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ORIGINAL ARTICLE

Beyond the Golden Hours: M2 Thrombectomy Outcomes Within and Beyond 6 Hours

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ABSTRACT

Introduction: Mechanical thrombectomy (MT) is an established treatment for large vessel occlusions in acute ischemic stroke (AIS), but It's role in medium vessel occlusions (MeVOs), particularly M2 segment occlusions, remains less defined. This study aimed to evaluate the safety and efficacy of MT for M2 occlusions in two time windows: early (<6 hours) and late (6–24 hours).**Material and Methods:** In this single-center cohort study, 23 patients with confirmed M2 occlusions underwent MT from October 2021 to October 2024 and were categorized into two groups: early (<6 hours, n = 12) and late (6–24 hours, n = 11). Advanced imaging was used for late-window selection. Baseline characteristics, procedural data, and outcomes, reperfusion success (modified TICI 2b/3), neurological improvement (NIHSS), functional recovery (mRS ≤2), and complications were analyzed.**Results:** The successful reperfusion rates were similar between the early and late groups (75% vs. 73%, P = 0.373). Both groups demonstrated significant neurological improvement (NIHSS change: early 6 ± 3, late 7 ± 3; P = 0.926) and favorable 3-month outcomes (mRS ≤ 2: early 66.7%, late 72.7%; P = 0.831). Procedural times were longer in the late group (52.91 vs. 42.50 minutes, P = 0.088), though not statistically significant. Complication rates were low and comparable.**Conclusion:** MT for M2 occlusions appears safe and effective in both early and late windows when guided by advanced imaging. Larger studies are warranted to confirm these findings.

Keywords: Mechanical thrombectomy; rTPA; M2 segment; catheter retrieval.

INTRODUCTION

Ischemic stroke is a leading cause of morbidity and mortality worldwide, with timely reperfusion being a critical factor in improving outcomes. Mechanical thrombectomy (MT) has revolutionized the treatment of large vessel occlusions (LVOs) of the anterior circulation,

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particularly when performed within the early time window of 6 hours (1, 2). However, recent trials, including DAWN and DEFUSE-3, have expanded the indications for MT by demonstrating its safety and efficacy in selected patients presenting in the late window (6-24 hours) based on advanced imaging criteria (3, 4). While these trials primarily focused on proximal occlusions, such as the internal carotid artery or M1 segment of the middle cerebral artery (MCA), the role of MT in medium vessel occlusions (MeVOs), such as the M2 segment of the MCA, remains less defined (5).

M2 occlusions represent a unique subset of ischemic strokes due to their more distal location, smaller vessel size, and potentially lower clot burden (6). Despite these differences, successful reperfusion in M2 occlusions has had significant clinical benefits (7). However, the safety and efficacy of MT in M2 occlusions, particularly in late-window cases, require further investigation to guide clinical practice (8).

We hypothesize that mechanical thrombectomy for M2 segment occlusions of the middle cerebral artery (MCA) yields comparable safety and efficacy outcomes in both early (<6 hours) and late (6–24 hours) time windows when patient selection is guided by advanced imaging criteria**.**

The primary aim of this study is to compare the safety and efficacy of mechanical thrombectomy (MT) for M2 segment MCA occlusions performed in the early (<6 hours) **versus** late (6–24 hours) time windows. Specifically, we assess**:** Reperfusion success, as measured by the modified Thrombolysis in Cerebral Infarction (mTICI) score. Neurological improvement**,** via changes in the NIH Stroke Scale (NIHSS). Functional outcomes, using the modified Rankin Scale (mRS) at 3 months. Procedural characteristics**,** including duration and number of thrombectomy passes. Complication rates**,** including hemorrhagic transformation and mortality.

By addressing these objectives, the study aims to contribute to the evidence base guiding thrombectomy decisions in medium vessel occlusions beyond traditional time windows.

This study primarily aims to compare the rates of successful reperfusion, defined as modified TICI 2b/3, in patients undergoing early versus late-window mechanical thrombectomy (MT). In addition, we will assess functional outcomes, measured by the Modified Rankin Scale (mRS), and stroke severity, as determined by the National Institutes of Health Stroke Scale (NIHSS), while investigating complication rates, including hemorrhagic transformation and mortality, associated with MT in each time window. Furthermore, the study will provide insights into the procedural characteristics and factors that influence outcomes in M2 occlusions. By addressing these objectives, our research seeks to bridge the existing knowledge gap regarding the optimal management of M2 occlusions and to refine MT indications and protocols in an era characterized by advanced imaging and individualized care.

PATIENTS AND METHODS

Study Design, Study Setting, and Ethical Approval

Our study is a descriptive cohort study conducted at Ain Shams University Hospitals. The study aimed to compare the safety and efficacy of MT with specific imaging-based eligibility criteria in patients with medium-vessel occlusions (M2 segment of the middle cerebral artery, MCA) based on the time window of intervention: an early-onset group with the last well-known time ≤ 6 hours; and a late-onset group with last well-known time > 6 hours but ≤ 24 hours. This study was conducted over a 3-year period, from October 2021 to October 2024, at Ain Shams

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University Hospital, within a highly equipped stroke unit (Ain Shams University Stroke Unit, featuring a 15-bed ICU and 10 intermediate beds, equipped with a Siemens ARTIS icono angio suite).

The study received approval from Assiut University's Faculty of Medicine ethics committee (IRB: 17200628) and was registered on ClinicalTrials.gov (NCT05091320). In accordance with the principles of the Declaration of Helsinki, written informed consent was obtained from all participants or their relatives.

Eligibility Criteria

Inclusion Criteria: patients with confirmed M2 segment MCA occlusion using CTA or MRA. Early-onset group: symptom onset ≤ 6 hours. Late-onset group: symptom onset > 6 hours and ≤ 24 hours. Diffusion-weighted MR imaging (DWI) and T2-weighted or fluid-attenuated inversion recovery (FLAIR) mismatch without clear infarct demarcation (DWI-FLAIR mismatch was defined as an ischaemic DWI lesion with no corresponding signal change on the FLAIR sequences. Partial mismatch was defined as a corresponding FLAIR signal change smaller than the DWI hyperintensity (9). No hypoattenuation on CT imaging. Exclusion Criteria: patients with large infarcts, contraindications for thrombectomy, or poor baseline functional status mRS > 4.

Clinical evaluation

All patients were clinically assessed by a skilled neurologist upon admission. A complete history was taken, including demographics as age and sex, and the vascular risk factors included (hypertension, hyperlipidemia, ischemic heart disease, atrial fibrillation (AF), diabetes mellitus (DM), and smoking). All patients were evaluated clinically at the time of presentation using the mRS and NIHSS, as well as radiologically with a CT scan and either CT angiography or MR angiography (whichever was available at the time of admission). Patients were also clinically re-evaluated on follow-up using the NIHSS (10). (most of the patients were revised 2 to 3 times as a follow-up for reassessment)

Procedural Metrics: Time to intervention, procedural duration, and method of thrombectomy.

Outcomes: 1-Recanalization success (TICI score), 2-Complications: procedural complications, reperfusion injury. 3-Functional and clinical outcomes: NIHSS, Modified Rankin Scale (mRS) at discharge and 3 months post-procedure.

Interventional Procedure

Digital subtraction angiography (DSA) was performed under general anesthesia. Mechanical thrombectomy techniques included: 1-Stent retriever: Solitaire (Solitaire: Medtronic; FR; ev3 Neurovascular, Irvine, CA). 2-Aspiration catheter: Sofia 5F (Sofia 5F: MicroVention Terumo). 3-Combined technique: Stent retriever plus aspiration catheter. A guiding catheter (8F soft tip) was introduced to the petrous segment of the internal carotid artery (ICA), and the thrombectomy technique was individualized. Post-thrombectomy DSA was performed to assess recanalization using the Thrombolysis in Cerebral Infarction (mTICI) score.

The scale was used to evaluate the outcome of the angiographic procedure. Namely, it assesses the reconstitution of the primary occluded vessel and the reperfusion of its distal vasculature. mTICI ranges from 0 to 3, where 0= represents no reperfusion while 3 = represents total reperfusion within the territory of the occluded artery (11). Reconstitution was considered successful if the mTICI score was 2b/3 after thrombectomy (12).

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Follow-up:

Clinical and functional outcomes were assessed at 3 months using the mRS scale to evaluate the extent of functional neurological disability. It encompasses a spectrum of severity, from no symptoms to mild disability (0-2), moderately severe disability (3-4), and severe/death (5-6) (13).

Statistical analysis:

Data were analyzed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY). Continuous variables were assessed for normality using the Shapiro-Wilk test and were presented as mean ± standard deviation (SD). Categorical variables were expressed as frequencies and percentages. Comparisons between group 1 [early (<6 hours)] and group 2 [late (6–24 hours)] were performed using the Mann-Whitney U test. Categorical variables were compared using the Chi-square test or Fisher's exact test, depending on data distribution and expected cell counts. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Twenty-three patients with M2 occlusion were classified into two groups based on the time of onset of presentation. The first group presented less than 6 hours after onset and had a mean age of 60.08 ± 5.84 SD. The second group presented more than 6 hours but less than 24 hours after onset, with a mean age of 59.27±13.10 years. There were no significant differences in baseline demographic criteria (age, sex, and vascular risk factors) between the groups, except for a higher proportion of smokers in group 2 (see Table 1).

Table 1: Baseline Demographics, Risk Factors, and Initial Clinical Presentation

Parameter	**Group 1 (<6h, n=12)**	**Group 2 (>6h, n=11)**	**P-value**
Age (mean ± SD)	60.08 ± 5.84	59.27 ± 13.10	0.459
Female Sex, n (%)	7 (58.3%)	3 (27.3%)	0.142
Hypertension, n (%)	8 (66.7%)	10 (90.9%)	0.168
Diabetes Mellitus, n (%)	7 (58.3%)	9 (81.8%)	0.232
Hyperlipidemia, n (%)	8 (66.7%)	8 (72.7%)	0.232
Atrial fibrillation, n (%)	3 (25.0%)	1 (9.1%)	0.325
Ischemic Heart Disease, n (%)	6 (50.0%)	5 (45.5%)	0.831
Smoking, n (%)	2 (16.7%)	7 (63.6%)	0.024
NIHSS (mean ± SD)	13 ± 3	14 ± 3	0.277
Onset to presentation (min, mean ±	305 ± 49	425 ± 56	0.001

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SD)			

There were no significant differences in procedural details between the two groups (Table 2). Mean procedural time and the number of thrombectomy passes were similar, and the majority of cases in both groups were treated using the combined technique.

Clinical outcomes were also comparable (Table 2). Successful reperfusion (modified TICI 2b/3) was achieved in 75% (9 patients) in the early group and 73% (8 patients) in the late group. Both groups showed similar neurological improvement, with a mean NIHSS reduction of 6–7 points.

One death occurred in the early group due to sudden unexpected death on the second day despite successful reperfusion. Hemorrhagic complications were low in both groups: one symptomatic hemorrhage in the early group and one asymptomatic hemorrhage in the late group..

Table 2: Procedural Details and Outcomes

Parameter	**Group 1 (<6h, n=12)**	**Group 2 (>6h, n=11)**	**P-value**
Procedural time (min, mean ± SD)	42.50 ± 12.7	52.91 ± 13.49	0.088
Number of Trials (mean ± SD)	3.0 ± 0.79	3.0 ± 0.77	0.156
Mortality, n (%)	1 (8.3%)	0 (0.0%)	0.166
Hemorrhage, n (%)			
- Symptomatic	1 (8.3%)	0 (0.0%)	0.628
- Asymptomatic	1 (8.3%)	1 (9.1%)	
Good Outcome (mRS ≤ 2), n (%)	8 (66.7%)	8 (72.7%)	0.831
NIHSS Improvement (mean ± SD)	6 ± 3	7 ± 3	0.926
TICI 2b/3 Reperfusion, n (%)	9 (75.0%)	8 (72.7%)	0.373
Thrombectomy Technique			
- Mixed (Stent + Aspiration)	9 (75.0%)	7 (63.6%)	0.786
- Stent Retriever Only	1 (8.3%)	3 (27.3%)	
- Aspiration Only	2 (16.7%)	1 (9.1%)	

DISCUSSION

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This was a comparative observational study in patients with M2-MCA occlusion designed to evaluate the feasibility and safety of mechanical thrombectomy in a late time window (up to 24 hours after symptom onset or last known well time). Patients were classified into two groups: early (<6 hours) and late (6 – 24 hours), depending on the time of intervention.

In terms of baseline characteristics, both groups (<6 hours and >6 hours) were comparable in demographics, vascular risk factors, initial stroke severity (NIHSS), as well as reperfusion success, functional recovery, and complication rates. Only smoking was significantly higher in the late-window group. Most studies, such as Goyal and colleagues (2021) and Jovin and colleagues (2018), report no significant differences in baseline demographics or stroke risk factors between early and late thrombectomy groups. Smoking, however, is often associated with worse stroke outcomes (14, 15).

The rate of successful reperfusion (modified TICI 2b/3) in our study was 75% in the early group and 73% in the late group. These rates are consistent with the findings from major trials such as the DAWN and DEFUSE-3 studies, which reported high reperfusion success rates (>70%) in late-window thrombectomy cases. Similarly, studies focusing on M2 occlusions, such as those by Grossberg and colleagues (2020) (16) and Berger and colleagues (2024) (17), reported comparable recanalization rates regardless of the time window. A systematic review by Menon and colleagues (2019) also found no significant difference in recanalization success between early and late thrombectomy for M2 occlusions. This suggests that the technical efficacy of thrombectomy is not significantly influenced by the time elapsed since symptom onset, provided that appropriate imaging criteria are used (18).

Good functional outcomes (mRS ≤2 at 3 months) were achieved in 66.7% of the early group and 72.7% of the late group (P = 0.831). These outcomes mirror the results from DAWN and DEFUSE-3, which demonstrated that patients selected for late-window thrombectomy based on advanced imaging criteria (e.g., DWI/FLAIR mismatch or small infarct core) achieve outcomes comparable to those treated within the traditional time frame. Furthermore, Berger and colleagues (2024) highlighted that distal vessel occlusions, such as M2, are equally amenable to late thrombectomy with favorable outcomes (17).

The improvement in NIHSS scores before and after thrombectomy was similar between groups (6 ± 3 vs. 7 ± 3). This finding is supported by studies, such as those by Lapergue and colleagues (2020), which demonstrated no significant differences in NIHSS improvement between early and late thrombectomy cases for M2 occlusions (19). This is slightly less than that reported by Berger and colleagues (2024) (17) and Wirtz and colleagues (2021) (20), who found an increase in NIHSS of 9 and 8 points, respectively, in 24 hours. Nevertheless, the observed neurological recovery underscores the importance of achieving reperfusion, even in extended time windows. Indeed, Kurmann and colleagues (2022) found that a > 4-point improvement in 24 hours post-thrombectomy leads to better clinical outcomes (21).

In terms of procedural details, the procedural times were slightly longer in the late group (52.91 ± 13.49 minutes vs. 42.50 ± 12.70 minutes, P = 0.088), likely reflecting the increased complexity of late-window cases, such as more organized clots or delayed intervention logistics. Nevertheless, the number of thrombectomy trials (mean = 3 in both groups) and techniques used were comparable, with a predominance of the combined technique. These findings align with

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Jumaa and colleagues (2021), who observed similar procedural characteristics in early and late thrombectomy cases (22).

Regarding the complications and mortality, the mortality was low, with one case (8.3%) in the early group and none in the late group. Hemorrhagic complications were rare and comparable between groups, with one symptomatic and one asymptomatic hemorrhage in the early group and one asymptomatic hemorrhage in the late group. This is better than what was reported by Limaya and colleagues (2023) (23), and consistent with Menon and colleagues (2019) (18) and Herzberg and colleagues (2022) (24), who reported low rates of complications and mortality in late-window thrombectomy, emphasizing the safety of the procedure when guided by imaging-based criteria. DAWN and DEFUSE-3 trials also reported low mortality rates (<15%) in late-window thrombectomy patients (18, 24), which were consistent with our findings.

Our findings support the growing evidence that late-window thrombectomy is a safe and effective option for patients with M2 occlusions when advanced imaging techniques are used to select candidates. The comparable outcomes in early and late groups underscore the importance of individualized decision-making based on imaging and clinical factors rather than rigid time constraints. This approach can potentially expand the number of eligible patients for thrombectomy, particularly those presenting beyond the traditional 6-hour window or with wake-up strokes.

Strength of the study

The study provides valuable insights into the outcomes of mechanical thrombectomy in M2 occlusions within different time windows, contributing to the limited data on this topic. Advanced imaging techniques were used for patient selection, ensuring optimal eligibility and minimizing risks associated with late-window interventions. Comprehensive data collection on procedural details, complications, and functional outcomes enhances the robustness of the analysis.

Limitations of the study

This study has several limitations that warrant consideration. Foremost, its retrospective and single-center design introduces potential selection and information biases, limiting the generalizability of the findings to broader populations. Such designs are susceptible to unmeasured confounding factors and may not capture all relevant variables that influence outcomes. The small sample size further restricts the statistical power to detect significant differences between early and late intervention groups, increasing the risk of Type II errors. Additionally, the absence of a control group receiving the best medical management precludes direct comparisons to non-interventional treatments, limiting the ability to ascertain the true efficacy of mechanical thrombectomy in this context. The study also lacks standardized assessments of collateral circulation and clot characteristics, factors known to influence outcomes in acute ischemic stroke. Moreover, the follow-up period was limited to three months, which may not fully capture long-term functional outcomes or delayed complications. Lastly, the definition of M2 occlusions can vary across studies, and without a universally accepted classification, comparisons and generalizations become challenging. These limitations underscore the need for larger, multicenter, prospective studies with standardized protocols to validate and expand upon these findings (25).

Recommendations

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Larger multicenter, randomized trials are needed to validate the safety and efficacy of thrombectomy in extended time windows for M2 occlusions. Future studies should explore the role of advanced imaging modalities in refining patient selection criteria and optimizing outcomes. Research should focus on identifying specific subgroups of patients who may benefit most from late-window thrombectomy based on clinical and imaging characteristics. Long-term follow-up studies are crucial for evaluating the durability of functional recovery and quality-of-life outcomes.

CONCLUSION

This study demonstrates that mechanical thrombectomy for M2 segment occlusions is equally effective and safe in both early and late time windows when advanced imaging is utilized for patient selection. These findings align with existing literature and highlight the potential to extend thrombectomy indications to a broader range of patients, ultimately improving outcomes for those with ischemic strokes involving distal vessel occlusions.

STATEMENT AND DECLARATIONS:

Declaration of competing interest:
All authors disclose no conflict of interest related to this study.
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Data availability statement:
All data generated or analyzed during this study are available from the corresponding author upon request.

REFERENCES :

1. Channing Hui PT, Mahammed Z. Khan Suheb, Laryssa Patti Ischemic Stroke. In: [Internet]. IS, editor.: Treasure Island (FL): StatPearls Publishing; 2025 Jan-. ; [Updated 2024 Apr 20].
2. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. New England Journal of Medicine. 2018;378(1):11-21.
3. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. New England Journal of Medicine. 2018;378(8):708-18.
4. Navia P, Schramm P, Fiehler J. ADAPT technique in ischemic stroke treatment of M2 middle cerebral artery occlusions in comparison to M1 occlusions: Post hoc analysis of the PROMISE study. Interventional Neuroradiology. 2020;26(2):178-86.
5. Limaye K, Bryant A, Bathla G, Dai B, Al Kasab S, Shaban A, et al. Computed tomography angiogram derived from computed tomography perfusion done with low iodine

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volume protocol preserves diagnostic yield for middle cerebral artery-M2 occlusions. Journal of Stroke and Cerebrovascular Diseases. 2019;28(12):104458.
6. Saver JL, Chapot R, Agid R, Hassan AE, Jadhav AP, Liebeskind DS, et al. Thrombectomy for distal, medium vessel occlusions: a consensus statement on present knowledge and promising directions. Stroke. 2020;51(9):2872-84.
7. Zhou H, Zhong W, Zhang T, Xu C, Zhong G, Xie G, et al. Comparing Outcomes of Thrombectomy Versus Intravenous Thrombolysis Based on Middle Cerebral Artery M2 Occlusion Features. Stroke. 2024;55(6):1592-600.
8. Lima FO, Furie KL, Silva GS, Lev MH, Camargo ÉC, Singhal AB, et al. Prognosis of untreated strokes due to anterior circulation proximal intracranial arterial occlusions detected by use of computed tomography angiography. JAMA neurology. 2014;71(2):151-7.
9. Thomalla G, Cheng B, Ebinger M, Hao Q, Tourdias T, Wu O, et al. DWI-FLAIR mismatch for the identification of patients with acute ischaemic stroke within 4·5 h of symptom onset (PRE-FLAIR): a multicentre observational study. Lancet Neurol. 2011;10(11):978-86.
10. Brott T, Adams Jr HP, Olinger CP, Marler JR, Barsan WG, Biller J, et al. Measurements of acute cerebral infarction: a clinical examination scale. Stroke. 1989;20(7):864-70.
11. Tomsick T. Timi, tibi, tici: I came, i saw, i got confused. American Journal of Neuroradiology. 2007;28(2):382-4.
12. Flores A, Tomasello A, Cardona P, De Miquel MA, Gomis M, Bermejo PG, et al. Endovascular treatment for M2 occlusions in the era of stentrievers: a descriptive multicenter experience. Journal of NeuroInterventional Surgery. 2015;7(4):234-7.
13. van Swieten JC, Koudstaal P, Visser M, Schouten H, Van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. stroke. 1988;19(5):604-7.
14. Goyal M, Ospel JM. Letter by Goyal and Ospel Regarding Article,"Multimodal Predictive Modeling of Endovascular Treatment Outcome for Acute Ischemic Stroke Using Machine-Learning". Stroke. 2021;52(2):e83-e4.
15. Jovin TG. MRI-guided intravenous Alteplase for stroke—still stuck in time. Mass Medical Soc; 2018. p. 682-3.
16. Grossberg JA, Rebello LC, Haussen DC, Bouslama M, Bowen M, Barreira CM, et al. Beyond large vessel occlusion strokes: distal occlusion thrombectomy. Stroke. 2018;49(7):1662-8.
17. Berger MC, Simgen A, Dietrich P, Naziri W. Efficacy of Mechanical Thrombectomy in Medium Vessel Occlusions of the MCA in the Extended-Time Window. medRxiv. 2024:2024.06. 16.24309009.
18. Menon BK, Hill MD, Davalos A, Roos YB, Campbell BC, Dippel DW, et al. Efficacy of endovascular thrombectomy in patients with M2 segment middle cerebral artery occlusions: meta-analysis of data from the HERMES Collaboration. Journal of neurointerventional surgery. 2019;11(11):1065-9.
19. Lapergue B, Blanc R, Costalat V, Desal H, Saleme S, Spelle L, et al. Effect of thrombectomy with combined contact aspiration and stent retriever vs stent retriever alone on revascularization in patients with acute ischemic stroke and large vessel occlusion: the ASTER2 randomized clinical trial. Jama. 2021;326(12):1158-69.
20. Wirtz MM, Hendrix P, Goren O, Beckett LA, Dicristina HR, Schirmer CM, et al. Predictor of 90-day functional outcome after mechanical thrombectomy for large vessel

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occlusion stroke: NIHSS score of 10 or less at 24 hours. Journal of neurosurgery. 2019;134(1):115-21.
21. Kurmann CC, Beyeler M, Grunder L, Lang MF, Piechowiak EI, Meinel TR, et al. Association of the 24-hour National Institutes of Health Stroke Scale after mechanical thrombectomy with early and long-term survival. Stroke: Vascular and Interventional Neurology. 2022;2(4):e000244.
22. Jumaa MA, Castonguay AC, Salahuddin H, Jadhav AP, Limaye K, Farooqui M, et al. Middle cerebral artery M2 thrombectomy in the STRATIS Registry. Stroke. 2021;52(11):3490-6.
23. Limaye K, Koo AB, Havenon Ad, Kasab SA, Bohnstedt B, Maier IL, et al. Safety and Efficacy of MCA-M2 Thrombectomy in Delayed Time Window: A Propensity Score Analysis From the STAR Registry. Stroke: Vascular and Interventional Neurology. 2023;3(3):e000664.
24. Herzberg M, Dorn F, Trumm C, Kellert L, Tiedt S, Feil K, et al. Middle cerebral artery M2 thrombectomy: safety and technical considerations in the German Stroke Registry (GSR). Journal of Clinical Medicine. 2022;11(15):4619.
25. Coutinho J, Liebeskind D, Slater L-A, Nogueira R, Baxter B, Levy E, et al. Mechanical thrombectomy for isolated M2 occlusions: a post hoc analysis of the STAR, SWIFT, and SWIFT PRIME studies. American Journal of Neuroradiology. 2016;37(4):667-72.

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ORIGINAL ARTICLE

Assessment of Outcomes Following Laparoscopic Transabdominal Retro-Muscular (TARM) Hernia Repair

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ABSTRACT

Background: Laparoscopic trans abdominal retro-muscular (TARM) repair offers potential advantages via placing the mesh in the retro-rectus space, reducing contact with intra-abdominal viscera and minimizing postoperative pain and adhesions. **Objectives**: To assess the short- and mid-term results of laparoscopic TARM hernia repair in cases with non-complicated ventral hernias. **Methodology**: This prospective research involved 25 cases with non-complicated ventral hernia treated at Aswan University Hospitals. Inclusion criteria were cases aged ≥18 years and both sexes. Patients with recurrent, complicated, or emergency hernias were excluded. TARM repair was performed using three ports, with mesh placement in the retro-muscular space after defect closure. **Results**: The mean age was 39.56 ± 11.54 years, with 56% females and a mean BMI of 31.28 ± 3.09 kg/m². Para umbilical hernia was most common (72%). The mean operative time was 104.44 ± 11.47 minutes, and median blood loss was fifteen milliliters. Complications during the operation happened in 16% of cases. The median hospital stay was 1 day. **Conclusion**: Laparoscopic TARM hernia repair is a safe and effective minimally invasive option, with low complication rates, short hospital stay, and no recurrence in short- to mid-term follow-up.

Keywords: Ventral hernia, Laparoscopic repair, Retro-muscular mesh, TARM, Surgical outcomes

INTRODUCTION

Ventral hernias are described as a defect of the fascia in the anterior wall of abdomen with or without a bulge. The manifestations range from minor cosmetic issues to extensive pain and fatal conditions like incarceration, bowel obstruction, perforation and strangulation. Though ventral hernia repair is considered as one of the commonest surgical procedures performed daily all over the world, there is still a debate about the ideal method for surgical repair due to high recurrence rate ranging from (10 %- 40 %) **(1,2)**.

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Every year, around (350,000) ventral hernia surgeries are performed worldwide. General surgeons are responsible for repairing these abdominal wall abnormalities **(3,4)**.
In most cases, a history and physical examination are sufficient to diagnose an abdominal hernia, although extreme obesity, a key risk factor, can limit the examination. Because hernias can vary with exercise or even standing, it is critical that the patient should be evaluated in a variety of situations **(4,5)**. A variety of adjunct assessments, like ultrasound or CT scan, can be done to aid in diagnosis **(5,6)**.
Ventral hernia can be repaired by laparoscopic or open approach. Trans-Abdominal Retro-Muscular Mesh Repair (TARM) was introduced as a cost-effective laparoscopic approach utilizing polypropylene mesh placed in the retro-rectus space **(6,7)**.
The 1^{ry} benefit of TARM is utilizing the traditional polypropylene mesh being located in the retro rectus space outside the peritoneal cavity with minimal fixation thus protecting the bowel from direct contact with the mesh and thus reducing the postsurgical pain and adhesions **(8,9,10)**.
This current study research is to assess the result following Laparoscopic Transabdominal Retro-Muscular (TARM) Hernia Repair.

PATIENTS AND METHODS

This prospective research has been performed on 25 cases admitted to Aswan university hospitals with non- complicated ventral hernia. This study was done in General surgery department Aswan university hospitals
Inclusion criteria: Studied cases with non-complicated ventral hernia**,** patients aged eighteen years and above, both sexes and size of defect from 1cm to 5cm
Exclusion criteria: Patients with recurrent ventral hernia**,** pregnant patients and emergency cases

Methods

Preoperatively, demographic information has been gathered, and all patients underwent a clinical examination to confirm the diagnosis. Radiological assessment was performed using pelvi-abdominal ultrasound for all involved cases and some cases assessed with CT scan . Laboratory investigations included complete blood count (CBC) and coagulation profile.

Procedure

The laparoscopic transabdominal retro-muscular (TARM) hernia repair using three ports was performed under general anesthesia with the cases in the French position, and the abdomen has been prepped and draped in a sterile manner. Pneumoperitoneum was established with carbon dioxide at a pressure of 12–15 millimeters of mercury.A 10–12 mm infraumbilical trocar was placed for the laparoscope, and two 5 millimeters working ports were inserted laterally under direct vision. The hernia defect and sac were identified and carefully dissected using an ultrasonic harmonic scalpel, preserving adjacent structures such as bowel loops, omentum, and blood vessels, and the hernia contents were gently reduced into the abdominal cavity. The retro-muscular space was developed by making a six to eight centimeters transverse incision on the peritoneum and posterior rectus sheath, five to six centimeters proximal to the defect, followed by blunt dissection to separate the rectus muscle from the posterior sheath and extend the space superiorly, inferiorly, and laterally to allow adequate mesh placement. The hernial defect was

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closed with No. 0 PDS or Vicryl sutures, and a synthetic mesh was trimmed to ensure at least eight centimeters overlap beyond the defect before insertion into the retro-muscular space. The mesh was fixed using absorbable tacks or sutures, and the posterior rectus sheath and peritoneum were closed with Vicryl sutures. Pneumoperitoneum was released, trocars were removed, and port sites have been closed through absorbable sutures or surgical glue.

RESULTS

Table 1. Patients' characteristics in our study .

	Number of cases : (n = 25)	
Age (years) **Range** **Mean ± SD**	**21 – 60** **39.56 ± 11.54**	
Sex	**No.**	**%**
Female	**14**	**56.0**
Male	**11**	**44.0**
BMI (kg/m^2) **Range** **Mean ± SD**	**26.2 – 35.4** **31.28 ± 3.09**	
Comorbidities	**No.**	**%**
Diabetes	**6**	**24.0**
Steroids	**1**	**4.0**
COPD	**3**	**12.0**
Hypertension	**9**	**36.0**
Inflammatory bowel disease	**2**	**8.0**
Smoking	**3**	**12.0**
ASA	**No.**	**%**
II	**17**	**68.0**
III	**8**	**32.0**

Table 1. shows the demographic and baseline clinical characteristics of our cases , the mean age was 39.56 ± 11.54 years, with a slight female predominance (56%). The mean BMI of 31.28 ± 3.09 kg/m². Common comorbidities included hypertension (36%), diabetes (24%), and COPD (12%), (4%) or had inflammatory bowel disease (8%). The American Society of Anesthesiologists (ASA) classification, 68% of patients were ASA II, while 32% of patients were ASA III.

Table 2. Hernia Characteristics in this study .

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	Number of cases (n = 25)	
Hernia- specific history	**No.**	**%**
Prior open abdomen	**2**	**8.0**
Hernia type	**No.**	**%**
Epigastric	**3**	**12.0**
Paraumbilical	**18**	**72.0**
Umbilical	**4**	**16.0**
Hernia width (cm.) **Range** **Mean ± SD**	**1.5 – 5** **3.34 ± 1.19**	

Table 2. shows Hernia Characteristics of this study , history of open abdomen was reported in 8% of patients. The most common hernia type was paraumbilical (72%), followed by umbilical (16%) and epigastric (12%). The mean hernia width was 3.34 ± 1.19 cm, ranging from 1.5 to 5 cm.

Table 3. Operative and Postoperative Outcomes in this study .

	Number of caeses (n = 25)	
Operative Time **Range** **Mean ± SD**	**85 – 124** **104.44 ± 11.47**	
Blood loss **Range** **Medien (IQR)**	**10 – 60** **50 (40 – 60)**	
Intra Operative complications	**N**	**%**
Peritoneal tear	**1**	**4.0**
Serosal tear	**0**	**0.0**
Hematoma	**1**	**4.0**
Conversion to open	**1**	**4.0**

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Minor bleeding	**2**	**8.0**
LOS (days) **Range** **Medien (IQR)**	**1 – 3** **1 (1 – 1)**	

Table 3. shows Operative and Postoperative Results of this study. The mean operative duration was 104.44 ± 11.47 minutes, with a range of 85 to 124 minutes. Median intraoperative blood loss was 50 milliliters (IQR: 40–60 milliliters). Intraoperative complications were infrequent, with peritoneal tear, hematoma, and conversion to open surgery each occurring in 4% of cases, and minor bleeding reported in 8% of cases. The length of hospital stay varied from 1 to 3 days, with a median stay of 1 day (IQR: 1–1).

Table 4. Short- and Mid-Term Postoperative Complications in the studied group.

	Number of cases (n = 25)	
1-month Complications	**No.**	**%**
Postoperative SSI	**1**	**4.0**
Bowel obstruction	**0**	**0.0**
Seroma	**2**	**8.0**
Ileus	**1**	**4.0**
Mesh infection	**0**	**0.0**
Overall complication	**4**	**16.0**
3-months complication	**No.**	**%**
Chronic Postoperative pain and neuropathy	**3**	**12.0**
6-12 months complication	**No.**	**%**
Recurrence	**0**	**0.0**

Table 4. shows Short- and Mid-Term Postoperative Complications founded in this study. Within the first month, the overall complication rate was sixteen percent, with seroma being the most frequent complication (8%), followed by postoperative surgical site infection (4%) and ileus (4%). No cases of bowel obstruction or mesh infection were reported. At 3 months, 12% of

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patients experienced chronic postoperative pain or neuropathy. No hernia recurrence was observed during the 6-12 months' follow-up period.

Discussion

Regarding the demographic and baseline clinical characteristics of the TARM group, the mean age was (39.56 ± 11.54) years, with a slight female predominance (56%). The mean BMI of (31.28 ± 3.09) kg/m². Common comorbidities included hypertension (36%), diabetes (24%), and COPD (12%), (4%) or had inflammatory bowel disease (8%). There were (12.0%) smokers. The ASA classification, (68%) of patients were ASA II, while (32%) of patients were ASA III.

Similarly, there outcomes were in line with **Hassan et al.**, **(5)** who compared the efficacy and safety between laparoscopic transabdominal retro muscular mesh (TARM) repair and laparoscopic (IPOM) repair in the treatment of patients with ventral hernia as they revealed that regarding the TARM group, the mean age was (41.0±9.5) years, females were more than males (75% vs. 25%), the mean BMI was (29.45±6.46) kg/m², there were (8.3%) smokers, 75% of patients had comorbidity-free status. Regarding comorbidities, COPD was present in (4.2%) of patients, diabetes in (12.5%), and both diabetes and hypertension in (8.3%).

As well, **Assy et al.**, **(10)** who aimed to assess the primary and secondary results of laparoscopic trans-abdominal Retro muscular (TARM) repair as a novel minimally invasive method for ventral hernia, conducted their study on (73) patients underwent TARM with mean age (45.6 ± 7.23) years. most of the included patients were females (69.9%).

In terms of Hernia Characteristics of the TARM group, history of open abdomen was reported in (8%) of patients. The most common hernia type was paraumbilical (72%), followed by umbilical (16%) then epigastric (12%). The mean hernia width was (3.34 ± 1.19) cm, ranging from (1.5 to 5) cm.

In alignment with the current study, **Aziz et al.**, **(11)** who aimed to compare and assess the early results of transabdominal retro muscular mesh repair of non-complicated 1ry ventral hernia with an average size of the defect under five centimeters against the classic IPOM repair, reported that the most common hernia type was paraumbilical (72.0%), meanwhile it followed by epigastric (24.0%) then umbilical (4.0%) in their study.

As well, the study agreed with **Hassan et al.**, **(5)**, as they revealed that the distribution of umbilical (41.7%) was more relevant than epigastric type (25%) and the mean hernia width in their study was (3.95±1.47) cm.

Concerning operative and postoperative results of the TARM group. The mean operative durations was (104.44 ± 11.47) minutes, with a range of (85 to 124) minutes. Median intraoperative blood loss was (50) milliliters [IQR: 40–60 milliliters]. Intraoperative complications were infrequent, with peritoneal tear, hematoma, and conversion to open surgery each occurring in (4%) of cases, and minor bleeding reported in (8%) of cases. The length of hospital stays varied from (1 to 3) days, with a median stay of (1) day [IQR: 1–1].

In the study of **Masurkar**, **(12)** who aimed at progressing this method (TARM) utilizing a familiar and ergonomic port geometry, they reported that the mean operating time, loss of blood and length of stay were (192) minutes, (35.2) milliliters and (5) days, correspondingly. Conversion to open, occurring in (3.4%) of cases. The technique might be the reason of not getting near values to the current outcomes.

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In agreement with the current outcomes, **Aziz et al.**, **(11)** revealed that in the TARM group, the mean operative time was (108.40 ±9.43) minutes. they reported that the intraoperative complications have been detected in eight cases (32.0%), all of which involved peritoneal flap (PPF) tears. Despite this, the majority of patients (17, 68.0%) had no intraoperative complications. Notably, there were no cases of intraoperative bleeding (0%).

As regards short- and mid-Term complications following the operation detected in the TARM group. Within the first month, the total complication rate was (16%), with seroma being the most frequent complication (8%), followed by postoperative surgical site infection (4%) and ileus (4%). No cases of bowel obstruction or mesh infection were reported. At (3) months, (12%) of patients experienced chronic postoperative pain or neuropathy. No hernia recurrence was observed during the (6-12) month follow-up period.

In agreement with the obtained findings , **Aziz et al.**, **(11)** demonstrated that regarding postoperative complications, seroma was reported in 1 patient (4.0%), and wound infection was noted in 1 patient (4.0%), meanwhile no cases (0%) had mesh infection.

In contrast, **Assy et al.**, **(10)** who concluded that laparoscopic TRAM Mesh Repair approach in managing ventral hernia with high efficacy and good outcome, Laparoscopic TARM has been demonstrated to be efficient for repairing small hernias, they reported that recurrence occurred in (5.5%) of cases. This discrepancy may be attributed to differences in patient selection, surgical technique, or follow-up duration. Meanwhile they also agreed with the presented findings as they reported that the most reported postoperative complication was seroma (16.4%). Postoperative ileus was reported in (4.1%) and wound infection were reported in (2.7%) of patients.

CONCLUSION

Laparoscopic transabdominal retro-muscular (TARM) hernia repair demonstrated favorable short- and mid-term outcomes, with low complication rates, minimal intraoperative risks, and no hernia recurrence throughout monitoring. It appears to be a safe and effective minimally invasive option for ventral hernia repair.

This minimally invasive technique provided reduced pain following the operation, shorter hospital stay, quicker recovery, reduced recurrence rates due to strong retro-muscular reinforcement, and improved cosmetic outcomes.

REFERENCES

1. Shahdhar M, Sharma A. Laparoscopic ventral hernia repair: extraperitoneal repair. Ann Laparosc Endosc Surg. 2018;3(9).
2. Chowbey PK, Sharma A, Khullar R, Mann V, Baijal M, Vashistha A. Laparoscopic ventral hernia repair. Journal of Laparoendoscopic & Advanced Surgical Techniques. 2000 Apr;10(2):79-84.
3. Schlosser KA, Arnold MR, Otero J, Prasad T, Lincourt A, Colavita PD, et al. Deciding on optimal approach for ventral hernia repair: laparoscopic or open. J Am Coll Surg. 2019;228(1):54–65.

***Corresponding author: Ahmed Abdelmotaleb Mohamed Hasan, Mobil:01114515852, Email: drahmedabdelmotaleb@gmail.com**

4. de'Angelis N, Schena CA, Moszkowicz D, Kuperas C, Fara R, Gaujoux S, Gillion JF, Gronnier C, Loriau J, Mathonnet M, Oberlin O. Robotic surgery for inguinal and ventral hernia repair: a systematic review and meta-analysis. Surgical Endoscopy. 2024 Jan;38(1):24-46.
5. Hassan AHA, Hassan Sadek MAR, Ibrahim IM, AbdAllah Zaitoun M. A comparative study between laparoscopic trans-abdominal retromuscular repair and intraperitoneal onlay mesh repair techniques in ventral hernia. Egypt J Surg. 2023;42(3).
6. Roy A, Bhoi D, Chhabra A, Mohan VK, Darlong V, Prasad G. Quadratus lumborum block vs. transversus abdominis plane block in laparoscopic trans-abdominal pre-peritoneal repair of inguinal hernia in adults: A randomised controlled trial. Indian journal of anaesthesia. 2023 Feb 1;67(2):207-15.
7. Smolevitz J, Jacobson R, Thaqi M, Millikan S, Millikan KW. Outcomes in complex ventral hernia repair with anterior component separation in class III obesity patients. Am J Surg. 2018;215(3):458–61.
8. Kudsi OY, Gokcal F, Bou-Ayash N, Watters E, Pereira X, Lima DL, Malcher F. A comparison of outcomes between class-II and class-III obese patients undergoing robotic ventral hernia repair: a multicenter study. Hernia. 2022 Dec;26(6):1531-9.
9. Awad PB, Hassan BH, Kashwaa MF, Abdel-Maksoud IM. A comparative study between open pre-peritoneal approach versus laparoscopic trans-abdominal pre-peritoneal approach in recurrent inguinal hernia repair: a prospective cohort study. Hernia. 2024 Apr;28(2):629-35.
10. Assy EE, Elmoghazy MB, Negm AMR, Hamed MAA. Laparoscopic trans-abdominal retro muscular mesh repair of ventral abdominal wall hernia. Int J Heal Sci. 2025;0(0):0–0.
11. Aziz MA, Elzeftawy S, Shemes A, Elghrieb A, Abdelmaksood M, Shetiwy M. Transabdominal retro muscular versus intraperitoneal onlay mesh repair of ventral hernia: a randomized controlled study. Egypt J Surg. 2023;42(3).
12. Masurkar AA. Laparoscopic Trans-Abdominal Retromuscular (TARM) Repair for Ventral Hernia: A Novel, Low-Cost Technique for Sublay and Posterior Component Separation. World J Surg. 2020;44(4):1081–5.

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ORIGINAL ARTICLE

Feasibility, Safety, and Usefulness of Bronchoscopic Cryotechnique in Management of Endobronchial Lesions

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ABSTRACT

Background: Endobronchial lesions can cause significant airway obstruction and pose diagnostic and therapeutic challenges. Bronchoscopic cryotherapy, a minimally invasive technique that uses extreme cold to ablate pathological tissue, is increasingly used for both diagnostic and palliative purposes. ***Objective:*** To evaluate the feasibility, safety, and therapeutic outcomes of bronchoscopic cryotechnique in managing endobronchial lesions at Kasr Al Ainy Hospital, Cairo University. ***Methods:*** This prospective study included 68 patients with endoscopically visible endobronchial lesions. Depending on clinical indication, patients underwent cryobiopsy or cryotherapy (cryoablation or cryorecanalization) via flexible bronchoscopy. Outcomes assessed included airway patency, symptom relief, and complications. ***Results:*** The mean age was 36.9 ± 20 years, with 63.2% males. Complete airway recanalization was achieved in 77.9% of cases, partial in 17.7%, and failure occurred in 4.4%. Significant symptomatic improvement in cough, dyspnea, and hemoptysis was noted ($p < 0.05$). The procedure was generally well-tolerated; bleeding occurred in 35.3% of cases, while serious complications were rare. ***Conclusion:*** Bronchoscopic cryotherapy is a safe and effective intervention for endobronchial lesions, offering substantial symptomatic relief with minimal risk. It represents a valuable palliative option for non-surgical patients with obstructive airway lesions.

Keywords:

Bronchoscopic cryotherapy, Endobronchial lesions, Cryobiopsy, Cryoablation, Cryorecanalization, Airway obstruction, Flexible bronchoscopy, Palliative treatment, Symptom relief, Airway recanalization

INTRODUCTION

Endobronchial lesions, whether benign or malignant, pose significant diagnostic and therapeutic challenges, especially when causing central airway obstruction. Primary tumors of the tracheobronchial tree are relatively uncommon but can lead to life-threatening conditions due to bronchial obstruction, bleeding, or recurrent infections **[1]**. Malignant lesions such as squamous cell carcinoma, adenocarcinoma, and carcinoid tumors remain the predominant histological types, whereas benign endobronchial tumors like hamartomas, lipomas, and papillomas comprise a smaller proportion, accounting for approximately 1–10% of bronchopulmonary neoplasms **[2]**.

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Traditional management of endobronchial tumors involves surgical resection, chemotherapy, and radiotherapy. However, for patients who are non-surgical candidates or present with high-risk airway compromise, bronchoscopic interventions have emerged as critical therapeutic alternatives. Among these, bronchoscopic cryotherapy—a technique that utilizes extreme cold temperatures to ablate pathological tissue—has demonstrated increasing utility in both diagnostic and palliative settings **[3, 4]**.

Cryotechnique achieves tissue destruction through both immediate mechanisms, such as intracellular ice crystal formation, and delayed effects, including vascular stasis and apoptosis **[5, 6]**. The freezing-thawing cycles induce cytotoxicity, causing cell membrane rupture and ischemia, particularly effective in highly vascular and cellular lesions **[7]**. Notably, cryotherapy is associated with a favorable safety profile—it avoids the risks of bronchial perforation, electrical injury, or airway fire, which are potential hazards in other thermal ablative modalities **[4]**.

Despite its advantages, the outcomes of bronchoscopic cryotherapy depend on lesion characteristics and procedural expertise. Complete or partial airway recanalization, improvement in clinical symptoms (e.g., cough, hemoptysis, dyspnea), and minimal complications have been reported in various studies, though factors predicting successful outcomes remain underexplored **[8, 9]**.

Accordingly, this study aims to assess the feasibility, safety, and usefulness of bronchoscopic cryotechnique in managing endobronchial lesions. It also seeks to identify the clinical features and predictors of procedural success, thereby optimizing patient selection and procedural planning in respiratory endoscopy.

PATIENTS AND METHODS

This prospective clinical study was conducted over a one-year period at the bronchoscopy unit of Kasr Al Ainy Hospital, Cairo University. A total of 68 patients with endoscopically visible endobronchial lesions were enrolled. Inclusion criteria were the presence of symptomatic endobronchial masses confirmed by preliminary imaging and flexible bronchoscopy. Informed written consent was obtained from all participants prior to the procedure.

Flexible bronchoscopic procedures were performed using the **Olympus BF-1T180 videobronchoscope.** Cryotherapeutic interventions were carried out with the Erbe Cryo 2 system, utilizing 1.9 mm or 2.4 mm flexible cryoprobes, and liquefied nitrous oxide (N_2O) as the cryogen. The cryoprobe was inserted through the working channel of the bronchoscope and placed directly onto the lesion. Freezing was activated via foot pedal and maintained for 30–60 seconds per application.

Cryotherapy was applied in two techniques:

- **Cryoablation**: Inducing tissue necrosis through targeted freezing.
- **Cryorecanalization**: Mechanically removing obstructive lesions by freezing and extracting tissue adhered to the probe.

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The selection of cryotechnique was individualized based on lesion characteristics (size, location, degree of airway obstruction) and the patient's clinical stability. In cases where tissue sampling was indicated, **cryobiopsy** was performed by freezing the target tissue and withdrawing the bronchoscope and probe en bloc to retrieve an intact specimen.

Patients underwent pre- and post-procedural clinical assessments, including evaluation of **cough**, **dyspnea**, and **hemoptysis**, with severity graded using the following standardized scales:

- **Cough**:
    - Grade 0: No cough
    - Grade I: Occasional, non-disruptive
    - Grade II: Frequent and functionally limiting
- **Dyspnea** *(Modified Medical Research Council [mMRC] Scale)*:
    - Grade 0: Dyspnea only on strenuous exertion
    - Grade I: On hurrying or uphill walking
    - Grade II: Slower walking than peers
    - Grade III: Stops after ~100 meters
    - Grade IV: Breathless at rest or during dressing
- **Hemoptysis**:
    - Grade 0: None
    - Grade I: Intermittent blood-streaked sputum
    - Grade II: Frequent or mild active bleeding

Bronchoscopic outcomes were categorized as:

- **Complete canalization**: Full restoration of airway patency
- **Partial canalization**: Clinically significant but incomplete clearance
- **Failure**: No improvement in luminal patency

All procedural complications were documented, with a particular focus on **bleeding**, the most common adverse event. Bleeding severity was graded from I (mild) to IV (life-threatening). Minor bleeding was controlled with cold saline or diluted epinephrine, while higher-grade bleeding necessitated adjunctive interventions. Other complications, including respiratory failure,

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pneumomediastinum, and mortality—were also systematically recorded.

RESULTS

The study included 68 patients with endobronchial lesions. The mean age of patients was 36.92 ± 20.02 years old, the male represented 63.2% of patients and females represented 36.8% of patients; 47.1% of the patients were smokers. Regarding comorbidities; HTN (19.1%), Recurrent chest infections (11.8%), COPD (8.8%) and DM (5.9%). (Table 1).

Table 1: Demographic Data of the Studied Group (N = 68)

Variable	Category	No. (%)
Age (years)	< 30	23 (33.8%)
	30 – 50	25 (36.8%)
	> 50	20 (29.4%)
	Mean ± SD	**36.92 ± 20.02**
	Median (Range)	**40.5 (1.5–70.0)**
Sex	Male	43 (63.2%)
	Female	25 (36.8%)
Smoking History	Smoker	32 (47.1%)
	Non-smoker	36 (52.9%)
Co-morbidities	Diabetes Mellitus (DM)	4 (5.9%)
	Hypertension (HTN)	13 (19.1%)
	Chronic Obstructive Pulmonary Disease (COPD)	6 (8.8%)
	Recurrent Chest Infections	8 (11.8%)
	None	32 (47.1%)

Patients were categorized according to lesion laterality: 47 had right-sided lesions and 21 had left-sided lesions. There was no statistically significant difference between both sides for cryotherapy (P>0.05) (Table 2).

Table 2: Cryotherapy Outcomes According to Lesion Site

Variable	Right (n = 47)	Left (n = 21)	P-value
	No. (%)	No. (%)	
Duration of the Procedure (min)			**0.560**
< 30	16 (34.0%)	10 (47.6%)	
30 – 45	15 (31.9%)	5 (23.8%)	
> 45	16 (34.0%)	6 (28.6%)	
Outcome			**0.367**
Complete canalization	37 (78.7%)	16 (76.2%)	
Partial canalization	9 (19.1%)	3 (14.3%)	
Failed	1 (2.1%)	2 (9.5%)	
Number of Sessions			**0.482**
One	38 (80.9%)	19 (90.5%)	
Two	9 (19.1%)	2 (9.5%)	

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There was statistically significant improvement of symptoms such as cough, dyspnea and hemoptysis after cryotherapy (P<0.05). However, chest pain improved post cryotherapy without statistically significant difference (Table 3).

Table 3: Symptom Severity Before and After Cryotherapy (n = 68)

Symptom	Grade	Before Cryotherapy	After Cryotherapy	P-value
		No. (%)	No. (%)	
Cough	No cough	4 (5.9%)	32 (47.1%)	**0.000***
	Grade I	26 (38.2%)	29 (42.6%)	
	Grade II	38 (55.9%)	7 (10.3%)	
Dyspnea	No dyspnea	3 (4.4%)	32 (47.1%)	**0.000***
	Grade I	12 (17.6%)	15 (22.1%)	
	Grade II	25 (36.8%)	17 (25.0%)	
	Grade III	20 (29.4%)	4 (5.9%)	
	Grade IV	8 (11.8%)	0 (0.0%)	
Hemoptysis	Yes	28(41.2%)	11 (16.2%)	**0.001***
	No	40 (58.8%)	57 (83.8%)	
Chest Pain	Yes	7 (10.3%)	2 (2.9%)	0.165
	No	61 (89.7%)	66 (97.1%)	

Bronchoscopic cryotherapy was well tolerated, with the majority (64.7%) of patients experiencing no bleeding. Mild to moderate bleeding (Grades I–II) was observed in 26.5% of cases, while severe bleeding (Grades III–IV) occurred in 8.8%. Non-bleeding complications included pneumomediastinum in 4.4%, respiratory failure (Type I and II) in a combined 4.4%, and isolated cases (1.5% each) of perforation, segmental collapse, and mortality. Notably, no cases of pneumothorax were reported (Table 4).

Table 4: Reported Complications Following Bronchoscopic Cryotherapy (n = 68)

Complication	No.	%
Bleeding Severity		
No bleeding	44	64.7%
Grade I (mild)	10	14.7%
Grade II (moderate)	8	11.8%
Grade III (severe)	4	5.9%
Grade IV (life-threatening)	2	2.9%
Other Complications		
Respiratory failure (type I)	1	1.5%
Respiratory failure (type II)	2	2.9%
Pneumothorax	0	0.0%
Pneumomediastinum	3	4.4%
Perforation	1	1.5%
Collapse	1	1.5%
Mortality	1	1.5%

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DISCUSSION

Bronchoscopic cryotherapy has emerged as a pivotal therapeutic modality in managing endobronchial lesions, especially in cases with airway obstruction due to malignant or benign pathology. Various bronchoscopic interventions such as laser ablation, electrocautery, argon plasma coagulation, stenting, and photodynamic therapy have been employed, with the choice of intervention guided by the lesion's nature, obstruction severity, patient condition, and institutional expertise **[10]**.

Cryotherapy, first introduced in the 1970s **[11]**, utilizes rapid freezing to induce cell death via apoptosis and vascular stasis. Its proven safety, cost-effectiveness, and ability to be applied via flexible bronchoscopy make it an attractive option for both palliative and diagnostic purposes **[4, 12]**. In Egypt, multiple studies have supported its use, including those by Mohamed and El-Din (2016) **[13]**, Abd El Hafez et al. (2017) **[14]**, Elkolaly et al. (2017) **[15]**, and most recently, Fadaly et al. (2023) **[16]**, highlighting its versatility across benign and malignant settings.

In our current study, conducted on 68 patients with endobronchial lesions, cryotherapy demonstrated high feasibility and effectiveness. Complete airway canalization was achieved in 77.9%, partial canalization in 17.7%, and failure in only 4.4%. These findings align with Mohamed and El-Din (2016), who reported >50% recanalization in 85% of patients **[13]**, and Hetzel et al. (2012), who showed complete or partial responses in 83% of cases **[17]**. Minor variations in success rates across studies could be attributed to differences in lesion type, operator expertise, and patient selection.

Importantly, this study found statistically significant improvements in cough, dyspnea, and hemoptysis following cryotherapy ($p < 0.05$), confirming prior observations by El-Helbawya et al. (2019) and Fadaly et al. (2023) **[4, 16]**. Improvement in chest pain was noted but was not statistically significant. The success in symptom relief can be mechanistically explained by cryotherapy's ability to reduce tumor burden and restore airway patency, alongside its hemostatic properties mediated by vasoconstriction and microthrombus formation **[4]**.

The mean age in this study was 36.9 years, younger than in other cohorts such as El-Helbawya et al. (2019) and Abd El Hafez et al. (2017) **[4, 14]**. This discrepancy is largely attributable to the high proportion of foreign body cases in our series, particularly among pediatric and young adult patients. This also explains the observed right-side predominance in lesion location (69.1%), consistent with anatomical predisposition and prior findings by Purohit et al. (2023) and Ulas et al. (2022) **[18, 19]**.

In terms of procedural logistics, most patients required only one session (83.8%), with the procedure typically lasting under 45 minutes. This is favorable compared to studies like Elkolaly et al. (2017), where up to four sessions were sometimes necessary. The need for multiple sessions in other reports may reflect operator experience, lesion complexity, or tumor burden **[15]**.

Our study reported a 35.3% bleeding rate, primarily Grade I, with other complications such as respiratory failure (4.4%), pneumomediastinum (4.4%), and perforation (1.5%) being infrequent. This aligns with global safety profiles reported by Mohamed and El-Din (2016), and Hetzel et al.

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(2012), confirming the safety of cryotherapy when performed by experienced bronchoscopists **[13, 17]**.

Beyond therapeutic ablation, cryobiopsy was employed for diagnostic purposes and demonstrated high safety and feasibility. Our findings are reinforced by studies like those by Ibrahim et al. (2022) **[20]**, Schumann et al. (2010) **[21]**, and Rubio et al. (2013) **[22]**, which reported diagnostic yields ranging from 83% to over 95%, with no significant increase in complications compared to forceps biopsy. Cryobiopsy offers the additional advantage of obtaining larger tissue samples with fewer artifacts **[17]**, making it increasingly valuable in histopathological evaluation of airway lesions.

While cryotherapy offers clear advantages, it does have limitations. The delayed onset of tissue necrosis necessitates repeated bronchoscopies for debridement and makes it less suitable in emergent airway obstruction **[4]**. Nonetheless, its safety profile, cost-efficiency, and symptom-relieving efficacy reinforce its role as a primary modality in the interventional pulmonologist's toolkit.

CONCLUSION

In conclusion, bronchoscopic cryotechnique is a feasible, effective, and safe modality for the management of endobronchial lesions. It demonstrated high rates of airway recanalization and resulted in significant improvement in respiratory symptoms, particularly cough, dyspnea, and hemoptysis. The procedure was well-tolerated, associated with a low complication rate, and typically required a limited number of sessions. As a minimally invasive intervention, cryotherapy holds substantial therapeutic value and should be considered an integral component of palliative bronchoscopy, especially in patients who are not candidates for surgical or conventional therapies.

REFERENCES

1. Insler JE, Seder CW, Furlan K, Mir F, Reddy VB, Gattuso P. Benign endobronchial tumors: a clinicopathologic review. Frontiers in surgery. 2021;8:644656.
2. Agarwal A, Agrawal A, Alagusundarmoorthy S, Meena N. Benign endobronchial neoplasms: a review. J Pulm Respir Med. 2015;5(275):2.
3. Gasparini S, Bonifazi M. Management of endobronchial tumors. Current Opinion in Pulmonary Medicine. 2016;22(3):245-51.
4. El-Helbawya R, Hussein SA, Tawab AMA. Fiberoptic bronchoscopic cryotherapy for endobronchial lung cancer: outcomes and predictors of success. The Egyptian Journal of Chest Diseases and Tuberculosis. 2019;68(3):394-403.
5. Baust J, Gage A, Johansen TB, Baust J. Mechanisms of cryoablation: clinical consequences on malignant tumors. Cryobiology. 2014;68(1):1-11.
6. Xu K. Cryobiology: mechanism of action and reaction to freezing. Modern cryosurgery for cancer: World Scientific; 2012. p. 123-70.
7. Prohaska J, Jan AH. Cryotherapy in dermatology. StatPearls [Internet]: StatPearls Publishing; 2023.
8. Fesseha H, Yilma T. Cryosurgery: Its principles and application-A Review. CPQ Med. 2020;10(2):1-18.

*Corresponding author: Omar Tarek Mahfouz, Mail: omartmahfouz@gmail.com, Mobile: 010 97878972

9. Colella S, Ravaglia C, Tomassetti S, Gurioli C, Gurioli C, Poletti V. Cryotherapy: application in the airways. Interventions in Pulmonary Medicine. 2018:139-53.
10. Rashad A, Badawy MS, Ali MM, Mansour H, Abdel-Bary M. The value of endobronchial cryotherapy in the management of malignant endobronchial obstruction in patients with inoperable NSCLC: a prospective analysis of clinical and survival outcomes. The Egyptian Journal of Bronchology. 2021;15:1-8.
11. Neel III HB, Farrell KH, Desanto LW, Payne WS, Sanderson DR. Cryosurgery of respiratory structures. I. Cryonecrosis of trachea and bronchus. The Laryngoscope. 1973;83(7):1062-71.
12. Niu L, Xu K, Mu F. Cryosurgery for lung cancer. Journal of thoracic disease. 2012;4(4):408.
13. Mohamed AS, El-Din MAA. Fiberoptic bronchoscopic cryo-ablation of central bronchial lung cancer. Egyptian Journal of Chest Diseases and Tuberculosis. 2016;65(2):527-30.
14. Abd El Hafez SAM, El Badrawy MK, Ali RE, Hadidy TE, aAbd Allah MS. Argon plasma coagulation versus cryotherapy in alleviation of endobronchial obstruction via fiberoptic bronchoscope. Egyptian Journal of Chest Diseases and Tuberculosis. 2017;66(1):181-6.
15. Elkolaly RM, Korraa EE-DA, Ibrahim IS. Electrocautery and cryotherapy in inoperable malignant lung lesions. Egyptian Journal of Bronchology. 2017;11:74-80.
16. Fadaly AS, Tawfek AES, Elsharawy M, AboZaid MM, Said AM, Elfakharany K. Bronchoscopic Cryotherapy in The Treatment of Endobronchial Typical Carcinoid. The Egyptian Journal of Hospital Medicine. 2023;90(1):1075-81.
17. Hetzel J, Eberhardt R, Herth F, Petermann C, Reichle G, Freitag L, et al. Cryobiopsy increases the diagnostic yield of endobronchial biopsy: a multicentre trial. European Respiratory Journal. 2012;39(3):685-90.
18. Purohit K, Grandfield S, Dhamija A, Abbasi A. Foreign body aspiration mimicking an endobronchial neoplasm: a case report and review of the literature. Cureus. 2023;15(3).
19. Ulas AB, Aydin Y, Eroglu A. Foreign body aspirations in children and adults. The American Journal of Surgery. 2022;224(4):1168-73.
20. Shouhdy Taha Ibrahim M, Ali Abu-Naglah A, Mohamed Ali Ewis A, Mohamed Ibrahim Tealeb A-S. EVALUATION OF CRYOPROBE BIOPSY IN DIAGNOSIS OF ENDOBRONCHIAL TUMORS. Al-Azhar Medical Journal. 2022;51(1):409-16.
21. Schumann C, Hetzel M, Babiak AJ, Hetzel J, Merk T, Wibmer T, et al. Endobronchial tumor debulking with a flexible cryoprobe for immediate treatment of malignant stenosis. The Journal of Thoracic and Cardiovascular Surgery. 2010;139(4):997-1000.
22. Rubio ER, Le SR, Whatley RE, Boyd MB. Cryobiopsy: should this be used in place of endobronchial forceps biopsies? BioMed research international. 2013;2013(1):730574.

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ORIGINAL ARTICLE

Comparative Analysis of Local Breast Tissue Flap Techniques for Reconstruction Following Centro-Partial Breast-Conserving Surgery: A Clinical, Oncological and Cosmetic Evaluation

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ABSTRACT

Background: Breast-conserving surgery (BCS) is the standard of care for early-stage breast cancer, but large resections may compromise cosmetic outcomes, particularly in women with small breast volumes. Local perforator-based flaps represent a muscle-sparing option for volume replacement. **Objective**: To compare clinical, oncological, and cosmetic outcomes of different local perforator flaps—AICAP/MICAP, LICAP, LTAP, and combined LICAP+LTAP—after centro-partial BCS. **Methods**: A prospective study of 69 patients undergoing centro-partial BCS with immediate local perforator flap reconstruction was performed. Patient demographics, tumor characteristics, surgical data, complications, and patient-reported satisfaction (5-point Likert scale) were analyzed .cross flap groups. **Results**: No significant differences were found among flap groups regarding age, comorbidities, tumor size, operative time, complications, or patient satisfaction ($p > 0.05$). Significant associations were observed only for tumor location ($p < 0.05$) and bra cup size ($p < 0.05$), reflecting flap selection preferences. All flap types achieved satisfactory clinical and cosmetic outcomes with low complication and reoperation rates. **Conclusion**: Local perforator flaps provide safe, reliable, and muscle-preserving reconstruction following centro-partial BCS. Flap choice is primarily determined by tumor location and breast anatomy.

Keywords

breast-conserving surgery, oncoplastic breast surgery, perforator flap, LICAP, LTAP, AICAP

INTRODUCTION

Breast cancer remains the most frequently diagnosed malignancy worldwide, with over 2.3 million new cases reported in 2020.[1]

Breast-conserving surgery (BCS), combined with radiotherapy, is the standard of care for early-stage disease, offering survival outcomes comparable to mastectomy while preserving breast aesthetics.[2] However, in women with small breast volumes, wide resections involving more than 20% of breast tissue often lead to unsatisfactory cosmetic outcomes.[3] Traditional techniques such as the latissimus dorsi (LD) flap provide

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reliable reconstruction but sacrifice muscle, resulting in donor-site morbidity and functional impairment.[4] Recent advances in the understanding of chest wall vascular anatomy have enabled the use of muscle-sparing perforator flaps such as the anterior/medial intercostal artery perforator (AICAP/MICAP), lateral intercostal artery perforator (LICAP), and lateral thoracic artery perforator (LTAP) flaps.[5], [6], [7] These flaps offer reliable volume replacement with reduced morbidity.[8] Despite their growing use, limited data exist comparing outcomes between different flap types, particularly in centro-partial resections. This study aimed to evaluate and compare the clinical, oncological, and cosmetic outcomes of AICAP/MICAP, LICAP, LTAP, and combined LICAP+LTAP flaps following centro-partial BCS.

PATIENTS AND METHODS

This prospective study included 69 patients with early-stage breast cancer who underwent centro-partial BCS and immediate reconstruction with local perforator-based flaps at Aswan University. Inclusion criteria were central or partial tumors requiring resection of >20% breast parenchyma. Exclusion criteria included locally advanced disease, prior ipsilateral surgery or radiotherapy, and severe comorbidities.

Preoperative evaluation included clinical examination, imaging, and histopathology. Tumor size, location, and bra/cup size were documented. Flaps were designed based on preoperative Doppler mapping of perforators.

Surgical technique: All patients underwent wide local excision with clear margins. Reconstruction utilized one of the following:
- AICAP/MICAP flaps (parasternal perforators)
- LICAP flaps (lateral intercostal artery perforators)
- LTAP flaps (lateral thoracic artery perforators)
- Combined LICAP+LTAP flaps

Flaps were raised in a suprafascial plane and rotated into the defect. Donor sites were closed primarily.

Outcomes measured included operative time, complications (infection, necrosis, dehiscence, seroma, hematoma), reoperations, and satisfaction (5-point Likert scale). Data were analyzed using SPSS with significance set at $p < 0.05$.

RESULTS

Patient demographics showed no significant differences between groups regarding age or comorbidities. Tumor size, operative time, complications, or patient satisfaction and focality were comparable across groups. Significant associations were noted only in relation to tumor location ($p < 0.05$) and bra cup size ($p < 0.05$), reflecting flap selection based on anatomical considerations. Mean operative time ranged between 120 and 156 minutes without significant variation. Complications were infrequent, with isolated cases of dehiscence, seroma, or partial necrosis, and no complete flap losses. Patient satisfaction was high across all groups, with the majority rating outcomes as 'Good' or 'Excellent' on the Likert scale. No significant differences in satisfaction were observed.

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Table 1. Patients' characteristics among the types of flaps groups.

	AICAP/MICAP Num.=12	LICAP Num.=30	LICAP + LTAP Num.=6	LTAP Num.=21	p-value
Age (years) Mean ±SD	44 ±7.70	40.6 ±12.13	55.5 ±6.36	38.71 ±14.09	0.372
Oral contraception	9 (75%)	24 (80%)	6 (100%)	18 (85.7%)	0.878
Hormone replacement therapy	0 (0%)	3 (10%)	0 (0%)	0 (0%)	0.715
Diabetes	0 (0%)	6 (20%)	0 (0%)	3 (14.3%)	0.720
Hypertension	3 (25%)	12 (40%)	0 (0%)	9 (42.9%)	0.669
Neoadjuvant chemotherapy	6 (50%)	3 (10%)	0 (0%)	9 (42.9%)	0.235
Corticosteroid therapy	3 (25%)	6 (20%)	0 (0%)	0 (0%)	0.516

P value below 0.05 is statistically significant, P above 0.05: Not significant, p below 0.001 is highly significant, SD: standard deviation.

There was statistically insignificant variance among the types of flap groups regarding age, oral contraception, diabetes, hormone replacement therapy, hypertension, neoadjuvant chemotherapy, and corticosteroid therapy ($p > 0.05$). (Table 1)

Table (2): Bra size among the types of flaps groups.

	AICAP/MICAP N=12	LICAP N=30	LICAP + LTAP N=6	LTAP N=21	p-value
Bra size					
32–35	3 (25%)	6 (20%)	0 (0%)	9 (42.9%)	0.588
36–39	9 (75%)	15 (50%)	3 (50%)	9 (42.9%)	0.776
≥ 40	0 (0%)	9 (30%)	3(50%)	3 (14.3%)	0.443
Cup size					
A	0 (0%)	3 (10%)	0 (0%)	9 (42.9%)	0.186
B	12 (100%)	18 (60%)	3 (50%)	3 (14.3%)	**0.047***
C	0 (0%)	6 (20%)	0 (0%)	9 (42.9%)	0.318
D	0 (0%)	3 (10%)	3 (50%)	0 (0%)	0.146

There was statistically insignificant variance among the types of flap groups regarding bra size, cup size A, cup size D, and cup size C (p above 0.05), while there was statistically significant variance among the types of flap groups regarding cup size B (p below 0.05). (Table 2)

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Table (3): Tumor Characteristics among the types of flaps groups.

	AICAP/MICAP N=12	**LICAP N=30**	**LICAP + LTAP N=6**	**LTAP N=21**	**p-value**
Size (mm) Medien (range)	25.5 (9-61)	24.5 (8-55)	44.5 (17-72)	19 (9-48)	0.667
Palpable mass	9 (75%)	18 (60%)	3 (50%)	21 (100%)	0.254
Location					
LIQ (lower inner quadrant)	9 (75%)	0 (0%)	0 (0%)	0 (0%)	<0.001
LOQ (lower outer quadrant)	3 (25%)	0 (0%)	0 (0%)	0 (0%)	0.174
LQT (lower quadrant transition)	0 (0%)	6 (20%)	0 (0%)	0 (0%)	0.415
OQT (outer quadrant transition)	0 (0%)	3 (10%)	3 (50%)	0 (0%)	0.146
UOQ (upper outer quadrant)	0 (0%)	21 (70%)	0 (0%)	15 (71.4%)	0.031*
UQT (upper quadrant transition)	0 (0%)	0 (0%)	3 (50%)	6 (28.6%)	0.111
Focality					
Unifocal	9 (75%)	6 (20%)	3 (50%)	3 (14.3%)	0.139
Multifocal	3 (25%)	24 (80%)	3 (50%)	18 (85.7%)	
Definitive diagnosis					
In situ	3 (25%)	6 (20%)	0 (0%)	6 (28.6%)	0.851
Invasive	9 (75%)	24 (80%)	6 (100%)	15(71.4%)	

There was statistically insignificant variance among the types of flap groups regarding size, palpable mass, LQT (lower quadrant transition), UQT (upper quadrant transition), LOQ (lower outer quadrant), OQT (outer quadrant transition), focality, and definitive diagnosis ($p > 0.05$), while there was statistically significant variance among the types of flap groups regarding LIQ (lower inner quadrant) and UOQ (upper outer quadrant) ($p < 0.05$). (Table 3)

Table (4): Surgical data among the types of flaps groups.

	AICAP/MICAP N=12	**LICAP N=30**	**LICAP + LTAP N=6**	**LTAP N=21**	**p-value**
Duration of surgery (min) Mean ±SD	120.75 ±24.00	127.7 ±29.91	156 ±8.84	118.71 ±31.96	0.452
Surgical drain	6 (50%)	24 (80%)	6 (100%)	18 (85.7%)	0.443
Complications					

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Infection	0 (0%)	0 (0%)	3 (50%)	3 (14.3%)	0.116
Flap necrosis	0 (0%)	0 (0%)	0 (0%)	3 (14.3%)	0.496
Dehiscence	0 (0%)	9 (30%)	0 (0%)	0 (0%)	0.213
Seroma	0 (0%)	3 (10%)	0 (0%)	6 (28.6%)	0.480
Hematoma	0 (0%)	0 (0%)	0 (0%)	3 (14.3%)	0.496
Reoperations	0 (0%)	6 (20%)	0 (0%)	6 (28.6%)	0.589

There was statistically insignificant variance among the types of flap groups regarding duration of surgery, surgical drain, and complications ($p > 0.05$). (Table 4)

Table 5. Satisfaction among the types of flaps groups.

	AICAP/MICAP N=12	**LICAP N=30**	**LICAP + LTAP N=6**	**LTAP N=21**	**p-value**
Satisfaction					
2 (Poor)	0 (0%)	0 (0%)	0 (0%)	3 (14.3%)	0.496
3 (Fair)	0 (0%)	6 (20%)	0 (0%)	3 (14.3%)	0.720
4 (Good)	6 (50%)	6 (20%)	6 (100%)	3 (14.3%)	0.083
5 (Excellent)	6 (50%)	18 (60%)	0 (0%)	12 (57.1%)	0.474

There was statistically insignificant variance among the types of flaps groups regarding Satisfaction $P > 0.05$. (Table 5)

DISCUSSION

This study demonstrated that local perforator flaps provide safe and effective reconstruction following centro-partial BCS. The absence of significant differences in complications or satisfaction suggests that flap choice should be tailored primarily to tumor location and breast anatomy. Our findings align with previous reports by Hamdi et al.[9], [10], [11] and McCulley et al.,[12] who emphasized the safety and reliability of LICAP, AICAP, and LTAP flaps. The low morbidity observed is consistent with the muscle-sparing nature of these procedures, offering advantages over the traditional LD flap. Strengths of this study include detailed surgical technique description and comparative analysis of multiple flap types. However, limitations include the small sample size, prospective design, and reliance on subjective satisfaction scores without standardized objective assessment.

CONCLUSION

Local perforator flaps (AICAP/MICAP, LICAP, LTAP, and combined LICAP+LTAP) represent reliable, muscle-preserving techniques for reconstruction after centro-partial breast-conserving surgery. All flap types achieved comparable safety, oncological adequacy, and cosmetic outcomes. Flap selection is best guided by tumor location and breast anatomy.
rather than differences in outcomes.
These results support the broader adoption of perforator flaps in oncoplastic surgery.

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REFERENCES

[1] H. Sung *et al.*, "Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries," *CA. Cancer J. Clin.*, vol. 71, no. 3, pp. 209–249, 2021.

[2] A. Ciabattoni *et al.*, "AIRO breast cancer group best clinical practice 2022 update," *Tumori J.*, vol. 108, no. 2_suppl, pp. 1–144, 2022.

[3] A. Karakatsanis *et al.*, "Chest wall perforator flaps are safe and can decrease mastectomy rates in breast cancer surgery: multicentre cohort study," *Br. J. Surg.*, vol. 111, no. 11, p. znae266, 2024.

[4] J. H. Højvig, M. Henriksen, C. R. Bartholdy, and C. T. Bonde, "Donor-site morbidity following breast reconstruction with a latissimus dorsi flap–A prospective study," *J. Plast. Reconstr. Aesthetic Surg.*, vol. 75, no. 7, pp. 2205–2210, 2022.

[5] C. M. Nava, G. Zinner, J. Martineau, and C. M. Oranges, "Chest Wall Perforator Flaps in Partial Breast Reconstruction: A Systematic Review and Meta-analysis," *Plast. Reconstr. Surgery–Global Open*, vol. 13, no. 8, p. e6996, 2025.

[6] S. Soumian, R. Parmeshwar, M. Chandarana, S. Marla, S. Narayanan, and G. Shetty, "Chest wall perforator flaps for partial breast reconstruction: surgical outcomes from a multicenter study," *Arch. Plast. Surg.*, vol. 47, no. 02, pp. 153–159, 2020.

[7] C. S. Hakakian, R. A. Lockhart, D. A. Kulber, and J. A. Aronowitz, "Lateral intercostal artery perforator flap in breast reconstruction: a simplified pedicle permits an expanded role," *Ann. Plast. Surg.*, vol. 76, pp. S184–S190, 2016.

[8] L. Galassi, G. Harder, F. Facchinetti, A. Cordovana, and R. Gilardi, "Immediate Breast Reconstruction with LICAP and AICAP Flaps: A Retrospective Evaluation of Surgical Outcomes and Patient Satisfaction," *J. Oman Med. Assoc.*, vol. 2, no. 1, p. 5, 2025.

[9] M. Hamdi, K. Van Landuyt, S. Monstrey, and P. Blondeel, "Pedicled perforator flaps in breast reconstruction: a new concept," *Br. J. Plast. Surg.*, vol. 57, no. 6, pp. 531–539, 2004.

[10] M. Hamdi and B. De Frene, "Pedicled perforator flaps in breast reconstruction," in *Seminars in plastic surgery*, Copyright© 2006 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New …, 2006, pp. 73–78.

[11] M. Hamdi, A. Spano, K. Van Landuyt, K. D'Herde, P. Blondeel, and S. Monstrey, "The lateral intercostal artery perforators: anatomical study and clinical application in breast surgery," *Plast. Reconstr. Surg.*, vol. 121, no. 2, pp. 389–396, 2008.

[12] S. J. McCulley, M. V Schaverien, V. K. M. Tan, and R. D. Macmillan, "Lateral thoracic artery perforator (LTAP) flap in partial breast reconstruction," *J. Plast. Reconstr. Aesthetic Surg.*, vol. 68, no. 5, pp. 686–691, 2015.

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ORIGINAL ARTICLE

Evaluation of the Impact of Cetuximab Plus FOLFIRI on Progression-Free Survival in Patients with Newly Diagnosed Metastatic Colorectal Cancer

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ABSTRACT

Background: Metastatic colorectal cancer (mCRC) continues to be a predominant cause of cancer-associated morbidity and death globally. Standard first treatment often includes combination chemotherapy, such as FOLFIRI. The incorporation of tailored biological agents has demonstrated enhancement in therapeutic outcomes for specific patients. **Objectives:** This study aimed to assess the progression-free survival of FOLFIRI chemotherapy with or without cetuximab. **Methodology:** Prospective research was performed at Ain Shams University Hospitals between December 2016 and December 2019, including 40 patients with newly diagnosed K-RAS/N-RAS wild-type mCRC. Patients were randomized into two groups: Protocol 1 (cetuximab + FOLFIRI, n = 20) and Protocol 2 (FOLFIRI alone, n = 20). Patients were evaluated clinically, biochemically, and radiologically every 3 months for one year. Progression-free survival (PFS) was analyzed by Kaplan–Meier method. **Results:** The first radiological assessment indicated a preference for Protocol 1 (95% compared to 60%, p = 0.02). Subsequent evaluations and tumor markers revealed no substantial discrepancies. The median progression-free survival (PFS) was markedly extended with Protocol 1 (9 months vs to 6 months, p = 0.004). **Conclusion:** The addition of cetuximab to FOLFIRI significantly improved progression-free survival and radiological response in K-RAS/N-RAS wild-type mCRC patients.

Keywords: mCRC, cetuximab, FOLFIRI, EGFR, PFS.

INTRODUCTION

Colorectal cancer is the third most prevalent cause of new cancer cases and cancer-related deaths in the United States, with an estimated 136,830 new diagnoses, comprising 96,830 cases of colon cancer and about 40,000 instances of rectal cancer. In that year, almost 50,310 persons died from these malignancies combined, demonstrating a significant trend of declining death rates for both sexes over the past two decades; precisely, from 2006 to 2010, the yearly decrease was 2.5% for men and 3.0% for women. The observed declines signify reductions in incidence rates along with improvements in early diagnosis and treatment techniques. Between 50% and 60% of patients diagnosed with colorectal

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cancer (CRC) develop colorectal metastases, with 80% to 90% of these patients exhibiting unresectable metastatic liver disease (1).

Colorectal cancer metastasizes in around 25% of individuals after diagnosis, with approximately 50% eventually progressing to metastatic CRC (mCRC). Metastatic colorectal cancer (mCRC) is predominantly treated with chemotherapy. Standard regimens, such as FOLFOX4, FOLFIRI, and XELOX, successfully manage tumor proliferation and enhance overall survival (OS) and disease-free survival (DFS) in patients; yet, they are linked to considerable adverse effects (2).

Metastatic illness generally develops metachronously after therapy for locoregional colorectal cancer, with the liver recognized as the primary site of involvement. Approximately 20% to 34% of individuals with colorectal cancer present with synchronous liver metastases. The treatment of metastatic colorectal cancer (mCRC) has significantly progressed during the last decade. In the last ten years, significant improvements have been noted in response rates, progression-free survival (PFS), and overall survival (OS) in patients with metastatic colorectal cancer (mCRC) (3).

The substantial improvement is chiefly ascribed to the recent introduction of innovative chemotherapy combinations and new therapeutic agents that target the molecular mechanisms implicated in colorectal carcinogenesis, including monoclonal antibodies (mAb) against the epidermal growth factor receptor (EGFR) and mAb against vascular endothelial growth factors (4).

Recent breakthroughs in targeted therapy suggest that the combination of chemotherapy with monoclonal antibodies as targeted therapeutics can prolong the life of patients with advanced colon cancer by more than 24 months. Cetuximab, a recombinant chimeric immunoglobulin G1 monoclonal antibody that targets EGFR, exhibits synergistic anticancer effects when used alongside chemotherapy (5).

Cetuximab, the first EGFR-targeting monoclonal antibody approved for metastatic colorectal cancer (mCRC), is categorized as a chimeric IgG1 antibody. This chemical has a higher affinity for EGFR Domain III compared to natural ligands such as EGF and TGF-α, therefore effectively obstructing ligand-induced receptor activation. Cetuximab promotes the internalization of EGFR, hence facilitating the downregulation of EGFR-dependent signaling. Cetuximab is associated with an increased frequency of infusion responses due to its chimeric properties. Pharmacokinetic disparities are seen in cetuximab's non-linear clearance and prolonged half-life, while panitumumab exhibits both linear and non-linear clearance processes, accompanied by a shorter half-life (6).

This research is to assess the effectiveness of cetuximab in combination with conventional irinotecan-based chemotherapy (infusional fluorouracil, leucovorin, and irinotecan [FOLFIRI]) as a first-line therapy for metastatic colorectal cancer (mCRC) that expresses the epidermal growth factor receptor.

PATIENTS AND METHODS

Study Design and Setting

This prospective, randomized trial was carried out at the Clinical Oncology Department, Ain Shams University, and Ain Shams Specialized Hospitals between December 2016 and December 2019.

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Patient Population

Forty patients with newly diagnosed metastatic colorectal cancer (mCRC) , wild-type *K-RAS*/*N-RAS* were enrolled. Patients were randomized equally into two groups:

- **Arm A (n = 20):** Cetuximab (500 mg/m²) followed by the FOLFIRI regimen, which included irinotecan (180 mg/m², day 1), leucovorin (200 mg/m², days 1–2), and fluorouracil (400 mg/m² bolus, then 600 mg/m² as a 22-hour infusion on days 1–2).
- **Arm B (n = 20):** FOLFIRI regimen alone, with the same dosing protocol.

Eligibility Criteria

Inclusion criteria included participants aged 18–75 years with histologically proven metastatic colorectal cancer (mCRC) (K-RAS, N-RAS wild-type), possessing at least one detectable lesion, no prior exposure to EGFR-targeted treatment or systemic chemotherapy for mCRC, an ECOG performance status of ≤2, and sufficient hematologic, hepatic, and renal function. The exclusion criteria were absence of EGFR expression, non-metastatic illness, previous systemic therapy, surgical intervention as the primary treatment, uncontrolled comorbidities, current infection, or psychiatric/social issues that impede compliance.

Baseline Assessment

The pretreatment assessment comprised a comprehensive medical history and physical examination, laboratory analyses [CBC, liver and renal function tests, carcinoembryonic antigen (CEA), CA19.9, KRAS/NRAS testing], and contrast-enhanced CT imaging of the chest, abdomen, and pelvis.

Follow-Up and Response Evaluation

Patients were monitored every 3 months for one year. Follow-up included clinical assessment, laboratory tests, and imaging with contrast-enhanced CT. Tumor response was evaluated utilizing the RECIST 1.1 criteria, tumors are categorized as complete response (CR), partial response (PR), stable disease (SD), or progressing disease (PD).

Study Endpoints

The **primary endpoint** was progression-free survival (PFS).

Statistical Analysis

SPSS 15.0 (SPSS Inc., Chicago, IL) was used to analyze patient demographics, tumor features, treatment specifics, clinical responses, and quality of life. Quantitative data were reported as mean ± SD for normally distributed variables or median with interquartile range for non-parametric data. We used frequencies and percentages for categorical variables. Group comparisons used the Student's t-test or Mann–Whitney U test for continuous variables and Chi-square or Fisher's exact for categorical variables. Using the Kaplan–Meier method and the log-rank test, survival curve differences were examined. Two-tailed p-values under 0.05 were statistically significant.

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RESULTS

Table 1: Baseline Demographic

		Group								t*	P value
		Protocol 1 (N=20)				Protocol 2 (N=20)					
		Min.	Max.	Mean	SD	Min.	Max.	Mean	SD		
Age		49.00	79.00	62.25	7.76	50.00	70.00	60.05	6.01	1.00	0.32 NS
		N		%		N		%		X^{2**}	P value
Age	<60	9		45.0%		15		75.0%		**3.75**	**0.05 S**
	>=60	11		55.0%		5		25.0%			
Sex	Male	13		65.0%		10		50.0%		0.92	0.34 NS
	Female	7		35.0%		10		50.0%			
Marital status	Married	19		95.0%		20		100.0%		1.03 FE	1.00 NS
	Single	1		5.0%		0		0.0%			
Family history	Negative	9		45.0%		11		55.0%		0.40	0.53 NS
	Positive	11		55.0%		9		45.0%			
Medical History	Negative	8		40.0%		10		50.0%		0.40	0.53 NS
	Positive	12		60.0%		10		50.0%			

The baseline characteristics of the studied patients in both Protocol 1 (n = 20) and Protocol 2 (n = 20) groups were compared .

The mean age of patients in Protocol 1 was 62.25 ± 7.76 years (range: 49–79 years), while in Protocol 2 the mean age was slightly lower at 60.05 ± 6.01 years (range: 50–70 years). The difference in mean age between the two groups did not reach statistical significance (t = 1.00, p = 0.32, NS). However, when patients were categorized by age groups, a statistically significant difference was observed: patients <60 years were more frequent in Protocol 2 (75.0%) compared to Protocol 1 (45.0%), whereas patients ≥60 years were more prevalent in Protocol 1 (55.0%) compared to Protocol 2 (25.0%) (χ^2 = 3.75, p = 0.05, significant).

Regarding sex distribution, males predominated in Protocol 1 (65.0%) compared to 50.0% in Protocol 2, while females were more represented in Protocol 2 (50.0% vs. 35.0%). However, this difference was not statistically significant (χ^2 = 0.92, p = 0.34, NS).

As for marital status, nearly all patients were married in both groups (95.0% in Protocol 1 and 100.0% in Protocol 2), with only one single patient in Protocol 1; this difference was not significant (Fisher's Exact test, p = 1.00, NS).

With respect to family history, 55.0% of patients in Protocol 1 reported a positive family history compared to 45.0% in Protocol 2, with no significant difference between the two groups (χ^2 = 0.40, p = 0.53, NS).

Similarly, medical history showed no significant difference between the two groups: 60.0% of patients in Protocol 1 and 50.0% in Protocol 2 had a positive medical history (χ^2 = 0.40, p = 0.53, NS).

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Table 2: Comparison between both studied groups as regards Tumor criteria:

		Group								Z*	P value
		Protocol 1 (N=20)				Protocol 2 (N=20)					
		Min.	Max.	Median	IQR	Min.	Max.	Median	IQR		
CEA		1.40	420.00	42.00	16.50-226	1.10	257.00	64.50	28.75-133.50	0.11	0.91 NS
CA19-9		2.00	529.00	14.25	8.95-87	1.80	220.00	19.90	13-50	0.04	0.97 NS
		N		%		N		%		X^{2**}	P value
tumor site	Right colon	2		10.0%		0		0.0%		3.32 FE	0.78 NS
	Left colon	4		20.0%		2		10.0%			
	sigmoid colon	6		30.0%		8		40.0%			
	cecum	3		15.0%		3		15.0%			
	Transverse colon	1		5.0%		1		5.0%			
	Rectal/ rectosigmoid	4		20.0%		6		30.0%			
Lung	Yes	6		30.0%		6		30.0%		0.00	1.00 NS
	No	14		70.0%		14		70.0%			
Liver	Yes	18		90.0%		18		90.0%		0.00	1.00 NS
	No	2		10.0%		2		10.0%			
Bone	Yes	3		15.0%		0		0.0%		3.24 FE	0.23 NS
	No	17		85.0%		20		100.0%			

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Peritoneum	Yes	6	30.0%	4	20.0%	0.53	0.47 NS
	No	14	70.0%	16	80.0%		
Pleural effusion	Yes	1	5.0%	4	20.0%	2.06 FE	0.34 NS
	No	19	95.0%	16	80.0%		
Ascites	Yes	2	10.0%	3	15.0%	0.23 FE	1.00 NS
	No	18	90.0%	17	85.0%		
LN	Yes	7	35.0%	4	20.0%	1.13	0.29 NS
	No	13	65.0%	16	80.0%		
Biopsy	infiltrating Ad C GII	17	85.0%	16	80.0%	2.72 FE	0.54 NS
	infiltrating Ad C GIII	2	10.0%	2	10.0%		
	signet ring C	0	0.0%	2	10.0%		
	musinous secreting ad C	1	5.0%	0	0.0%		

Regarding tumor site, sigmoid colon involvement was most common (30.0% in Protocol 1 vs. 40.0% in Protocol 2), followed by rectal/rectosigmoid tumors (20.0% vs. 30.0%). Right colon tumors were seen only in Protocol 1 (10.0%), while signet-ring carcinoma of the rectum was exclusively reported in Protocol 2 (10.0%). No statistically significant difference in tumor site distribution was found (Fisher's Exact test, p = 0.78, NS).

As for metastatic distribution:

Lung metastasis was present in 30.0% of patients in both groups (p = 1.00, NS).

Liver metastasis was the most common site, detected in 90.0% of both groups (p = 1.00, NS).

Bone metastasis was observed in 15.0% of Protocol 1 patients but absent in Protocol 2, with no statistically significant difference (Fisher's Exact test, p = 0.23, NS).

Peritoneal deposits were seen in 30.0% of Protocol 1 patients and 20.0% of Protocol 2 patients (p = 0.47, NS).

Pleural effusion was reported in 5.0% of Protocol 1 compared to 20.0% in Protocol 2, but this difference did not reach significance (Fisher's Exact test, p = 0.34, NS).

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Ascites was present in 10.0% of Protocol 1 patients and 15.0% of Protocol 2 patients (p = 1.00, NS). Lymph node involvement was more frequent in Protocol 1 (35.0%) compared to Protocol 2 (20.0%), though not statistically significant ($\chi^2 = 1.13$, p = 0.29, NS).

Table 3: Treatment Response Evaluations

Evaluation	Parameter	Protocol 1	Protocol 2	P-value
First Evaluation	**Radiological, n (%)**	N=20	N=20	**0.02**
	Stable Disease/Regression	19 (95.0)	12 (60.0)	
	Progression	1 (5.0)	8 (40.0)	
Second Evaluation	**Radiological, n (%)**	N=19	N=12	0.24
	Stable Disease/Regression	12 (63.2)	5 (41.7)	
	Progression	7 (36.8)	7 (58.3)	
Third Evaluation	**Radiological, n (%)**	N=12	N=5	0.52
	Stable Disease/Regression	3 (25.0)	0 (0.0)	
	Progression	9 (75.0)	5 (100.0)	
Fourth Evaluation	**Radiological, n (%)**	N=3	-	-
	Progression	3 (100.0)	-	

Table (3): shows that at first evaluation, radiological response was significantly better in Protocol 1, with 95% achieving stable disease/regression compared to 60% in Protocol 2 ($p = 0.02$). Subsequent evaluations showed a trend toward improved outcomes in Protocol 1, although differences were not statistically significant.

Across sequential evaluations, our study observed that renal and hepatic function remained generally preserved in both treatment arms. However, abnormalities were more frequent in the FOLFIRI group (Protocol 2). At the first evaluation, CBC abnormalities were slightly higher in Protocol 2 (25% vs. 15%), with only isolated cases of ALT and bilirubin elevation (5%). By the second evaluation, hematologic abnormalities increased to 41.7% in Protocol 2, compared to 15.8% in Protocol 1, alongside ALT (8.3%) and bilirubin elevations (up to 25%), both confined to the FOLFIRI group (Protocol 2) group. At the third evaluation, the disparity widened: CBC abnormalities were present in 60% of Protocol 2 versus 33.3% of Protocol 1, and hepatic toxicity also rose (ALT 20%, bilirubin 40%). In the fourth evaluation (Protocol 1 only), CBC abnormalities persisted (66.7%),

Table 4: Progression-Free Survival Analysis

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Group	Median PFS (months)	95% CI	Mean PFS (months)	95% CI	Log-Rank Test
Protocol 1	9.00	7.96 - 10.04	8.10	7.05 - 9.15	$\chi^2 = 8.435$
Protocol 2	6.00	4.37 - 7.63	5.55	4.48 - 6.62	**p = 0.004**
Overall	**6.00**	**4.69 - 7.31**	**6.83**	**5.98 - 7.67**	

PFS = Progression-Free Survival; CI = Confidence Interval.

Table (4): shows that Progression-free survival (PFS) was significantly longer in Protocol 1 compared to Protocol 2 (median 9.0 vs. 6.0 months, log-rank p = 0.004), confirming superior disease control with Protocol 1.

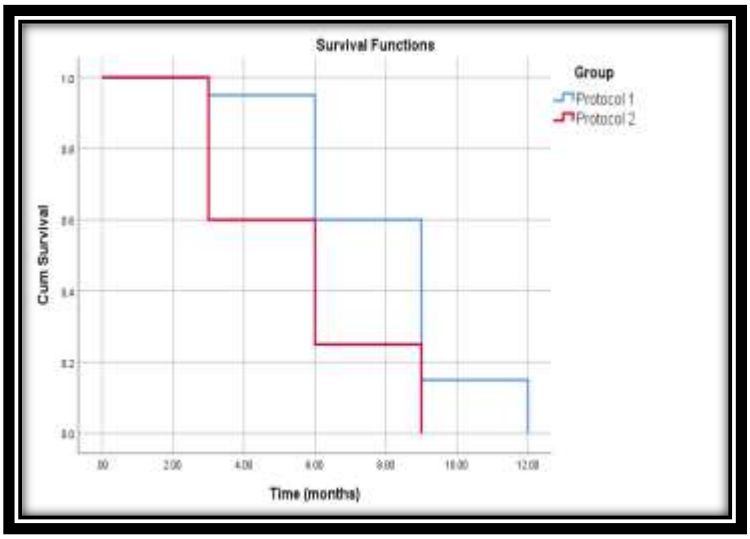

Fig. (3): Kaplan-Meier analysis for progression-free survival

DISCUSSION

Metastatic colorectal cancer (mCRC) poses a major therapeutic challenge, with nearly half of patients developing metastatic disease during the course of illness. Standard chemotherapy regimens, including FOLFIRI, FOLFOX, and XELOX, have modestly improved survival but remain limited in durability of response and are burdened with toxicity (2). The use of monoclonal antibodies like cetuximab, which targets the epidermal growth factor receptor (EGFR), has notably improved treatment strategies, especially for patients with RAS wild-type tumors.
The current study indicates that patients administered FOLFIRI in conjunction with cetuximab demonstrated significantly enhanced radiological tumor regression at early evaluation relative to those treated with FOLFIRI alone ($p < 0.05$). The results align with those of Shi et al. (7), who observed a

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significantly higher objective response rate (ORR) with cetuximab β combined with FOLFIRI (69.1% compared to 42.3%; odds ratio 3.09; 95% CI, 2.28–4.19; $p < 0.001$). Importantly, this translated into increased surgical conversion rates for metastases with curative intent (7.4% vs. 1.6%; $p = 0.002$), highlighting the clinical relevance of early tumor shrinkage in enabling potentially curative resection for patients initially considered unresectable.

Comparable evidence was reported by Cremolini et al. (8), who observed higher secondary resection rates following four months of FOLFOXIRI plus cetuximab induction therapy. This supports the concept that intensifying first-line treatment with triplet chemotherapy in combination with an anti-EGFR agent remains a valuable strategy for patients with liver-limited disease where secondary resection is feasible. Consistent with this, Heinemann et al. (1) demonstrated a significantly greater proportion of patients achieving early tumor shrinkage with FOLFIRI plus cetuximab (70% vs. 50%; $p = 0.0004$), along with a deeper overall response (50% vs. 33%; $p < 0.0001$).

This study demonstrates that patients receiving FOLFIRI in combination with cetuximab experienced significantly longer progression-free survival (PFS) than those treated with FOLFIRI alone ($p < 0.05$). The findings are consistent with prior reports. Xuan et al. (9) showed that induction therapy using cetuximab and chemotherapy significantly enhanced progression-free survival in patients with RAS wild-type metastatic colorectal cancer, while maintaining an acceptable toxicity profile. Qin et al. (10) demonstrated that the incorporation of cetuximab into the FOLFOX-4 regimen significantly enhanced progression-free survival (PFS) (HR, 0.69; 95% CI, 0.54–0.89; $p = 0.004$), resulting in an increase in median survival from 7.4 to 9.2 months. Holch et al. (6) confirmed the survival benefits associated with cetuximab-based regimens in this context.

Additional supporting evidence is derived from a critical phase III trial conducted in China, which randomized 505 patients with RAS/BRAF wild-type metastatic colorectal cancer to receive cetuximab β in combination with FOLFIRI or FOLFIRI monotherapy. The cetuximab cohort exhibited a notably extended median progression-free survival (13.1 months compared to 9.6 months; HR 0.639, $p = 0.004$) and overall survival (28.3 months versus 23.1 months; HR 0.729, $p = 0.024$).

A meta-analysis conducted by Azeem et al. (11), which included 25 studies and 3,788 patients, confirmed the survival advantage, demonstrating enhanced progression-free survival (HR 0.79) and overall survival (HR 0.78) with cetuximab-based therapy. Likewise, Yoshino et al. (12) found that EGFR inhibitors combined with chemotherapy were superior to bevacizumab-based regimens in RAS wild-type, left-sided mCRC, underscoring the importance of tumor location in treatment selection.

Consistent results have been reported by Wu et al. (13), who observed significantly improved OS and PFS with cetuximab-based therapy compared to chemotherapy alone. Mechanistically, cetuximab blocks ligand-dependent EGFR activation and induces antibody-dependent cellular cytotoxicity, thereby enhancing chemosensitivity and tumor regression (14). These effects translate clinically into longer disease control, higher response rates, and improved potential for curative resections.

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CONCLUSION

In conclusion, our findings confirm that adding cetuximab to irinotecan-based chemotherapy provides a significant PFS advantage in patients with RAS wild-type mCRC. Together with evidence from international trials and meta-analyses, this supports cetuximab as a cornerstone of modern first-line therapy, particularly for patients with left-sided tumors.

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REFERENCES

1. **Heinemann, V., von Weikersthal, L. F., Decker, T., Kiani, A., Kaiser, F., Al-Batran, S. E., ... & Stintzing, S. (2021).** FOLFIRI plus cetuximab or bevacizumab for advanced colorectal cancer: final survival and per-protocol analysis of FIRE-3, a randomised clinical trial. British journal of cancer, 124(3), 587-594.
2. **Boige, V., Blons, H., François, E., Abdelghani, M. B., Phelip, J. M., Le Brun-Ly, V., ... & Bouché, O. (2023).** Maintenance therapy with cetuximab after FOLFIRI plus cetuximab for RAS wild-type metastatic colorectal cancer: A phase 2 randomized clinical trial. JAMA Network Open, 6(9), e2333533-e2333533.
3. **Fischer, L. E., Stintzing, S., von Weikersthal, L. F., Modest, D. P., Decker, T., Kiani, A., ... & Heinemann, V. (2022).** Efficacy of FOLFIRI plus cetuximab vs FOLFIRI plus bevacizumab in 1st-line treatment of older patients with RAS wild-type metastatic colorectal cancer: an analysis of the randomised trial FIRE-3. British Journal of Cancer, 127(5), 836-843.
4. **Wu, J., Wang, Z., Jin, C., Ren, H., Hu, Y., Yang, B., & Hu, Y. (2021).** Effect of cetuximab combined with chemotherapy in treating metastatic colorectal cancer and its prognostic analysis. J buon, 26(1), 101-108.
5. **Cremolini, C., Antoniotti, C., Rossini, D., Lonardi, S., Loupakis, F., Pietrantonio, F., ... & Banzi, M. (2020).** Upfront FOLFOXIRI plus bevacizumab and reintroduction after progression versus mFOLFOX6 plus bevacizumab followed by FOLFIRI plus bevacizumab in the treatment of patients with metastatic colorectal cancer (TRIBE2): a multicentre, open-label, phase 3, randomised, controlled trial. The Lancet Oncology, 21(4), 497-507.
6. **Holch, J. W., Held, S., Stintzing, S., von Weikersthal, L. F., Decker, T., Kiani, A., ... & Heinemann, V. (2020).** Relation of cetuximab-induced skin toxicity and early tumor shrinkage in metastatic colorectal cancer patients: results of the randomized phase 3 trial FIRE-3 (AIO KRK0306). Annals of Oncology, 31(1), 72-78.
7. **Shi, Y., Ba, Y., Wang, J., Xiong, J., Gu, K., Chen, Y., ... & Hou, S. (2025).** First-line treatment of anti-EGFR monoclonal antibody cetuximab β plus FOLFIRI versus FOLFIRI alone in Chinese patients with RAS/BRAF wild-type metastatic colorectal cancer: a randomized, phase 3 trial. Signal Transduction and Targeted Therapy, 10(1), 147.
8. **Cremolini, C., Antoniotti, C., Rossini, D., Lonardi, S., Loupakis, F., Pietrantonio, F., ... & Banzi, M. (2020).** Upfront FOLFOXIRI plus bevacizumab and reintroduction after progression

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versus mFOLFOX6 plus bevacizumab followed by FOLFIRI plus bevacizumab in the treatment of patients with metastatic colorectal cancer (TRIBE2): a multicentre, open-label, phase 3, randomised, controlled trial. The Lancet Oncology, 21(4), 497-507.

9. **Xuan, T., Wang, Z., Meng, S., Li, J., Li, J., Cao, F., & Qu, L. (2024).** Efficacy and safety of maintenance therapy using cetuximab in patients with metastatic colorectal cancer: retrospective study. Cancer Management and Research, 185-197.
10. **Qin, S., Li, J., Wang, L., Xu, J., Cheng, Y., Bai, Y., ... & Liu, T. (2018).** Efficacy and tolerability of first-line cetuximab plus leucovorin, fluorouracil, and oxaliplatin (FOLFOX-4) versus FOLFOX-4 in patients with RAS wild-type metastatic colorectal cancer: the open-label, randomized, phase III TAILOR trial. Journal of Clinical Oncology, 36(30), 3031-3039.
11. **Azeem, M., Ur Rehman, A., Rasheed, S., Shahzad, A., Javed, M. H., Jamil, Q. A., ... & Al-Tamimi, S. K. (2025).** The impact of combining cetuximab with the traditional chemotherapy regimens on clinical effectiveness in metastatic colorectal cancer: a systematic review and meta-analysis. BMC cancer, 25(1), 331.
12. **Yoshino, T., Hooda, N., Younan, D., Muro, K., Shitara, K., Heinemann, V., ... & Stintzing, S. (2024).** A meta-analysis of efficacy and safety data from head-to-head first-line trials of epidermal growth factor receptor inhibitors versus bevacizumab in adult patients with RAS wild-type metastatic colorectal cancer by sidedness. European Journal of Cancer, 202, 113975.
13. **Wu, J., Wang, Z., Jin, C., Ren, H., Hu, Y., Yang, B., & Hu, Y. (2021).** Effect of cetuximab combined with chemotherapy in treating metastatic colorectal cancer and its prognostic analysis. J buon, 26(1), 101-108.
14. **Elshorbagy, S., Nada, Y., Saadawy, I. M., & Haggag, R. (2023).** Anti-Epithelial Growth Factor Receptors for Prognosis in Management of Metastatic Colorectal Cancer. The Egyptian Journal of Hospital Medicine, 90(1), 1527-1533.
15. 90(1), 1527-1533.

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ORIGINAL ARTICLE

Determinant of Patient Satisfaction and Outcomes of Local Breast Tissue Flaps in Central Breast-Conserving Surgery: A prospective Cohort Study

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ABSTRACT

Background: Central breast tumors pose challenges for breast-conserving surgery (BCS), as excision may affect aesthetics and symmetry. Local tissue flaps are increasingly used for reconstruction, but evidence on outcomes and satisfaction is limited. **Objective**: To evaluate surgical outcomes and patient-reported satisfaction after local flap reconstruction following centro-partial BCS, with focus on aesthetics, complications, and quality of life. **Methods**: A prospective cohort of 69 women with central breast cancer underwent centro-partial BCS and immediate reconstruction using local tissue flaps. Collected data included demographics, breast size, tumor features, flap type/movement, operative details, and complications. Satisfaction was measured with a validated questionnaire and categorized as poor, fair, good, or excellent. Associations between satisfaction and clinical or surgical factors were analyzed. **Results**: Overall satisfaction was high: 52.2% rated outcomes excellent and 30.4% good. Tumor size (p=0.006) and focality (p=0.038) were significantly associated with satisfaction. Flap type, flap movement, and operative time showed no influence. Complications—including infection (p=0.006), flap necrosis (p<0.001), seroma (p=0.028), and reoperations (p<0.001)—were strongly linked to lower satisfaction. **Conclusion**: Local flap reconstruction after centro-partial BCS yields favorable aesthetic and satisfaction outcomes. Tumor factors and complications influence satisfaction more than flap type or surgical technique.

Keywords

breast cancer, central breast tumors, oncoplastic surgery, local tissue flap, patient satisfaction

INTRODUCTION

Breast cancer is the most common malignancy among women worldwide, with central breast tumors representing a particular surgical challenge due to the involvement of the nipple-areolar complex and central breast contour.[1]

Breast-conserving surgery (BCS) combined with radiotherapy is standard for early-stage disease, howeverin central tumors, large excisions may compromise breast symmetry and aesthetics. Oncoplastic techniques have been developed to address these challenges by integrating oncological resection with immediate reconstruction.[2] Local breast tissue flaps provide a muscle-sparing option that preserves breast contour while avoiding donor-site morbidity of larger myocutaneous flaps.[3], [4]

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Despite their increasing use, evidence on satisfaction, quality of life, and complication impact after central BCS reconstruction with local flaps remains limited.[5]

This study aimed to evaluate surgical outcomes and patient satisfaction following local tissue flap reconstruction after centro-partial BCS, with a focus on aesthetic satisfaction and quality-of-life outcomes.

PATIENTS AND METHODS

Study Design and Population: This prospective cohort study included 69 women aged 18 years or older with central breast cancer who underwent centro-partial BCS with immediate reconstruction using local tissue flaps at Aswan University. Exclusion criteria were incomplete medical records, loss to follow-up, prior breast surgery or radiotherapy, metastatic disease, and male patients.

Data Collection: Clinical data included demographics, comorbidities, hormonal therapy, and neoadjuvant chemotherapy. Breast size and cup size were recorded. Tumor characteristics included size, location, focality, and pathology. Surgical details comprised flap type (AICAP/MICAP, LICAP, LTAP, or LICAP+LTAP), flap movement (rotation, advancement, folded), operative time, and drain use. Postoperative complications (infection, necrosis, seroma, dehiscence, hematoma) and reoperations were documented.

Outcomes: The primary outcome was patient-reported satisfaction with aesthetic results, categorized as poor, fair, good, or excellent, using a validated satisfaction tool. Secondary outcomes were complication rates and reoperations.

Statistical Analysis: Data were analyzed using SPSS software. Continuous variables were expressed as mean ± SD or median (range), and categorical variables as frequencies. Comparisons were performed using Chi-square/Fisher's exact test for categorical data and ANOVA/Kruskal–Wallis test for continuous variables. A p-value <0.05 was considered significant.

RESULTS

Patient Satisfaction: Of 69 patients, 52.2% rated outcomes as excellent, 30.4% as good, 13.0% as fair, and 4.3% as poor. Tumor size ($p=0.006$) and focality ($p=0.038$) were significantly associated with satisfaction. Flap type, flap movement, operative time, and drain use did not significantly influence satisfaction.

Complications: Postoperative complications were uncommon but significantly affected satisfaction. Infection ($p=0.006$), flap necrosis ($p<0.001$), seroma ($p=0.028$), and reoperations ($p<0.001$) were strongly associated with poor satisfaction. No complete flap losses occurred. Overall, complications were the most consistent predictor of reduced satisfaction, while technical and anatomical variables had minimal impact.

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Table 1. Patients' characteristics among satisfaction groups.

	Poor	Fair	Good	Excellent	p-value
	N=3	N=9	N=21	N=36	
Age (years)					
Mean ±SD	31 ±0	35.66 ±12.66	45.28 ±11.91	42.41 ±12.50	0.564
Oral contraception	3 (100%)	9 (100%)	21 (100%)	24 (66.7%)	0.217
Hormone replacement therapy	0 (0%)	3 (33.3%)	0 (0%)	0 (0%)	0.072
Diabetes	0 (0%)	0 (0%)	3 (14.3%)	6 (16.7%)	0.861
Hypertension	0 (0%)	3 (33.3%)	3 (14.3%)	18 (50%)	0.3825
Neoadjuvant chemotherapy	0 (0%)	0 (0%)	3 (14.3%)	15 (41.7%)	0.330
Corticosteroid therapy	0 (0%)	3 (33.3%)	3 (14.3%)	3 (8.3%)	0.686

P value >0.05: Not significant, P value <0.05 is statistically significant, p<0.001 is highly significant, SD: standard deviation.

Table1 shows that, there was statistically insignificant variance among satisfaction groups regarding Age, Oral contraception, Hormone replacement therapy, Diabetes, Hypertension, Neoadjuvant chemotherapy, and Corticosteroid therapy.

Table 2. Bra size among satisfaction groups.

	Poor	Fair	Good	Excellent	p-value
	N=3	N=9	N=21	N=36	
Bra size					
32–35	3 (100%)	3 (33.3%)	0 (0%)	9 (25%)	**0.048***
36–39	0 (0%)	6 (66.7%)	12 (57.1%)	21 (58.3%)	0.621

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≥ 40	0 (0%)	0 (0%)	9(42.9%)	6 (16.7%)	0.372
Cup size					
A	3 (100%)	3 (33.3%)	0 (0%)	3(8.3%)	**0.007***
B	0 (0%)	6 (66.7%)	12 (57.1%)	21 (58.3%)	0.621
C	0 (0%)	0 (0%)	3 (14.3%)	12 (33.3%)	0.514
D	0 (0%)	0 (0%)	6 (28.6%)	0 (0%)	0.171

Table 2 shows that, there was no statistically significant difference among satisfaction groups regarding Bra size (36–39), Bra size ≥ 40, Cup size B, Cup size C, and Cup size D, while there was statistically significant variance among satisfaction groups regarding Bra size (32–35), and Cup size A.

Table 3. Tumor Characteristics among satisfaction groups.

	Poor N=3	**Fair** N=9	**Good** N=21	**Excellent** N=36	**p-value**
Size (mm) Medien (range)	9	35 (20-48)	23 (9-72)	24.5 (8-55)	**0.006***
Palpable mass	3 (100%)	9 (100%)	15 (71.4%)	27 (75%)	0.623
Location					
LIQ (lower inner quadrant)	0 (0%)	0 (0%)	6 (28.6%)	3 (8.3%)	0.508
LOQ (lower outer quadrant)	0 (0%)	0 (0%)	0 (0%)	3 (8.3%)	0.811
LQT (lower quadrant transition)	0 (0%)	0 (0%)	0 (0%)	3 (8.3%)	0.811
OQT (outer quadrant transition)	0 (0%)	3 (33.3%)	3 (14.3%)	31 (8.3%)	0.686

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• **UOQ (upper outer quadrant)**	• 3 (100%)	• 3 (33.3%)	• 9 (42.9%)	• 21 (58.3%)	• 0.621
• **UQT (upper quadrant transition)**	• 0 (0%)	• 3 (33.3%)	• 3 (14.3%)	• 3 (8.3%)	• 0.686
• **Focality**					
• **Unifocal**	• 0 (0%)	• 0 (0%)	• 5 (71.4%)	• 6 (16.7%)	• **0.038***
• **Multifocal**	• 3 (100%)	• 9 (100%)	• 6 (28.6%)	• 30 (83.3%)	
• **Definitive diagnosis**					
• **In situ**	• 0 (0%)	• 0 (0%)	• 3 (14.3%)	• 12 (33.3%)	• 0.514
• **Invasive**	• 3 (100%)	• 9 (100%)	• 18 (85.7%)	• 24 (66.7%)	

Table 3 shows that, there was statistically insignificant variance among satisfaction groups regarding Palpable mass, LIQ (lower inner quadrant), LOQ (lower outer quadrant), LQT (lower quadrant transition), OQT (outer quadrant transition), UOQ (upper outer quadrant), UQT (upper quadrant transition), and Definitive diagnosis, while there was statistically significant variance among satisfaction groups regarding Size, and Focality.

Table 4. Flaps characteristics among satisfaction groups.

•	• **Poor**	• **Fair**	• **Good**	• **Excellent**	• **p-value**
	• N=3	• N=9	• N=21	• N=36	
• Types of flaps					
• **AICAP/MICAP**	• 0 (0%)	• 0 (0%)	• 6 (28.6%)	• 6 (16.7%)	• 0.692
• **LICAP**	• 0 (0%)	• 6 (66.7%)	• 6 (28.6%)	• 18 (50%)	• 0.519
• **LICAP + LTAP**	• 0 (0%)	• 0 (0%)	• 6 (28.6%)	• 0 (0%)	• 0.171
• **LTAP**	• 3 (100%)	• 3 (33.3%)	• 1 (14.3%)	• 12 (33.3%)	• 0.360

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• **Movement of the flap**					
• **Rotation**	• 3 (100%)	• 3 (33.3%)	• 15 (71.4%)	• 27 (75%)	•
• **Folded**	• 0 (0%)	• 6 (66.7%)	• 3 (14.3%)	• 9 (25%)	• 0.802
• **Advancement**	• 0 (0%)	• 0 (0%)	• 3(14.3%)	• 0 (0%)	

Table 4 shows that, there was statistically insignificant difference among satisfaction groups regarding Types of flaps, and Movement of the flap.

Table 5. Surgical data among satisfaction groups.

	Poor	**Fair**	**Good**	**Excellent**	**p-value**
	N=3	N=9	N=21	N=36	
Duration of surgery (min) Mean ±SD	159 ±0	124.66 ± 32.57	130.85 ±34.20	121.16 ±26.31	0.634
Surgical drain	3 (100%)	9 (100%)	21 (100%)	21 (58.3%)	0.118
Complications					
Infection	3 (100%)	0 (0%)	3 (14.3%)	0 (0%)	**0.006***
Flap necrosis	3(100%)	0 (0%)	0 (0%)	0 (0%)	**<0.001***
Dehiscence	0 (0%)	3 (33.3%)	6 (28.6%)	0 (0%)	0.209
Seroma	0 (0%)	6 (66.7%)	0 (0%)	3 (8.3%)	**0.028***
Hematoma	0 (0%)	0 (0%)	0 (0%)	3 (8.3%)	0.811
Reoperations	3 (100%)	9 (100%)	0 (0%)	0 (0%)	**<0.001***

P value >0.05: Not significant, P value <0.05 is statistically significant, p<0.001 is highly significant, SD: standard deviation.

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Table 5 shows that, there was no statistically significant difference among the types of flaps groups regarding Duration of surgery, Surgical drain, Dehiscence, and Hematoma, while there was statistically significant difference among the types of flaps groups regarding Infection, Flap necrosis, Seroma, and Reoperations.

DISCUSSION

This study highlights that reconstruction with local tissue flaps after central BCS achieves high levels of satisfaction, with over 80% of patients rating outcomes as good or excellent. The strongest determinants of dissatisfaction were postoperative complications, while flap type or movement did not significantly affect outcomes. These findings emphasize that surgical precision and minimizing complications are more critical for patient experience than flap selection.

Comparison with Literature: Our results align with Krzos et al., who reported stable satisfaction post-BCS regardless of age or treatment variables.[6]

Similarly, Barkai et al. and Leser et al. found that patient satisfaction did not significantly differ across surgical techniques when good oncological and reconstructive principles were followed.[7], [8]

In contrast, complications such as infection or necrosis were consistently linked to dissatisfaction, supporting reports from Ho et al. and Colakoglu et al.[9], [10]

Breast size showed some association with satisfaction, as smaller cup sizes tended toward higher satisfaction, echoing findings from Kim et al. and Shamsunder et al.[11], [12]

Strengths and Limitations: This study draws its strength from being one of thefew regional studies addressing satisfaction after central BCS reconstruction with local flaps. Limitations include small sample size, limited follow-up, and reliance on subjective satisfaction measures rather than objective tools such as BCCT.core. Future studies should be multicenter, and incorporate validated quality-of-life instruments to better capture patient perspectives.

CONCLUSION

Local tissue flap reconstruction after centro-partial breast-conserving surgery is safe, effective, and associated with high patient satisfaction. Satisfaction is influenced primarily by tumor factors and postoperative complications, rather than flap type or surgical duration. Complication prevention remains critical to improving quality of life.

REFERENCES

[1] K. M. Cuthrell and N. Tzenios, “Breast cancer: updated and deep insights,” *Int. Res. J. Oncol.*, vol. 6, no. 1, pp. 104–118, 2023.

[2] M. Zwakman *et al.*, “Long-term quality of life and aesthetic outcomes after breast conserving surgery in patients with breast cancer,” *Eur. J. Surg. Oncol.*, vol. 48, no. 8, pp. 1692–1698, 2022.

[3] D. Rossi *et al.*, “The genetics of Richter syndrome reveals disease heterogeneity and predicts survival

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after transformation," *Blood, J. Am. Soc. Hematol.*, vol. 117, no. 12, pp. 3391–3401, 2011.

[4] V. Vindigni, F. Marena, C. Zanettin, and F. Bassetto, "Breast reconstruction: the oncoplastic approach," *J. Clin. Med.*, vol. 13, no. 16, p. 4718, 2024.

[5] M. F. Scaglioni, F. Martini, and M. Meroni, "Present and Future of Autologous Breast Reconstruction: Advancing Techniques to Minimize Morbidity and Complications, Enhancing Quality of Life and Patient Satisfaction," *J. Clin. Med.*, vol. 14, no. 8, p. 2599, 2025.

[6] A. Krzos, A. Stanisławek, M. Jędrych, M. Łuczyk, and B. Ślusarska, "Satisfaction with the aesthetic effect and quality of life for women after breast conserving therapy (BCT)—preliminary research," *Int. J. Environ. Res. Public Health*, vol. 16, no. 23, p. 4682, 2019.

[7] E. Barkai, Y. Namir, O. Golan, Y. Barnea, E. Arad, and T. S. Menes, "Patient Satisfaction and Surgical Outcome After Oncoplastic Reconstruction following Radical Lumpectomy Versus Standard Lumpectomy: A Retrospective Cohort Study," *Eur. J. Breast Heal.*, vol. 18, no. 2, p. 127, 2022.

[8] C. Leser *et al.*, "Patient satisfaction after breast cancer surgery: A prospective clinical trial," *Wien. Klin. Wochenschr.*, vol. 133, no. 1, pp. 6–13, 2021.

[9] G. Ho, T. J. Nguyen, A. Shahabi, B. H. Hwang, L. S. Chan, and A. K. Wong, "A systematic review and meta-analysis of complications associated with acellular dermal matrix-assisted breast reconstruction," *Ann. Plast. Surg.*, vol. 68, no. 4, pp. 346–356, 2012.

[10] S. Colakoglu *et al.*, "Impact of complications on patient satisfaction in breast reconstruction," *Plast. Reconstr. Surg.*, vol. 127, no. 4, pp. 1428–1436, 2011.

[11] J. B. Kim, J. R. Eom, J. W. Lee, J. Lee, H. Y. Park, and J. D. Yang, "Utility of two surgical techniques using a lateral intercostal artery perforator flap after breast-conserving surgery: a single-center retrospective study," *Plast. Reconstr. Surg.*, vol. 143, no. 3, pp. 477e-487e, 2019.

[12] M. G. Shamsunder *et al.*, "Understanding preoperative breast satisfaction among patients undergoing mastectomy and immediate reconstruction: BREAST-Q insights," *Plast. Reconstr. Surg.*, vol. 148, no. 6, pp. 891e-902e, 2021.

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ORIGINAL ARTICLE

Impact of Cetuximab Addition to FOLFIRI as First-Line Therapy for Metastatic Colorectal Cancer on Patient Quality of Life

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ABSTRACT

Background: Epidermal growth factor receptor (EGFR)–expressing metastatic colorectal cancer (mCRC) with wild-type K-RAS/N-RAS may benefit from anti-EGFR targeted therapy. **Objective:** This study evaluated the efficacy and quality-of-life outcomes of FOLFIRI chemotherapy with or without cetuximab. **Patients and Methods:** A prospective study was conducted at Ain Shams University Hospitals between December 2016 and December 2019, including 40 patients with newly diagnosed EGFR-expressing, K-RAS/N-RAS wild-type mCRC. Patients were randomized into two groups: Protocol 1 (cetuximab + FOLFIRI, n = 20) and Protocol 2 (FOLFIRI alone, n = 20). Patients were evaluated clinically, biochemically, and radiologically every 3 months for one year. Quality of life (QoL) was assessed using a structured questionnaire. **Results:** QoL scores were significantly better in Protocol 1 across general ($p < 0.001$), physical ($p = 0.004$), psychological ($p = 0.04$), familial ($p = 0.04$), and economic ($p = 0.05$) domains. Median PFS was significantly longer with Protocol 1 (9 vs. 6 months, $p = 0.004$). **Conclusion:** In conclusion, our study reinforces that combining cetuximab with FOLFIRI not only enhances oncologic outcomes but also preserves, and in some domains improves, patient-reported quality of life.

Keywords: metastatic colorectal cancer, cetuximab, FOLFIRI, EGFR, quality of life

INTRODUCTION

Colorectal cancer ranks as the third most prevalent cause of new cancer diagnoses and cancer-related fatalities in the United States, with an anticipated 136,830 new cases (96,830 cases of colon cancer and about 40,000 instances of rectal cancer projected for diagnosis). In that year, around 50,310 individuals succumbed to these malignancies together, exhibiting a notable trend of decreasing death rates in both genders over the preceding twenty years; from 2006 to 2010, the rate diminished by 2.5%

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year in men and by 3.0% annually in women. These reductions indicate diminishing incidence rates and advancements in early diagnosis and treatment (1).

Approximately 50% to 60% of individuals diagnosed with colorectal cancer (CRC) develop colorectal metastases, and 80% to 90% of these individuals present with unresectable metastatic liver disease. (2).

Colorectal cancer has metastasized in around 25% of patients upon diagnosis and will ultimately advance to metastatic CRC (mCRC) in about 50% of patients. Currently, metastatic colorectal cancer (mCRC) is mostly treated with chemotherapy. Standard chemotherapy regimens, including FOLFOX4, FOLFIRI, and XELOX, can inhibit tumor proliferation and prolong overall survival (OS) and disease-free survival (DFS) in patients; however, they also induce significant adverse effects (3).

Metastatic illness typically arises metachronously following therapy for locoregional colorectal cancer, with the liver being the predominant site of involvement. Nonetheless, 20% to 34% of individuals with colorectal cancer exhibit synchronous liver metastases. (4).

The management of metastatic colorectal cancer (mCRC) has advanced considerably in the past ten years. Over the past decade, notable advancements have been achieved in response rates, progression-free survival (PFS), and overall survival (OS) for patients with metastatic colorectal cancer (mCRC). This significant enhancement is primarily attributable to the recent implementation of novel chemotherapy combinations and new therapeutic agents that target molecular processes involved in colorectal carcinogenesis, such as monoclonal antibodies (mAbs) against the epidermal growth factor receptor (EGFR) or mAbs against vascular endothelial growth factors. Recent advancements in targeted therapy have demonstrated that chemotherapy, when paired with monoclonal antibodies as targeted agents, can extend the life of patients with advanced colon cancer by almost 24 months (6).

Cetuximab, a chimeric human/mouse immunoglobulin G1 monoclonal antibody targeting EGFR, elicits synergistic anticancer effects when administered with chemotherapy (7).

Cetuximab, the inaugural EGFR-targeting monoclonal antibody sanctioned for metastatic colorectal cancer (mCRC), is a chimeric IgG1 antibody. It selectively binds to the EGFR Domain III with more affinity than natural ligands like EGF and TGF-α, substantially inhibiting ligand-induced receptor activation. Cetuximab facilitates the downregulation of EGFR-dependent signaling by enhancing the internalization of EGFR. Cetuximab is linked to a higher incidence of infusion reactions because of its chimeric composition. Pharmacokinetic distinctions encompass cetuximab's non-linear clearance and extended half-life, whereas panitumumab demonstrates both linear and non-linear clearance processes along with a reduced half-life (8).

The objective of this study is to ascertain the efficacy of cetuximab in conjunction with conventional irinotecan-based chemotherapy (infusional fluorouracil, leucovorin, and irinotecan [FOLFIRI]) as a first-line treatment for metastatic colorectal cancer (mCRC) that expresses the epidermal growth factor receptor.

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PATIENTS AND METHODS

Study Design and Setting

This was a prospective, randomized study conducted at the Clinical Oncology Department, Ain Shams University and Ain Shams Specialized Hospitals, during the period from December 1, 2016, to December 1, 2019.

Patient Population

A total of 40 patients with newly diagnosed epidermal growth factor receptor (EGFR)-expressing metastatic colorectal cancer (mCRC) harboring wild-type K-RAS and N-RAS were enrolled. Patients were randomized into two equal groups:

- **Arm A (n = 20):** Patients received Cetuximab (500 mg/m²) followed by FOLFIRI regimen, consisting of Irinotecan (180 mg/m², day 1), leucovorin (200 mg/m², days 1–2), fluorouracil (400 mg/m² bolus, then 600 mg/m² as 22-hour continuous infusion on days 1–2).
- **Arm B (n = 20):** Patients received FOLFIRI regimen alone, using the same dosing protocol.

Inclusion Criteria

- Individuals aged 18 to 75 years.
- Histologically confirmed EGFR-expressing metastatic colorectal cancer (mCRC) with wild-type K-RAS and N-RAS, exhibiting at least one measurable lesion.
- No previous exposure to EGFR-targeted therapy or chemotherapy for metastatic colorectal cancer (mCRC).
- ECOG performance status of 2 or lower.
- Adequate hematologic function: ANC greater than 1500/mm³, platelets equal to or greater than 100,000/mm³, hemoglobin greater than 10 g/dL.
- Sufficient hepatic function: AST and ALT levels are ≤2.5 times the upper limit of normal (ULN), and bilirubin levels are ≤1.5 times the ULN.
- Adequate renal function is defined as serum creatinine levels not exceeding 1.5 times the upper limit of normal (ULN).
- Accessibility of patients for treatment and follow-up.

Exclusion Criteria

- Absence of EGFR expression.
- Non-metastatic colorectal cancer at initial presentation.
- Prior exposure to EGFR-targeted therapy and/or chemotherapy for mCRC.
- Patients undergoing primary surgical treatment for the primary tumor.
- Severe uncontrolled organ dysfunction or metabolic disease.
- Active uncontrolled infection, psychiatric illness, or social circumstances precluding compliance.

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Pretreatment Evaluation

All patients underwent:

1. **Clinical assessment:** complete history and physical examination.
2. **Laboratory investigations:** complete blood count (CBC), liver function tests (AST, ALT, bilirubin), renal profile (serum creatinine, urea), carcinoembryonic antigen (CEA), CA19.9, and KRAS/NRAS mutation testing.
3. **Radiological assessment:** contrast-enhanced CT of chest, abdomen, and pelvis to document baseline disease status.

Treatment Evaluation and Follow-Up

Patients in both arms were followed up for 12 months at 3-month intervals. Follow-up included:

- **Clinical evaluation:** assessment of metastatic symptoms and detection of new manifestations.
- **Laboratory evaluation:** CBC, liver and kidney function tests, CEA, and CA19.9.
- **Radiological evaluation:** Contrast-enhanced computed tomography of the chest, abdomen, and pelvis. Treatment response was evaluated using RECIST 1.1 criteria (Eisenhauer et al., 2009) and classified as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD).

Quality of Life Assessment

The evaluation of quality of life (QoL) utilized a structured questionnaire adapted from Nayak et al. (9), encompassing six domains: general well-being, physical well-being, psychological well-being, familial relationships, cognitive well-being, and economic well-being. Each item received a score on a 5-point Likert scale, where 1 represents the best and 5 signifies the worst. The scores for each domain were aggregated.

- General well-being: 3–15 points
- Physical well-being: 8–40 points
- Psychological well-being: 4–20 points
- Familial relationships: 3–15 points
- Cognitive well-being: 1–5 points
- Economic well-being: 2–10 points

Patient questionnaire

1- **General well-being** (3–15 points): Reflects the patient's perception of physical ability, confidence in financial management, and body image.

- Do you perceive your physical performance as being below your desired level?
- Do you feel uncertain about managing your financial needs?
- Are you dissatisfied with your body's appearance?

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2- **Physical well-being** (8–40 points): Captures pain, appetite, sleep quality, fatigue, mobility, and physiological functions.

- Are you currently experiencing any pain?
- Does your pain disrupt your daily activities?
- Do you experience any issues with your appetite?
- Do you experience any sleep issues?
- Do you experience fatigue?
- Are you unable to move physically as you typically do?
- Are you experiencing difficulties with urination?
- Do you experience difficulties with bowel movements?

3- **Psychological well-being** (4–20 points): Evaluates depression, sadness, fear of disability, and sense of purpose.

- Are you experiencing symptoms of depression?
- Does your experience of sadness or depression impact your daily functioning?
- Do you experience a fear of functional disability?
- Do you perceive an excess of time with no significant tasks at hand?

4- **Familial relationship** (3–15 points): Measures satisfaction with family support and freedom of emotional expression.

- Are you dissatisfied with your familial relationships?
- Do you feel unable to share your problems with your family members?
- Are you not receiving adequate support from your family members?

5- **Cognitive well-being** (1–5 points): Assesses memory and concentration difficulties.

- Do you have difficulty in remembering things?

6- **Economic well-being** (2–10 points): Reflects financial burden due to health status and satisfaction with responsibilities.

- Do you feel that your physical condition has resulted in reduced economic status?
- Are you not satisfied with your responsibilities ?

The cumulative scores were subjected to statistical analysis to evaluate the effect of treatment on patients' quality of life.

Statistical Analysis

Demographic data of patients, tumor characteristics, treatment methods, responses, and quality of life were collected and analyzed using SPSS version 15.0 (SPSS Inc., Chicago, IL). Quantitative data were presented as mean ± standard deviation (SD) or median with interquartile range, while qualitative variables were expressed as frequencies and percentages. Group comparisons utilized the Student's t-test or Mann–Whitney test for quantitative data, and the Chi-square or Fisher's exact test for qualitative data. Survival analysis was conducted using the Kaplan–Meier method, with comparisons

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of curves evaluated through the log-rank test. A two-tailed p-value below 0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics

Characteristic	Protocol 1 (N=20)	Protocol 2 (N=20)	P-value
Age, years			
Mean ± SD	62.25 ± 7.76	60.05 ± 6.01	0.32
≥60, n (%)	11 (55.0)	5 (25.0)	0.05
Sex, n (%)			
Male	13 (65.0)	10 (50.0)	0.34
Female	7 (35.0)	10 (50.0)	
Family History, n (%)	11 (55.0)	9 (45.0)	0.53
Medical History, n (%)	12 (60.0)	10 (50.0)	0.53
Presenting Symptom, n (%)			
Abdominal Pain	10 (50.0)	11 (55.0)	0.75
Bleeding per Rectum	7 (35.0)	9 (45.0)	0.52
Constipation	7 (35.0)	7 (35.0)	1.00

Table (1): shows that baseline demographic and clinical characteristics were largely comparable between the two groups, except for age distribution, where patients <60 years were more frequent in Protocol 2 (75% vs. 45%, $p = 0.05$). No significant differences were observed regarding sex, marital status, family or medical history and presenting symptoms.

Table 2: Baseline Tumor Characteristics

Characteristic	Protocol 1 (N=20)	Protocol 2 (N=20)	P-value
Tumor Markers, Median (IQR)			
CEA (ng/mL)	42.00 (16.50-226.00)	64.50 (28.75-133.50)	0.91
CA19-9 (U/mL)	14.25 (8.95-87.00)	19.90 (13.00-50.00)	0.97
Metastatic Site, n (%)			
Liver	18 (90.0)	18 (90.0)	1.00

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Lung	6 (30.0)	6 (30.0)	1.00
Peritoneum	6 (30.0)	4 (20.0)	0.47
Histopathology, n (%)			
Infiltrating Adeno. GII	17 (85.0)	16 (80.0)	0.54
Infiltrating Adeno. GIII	2 (10.0)	2 (10.0)	

Table (2): shows that no significant differences were observed regarding tumor markers (CEA, CA19-9), tumor site, metastatic pattern, or histopathology.

Table 3: Treatment Response Evaluations

Evaluation	Parameter	Protocol 1	Protocol 2	P-value
First Evaluation	**Radiological, n (%)**	N=20	N=20	**0.02**
	Stable Disease/Regression	19 (95.0)	12 (60.0)	
	Progression	1 (5.0)	8 (40.0)	
Second Evaluation	**Radiological, n (%)**	N=19	N=12	0.24
	Stable Disease/Regression	12 (63.2)	5 (41.7)	
	Progression	7 (36.8)	7 (58.3)	
Third Evaluation	**Radiological, n (%)**	N=12	N=5	0.52
	Stable Disease/Regression	3 (25.0)	0 (0.0)	
	Progression	9 (75.0)	5 (100.0)	
Fourth Evaluation	**Radiological, n (%)**	N=3	-	-
	Progression	3 (100.0)	-	

At first evaluation, radiological response was significantly better in Protocol 1, with 95% achieving stable disease/regression compared to 60% in Protocol 2 ($p = 0.02$). Subsequent evaluations showed a trend toward improved outcomes in Protocol 1, although differences were not statistically significant **(Table 3).**

Table 4: Quality of Life Domain Scores

Domain	Protocol 1 (N=20)	Protocol 2 (N=20)	P-value
	Mean ± SD	**Mean ± SD**	
General Condition	8.00 ± 2.36	10.40 ± 0.94	**<0.001**

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Physical	23.55 ± 6.79	28.80 ± 3.17	**0.004**
Psychological	9.70 ± 2.74	11.55 ± 2.76	**0.04**
Family Relationship	5.80 ± 2.17	7.05 ± 1.36	**0.04**
Economic	5.25 ± 1.86	6.25 ± 1.25	0.05
Cognitive	1.90 ± 1.07	2.50 ± 0.89	0.06

Quality-of-life assessment revealed significantly higher(worse) scores in Protocol 2 across most domains, including general condition ($p < 0.001$), physical ($p = 0.004$), psychological ($p = 0.04$), family relationships ($p = 0.04$), and economic aspects ($p = 0.05$), with no significant difference in cognitive function **(Table 4).**

General condition scores ranged from 4.00 to 12.00 in Protocol 1, with a mean of 8.00 ± 2.36. In Protocol 2, scores ranged from 9.00 to 12.00, with a significantly higher mean of 10.40 ± 0.94. The difference was highly significant ($t = 4.22$, $p < 0.001$, HS).

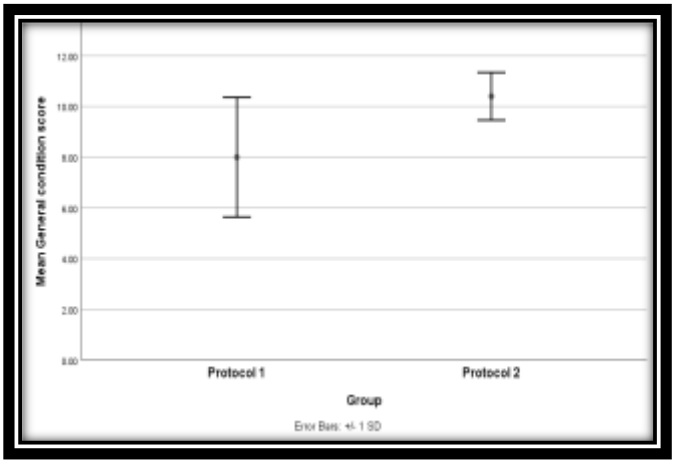

Fig. (1): Comparison between both studied groups as regards mean general condition score

Physical domain scores in Protocol 1 ranged between 10.00 and 32.00, with a mean of 23.55 ± 6.79, whereas in Protocol 2 scores ranged from 22.00 to 33.00, with a mean of 28.80 ± 3.17. This difference was statistically significant ($t = 3.13$, $p = 0.004$, HS), indicating superior physical well-being in Protocol 2.

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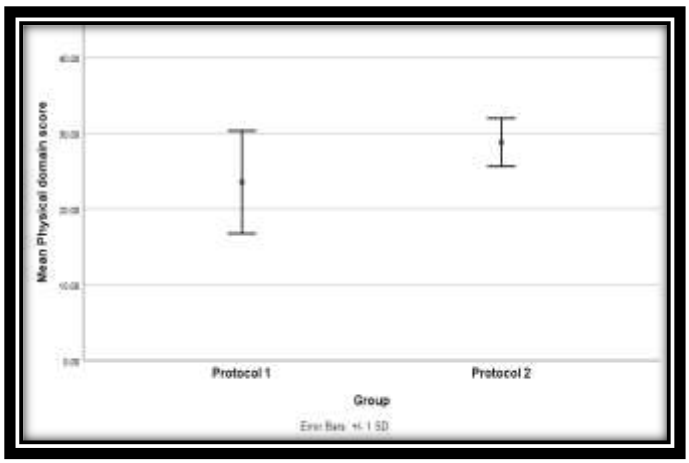

Fig. (2): Comparison between both studied groups as regards mean physical domain score

Psychological domain scores were also higher in Protocol 2 (mean 11.55 ± 2.76) compared to Protocol 1 (mean 9.70 ± 2.74). The difference was statistically significant (t = 2.13, p = 0.04, S).

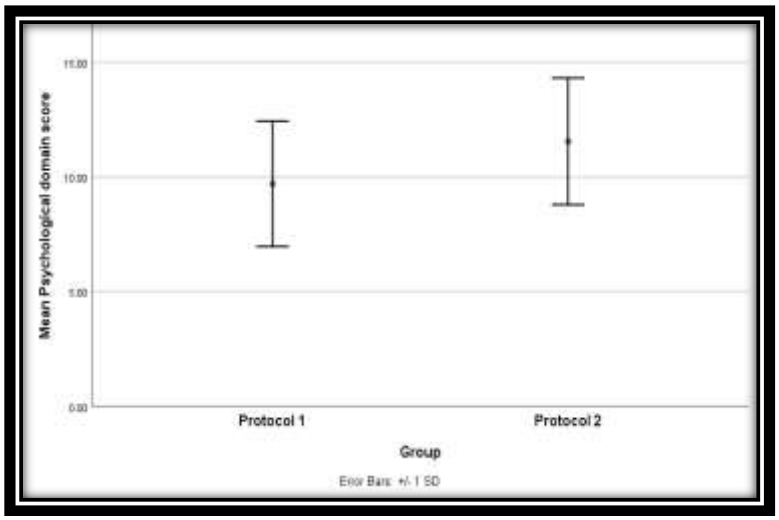

Fig. (3): Comparison between both studied groups as regards psychological domain score

Regarding **family relationship domain**, patients in Protocol 2 again reported higher scores (mean 7.05 ± 1.36) compared to Protocol 1 (mean 5.80 ± 2.17), with a statistically significant difference (t = 2.19, p = 0.04, S).

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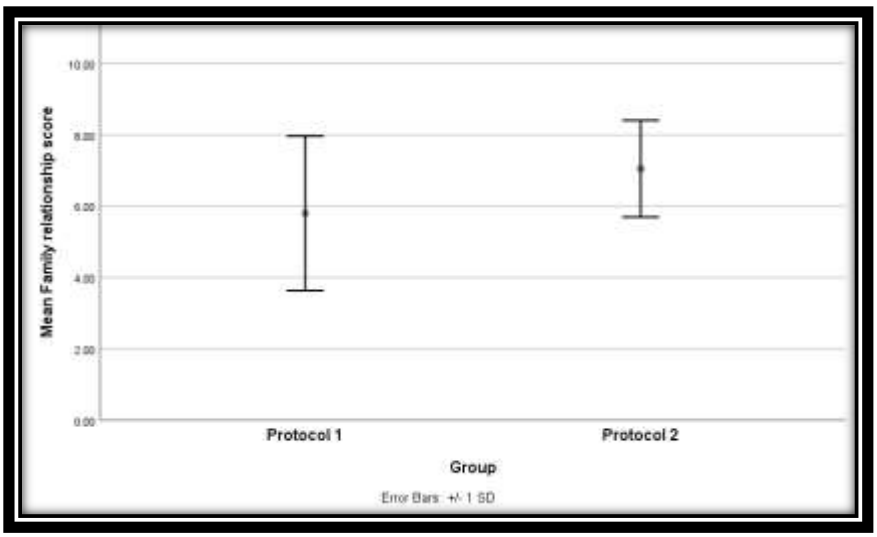

Fig. (4): Comparison between both studied groups as regards family relationship score

Economic domain scores were better in Protocol 2 (mean 6.25 ± 1.25) than Protocol 1 (mean 5.25 ± 1.86). The difference reached statistical significance (t = 1.99, p = 0.05, S).

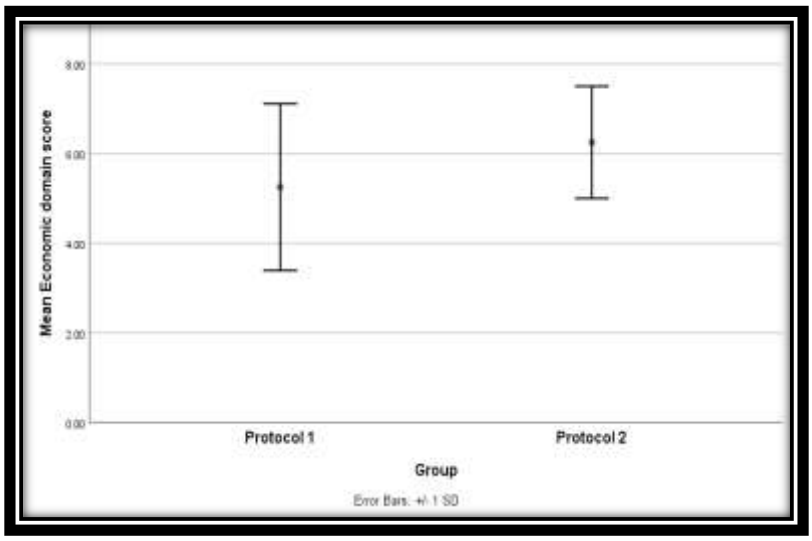

Fig. (5): Comparison between both studied groups as regards economic domain score

DISCUSSION

Colorectal cancer (CRC) is a major contributor to cancer-related morbidity and mortality globally, with nearly 25% of patients exhibiting metastases at diagnosis and around 50% advancing to metastatic disease throughout their course of illness. Standard chemotherapy regimens, including FOLFIRI, FOLFOX, and XELOX, have enhanced patient outcomes; however, they are linked to significant toxicities that can adversely affect patients' quality of life (QoL) (10).

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This study found no significant differences in laboratory parameters between the two treatment groups, indicating that the safety profile of the combination therapy was manageable and predictable, with no new safety concerns identified. The findings align with Wu et al. (11), who observed similar rates of bone marrow suppression, hepatic and renal dysfunction, and neurotoxicity in cetuximab-treated patients compared to those receiving chemotherapy alone ($p > 0.05$). Ocvirk et al. (12) demonstrated that FOLFIRI in combination with cetuximab was generally better tolerated than FOLFOX6 with cetuximab.

The incorporation of cetuximab into FOLFIRI as a first-line treatment for metastatic colorectal cancer signifies a significant therapeutic advancement, improving progression-free survival and overall survival, and response rates in RAS wild-type tumors without compromising quality of life. Clinical evidence indicates that patients maintain global health status and social functioning, while treatment-related toxicities, particularly dermatologic adverse events, are manageable with supportive care and seldom necessitate treatment discontinuation (13).

The development of targeted therapies such as cetuximab has provided additional survival benefits, particularly in patients with RAS wild-type tumors. However, concerns persist regarding whether the survival gains are achieved at the expense of QoL. In our study, patients receiving FOLFIRI plus cetuximab reported significantly better QoL outcomes compared to those receiving FOLFIRI alone, especially in physical, psychological, familial, and economic domains. Importantly, cognitive function remained unaffected, highlighting that treatment intensification did not impair higher-order functioning.

Our results align with Wu et al. (11), who demonstrated improved physical and emotional functioning scores in patients receiving cetuximab-based regimens, while role and cognitive functioning remained comparable between groups. Similarly, Boige et al. (10) reported sustained or improved QoL outcomes during cetuximab maintenance, particularly in physical well-being. Furthermore, the CRYSTAL trial and subsequent analyses confirmed that adding cetuximab to chemotherapy improved clinical efficacy without negatively impacting global health status or social functioning (14).

These findings collectively emphasize that the integration of cetuximab into first-line treatment does not compromise QoL, despite its unique toxicity profile, particularly dermatological side effects. With appropriate supportive care, these adverse events can be effectively managed, allowing patients to maintain overall well-being while benefiting from improved disease control.

CONCLUSION

In conclusion, our study reinforces that combining cetuximab with FOLFIRI not only enhances oncologic outcomes but also preserves, and in some domains improves, patient-reported quality of life. This dual advantage strengthens the case for cetuximab-based therapy in RAS wild-type mCRC, where both survival and QoL are critical determinants of treatment success.

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REFERENCES

1. **Holch, J. W., Ohnmacht, A. J., Stintzing, S., Heinrich, K., Weiss, L., Probst, V., ... & Heinemann, V. (2025).** FOLFIRI with cetuximab or bevacizumab in RAS wild-type metastatic colorectal cancer: Refining first-line treatment selection by combining clinical parameters: A post hoc analysis of the randomized open-label phase III trial FIRE-3/AIO KRK0306. European Journal of Cancer, 220, 115388.
2. **Sastre, J., García-Alfonso, P., Viéitez, J. M., Cano, M. T., Rivera, F., Reina-Zoilo, J. J., ... & de Prado, P. M. (2021).** Influence of BRAF and PIK3CA mutations on the efficacy of FOLFIRI plus bevacizumab or cetuximab as first-line therapy in patients with RAS wild-type metastatic colorectal carcinoma and< 3 baseline circulating tumour cells: the randomised phase II VISNÚ-2 study. ESMO open, 6(2), 100062.
3. **Alhajj, O., Noor, D. M., & Md Hanafiah, N. H. (2024).** Investigation on the cost–effectiveness of Cetuximab in treatment of colorectal cancer: a systematic review. Colorectal Cancer, 13(1), 2390822.
4. **Elsamany, S., Elsisi, G. H., Hassanin, F. A. M., Saleh, K., & Tashkandi, E. (2022).** Cost-effectiveness of first-line cetuximab in metastatic colorectal cancer in Saudi Arabia. Value in health regional issues, 28, 67-75.
5. **Tsai, H. L., Chen, Y. C., Yin, T. C., Su, W. C., Chen, P. J., Chang, T. K., ... & Wang, J. Y. (2022).** Comparison of UGT1A1 polymorphism as guidance of irinotecan dose escalation in RAS wild-type metastatic colorectal cancer patients treated with cetuximab or bevacizumab plus FOLFIRI as the first-line therapy. Oncology research, 29(1), 47.
6. **Pinto, C., Orlandi, A., Normanno, N., Maiello, E., Calegari, M. A., Antonuzzo, L., ... & Barone, C. (2024).** Fluorouracil, leucovorin, and irinotecan plus cetuximab versus cetuximab as maintenance therapy in first-line therapy for RAS and BRAF wild-type metastatic colorectal cancer: phase III ERMES study. Journal of Clinical Oncology, 42(11), 1278-1287.
7. **Dohan, A., Gallix, B., Guiu, B., Le Malicot, K., Reinhold, C., Soyer, P., ... & Hoeffel, C. (2020).** Early evaluation using a radiomic signature of unresectable hepatic metastases to predict outcome in patients with colorectal cancer treated with FOLFIRI and bevacizumab. Gut, 69(3), 531-539.
8. **Tintelnot, J., Ristow, I., Sauer, M., Simnica, D., Schultheiß, C., Scholz, R., ... & Stein, A. (2022).** Translational analysis and final efficacy of the AVETUX trial–Avelumab, cetuximab and FOLFOX in metastatic colorectal cancer. Frontiers in Oncology, 12, 993611.
9. **Nayak, M. G., George, A., Vidyasagar, M. S., Mathew, S., Nayak, S., Nayak, B. S., ... & Kamath, A. (2017).** Quality of life among cancer patients. *Indian journal of palliative care*, *23*(4), 445.
10. **Boige, V., Blons, H., François, E., Abdelghani, M. B., Phelip, J. M., Le Brun-Ly, V., ... & Bouché, O. (2023).** Maintenance therapy with cetuximab after FOLFIRI plus cetuximab for RAS wild-type metastatic colorectal cancer: A phase 2 randomized clinical trial. JAMA Network Open, 6(9), e2333533-e2333533.

Corresponding author: Mohamed Ibrahim, 01220339522, Email: Mohamed.s.ibrahim2024@gmail.com

11. **Wu, J., Wang, Z., Jin, C., Ren, H., Hu, Y., Yang, B., & Hu, Y. (2021).** Effect of cetuximab combined with chemotherapy in treating metastatic colorectal cancer and its prognostic analysis. J buon, 26(1), 101-108.

12. **Ocvirk, J., Brodowicz, T., Wrba, F., Ciuleanu, T. E., Kurteva, G., Beslija, S., ... & Zielinski, C. C. (2010).** Cetuximab plus FOLFOX6 or FOLFIRI in metastatic colorectal cancer: CECOG trial. World journal of gastroenterology: WJG, 16(25), 3133.

13. **Heinemann, V., von Weikersthal, L. F., Decker, T., Kiani, A., Kaiser, F., Al-Batran, S. E., ... & Stintzing, S. (2021).** FOLFIRI plus cetuximab or bevacizumab for advanced colorectal cancer: final survival and per-protocol analysis of FIRE-3, a randomised clinical trial. British journal of cancer, 124(3), 587-594.

14. **Saltz, L., Badarinath, S., Dakhil, S., Bienvenu, B., Harker, W. G., Birchfield, G., ... & Cohn, A. (2012).** Phase III trial of cetuximab, bevacizumab, and 5-fluorouracil/leucovorin vs. FOLFOX-bevacizumab in colorectal cancer. Clinical colorectal cancer, 11(2), 101-111.

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ORIGINAL ARTICLE

"The Impact of Ablation Site Complications on Outcomes in Radiofrequency Ablation for Osteoid Osteoma: A Prospective Cohort Study"

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ABSTRACT

Background: Osteoid osteoma is a benign bone-forming neoplasm. Radiofrequency ablation is a reliable treatment. **Objectives:** This work evaluates RFA ablation site complications and their impact on osteoid osteoma outcomes. **Methodology:** 30 osteoid osteoma patients were involved in the study, aged 4 to 37 years. The study included patients who were diagnosed radiologically, painful bone lesion, night pain relieved by NSAIDs, radiolucent nidus with surrounding sclerosis is depicted in CT images. The ablation site complications were assessed for their impact on the outcomes. **Results:** Most tumors were cortical (86.7%), mainly located in the diaphysis (70%), the femur being the most affected bone (46.7%). Patients' ages ranged from 4 to 37 years, an average of 17 years. Patients had pre-procedure pain scores between 5 and 9, mean of 7 ± 1.07, were on NSAIDs. 47% of patients experienced swelling. Patients reported significant reduction in pain immediately post-procedure, mean score of 8.6, compared to one week (mean 1.3) and six months (mean 0.9) post-procedure ($P < 0.001$). No reported cases of anesthesia-related complications, skin burns, fat necrosis, soft tissue infections, vasomotor instability, tendinitis or hematomas at RFA site. **Conclusion:** Radiofrequency ablation is reliable minimally invasive procedure for osteoid osteoma, with low ablation site complication rate and consistently positive results.

Keywords: Ablation Site Complications, Radiofrequency Ablation, Osteoid Osteoma

INTRODUCTION:

Necrosis injury in vascular structures and cutaneous necrosis is the most feared complication of RFA. It adds to other potential hazards such as infections, discomfort, bleeding, and post-ablation syndrome. Vascular access lesions, thromboembolic events (such as acute ischemic stroke, acute coronary syndrome, etc.), air embolism, valvular lesions, cardiac tamponade, coronary artery lesions, conduction system injuries, and cardiac insufficiency are all potential complications of ventricular tachycardia after RFA (**1)**

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As a result of its low cost, reduced complication rates, short or no hospital stays, and less-traumatic access for deep anatomical locations like the proximal femur and pelvis, as well as its high efficacy, CT-guided radiofrequency ablation has become more popular among physicians. There has been a lack of research in peer-reviewed journals regarding the frequency and severity of problems associated with percutaneous drilling and ablation, in addition to the therapeutic outcomes of treatment **(2)**.

Some of the known side effects of this procedure include temporary paralysis of the extensor hallucis longus muscle, superficial skin burns, cellulitis, an osteo-cutaneous fistula that needed to be surgically debrided, a short-lived palsy of the muscle, and temporary numbness of the thigh over an ablation tract. A femoral shaft fracture at 4 weeks post-pecedure was documented in an older investigation using CT-guided drilling without RFA; however, this operation entailed using a 7-mm bit to drill the nidus. Nevertheless, no recorded cases of vascular injury, irreversible nerve injury, or fracture were found when the English literature evaluation was limited to only articles that used RFA procedures **(3)**.

CT-guided RFA is recognized as a reliable and minimally invasive treatment for OO; most literature reports its safety and technical success. However, there are limited reports on the complications at the ablation site, such as infections, fractures, burns, and neural injuries, which can affect final patient outcomes, including functional recovery, pain relief, and quality of life. **(4-6)**

We hypothesize that these complications at the ablation site negatively impact patient outcomes, increase the morbidity rate, prolong recovery time, and worsen the quality of life.

This work aimed to evaluate the impact of ablation site complications on outcomes in radiofrequency ablation for osteoid osteoma.

PATIENTS AND METHODS:

Thirty individuals with osteoid osteoma, aged four to thirty-seven, participated in this prospective study. Participants included those with a radiologic diagnosis of osteoid osteoma, a painful bone lesion characterized by pain that worsens at night and is relieved by oral NSAIDs, along with CT images showing a radiolucent nidus surrounded by cortical thickening and bony sclerosis. The Ethical Committees of Cairo University, Al-Kasr El-Ainy Hospital, and Aswan University Hospital approved the research. The informed consent was signed by the patients.

Lesions in the hand or posterior arch of the vertebrae, tumors less than 1 cm from a major nerve, neurological injury, and any patient who has undergone surgery for the lesions were also excluded.

To prepare for a preprocedural examination, all patients underwent a clinical evaluation at the orthopedic outpatient clinic and received referral requests to the interventional radiology unit. The patient's suitability for anesthesia during the ablation procedure was confirmed through thorough clinical and laboratory assessments before the procedure.

RFA technique: All operations were carried out while under spinal or general anaesthesia. An 11-gauge Geotek Bone Needle was utilized to create osseous access following the identification of the nidus using 1–3 mm CT slices. Using a rigid RF Soloist single-needle electrode with a diameter of 1.57 mm, RFA was carried out for 4–5 minutes at 90°C using an RF3000 radiofrequency generator. If the tip of the RF electrode could be positioned inside the center of the nidus and heated to the appropriate temperature, the technique was considered technically successful. A persistent reduction in pain and a return to normal function without the need for further therapy were considered clinical successes.

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If symptoms persisted or recurred following RF ablation, treatments was considered secondarily effective if permanent alleviation had been achieved in the second procedure.

Clinical Follow-Up: One and six months after the procedure, follow-up assessments were conducted in the outpatient orthopedic clinic. Keeping track of any issues at the RFA site and brought on by anesthesia, such as hematoma, tendinitis, soft tissue infection, vasomotor instability, skin burn, and skin and fat necrosis. A change in oral NSAID intake after the surgery was evaluated, and the Visual Analog Scale (VAS) was utilized to determine post-procedure discomfort **(7)**.

The location, size, and volume of the lesion, as well as the presence or absence of calcification and cortical thickness, were all evaluated by CT imaging both before and immediately after the treatment.

Sample Size Calculation:

Using MedCalc software version 18.2.1, the sample size was determined according to research conducted by Pratali et al. (2019) that found an AUC of 0.947 in predicting severe osteoid osteoma lesions. The required sample size was thirty patients. At 0.8, the AUC's null hypothesis value was modified. Alpha was set at 0.05 and power to 0.9, respectively **(8)**.

Statistical analysis

The statistical analysis was conducted utilizing SPSS version 26 (IBM Inc., Armonk, NY, USA). The quantitative variables were expressed as means and standard deviations (SD). The qualitative elements were displayed as frequencies and percentages. For quantitative variables, the ANOVA test was used for intergroup comparison, and the T-test was used for comparisons between two durations. The Chi-square test or Fisher's exact test was employed to assess qualitative variables, as necessary. Statistical significance was denoted by a two-tailed P value below 0.05.

RESULTS:

The patients' ages varied from 4 to 37, with a mean of 17 ± 7.73 years. There were 18 males (60%), and 12 females (40%). (Table 1)

Table 1: Demographic data, Type of tumor, size of tumor, bone affected with the tumor, and pre-procedural cortical thickening (sclerosis) of the studied patients

		n=30
Age (years)	**Mean ± SD**	17 ± 7.73
	Range	4 – 37
Sex	**Male**	18 (60%)
	Female	12 (40%)
Type of tumor	**Cortical**	26 (86.67%)
	Medullary	3 (10%)
	Subperiosteal	1 (3.33%)
Site of tumor	**Diaphysis**	21 (70%)
	Metaphysis	3 (10%)
	Neck of femur	6 (20%)
Bone affected with the tumor	**Femur**	14 (46.67%)
	Tibia	12 (40%)
	Ulna	4 (13.33%)

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The study found that 26 patients (86.67%) had cortical tumors, 3 patients (10%) had medullary tumors, and 1 patient (3.33%) had subperiosteal tumors. Of the patients in the study, 21 (70%) had tumors at the diaphyseal region, 3 (10%) had tumors at the metaphyseal region, and 6 (20%) had tumors at the femur neck. Regarding the bone that the tumor impacted, among the patients in the study, 14 (46.67%) had femur tumors, 12 (40%) had tibia tumors, and 4 (13.33%) had ulna tumors. In this investigation, pre-procedural cortical sclerosis was observed in all 30 (100%) cases.

Complications: There were no documented instances of complications from anesthesia. There were no reported incidences of hematoma at the RFA site, tendinitis, vasomotor instability, soft tissue infection, skin burn, or fat necrosis.

Table (2): Pre-Procedure Pain Score, NSAIDs usage, and swelling in the studied patients

		N=30
Pain Score	Mean ± SD	7 ± 1.07
	Range	5 – 9
NSAIDs	Yes	30 (100%)
	No	0 (0%)
Swelling	Yes	14 (47%)
	No	16 (53%)

NSAIDs: Non-steroidal anti-inflammatory drugs.

The Pre-Procedure Pain Score in the studied patients ranged from 5- 9, with a mean of 7 ± 1.07. All patients in this study were on NSAIDs pre operatively. Regarding swelling, 14 (47%) patients had swelling pre operatively. [Table 2]

Table (3): Post procedural pain score comparison in the studied patients

		Pre procedure pain score	One week post procedure pain score	Six months post procedure pain score	P-value
Pain score	Mean ± SD	7 ± 1.07	1.3 ± 1.3	0.9 ± 1.93	< 0.001* P1= < 0.001* P2=< 0.001* P3=0.069
	Range	5 - 9	0 - 5	0 - 7	

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In terms of the pain score pre and post procedure, the one-week post procedure pain score and six months post procedure pain score were significantly lower than the pre procedure pain score (P<0.001). However, no significant difference was observed between the one-week post procedure pain score and six months post procedure pain score. [Table 3]

Illustration cases :

Case No. 1: A 19-year-old woman arrived at the orthopedic outpatient clinic complaining of left hip pain that had been alleviated by NSAIDs a year prior. The patient was sent to the interventional radiology unit for radiofrequency ablation after radiological studies revealed that she had a left femoral neck osteoid osteoma. After a successful radiofrequency ablation, the patient was released from the hospital two hours later in good health and without any problems.

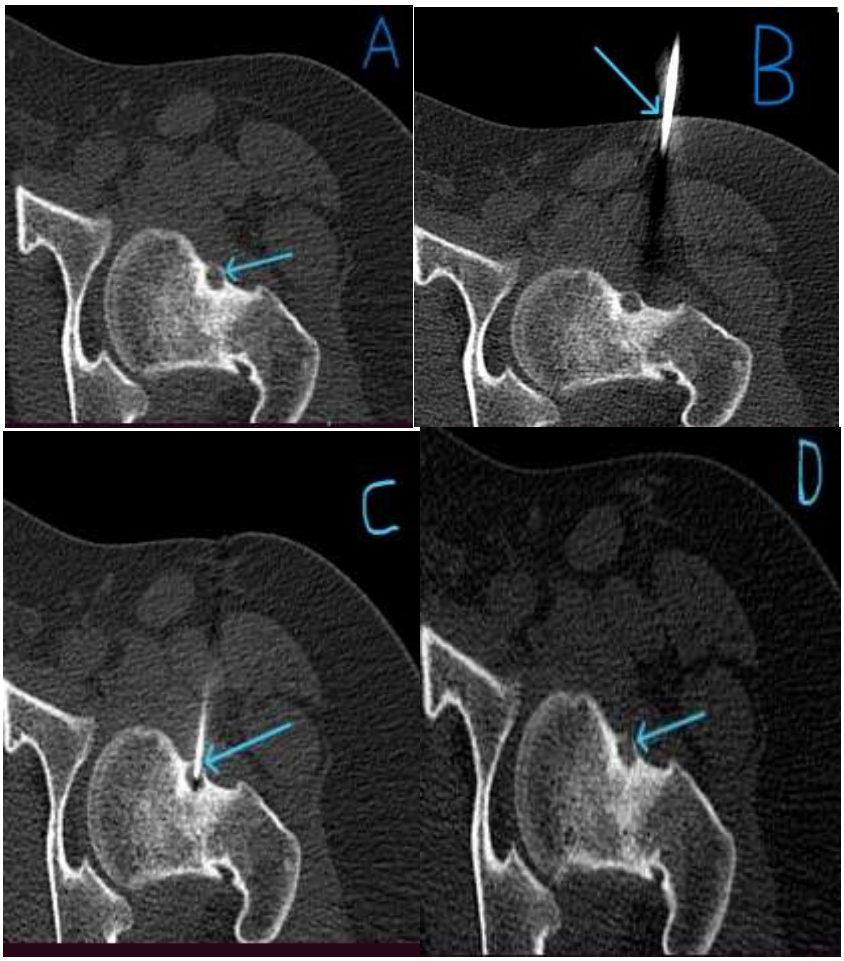

Figure (1): A) Pre-procedure axial CT image shows the hypodense nidus at the anterior cortex of the neck of the left femur surrounded by sclerotic bone reaction. B) During the procedure, axial CT image shows the bone needle entrance from the skin. C) During the procedure, axial CT image shows the tip of the RF electrode in the nidus. D) The immediately post-procedure axial CT image shows a good ablation zone with no complications at the ablation site.

Case No. 2: NSAIDs helped a 20-year-old woman who had been experiencing pain and edema in her left forearm for seven months. The pain was worse at night. She was referred to the interventional radiology unit after radiological evaluation revealed that she had left ulna

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osteoid osteoma. Under general anesthesia, the radiofrequency ablation was completed successfully, and the patient was discharged two hours later without any complications.

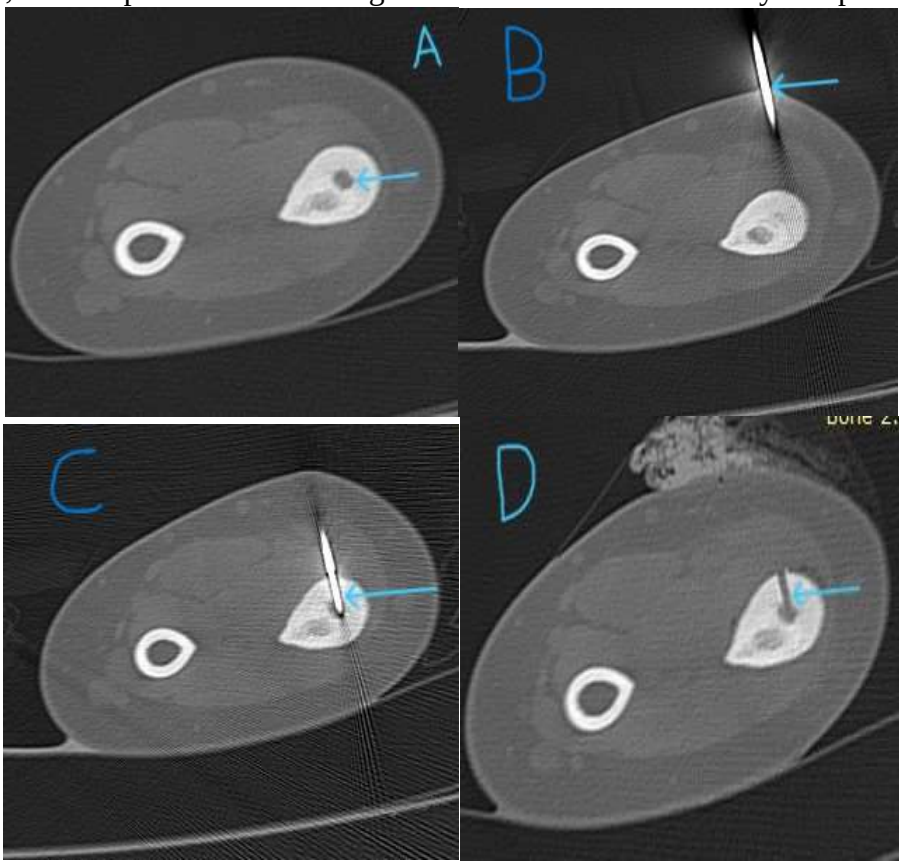

Figure (2): A) Pre-procedure axial CT image shows the hypodense nidus at the anterior cortex of the mid shaft of the left ulna with bone sclerosis and cortical thickening. B) During the procedure, axial CT image shows the bone needle entrance from the skin. C) During the procedure, the axial CT image shows the tip of the RF electrode in the nidus. D) The immediately post-procedure axial CT image shows a good ablation zone with no complications at the ablation site.

Case no.3: A 21-year-old male patient presented with right thigh pain of 9 months duration, the pain characteristics are consistent with osteoid osteoma pain criteria, increased at night, relieved by NSAIDs. After clinical and radiological assessment, the final diagnosis was the right femur osteoid osteoma. Radiofrequency ablation under spinal anaesthesia was successfully done, and the patient was discharged 2 hours after the procedure without complications.

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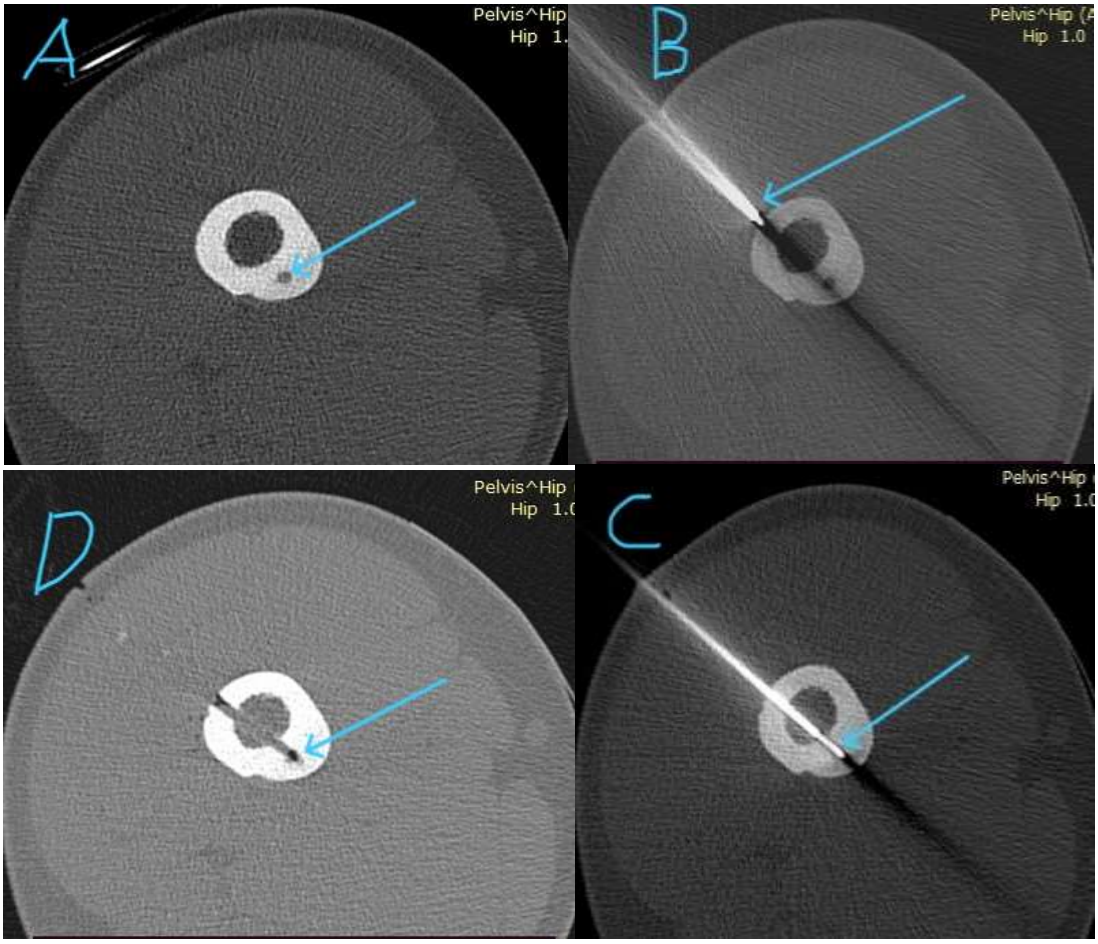

Figure (3): A) Pre-procedure axial CT image shows the hypodense nidus at the medial cortex of the right femoral shaft with bone sclerosis and significant cortical thickening. B) During the procedure, axial CT image shows the bone needle entrance from the lateral cortex. C) During the procedure, the axial CT image shows the tip of the RF electrode in the nidus. D) Immediately post-procedure axial CT image shows complete ablation of the nidus, no ablation site complications.

DISCUSSION

Osteoid osteomas typically cause nocturnal pain, relieved by NSAIDs. **(9,10)** Diagnosis is made using imaging techniques. **(11)** Management varies between conservative medical treatment, surgery, and minimally invasive treatments. Surgical resection and RFA are preferred due to NSAID limitations and prolonged natural history. **(12).** While RFA is a viable, safe, and effective option with fast-recovery time and few complications **(13).**

This prospective research was performed to assess the morbidity of the ablation site using RFA for the treatment of osteoid osteomas in 30 patients.

The average age of 17 ± 7.73 years (range 4–37) reflects a tendency towards adolescents and young adults. This aligns with prior work (14), who reported an average age of 16.8 years in 100 patients with osteoid osteoma. Likewise, another series (15) noted that most of their cases involved patients under the age of 25.

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Regarding sex, our study found a predominance of males (60% males, 40% females), which is consistent with the male-to-female ratio frequently reported in the literature. **(16, 17)**

In our series, concerning tumor type and location, most cases (86.67%) were cortical; 70% were situated in the diaphysis, and 86.67% occurred in the long bones of the lower limbs. This distribution aligns with findings reported in the literature, which identified cortical osteoid osteomas (18, 19), diaphyseal location (20,21), and lower limb long bones (3,10) as the most prevalent subtypes in their radiological analysis.

In our series, it is noteworthy that no complications related to RFA ablation sites were recorded. There were no anesthesia-related adverse events, hematoma, tendinitis, soft tissue infections, vasomotor changes, or skin burns. These findings are highly consistent with the excellent safety profile outlined in the existing literature. The referenced studies reported no severe complications (less than 1%) in their CT-guided RFA series, suggesting both efficacy and safety under image guidance**. (3,10,22)**

Our results show a statistically and clinically significant reduction in post-procedural pain scores. One week after ablation, the average pain score was 7, which decreased to 1.3 ± 1.3, and at six-month follow-up, it further dropped to 0.9 ± 1.93 ($P < 0.001$ for both). Similar findings **(3)** also reported a decrease to 1.2 at 1 week after ablation from a mean baseline of 7.4 and to 0.8 at 6 months. **(23,24**) showed comparable pain relief trends, with most patients reaching a full or nearly optimal symptomatic endpoint.

Although the scores at 1 week and 6 months post-ablation were significantly lower than the baseline values, there was no significant difference between them ($P = 0.069$), demonstrating that most therapeutic benefit occurs within the first week after ablation. This finding is consistent with the results of **(22**) in their study.

CT guidance offers high spatial resolution and rapid acquisition enabling near-real-time needle monitoring—advantages over MRI guidance**. (25).**
Our patients used NSAIDs for relief of symptoms, as in the case of this disease. Based on literature, osteoid osteoma pain is prostaglandin dependent and is typically responsive to aspirin or other NSAIDs (**26).** This therapeutic aspect not only enhances diagnostic capabilities but also underscores the inflammatory nature of the lesion. **(25)** found equally NSAID dependency in their study population, which had all achieved partial resolution before referral for curative RFA.
The onset of pain relief was rapid and effects were long-lasting, in agreement with the results obtained by **(24)** who reported >95% of their patients' symptom relief occurred within the first week after RFA.

Our results agree with recent research that confirms complications at the ablation site during RFA, such as infections, burns, hematomas, fractures, and injuries to nearby vessels or nerves, are uncommon when procedures are well-planned and guided by imaging. Most issues are minor and easily managed, indicating a generally safe practice. However, anatomical differences and variations in technique can increase risks, especially thermal damage to surrounding structures. As ablation application extends into more complex areas, ongoing caution and procedural improvements remain essential. **(27-29)**

We agree with the literature's recommendation to advance the field by establishing multicenter registries and adopting standardized complication grading systems, which will

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facilitate data sharing and enable comparisons of ablation techniques and emphasize long-term outcomes, especially for vulnerable groups and less common sites. Prioritizing rigorous methodology and collaboration can improve treatment safety and recovery for patients undergoing osteoid osteoma ablation. (28,29)

This study's limitations include a small sample size and brief follow-up, which may hinder generalization and detection of long-term complications of radiofrequency ablation for osteoid osteoma. Because the study was conducted at two centers, potential institutional biases could have influenced the resultAdditionally, the lack of a control group limits conclusions on whether observed complications are related to the procedure or how safety compares to other treatments.

CONCLUSION:

Osteoid osteoma can be treated effectively and safely with CT-guided RFA. In our cohort, no ablation-site complications were observed, and pain scores decreased significantly. The study recommends RFA as the first-line management for patients with osteoid osteoma.

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The author's contributions.

Abdelrhman M. Yousef: study design, performing the procedures, data collection, and writing the first and final drafts of the manuscript.
Omar Abdelaziz Ahmed: study design, writing, and reviewing of the manuscript.
Salah M.Maklad: study design, writing, and reviewing of the manuscript.
Ebeed Yasin Ibrahim: study design, writing the first draft, and final draft of the manuscript.

References:

1. Matin, S. F. & Ahrar, K. 2008. Nephron-sparing probe ablative therapy: long-term outcomes. Current opinion in urology, 18, 150-6.

2. Tordjman, M., Perronne, L., Madelin, G., Mali, R. D. & Burke, C. 2020. CT-guided radiofrequency ablation for osteoid osteomas: a systematic review. European radiology, 30,

3. Rosenthal, D. I., Hornicek, F. J., Torriani, M., Gebhardt, M. C. & Mankin, H. J. 2003. Osteoid osteoma: percutaneous treatment with radiofrequency energy. Radiology, 229, 171-5.

4. Yunus Oc , Kilinc BE, Cennet S, Boyacioglu MM, Ertugrul R, Varol A. Complications of Computer Tomography Assisted Radiofrequency Ablation in the Treatment of Osteoid Osteoma. Biomed Res Int. 2019 May 15;2019:4376851. doi: 10.1155/2019/4376851. PMID: 31223617; PMCID: PMC6541958.
5952-63.

5. Vogl TJ, Bialek M, Eichler K, Hammerstingl R, Bielfeldt J, Zangos S, Scholtz JE, Adwan H. 2024. Short- and Long-Term Outcomes after Radiofrequency Ablation of Osteoid Osteomas. J Pers Med. 2024 Apr 10;14(4):401. doi: 10.3390/jpm14040401. PMID: 38673028; PMCID: PMC11051171.

6. Singh DK, Kumar N, Rustagi A, Jalan D, Krishna LG, Sharma A. 2022. Percutaneous CT-guided radiofrequency ablation of osteoid osteoma: Potential Pitfalls and complications and how to avoid them. J Clin Orthop Trauma. 2022 Apr

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16;28:101869. doi: 10.1016/j.jcot.2022.101869. PMID: 35494487; PMCID: PMC9043674.

7. Delgado, D. A., Lambert, B. S., Boutris, N., McCulloch, P. C., Robbins, A. B., Moreno, M. R., et al. 2018. Validation of digital visual analog scale pain scoring with a traditional paper-based visual analog scale in adults. JAAOS Global Research & Reviews, 2, e088.

8. Pratali, R. R., Smith, J. S., Ancheschi, B. C., Maranho, D. A., Savarese, A., Nogueira-Barbosa, M. H., et al. 2019. A technique for dynamic cervical magnetic resonance imaging applied to cervical spondylotic myelopathy: a reliability study. Spine, 44, E26-E32.

9. Ghanaati, H., Firouznia, K., Rezaei, M., Shakiba, M. & Ghavami, N. 2020. Management of osteoid osteoma using radiofrequency ablation. Iran J Radiol, 17, e67216.

10. Rimondi, E., Mavrogenis, A. F., Rossi, G., Ciminari, R., Malaguti, C., Tranfaglia, C., & Ruggieri, P. 2012. Radiofrequency ablation for non-spinal osteoid osteomas in 557 patients. *European Radiology*, 22(1), 181–188.

11. Çakar, M., Esenyel, C. Z., Seyran, M., Tekin, A. Ç., Adaş, M., Bayraktar, M. K., et al. 2015. Osteoid osteoma treated with radiofrequency ablation. Advances in Orthopedics, 2015, 807274.

12. De Filippo, M., Russo, U., Papapietro, V. R., Ceccarelli, F., Pogliacomi, F., Vaienti, E., ... & Sverzellati, N. 2018. Thermal ablation of osteoid osteoma: Treatment outcome and efficacy using dynamic contrast-enhanced MRI. *Radiologia Medica*, 123(6), 451–457.

13. Jankharia, B. & Burute, N. 2009. Percutaneous radiofrequency ablation for osteoid osteoma: how we do it. Indian Journal of Radiology and Imaging, 19, 36-42.

14. Boscainos, P. J., Cousins, G. R., Kulshreshtha, R., Oliver, T. B., & Papagelopoulos, P. J. (2013). Osteoid osteoma. *Orthopedics*, 36(9), 792–800.

15. Cantwell, C. P., O'Byrne, J., & Eustace, S. 2004. Current trends in treatment of osteoid osteoma with an emphasis on radiofrequency ablation. *European Radiology*, 14(4), 607–617.

16. Jordan, R. W., Koç, T., Chapman, A. W. P., & Taylor, H. P. 2015. Osteoid osteoma of the foot and ankle—A systematic review. *Foot and Ankle Surgery*, 21(4), 228–234.

17. Kitsoulis, P., Mantellos, G., & Vlychou, M. 2006. Osteoid osteoma. *Acta Orthopaedica Belgica*, 72(2), 119–125.

18. Ebrahim, F. S., Jacobson, J. A., Lin, J., Housner, J. A., Hayes, C. W., & Resnick, D. 2001. Intraarticular osteoid osteoma: Sonographic findings in three patients with radiographic, CT, and MR imaging correlation. *American Journal of Roentgenology*, 177(6), 1391–1395.

19. Pinto, C. H., Taminiau, A. H., Vanderschueren, G. M., Hogendoorn, P. C., Bloem, J. L., & Obermann, W. R. 2002. Technical considerations in CT-guided radiofrequency thermal ablation of osteoid osteoma: tricks of the trade. *American Journal of Roentgenology*, 179(6), 1633–1642.

*Corresponding Author: Abdelrhman M.Yousef **,** Email: Abdelrhmanyousef9@gmail.com**. Mobile: 01159633858**

20. Papathanassiou, Z. G., Megas, P., Petsas, T., Papachristou, D. J., Nilas, J., & Siablis, D. 2008. Osteoid osteoma: diagnosis and treatment. *Orthopedics*, 31(11), 1118.

21. Park, J. H., Pahk, K., Kim, S., Lee, S. H., Song, S. H., & Choe, J. G. 2015. Radionuclide imaging in the diagnosis of osteoid osteoma. *Oncology Letters*, 10(2), 1131–1134.

22. Shields, D. W., Sohrabi, S., Crane, E. O., Nicholas, C., & Mahendra, A. 2018. Radiofrequency ablation for osteoid osteoma–Recurrence rates and predictive factors. *The Surgeon*, 16(3), 156–162.

23. Hoffmann, R.-T., Jakobs, T. F., Kubisch, C. H., Trumm, C. G., Weber, C., Duerr, H.-R., et al. 2010. Radiofrequency ablation in the treatment of osteoid osteoma—5-year experience. European journal of radiology, 73, 374-9.

24. Sung, K.-S., Seo, J.-G., Shim, J. S. & Lee, Y. S. 2009. Computed-tomography-guided percutaneous radiofrequency thermoablation for the treatment of osteoid osteoma—2 to 5 years follow-up. International orthopaedics, 33, 215-8.

25. Noordin, S., Allana, S., Hilal, K., Nadeem, N., Lakdawala, R., Sadruddin, A., & Uddin, N. (2018). Osteoid osteoma: Contemporary management. *Orthopedic Reviews*, 10(3), 108–119.

26. Campanacci, M., & Campanacci, M. 1999. *Osteoid osteoma*. In *Bone and Soft Tissue Tumors: Clinical Features, Imaging, Pathology and Treatment* (pp. 391–414).

27. Vogl TJ, Bialek M, Eichler K, Hammerstingl R, Bielfeldt J, Zangos S, Scholtz JE, Adwan H. Short- and Long-Term Outcomes after Radiofrequency Ablation of Osteoid Osteomas. J Pers Med. 2024 Apr 10;14(4):401.

28. **Abdalla BA, Abdullah HO, Nasralla HA, Ali RM, Omar SS, Ghafour AK, Asaad SK, Raoof SS, Tahir SH, Rashid RJ, Mohammed AA, Sabr NS, Hasan AH, Mustafa LJ, Salih AM, Kakamad FH.** The efficacy and safety of microwave ablation in managing osteoid osteoma: a systematic review. Case Reports Plast Surg Hand Surg. 2025 May 10;12(1):2503195.

29.**Igrec J, Smolle MA, Meszarics M, Godschachner TM, Steiner J, Feichtinger M, Talakic E, Portugaller RH, Leithner A, Fuchsjäger M, Brcic I**. A comparative study assessing the efficacy and safety of radiofrequency ablation versus surgical treatment for osteoid osteoma: retrospective analysis in a single institution. Insights Imaging. 2024 Mar 22;15(1):82.

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Review article

Blastocystis and Gut Microbiome: A Review of the Current Understanding

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ABSTRACT

Blastocystis spp. is an important enteric protozoan. With at least 40 subtypes, this parasite displays extensive genetic diversity. Gut microbiota, comprising multiple beneficial microorganisms, has a significance impact on the host's health. Research has demonstrated that Blastocystis colonization is associated with increased gut microbiome diversity and reduced *Bacteroides*, indicating a potential beneficial relation. The bidirectional influence between *Blastocystis* spp. and gut microbiota is complex, with distinct subtypes can display varying effects on the microbiome. Probiotics may be used in treating symptomatic blastocytosis, but the type and dosage of probiotics used for treatment, as well as their potential impact on *Blastocystis* species are still uncertain. This review highlights the need for more research to understand the relation between the gut microbiome and *Blastocystis* spp. with potential implications for development of novel therapeutic strategies.

Keywords: *Blastocystis*, Microbiome, Dysbiosis, Probiotics

A brief look at *Blastocystis* spp.

Blastocystis spp. is an intestinal protozoan infecting both human and most animals. *Blastocystis* spp. was identified in individuals who are either symptomatic or asymptomatic. This parasite is known as pleomorphic. There are vacuolar, granular, amoeboid, and cyst forms. Avacuolar and multivacuolar forms were also described, but rarely seen. Cysts are the only known transmissible forms as proved by experimental studies, and is transmitted feco-orally [1].

Research has revealed that *Blastocystis* has extensive genetic diversity, with at least 40 different subtypes (STs 1-21 and STs 23-44) found based on the SSU-rRNA gene. These subtypes are found in different hosts, involving man, rodents, birds, primates, and other mammals. Only STs1-10, ST12, ST14, ST16, ST23, ST35 and ST41 were isolated from humans. STs 1-4 considered the most prevalent in man, with prevalence about 90% [2].

The prevalence of *Blastocystis* spp. around the world is highly variable, with a rate of 10% in the developed countries and higher than 60% in the developing regions. There are great

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variations in the prevalence even between areas within the same country [3]. Furthermore, there are variations in the distribution and proportion of various subtypes worldwide. For instance, ST4 was reported to be is particularly prevalent in European areas and US while ST2 is prevalent within the non-industrialized countries [4]. Although no clear explanation for these variations has been found, various epidemiological and demographic criteria involving climatic alterations, geographical residence, cultural practices, contact with reservoirs & transmission methods are reflected in diversity and prevalence of subtypes isolated from humans [5].

A brief look at human gut microbiome:

A wide range of enteric microorganisms, including bacteria, viruses, protozoa, and fungi, make up the gut microbiome. These microorganisms work together to carry out critical functions related to nutrient and drug metabolism, preserve the structural integrity of the gut mucosal barrier, modulate immune responses as well as applying defence against external and opportunistic pathogens [6]. Research over the last few decades has demonstrated that the host's health is greatly affected by the gut microbiota [7].

The metabolic axis connects the host and the gut microbiome is considered one of the most significant axes within the body. Microbiota metabolism has a role in the digestive mechanisms, including digestion of fibers in addition to bile acid, lipids and sugars metabolism. So, gut microbiota is important for products many metabolic products, including neurotransmitters and vitamins, that are required for body organs and tissues to function properly [8].

The gut microbiota links with the central nervous system (CNS) with the enteric nervous system (ENS) via brain-gut axis (BGA). There is substantial evidence that bacterial colonization is necessary for the CNS and ENS to develop properly. Apart from maintaining gut homeostasis through communication with the CNS, gut microbiome has a key role in modulation of nociceptive sensory pathways implicated in visceral pain, intestinal motility and permeability in addition to maintenance of gut barrier [9].

Additionally, the gut microbiome interacts with the human immune system in a coordinated manner through certain receptors like Toll-like receptors (TLRs), or their byproducts, as short-chain fatty acids (SCFAs), that enhance the production of Immunoglobulin A by plasma cells, the microbiota helps the immune system in recognizing & eliminating opportunistic microorganisms. Immunoglobulin A prevents the adherence of bacteria to the epithelium, inhibiting further damage. Furthermore, Immunoglobulin A has a direct effect on the virulence of bacteria, preventing the infection [10]. This process is crucial for the local immune responses [11].

The alteration in gut microbiome is known "dysbiosis", can result from loss or overgrowth of certain agent, decrease in microbial diversity or gene mutations [12]. Dysbiosis is often characterized by decreased diversity and quantity of commensal bacteria, which is related to a variety of chronic disorders, including cancer, obesity, metabolic, neurologic, autoimmune,

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cardiac, vascular, and intestinal disorders as inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) [11].

RELATION BETWEEN *BLASTOCYSTIS* & GUT MICROBIOTA

The relation between *Blastocystis* spp. and gut microbiota is a topic of debate. Several studies have demonstrated that an increase in the diversity of gut microbiome and a decrease in *Bacteroides* are linked to the existence of *Blastocystis* spp.. Better health and a decreased risk of inflammatory disorders are generally related to high bacterial diversity [13]. *Bacteroides*, on the other hand, have been linked to disorders such as obesity, lower gastrointestinal tract inflammation, celiac disease, and colorectal cancer [14]. This implies that healthy microbiome is strongly related to existence of *Blastocystis* spp.

On the other hand, there have been also reports on the pathogenic potential of *Blastocystis* spp. [15]. For instance, it has been reported that beneficial bacteria like *Lactobacillus* and *Bifidobacterium* can be reduced by *Blastocystis* spp. [16]. Certain strains of *Lactobacillus* prevent opportunistic infections in the gastrointestinal tract [17], whereas *Bifidobacterium* is a protective bacterium with anti-inflammatory properties [18], while certain strains of *Lactobacillus* guard against gastrointestinal opportunistic infections [17].

Some gut protozoa, including *Entamoeba histolytica* and *Giardia lamblia* depends on the existence of gut microbiota to express their pathogenicity. Consequently, the question that thus emerges is whether or not a specific microbiome or dysbiosis is linked to *Blastocystis* colonization[19]. In this context, a study by Rajamanikam *et al* [20] highlighted the significant role of the gut microbiota in modulating the behavior of *Blastocystis* spp. This study demonstrated how the gut microbiota can cause asymptomatic *Blastocystis* spp. to exhibit pathogenic characteristics.

An in vitro co-incubation assay revealed a bidirectional influence between *Blastocystis* spp. and other microorganisms. The study by Yason *et al* [16] found that presence of gut bacteria increased the quantity of *Blastocystis* ST7. On the other hand, in the study by Deng *et al* [21], *Blastocystis* ST7 exhibited a selective effect on specific bacterial groups, it inhibited the growth of *Lactobacillus* sp. and the obligatory anaerobe *Bifidobacterium longum*, while enhanced the growth of the facultative anaerobe *Escherichia coli* (Figure 1).

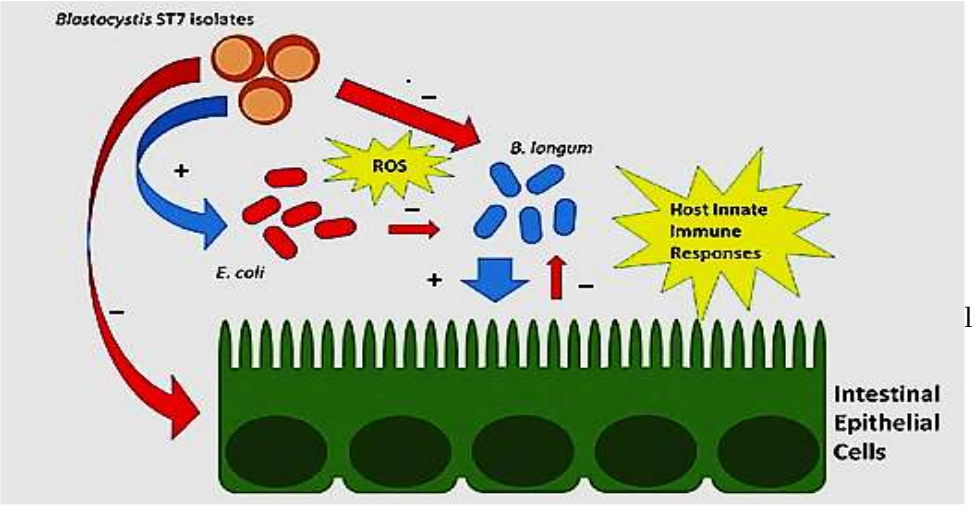

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Figure 1. *Blastocystis* spp. interactions with gut bacteria & its impact on the host. The gut microbiome may be selectively disrupted by *Blastocystis* spp.. *Bifidobacterium longum* was reduced by *Blastocystis* spp., however *Escherichia coli* was increased. This could occur through several mechanisms. *Blastocystis* spp. directly limit the viability of obligatory anaerobic bacteria through oxidative stress. *Bifidobacterium longum* bacteria can be inhibited by the immune response produced by *Blastocystis* spp.. *Bifidobacterium longum* is essential to prevent the damage of the intestinal epithelial barrier by *Blastocystis*. Positive and negative interactions are shown by blue and red arrows represent, respectively [16].

The complexity of *Blastocystis*, which harbors many genetically different subtypes, may be the reason of the conflicting views about its relation to gut microbiome. These distinct subtypes can display varying host ranges, colonization rate, drug resistance, and other biological characteristics. As a result, these dissimilarities can consequently impact how the parasite affects the gut microbiota. Therefore, depending on the subtype of *Blastocystis*, it has been proposed that the microbiota composition may change [22]. Recent studies by Yason *et al* [16] & Deng *et al* [23] found that the effects of *Blastocystis* ST4 and *Blastocystis* ST7 on the gut microbiota are different, potentially influencing the susceptibility to colitis. While *Blastocystis* ST7 aggravated the colitis induced experimentally in mice models with decrease in the abundance of *Lactobacillus* and *Bifidobacterium*, two beneficial bacteria. On the other hand, the infection with *Blastocystis* ST4 was found to improve the colitis through altering in the components of gut microbiota along with activating immune responses of T helper-2 and regulatory T-cells. (Figure 2)

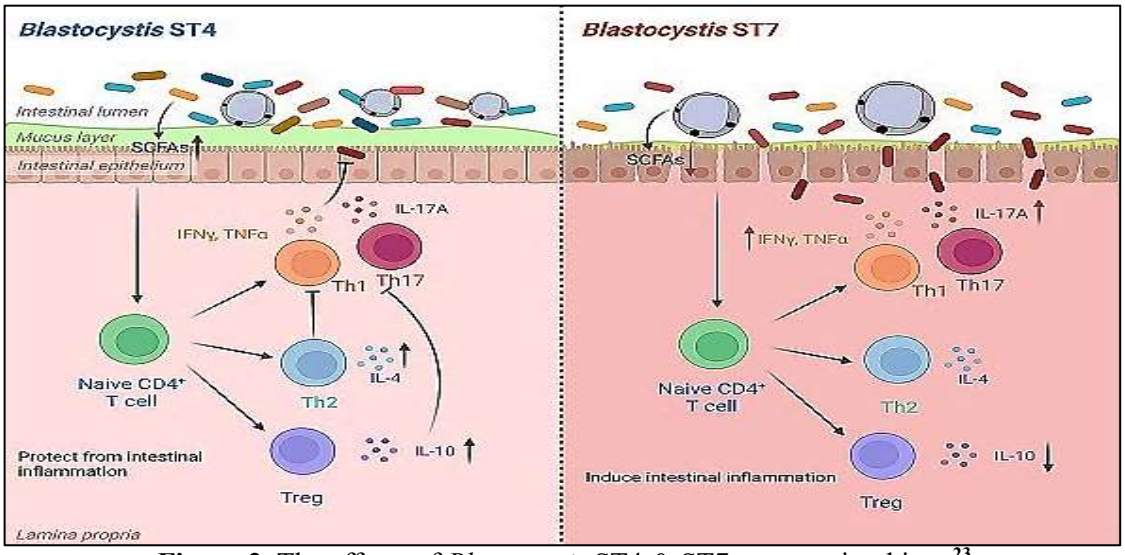

Figure 2. The effects of *Blastocystis* ST4 & ST7 on gut microbiota [23].

Blastocystis spp. and Probiotics

Probiotics are variety of live microorganisms that have good effects on the health. The strains of *saccharomyces boulardii* yeast, *Lactobacillus* and *Bifidobacterium* are the most widely utilized probiotics. Probiotics can reduce the parasite load and enhance therapeutic outcomes by modifying

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the gut microbiome and immune response of the host and preventing the growth of parasites. Additionally, probiotics have the ability to increase the quantity of beneficial bacteria, alter environment to be less favorable for colonization, compete pathogens for nutrition, trigger mucosal immunity, inhibit bacterial toxins and increase the secretion of mucus [24].

Infections with *Blastocystis* spp. can range in severity from mild to severe. Additionally, the presence of *Blastocystis* spp. does not always indicate that medical intervention is necessary. Metronidazole is the primary option if treatment is necessary for the symptomatic cases. Other drugs as Paromomycin and Trimethoprim/sulfamethoxazole may be suggested in case of resistance to metronidazole. Probiotics have been used for treatment of blastocystosis with variable results [24].

The type and dosage of probiotics used for treatment, as well as their potential impact on *Blastocystis* species are still uncertain. Apart from the belief that probiotics can be utilized to treat *Blastocystis* spp., some research argue that *Blastocystis* spp. are a part of healthy gut microbiome and could one day employed as probiotic[25].

CONCLUSION

Blastocystis exhibits complex interactions with gut microbiota, influencing its diversity and host's health. Different subtypes appear to exert distinct effects; while some have been associated with adverse health outcomes, others may contribute to enhanced microbial diversity and potentially beneficial impacts. This highlights the complex relation between this parasite and host's gut environment.

REFERENCES

1. **Abd-Elal SRM, El-Hady HA, Ahmed AM, Abd-Ellah AK (2024).** *Blastocystis*: A Mysterious Disregarded Parasite. *SJYR,4*. https://doi.org/10.21608/sjyr.2024.263883.1394
2. **Abd-Elal SRM, El Hady HA, Ahmed AM, Abd Ellah AK (2024).** *Blastocystis* and Irritable Bowel Syndrome: The Mysterious Link. *Aswan University Medical Journal*, 4(2):55-61.
3. **Abd Ellah AK, El Hady HA, Ahmed AM, Mohamed SR (2024).** Genetic characterization of *Blastocystis* spp. in patients with colorectal cancer, irritable bowel syndrome, and asymptomatic individuals in Sohag, Egypt. *PUJ*; 17(3):247-254 https://doi.org/10.21608/puj.2024.332991.1277
4. **Deng L, Wojciech L, Gascoigne NRJ, Peng G, Tan KSW. (2021).** New insights into the interactions between *Blastocystis*, the gut microbiota, and host immunity. *PLoS Pathog,* 17: 1009253.https://doi.org/10.1371/journal.ppat.1009253
5. **Alfellani MA, Stensvold CR, Vidal-Lapiedra A, Onuoha ES, Fagbenro-Beyioku AF, Clarck CG. (2013).** Variable geographic distribution of *Blastocystis* subtypes and its potential implications. *Acta Trop,* 126:11https://doi.org/10.1016/j.actatropica.2012.12.011

Corresponding author: Shimaa Refaey Mohamed mobile:01004920534, Email: shimaa.refaee@med.sohag.edu.eg

6. **Jandhyala S, Talukdar R, Subramanyam C, Vuyyuru H, Sasikala M, Reddy DN. (2015).** Role of the normal gut microbiota. *World J Gastroenterol*, 21: 8836-8847. https://doi.org/10.3748%2Fwjg.v21.i29.8787
7. **Fan Y. & Pedersen, O. (2021).** Gut Microbiota in Human Metabolic Health and Disease. *Nat Rev Microbiol*, 19: 55-71. https://doi.org/10.1038/s41579-020-0433-9
8. **Rebersek M. (2021).** Gut microbiome and its role in colorectal cancer. *BMC Cancer,* 21: 1-13. https://doi.org/10.1186/S12885-021-09054-2
9. **Carabotti M, Scirocco A, Maselli MA, Severi C. (2015).** The gut-brain axis: Interactions between enteric microbiota, central and enteric nervous systems. *Ann Gastroenterol,* 28: 203. https://www.researchgate.net/publication/274401121
10. **Gopalakrishnan V, Helmink BA, Spencer CN, Reuben A, Wargo JA. (2018).** The influence of the gut microbiome on Cancer, immunity, and Cancer immunotherapy. *Cancer Cell,* 33: 570-580. https://doi.org/10.1016/j.ccell.2018.03.015
11. **Ternes D, Karta J, Tsenkova WP, Haan S, Letellier E. (2020).** Microbiome in colorectal Cancer: how to get from Meta omics to mechanism? *Trends Microbiol*, 28: 401-423. https://doi.org/10.1016/j.tim.2020.01.001
12. **Kriss M, Hazleton KZ, Nusbacher NM, Martin CG, Lozupone CA. (2018).** Low diversity gut microbiota dysbiosis: Drivers, functional implications and recovery. *Curr Opin Microbiol*, 44: 34-40. https://doi.org/10.1016/j.mib.2018.07.003
13. **Loh G. & Blaut M. (2012).** Role of commensal gut bacteria in inflammatory bowel diseases. *Gut Microbes,* 3: 544-555. https://doi.org/10.4161/gmic.22156
14. **Vieira-Silva S, Falony G, Darzi Y, Lima-Mendez G, Garcia Yunta R, Okuda S, *et al.* (2016).** Species-function relationships shape ecological properties of the human gut microbiome. *Nature Microbiol,* 1. https://doi.org/10.1038/nmicrobiol.2016.88
15. **Poirier P, Wawrzyniak I, Vivare`s CP, Delbac F, El Alaoui H. (2012).** New insights into Blastocystis spp.: a potential link with irritable bowel syndrome. *PLoS Pathog,* 8: e1002545. https://doi.org/10.1371/journal.ppat.1002545
16. **Yason JA, Liang YR, Png CW, Zhang Y, Tan KSW. (2019).** Interactions between a pathogenic Blastocystis subtype and gut microbiota: in vitro and in vivo studies. *Microbiome,* 7: 30. https://doi.org/10.1186/s40168-019-0644-3
17. **Sales-Campos H, Soares SC, Oliveira CJ. (2019).** An introduction of the role of probiotics in human infections and autoimmune diseases. *Critical Rev Microbiol,* 45: 413-432. https://doi.org/10.1080/1040841X.2019.1621261
18. **Plaza-Dı´az J, Ruiz-Ojeda FJ, Vilchez-Padial LM, Gil A. (2017).** Evidence of the Anti-Inflammatory Effects of Probiotics and Synbiotics in Intestinal Chronic Diseases. *Nutrients,* 9. https://doi.org/10.3390/nu9060555
19. **Audebert C, Even G, Amandine Cian A, Loywick A, Merlin S, Viscogliosi E, Magali Chabé M. (2016).** Colonization with the enteric protozoa *Blastocystis* is associated with increased diversity of human gut bacterial microbiota. *Sci Rep,* 6: 25255. https://doi.org/10.1038/srep25255
20. **Rajamanikam A, Isa MNM, Samudi C, Devaraj S, Govind SK. (2023).** Gut bacteria influence *Blastocystis* sp. phenotypes and may trigger pathogenicity. *PLOS Negl Trop*

Corresponding author: Shimaa Refaey Mohamed mobile:01004920534, Email: shimaa.refaee@med.sohag.edu.eg

Dis, 17: e0011170. https://doi.org/10.1371/journal.pntd.0011170

21. **Deng L, Wojciech L, Png CW, Koh EY, Aung TT, Kioh DYQ, *et al*. (2022).** Experimental colonization with *Blastocystis* ST4 is associated with protective immune responses and modulation of gut microbiome in a DSS-induced colitis mouse model. *Cell Mol Life Sci,* 79: 245 https://doi.org/10.1007/s00018-022-04271-9
22. **Tito RY, Chaffron S, Caenepeel C, Lima-Mendez G, Wang J, Vieira-Silva S, *et al*. (2019).** Population-level analysis of *Blastocystis* subtype prevalence and variation in the human gut microbiota. *Gut,* 0: 1-10. https://doi.org/10.1136/gutjnl-2018-316106
23. **Deng L, Wojciech L, Png CW, Qin Kioh DY, Gu Y, Aung TT, Malleret B, Chan E, Peng G, Zhang Y, *et al.* (2023).** Colonization with two different *Blastocystis* subtypes in DSS-induced colitis mice is associated with strikingly different microbiome and pathological features. *Theranostics,* 13: 1165-1179.https://doi.org/10.7150/thno.81583
24. **Aykur M, Malatyalı E, Demirel F, Cömert-Koçak B, Gentekaki E, Tsaousis AD, Dogruman-Al F. (2024).** *Blastocystis*: A Mysterious Member of the Gut Microbiome. *Microorganisms*, *12*, 461. https://doi.org/10.3390/microorganisms12030461
25. **Andersen LO & Stensvold CR (2016).** *Blastocystis* in Health and Disease: Are We Moving from a Clinical to a Public Health Perspective? *J. Clin. Microbiol.*, *54*, 524–528.

Corresponding author: Shimaa Refaey Mohamed mobile:01004920534, Email: shimaa.refaee@med.sohag.edu.eg

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ORIGINAL ARTICLE

High Prevalence of Protozoan Infections: Current Status of Intestinal Parasitic Infections in Sohag Governorate, Egypt

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ABSTRACT

Intestinal parasitic infections (IPIs) continue to be significant health concern in numerous communities. Despite improvements in sanitation, IPIs remain a significant challenge in Egypt. These infections are caused by a wide range of protozoa and helminths through feco-oral transmission. This study aimed to detect the prevalence of different intestinal parasitic infections and compare between the current and previous situations in Sohag governorate, Egypt, with a focus on the rising prevalence of protozoan parasites like *Blastocystis* spp. In this cross-sectional study, 225 fecal samples were collected from different hospitals in Sohag governorate. All samples were examined by direct mount, Formalin Ethyl acetate Concentration Technique (FECT), modified Kinyoun's acid-fast staining and *in vitro* culture on modified Jones media enriched with 10% inactivated donkey serum. 60.44% of the participants were infected with at least one intestinal parasite. *Blastocystis* spp. was the most prevalent parasite (43.1%) followed by *Cryptosporidium* spp. (19.6%), *Entamoeba coli* (8.4%), *Entamoeba histolytica/dispar* (8%), *Giardia lamblia* (6.2%), *Cyclospora cayetanensis* (4.4%), *Hymenolepis nana* (0.8%).

Keywords: Intestinal Parasitic Infections, IPIs, polyparasitism.

INTRODUCTION:

Intestinal parasitic infections (IPIs) continue to be a significant health challenge in numerous communities particularly in the developing countries, stemming from poor hygiene, limited sources for clean water in addition to low socio-economic status. Despite advancements in diagnosis and treatment, IPIs continue to impact human productivity worldwide. About 3.5 billion persons are infected and 450 million exhibit manifestations. These infections are caused by a wide range of protozoa such as *Cryptosporidium* spp, *Entamoeba* spp., *G. lamblia, Blastocystis* spp, and helminths such as *H. nana*, *Ascaris*, Hookworm [1]. Parasitized persons typically exhibit variable manifestations such as nausea, vomiting, abdominal pain, diarrhea, dysentery, nutritional deficiencies and anemia. While all age groups can be infected by IPIs,

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children are more susceptible due to hygienic practices [2]. These parasites share the same route of transmission which is the feco-oral route. The main method for diagnosing IPIs is through fecal examination. Suitable control measures are crucial for effectively managing the IPIs. IPIs remain a significant problem in Egypt, even improvements in sanitation [3].

In this study, we aimed to detect the prevalence of different intestinal parasitic infections and compare between the current and previous situations in Sohag governorate, Egypt, with a focus on the rising prevalence of protozoan parasites like *Blastocystis* spp.

MATERIALS AND METHODS:

Ethical consideration:

The study was approved by the Medical Research Ethical Committee (MREC) of our faculty under the IRB registration No (Soh-med-22-10-16). It was registered at Clinical Trials.gov under registry No (NCT05580393). Individual written informed consents were obtained from enrolled participants after brief explanation of the study.

Study design This cross-sectional survey was conducted from November 2022 to November 2024.

Study population: 225 faecal specimens were collected from individuals (with or without gastrointestinal symptoms) attending outpatient clinics of different hospitals at Sohag governorate with exclusion of those who used anti-parasitic medications 10-14 days before the examination.

Parasitological methods:

All specimens were examined by direct mount, Formol-ethyl acetate concentration technique (FECT) and Modified Kinyoun's acid-fast staining [4].

For the detection of *Blastocystis* spp., 50 mg from every faecal specimen was inoculated in 5ml-capped tubes with Jones media containing 10% inactivated donkey serum and 1% yeast extract. The tubes then were incubated at room temperature (37^{o}C) for 2-3 days. A drop from the cultivated sample was put on a slide and examined under the microscope. The culture was not reported to be negative for *Blastocystis* spp. except after ten days [5,6].

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Statistical analysis

Data were entered into Microsoft Excel 2016 for tabulation and then analyzed. Medcalc and SPSS Statistics were used to analyze the results. Quantitative results were reported as mean ± standard deviation, while the qualitative results were reported as percentages and frequencies. Comparing qualitative data was done by using chi-square test (X^2). If *P*-value was less than 0.05, it was considered statistically significant.

RESULTS

Of all studied 225 participants, 136 (60.44%) were found to be infected with at least one intestinal parasite, while 89 (39.56%**)** were not infected **(Figure 1)**.

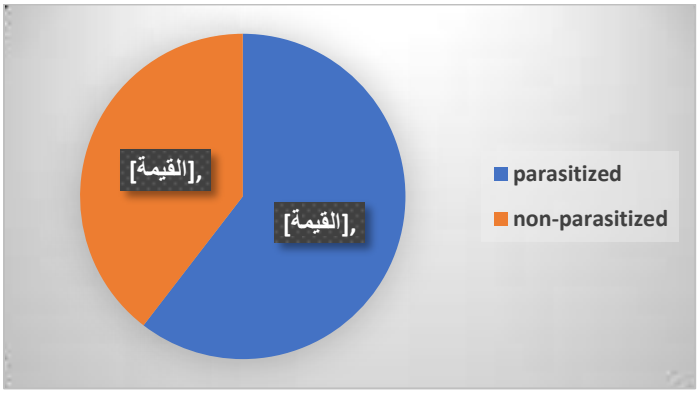

Figure 1. Incidence of intestinal parasitic infections among the studied participants (n=225).

60.3% of the infected individuals were infected with one intestinal parasite while 39.7% were infected with two or more intestinal parasites **(Table 1)**.

Table 1. Types of parasitism (n=136).

Parasitism	N	%
Monoparasitism	**82**	**60.3%**
Polyparasitism*	**54**	**39.7%**

***Polyparasitism= 2 or more parasite species**

Blastocystis spp. was the most prevalent parasite (43.1%) followed by *Cryptosporidium* spp (19.6%). *E. coli* was found in 19 cases with a prevalence of 8.4%, *E. histolytica/dispar* was found in 18 cases with a prevalence of 8%, *G. lamblia* was found in 14 cases with prevalence of 6.2%, *Cyclospora* was found in 10 cases with a prevalence of 4.4% while *H. nana* was found only in 2 cases with a prevalence of 0.8% **(Table 2)**.

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Table 2. Distribution of intestinal parasites.

	Total (n=225)	%
Blastocystis spp.	97	43.1%
Cryptosporidium spp.	44	19.6%
E. coli	19	8.4%
E. histolytica/dispar	18	8%
G. lamblia	14	6.2%
Cyclospora cayetanensis	10	4.4%
H. nana eggs	2	0.8%

Logistic regression analysis revealed that none of the studied socio-demographic factors (age, gender, residence, animal contact) were significantly associated with intestinal parasitic infection (*p* value > 0.05 for all) **(Table 3)**.

Table 3. Logistic regression analysis of socio-demographic factors associated with IPIs among 225 participants in Sohag Governorate.

		N. of tested (225)	N. of infected (136)	N. of non-infected (89)	Crude OR (95% CI)	*P* value
Age	15-29 y	61 (27.1%)	35 (25.7%)	26 (29.2%)	0.839 (0.462-1.53)	0.551
	30-44 y	51 (22.7%)	33 (24.3%)	18 (20.2%)	1.26 (0.660-2.42)	
	45-59 y	65 (28.9%)	36 (26.5%)	29 (32.6%)	0.745 (0.415-1.34)	
	60-75 y	48 (21.3%)	32 (23.5%)	16 (18%)	1.40 (0.718-2.74)	
Gender	Male	112 (49.8%)	63 (46.3%)	49 (55.1%)	0.704 (0.412-1.20)	0.201
	Female	113 (50.2%)	73 (53.7%)	40 (44.9%)		
Residence	Rural	129 (57.3%)	79 (58.1%)	50 (56.2%)	1.08 (0.630-1.85)	0.777
	Urban	96 (42.7%)	57 (41.9%)	39 (43.8%)		
Animal contact	Yes	103 (45.8%)	58 (42.6%)	45 (50.6%)	0.727 (0.425-1.24)	0.243
	No	122 (54.2%)	78 (57.4%)	44 (49.4%)		

Significant if *P* value < 0.05

DISCUSSION

This cross-sectional study conducted in Sohag governorate; Egypt revealed that (60.44%) of the tested participants were infected by at least one intestinal parasite. Previous studies

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conducted in 2013, 2016, 2017, 2020, 2022 in Sohag governorate reported different rates of parasitism 55%, 31%, 63.5%, 40%, 59%, respectively [7, 8, 3, 9, 10]. These disparities may be due to differences in the studied population and the used diagnostic techniques.

60.3% of the infected persons in the current study harbored only one gut parasite while 39.7% were infected by more than one parasite. Our findings were in accordance with the results of a cross-sectional study conducted in 2017 Sohag [3] where monoparasitism (40%) was higher than polyparasitism (23.5%).

Blastocystis spp. (43.1%) was found to be the most prevalent gut parasite in the present study. Our percentage was higher than that reported by other previous studies in Sohag governorate (10.5%, 3%, 5%) [3, 9, 10]. This may be attributed to the use of culture on modified Jones media for detection of *Blastocystis* spp. in our study.

Blastocystis spp. is one of the "emerging intestinal parasites" with high genetic diversity. Up to now, more than forty species detected in wide range of mammals but only sixteen species can infect man. There is still some confusion about its pathogenicity. While some claim it is commensal and causes no symptoms, others accuse it of having a close relation with some gastrointestinal disorders such as irritable bowel syndrome. The prevailing theory is that *Blastocystis* virulence is related to its species [11, 12]. In the last few years, *Blastocystis* spp. was reported to be the most detectable intestinal parasitic infection in numerous Egyptian and global surveys [13]. Up to now, *Blastocystis* spp. infection not included in the fecal examination reports. This not only due to the controversy of its pathogenicity but also few examiners trained to diagnose it.

Cryptosporidium (19.6%) was the second prevalent intestinal parasite in this study. This result was in accordance with Abd Ellah *et al*.[14] who found *Cryptosporidium* in 18% and lower than El Nadi *et al*.[3] and Abd El-Mawgood *et al*.[10] who reported *Cryptosporidium* prevalence 31.5% and 25%, respectively.

Consuming the infective oocysts in contaminated water is the main route for *Cryptosporidium* infection. Unfortunately, oocysts have the ability to survive in chlorine which commonly used in water treatment [15].

The prevalence of *E. histolytica/dispar* was 8% in our study. This rate is in accordance with the rates (9%, 8%) reported in Sohag in 2023 and 2024, respectively [14, 16]. Higher prevalence rates (13.2%, 11%, 13.2%) were reported in previous studies in Sohag in 2013, 2016, 2017, respectively [7, 8, 3].

G. lamblia was detected in 6.2% in the current study. This was lower than the results reported by Abd Ellah *et al.* [16] who reported *G. lamblia* in 4%, while higher prevalence rates

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(9.9%, 21%, 14.5%, 16%, 15%) in previous studies conducted in Sohag in 2013, 2016, 2017, 2022 and 2023, respectively [7, 8, 3, 10, 14].

The prevalence of *H. nana* was 0.8% in the present study. Previous studies were performed in Sohag governorate reported higher prevalence for *H. nana* (9.9%, 11%, 5%) in 2013, 2016, 2017, respectively[7, 8, 3]. Therefore, our findings indicate a shifting paradigm in the epidemiology of IPIs in Sohag, away from helminths and towards challenging protozoans, which will be discussed in the conclusion.

According to logistic regression analysis, there were no risk variables for intestinal parasitism related to age, residence, gender, animal contact. This is consistent with El Nadi *et al.* and Abd Ellah *et al.*[3, 14].

CONCLUSION

IPIs are still a health problem in our community. Despite IPIs were common in our study, only two cases were infected with helminthic parasites, and the majority were protozoa. The decreased helminthic parasitism may be related to the World Health Organization (WHO) mass deworming program in Egypt. Decrease in the prevalence of most protozoal infections may be attributed to the increased awareness and proper management of these infections. The use of new diagnostic methods increased the detection of some parasites like *Blastocystis* spp.

REFERENCES

1. **Shaldoum FM, Muhammad AA, Yassin MK, Gobaara IM. (2017):** Intestinal parasites associated to infection with *H. pylori* in Egypt. *Al Azhar Bull Sci.,* 9: 267-278.
2. **Elmonir W, Elaadli H, Amer A, El-Sharkawy H, Bessat M, Mahmoud SF, Atta MS, El-Tras WF (2021):** Prevalence of IPIs and their associated risk factors among preschool and school children in Egypt. *Plos one,* 16(9): e0258037.
3. **El-Nadi NAF, Omran EK, Ahmed NS, Fadel EF (2017):** Current status of intestinal parasites among elementary school children in Sohag, Egypt. *J. Adv. Parasitol.,* 4(2): 33-40.
4. **Garcia, L.S. (2016).** Diagnostic medical Parasitology. 6th Edition. *ASM Press*.
5. **Jones, M.S.; Ganac, R.D.; Hiser, G.; Hudson, N.R.; Le, A. and Whipps, C.M. (2008).** Detection of *Blastocystis* from stool samples using real-time PCR. *Parasitol Res,* 103:551-557.
6. **Piekara-Stępińska, A.; Gorczykowski, M. and Piekarska, J. (2018).** Suitability of selected culture media for *Blastocystis* spp. *Pol J Vet Sci,* 21: 815-817.
7. **Hamed AF, Yousef FMA, Omran EK, Ahmed AM (2013).** Common Parasitic Infestation among Rural Population in Sohag Governorate, Egypt. *J Am Sci*; 9(4):596-601.
8. **El-Nazer MM, Abd El Mawgood AA, Mohammed HS, Gaballa MR (2016):** Prevalence of intestinal parasites in patients with chronic kidney disease. M.Sc. Thesis, Faculty of Medicine, Sohag University.

Corresponding author: Shimaa Refaey Mohamed mobile:01004920534, Email: shimaa.refaee@med.sohag.edu.eg

9. **Mohamed SR, El Hady HA, Ahmed AM (2020).** Evaluation of Immunochromatographic Assay for Diagnosis of Cryptosporidiosis. *J Egypt Soc Parasitol*; 50(3): 477-482.
10. **Abd El-Mawgood AA, Ahmed AM, Hashem KZ, Abd Ellah AK (2022).** Immunochromatography Versus Microscopy for Diagnosis of *Entamoebia histolytica*/*dispar* Infection in Sohag University Hospitals, Egypt**.** *J Egypt Soc Parasitol;* 52(1): 139-144.
11. **Abd-Elal SRM, El-Hady HA, Ahmed AM, Abd-Ellah AK (2024).** *Blastocystis*: A Mysterious Disregarded Parasite. *SJYR*,*4*.
12. **Abd-Elal SRM, El Hady HA, Ahmed AM, Abd Ellah AK (2024).** *Blastocystis* and Irritable Bowel Syndrome: The Mysterious Link. *Aswan University Medical Journal*, 4(2):55-61.
13. **Ahmed H.K, Mohamed KA, Sheishaa GAA, Ali NE, El-Wakil ES, El-Badry AA (2022).** *Blastocystis* SPP. infection prevalence and associated patient characteristics as predictors among a cohort of symptomatic and asymptomatic Egyptians. *Int J Health Sci*, 6: 5839-5852.
14. **Abd Ellah AK, El-Nadi NA, Mahmoud SN, Abd El Mawgood AA (2023).** Evaluation of Feconomics® versus traditional techniques for diagnosis of intestinal parasitic infections among schoolchildren in Sohag, Egypt. *PUJ*; 16(3):177-182
15. **Latif B & Rossle N F (2015).** Cryptosporidiosis among children with diarrhoea in three Asian countries: A review**.** ***Asian Pacific Journal of Trop Biomed,*** 5(11), 885–888
16. **Abd Ellah AK, Ahmed AM, Ahmed NM, AL-Amir H. (2024).** Intestinal Parasitic Infections in Patients with Irritable Bowel Syndrome in Sohag, Egypt. *JESP*, 54: 277-282.

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ORIGINAL ARTICLE

Clinical outcomes after Minimally Invasive Trans-foraminal Lumbar Interbody Fusion (MI-TLIF) in treatment of degenerative lumbosacral spine diseases

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ABSTRACT

Background: Degenerative lumbar spine illness is one of the most common healthcare issues in the globe. The various treatment modalities relieve radicular symptoms but with limited results regarding the pain. Minimally Invasive Trans-foraminal Lumbar Interbody Fusion (MI-TLIF) one of these modalities. **Objective:** to evaluate the clinical outcomes and the patient satisfaction after using MI-TLIF for treatment of degenerative lumbosacral spine diseases. **Methods**: This is a prospective study that conducted on 30 patients with degenerative lumbosacral spine diseases presented to Aswan university hospital. The study included patients with degenerative disc disease, recurrent disc herniation, Grade 1 and 2 spondylolisthesis, post-laminectomy instability or Trauma requiring interbody fusion. **Results:** the mean patient's age was 55 ± 8 years, of them 12 were females and about 50% of participants didn't have any comorbidities. The mean ODI score preoperative, one month and 6 months was 57.8 %±12.42, 28.2 %. ± 12.1 and 18.1% ± 4.9 respectively with very high statistically significant differences (p-value < 0.001). Delayed post-operative complications were reported in 8 (26.6%) patients.**Conclusion:** MI-TLIF is a reliable, and effective technique, with significant clinical improvement, reasonably satisfaction rate, and low incidence of complications.

Keywords: Less invasive TLIF, Disc surgery ,Oswestry Disability Index.

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INTRODUCTION

One of the most common healthcare issues in the globe is degenerative lumbar spine illness. (1). The estimated annual prevalence of low back pain was 38.0%, and the estimated lifetime prevalence was 39.9%. The estimated mean prevalence of low back pain was 31.0%. (2)

Lumbar fusion has been utilized to treat degenerative diseases of the lumbar spine. (3) The available forms of the spinal fusion procedures has seen remarkable development in the last century which includes: Anterior Lumbar Interbody Fusion (ALIF) by Burs (4), Posterior Lumbar Interbody Fusion (PLIF) by Cloward (5), pedicle screws by Roy-Camille (1970) and Trans-foraminal Lumbar Interbody Fusion (TLIF) by harms and Rolinger. (6)

While open exposure and protracted retraction can cause tissue necrosis, which frequently results in harm to the soft tissues that surround the spine. During the surgical exposes, there is also a potential of harm to neurovascular structures. (3). Less invasive surgical exposures have been developed in an effort to lessen the drawbacks of conventional open exposures, such as infections and issues with wound healing. (7)

The posterior minimally invasive techniques to the lumbar spine have produced somewhat better outcomes. Less soft tissue dissection, preservation of the soft tissue envelope, and reduced blood loss are benefits of these methods. Additionally, because the posterior ligamentous components are unaffected, there is less chance of adjacent-level instability. (8) (9)**.** The current study aims to evaluate the patient satisfaction and 6 months follow-up clinical outcomes of Minimally Invasive Trans-foraminal Lumbar Interbody Fusion (MI-TLIF) in treatment of degenerative lumbosacral spine diseases.

PATIENTS AND METHODS

This is a Quasi-experimental study on patients presented to Aswan university hospital with any of the degenerative lumbosacral spine diseases in the period from May 2022 to May 2023.The protocol of the study was approved by IRP, Faculty of Medicine, Aswan University.

The study included patients with degenerative disc disease (DDD), recurrent disc herniation, Grade 1 and 2 spondylolisthesis, post-laminectomy instability or trauma requiring interbody fusion. No restriction on age or gender specific. Patients to be treated primarily, severe osteoporosis, distorted anatomy, or major vertebral deformities were excluded.

Patients were identified and demographic characteristics such as age, gender, smoking, duration of symptoms and location of the diseased segments were collected. Radiological investigations X-rays, Computed Tomography (CT) and MRI was done to confirm the diagnosis, evaluate facet joints, demonstrate the correct location of affected segment and detecting concomitant diseases.

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The surgical procedure was done according to Garg & Mehta (10). Post-operative follow up: Patients was subjected to early post-operative follow up and late follow up evaluation scheduled after one month, and six months. Standardized questionnaires and scores addressing the quality of life, patient satisfaction, sociodemographic characteristics and radiological measurements was addressed to patients. For clinical outcomes we used Oswestry Disability Index (ODI) which ranging from 0-100% (11).

Statistical Analysis: Data was collected, coded, and entered using Microsoft Excel software. Data analyses were done using SPSS version 25.0 and R version 4.1.1 software (R Core Team). According to the type of data, qualitative data represent as number and percentage, quantitative data represent by mean ± SD. Repeated-ANOVA was used to compare between the continuous measurement scale over time for each group. Post hoc used to detect the difference between each time point using holms correction. P- value was considered significant if it was < 0.05.

RESULTS

In this study we included 30 participants with mean ± SD age 55 ± 8 years, and the body mass index 27 ± 3, of them 60% were males, and 26.7% were smokers. There were 12 patients that have hypertension, and 8 patients were diabetic, while 46.6 % of participants didn't have any comorbidities. Regarding the clinical presentation 13 patients suffered from right radiculopathy, 12 patients had left radiculopathy while 5 patients suffered bilateral radiculopathy with mean ±SD follow up duration 9 ± 4 months. The mean ±SD operative time was 152±23 (ranged from 122 to 211) minutes, the mean ±SD C-arm duration was 213 ± 29 (ranged from 87 to 238) seconds and the mean essential blood loss was 199 ± 108 (ranged from 100 to 700) ml [Table 3].

Our study showed that the mean ±SD preoperative ODI score was 57.8 %±12.42, which decreased after one month post-operatively to be 28.2 %. ± 12.1 and reached 18.1% ± 4.9 after 6 months post-operative. There were very high statistically significant differences between the three time points (p-value < 0.001). After performing post hoc analysis, the difference between preoperative ODI score and after one month and 6 months was very highly statistically significant. Also, the difference between ODI score after one month and after 6 months was very highly statistically significant [Table 2].

Regarding to the intra-operative complication was dural tear in 2 (6.6%) patients. As regard to Delayed post-operative complications were 8 (26.6%) patients; 3 cases had superficial wound infection, one case suffered weakness of muscles and 4 cases developed foraminal canal stenosis [Table 3].

Our study found that patients' satisfaction was as follow; 2 were very dissatisfied, 5 were dissatisfied, 6 were neutral, 12 were satisfied and 5 were very satisfied. [Figure 2]

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Tables & figures

Table 1: Baseline characteristics

		Mean ± SD **Frequency (%)**
		55 ± 8
Gender	Male	18 (60.0%)
	Female	12 (40.0%)
Smoking	Yes	8 (26.7%)
	No	22 (73.3%)
Comorbidity	HTN	12 (40.0%)
	DM	8 (26.7%)
	IHD	1 (3.3%)
	CVS	2 (6.7%)
	No comorbidity	14 (46.6%)
Radiculopathy	RT	13 (43.3%)
	LT	12 (40.0%)
	Both	5 (16.7%)
BMI		27 ± 3
Duration of symptoms (months)		9 ± 4
Operative time (min)		152 ± 23
C-arm duration (sec)		213 ± 29
Essential blood loss (ml)		199 ± 108

BMI: Body Mass Index, SD: Standard deviation, HTN: Hypertension, DM: Diabetes Mellitus, IHD: ischemic heart diseases, CVS: Cerebro-Vascular stroke, Rt: Right, Lt: Left

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Table 2: Change in ODI score over time

	Mean ±SD	P-value
RM-ANOVA		
Pre-operative	57.8 ± 12.42	< 0.001***
After one month	28.2 ± 12.1	
After six months	18.1 ± 4.9	
Post hoc analysis		
	MD [95% CI]	
Pre Vs 1 month	31.7 [27.07 - 36.33]	< 0.0001***
Pre Vs 6 months	39.8 [34.96 - 44.64]	< 0.0001***
3 Vs 6 months	8.1 [5.6 - 10.59]	< 0.0001***

RM-ANOVA: repeated measure ANOVA, MD: Mean Difference, CI: Confidence interval.

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Table 3: Operative and post-operative complications

		Frequency (%)
Operative complications	No	27 (93.1%)
	Dural tear	2 (6.9%)
	Root injury	0 (0.0%)
	malposition hardware	0 (0.0%)
Delayed post-operative complications	No	22 (73.3%)
	superficial wound infection	3 (10.0%)
	weakness of muscles	1 (3.3%)
	foraminal canal stenosis	4 (13.3%)
	hardware failure	0 (0.0%)
	delayed skin wound healing	0 (0.0%)

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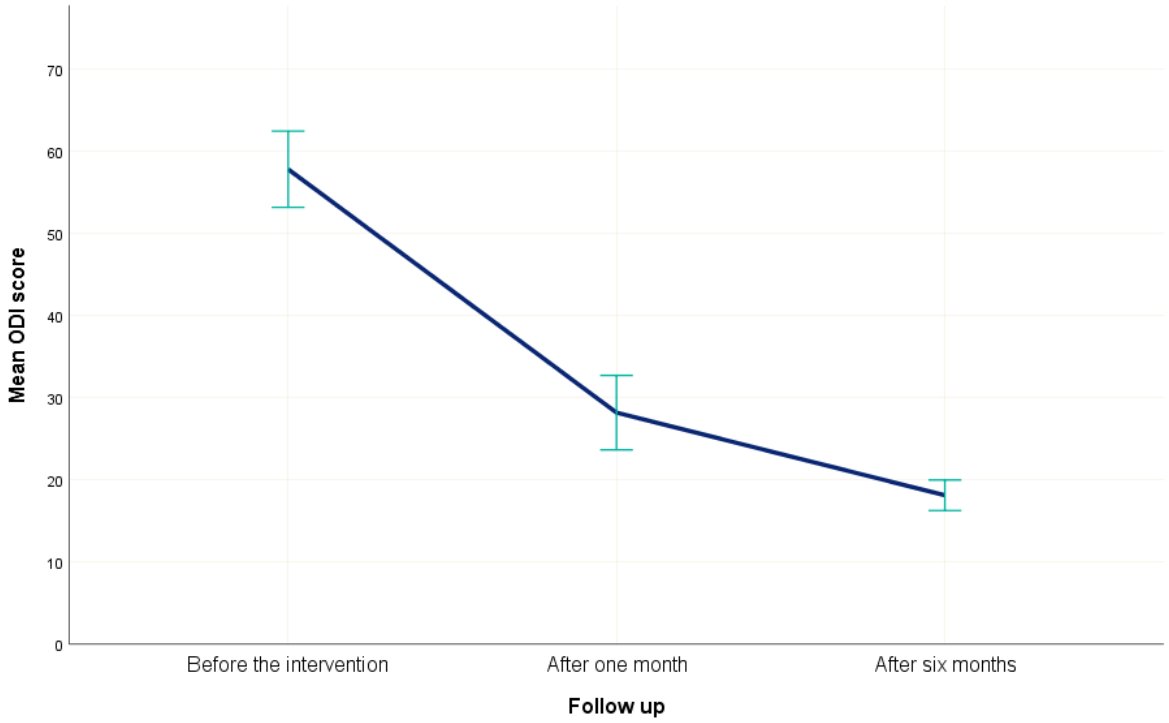

Figure 1: Line graph shows the change in ODI score

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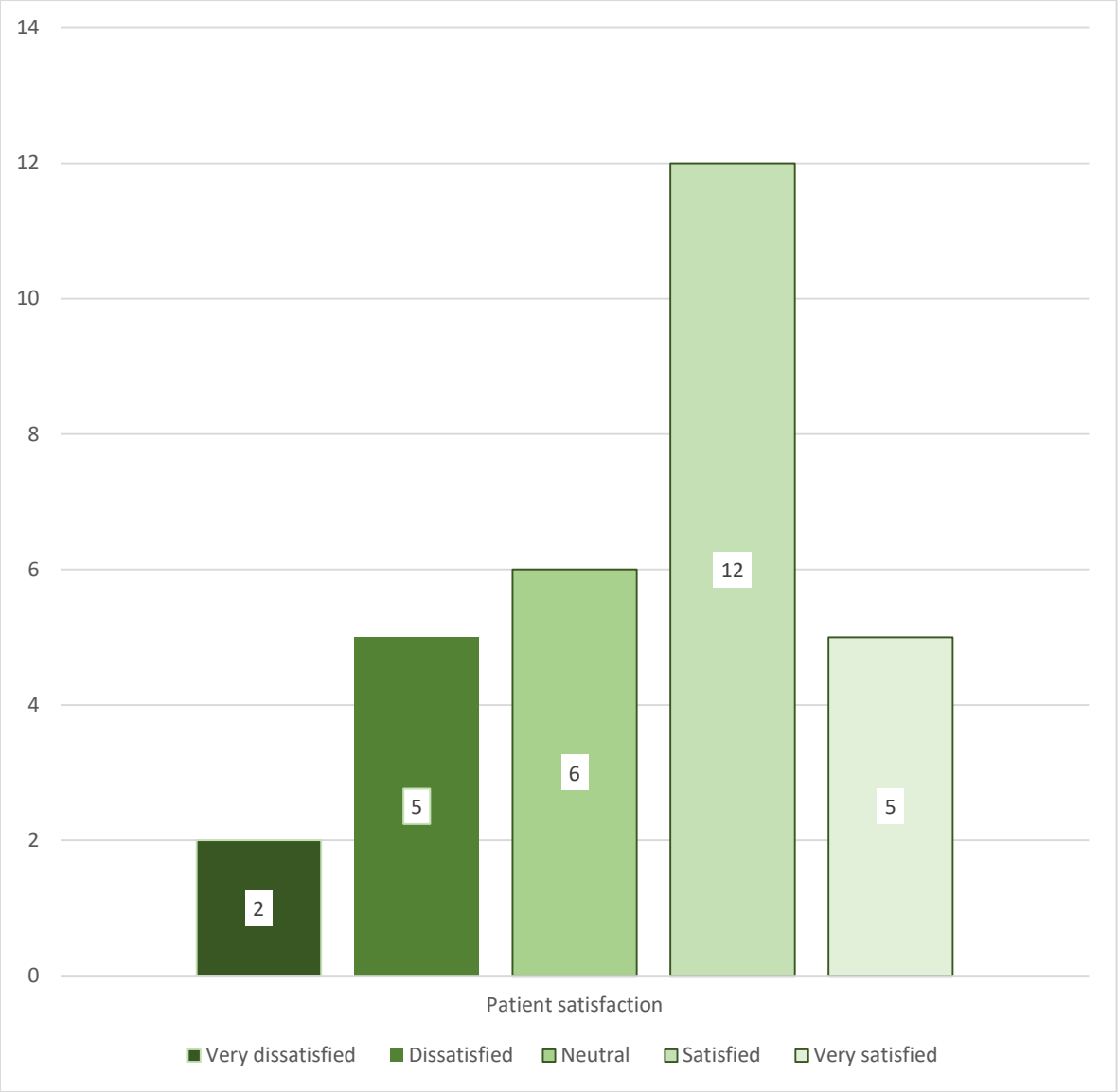

Figure 2: Patient satisfaction after one month's follows up

DISCUSSION

Degenerative lumbar spine remains a common healthcare problem. (1) The evolution of the spinal fusion procedures has seen remarkable development in the last century. Although the goals of all lumbar fusion surgeries whether open or minimally-invasive- remain the same, but excellent results were obtained with open TLIF. (12)

By employing smaller incisions and accessing the spine through paraspinal muscle-splitting surgical corridors, MI-TLIF causes significantly less soft tissue and muscle disruption.

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Technological advances, better magnification and illumination, modern tubular retractors and percutaneous screw systems and more frequent exposure of surgeons to minimally access surgery in their residency training has greatly contributed to the global success of MI – TLIF. (9)

So, we conducted this study aiming to evaluate the results of MI-TLIF in treatment of degenerative lumbosacral spine diseases and its impact on functional outcomes and patient satisfaction, where, 30 participants were included with mean ± SD age 55 ± 8 years and mean ± SD BMI 27 ± 3. Thirteen patients suffered from right radiculopathy; 12 patients had left radiculopathy while 5 patients suffered bilateral radiculopathy.The mean ± SD operative time was 152 ± 23 minutes, which was similar to the literature (13,14)

Regarding The C-arm duration in our study the mean ± SD of C-arm duration of MIS-TLIF procedures done was 213 ± 29 seconds. which is longer than Peng et al., 2009 (20) who reported mean C-arm duration about 105.5 seconds. Moreover, Gu et al., 2014 (21) reported c-arm duration was 45.3±11.7. Longer C-arm duration is inherited in MIS TLIF, and this is one of the shortage of this technique, especially when compared to the standard open TLIF. The higher radiation exposure in MIS-TLIF group could be explained by the longer duration of surgery when compared to the open TLIF group. Peng et al., 2009 (20) reported mean ± SD radiation time in MIS-TLIF and open TLIF groups (105.5 sec and 35.2 sec respectively).

In our study we found the mean ± SD essential blood loss for MIS-TLIF procedures was 199 ± 108 ml. Brodano et al., 2015 (14) reported similar results regarding mean ± SD essential blood loss in MIS-TLIF procedures which was 230 ml. While Peng et al., 2020 (16) and Terman et al., 2014 (15) had reported less amounts of essential blood loss in MIS-TLIF procedures with mean ± SD equals 88.33 ± 23.57 ml and 100 ml respectively. On the contrary of the c-arm duration, blood loss in our technique is one of the advantages as the intraoperative blood loss lesser than the open TLIF.

Our study shows that the only operative complication occurred was 2 (6.6%) cases with dural tear. Similar to our work, Terman et al., (15) reported 2 cases of dural tear among MIS-TLIF patients. Also reported 3 cases of dural tear and 5 cases of excessive blood loss among open TLIF participants. In our study, we didn't reported any case of device malposition while Peng et al., (16) had reported in their study 3 cases of device malposition in MIS-TLIF groups which and 13 cases in open TLIF groups this difference is statistically significant.

In our study, 8 (26.6%) participants suffered from delayed post-operative complications; 3 cases suffered from superficial wound infection which were resolved with antibiotics. There was a single case of muscle weakness and 4 cases of foraminal canal stenosis. Similar to our work, Fan et al., (13) have noticed 3 cases of wound infection among MIS-TLIF patients and 2 cases among open TLIF patients. Aoki et al., (17) reported one case of muscle weakness after open TLIF surgery. Lo et al., (18) reported only 2 cases of wound infections in open TLIF group.

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Our study showed that the mean ± SD pre-operative ODI score was 57.8 ± 12.42 % which reduced into 28.2 ± 12.1% after one month and reached 18% ± 4.9 after 6 months. The difference was statistically significant, and amount of reduction is of clinical importance as it reduced to the 2/3 of the beginning value.

There are little studies that reported ODI score one-month and six post-operative. One of them was Chen et al., (19) who reported the mean ± SD ODI score one month's post-operative was 22.90 ± 2.76 % and (16) who reported the mean ± SD ODI score one month's post-operative was 21.67 ± 1.74 %. While Peng et al., and Gu et al (20,21) reported the mean ± SD ODI score six months postoperative was 16.2 ± 3.4 % and 16.5 ± 2.0 % respectively.

The steep learning curve and the higher radiation exposure are the two main concerns that most surgeons still have with MI-TLIF. (22)

Our study has some limitations, as the accessible population was patients presented to Aswan university hospital only and therefore the results cannot be generalized to the worldwide population. Other limitation are small sample size, short follow-up, and lack of comparison with open-TLIF, so we recommend conducting randomized clinical trials that compare MIS with open TLIF with larger sample size to overcome these shortages.

CONCLUSION

The MI-TLIF is a reliable, and effective surgical technique, with significant clinical improvement, reasonably satisfaction rate, and low incidence of complications or failed back surgery syndrome, with concern to the higher radiation exposure.

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Conflict of Interest: The Authors declare that there is no conflict of interest

REFERENCES

1. Gooch CL, Pracht E, Borenstein AR. The burden of neurological disease in the United States: A summary report and call to action. Ann Neurol [Internet]. 2017 Apr;81(4):479–84. Available from: https://onlinelibrary.wiley.com/doi/10.1002/ana.24897
2. Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, et al. A systematic review of the global prevalence of low back pain. Arthritis Rheum [Internet]. 2012 Jun;64(6):2028–37. Available from: https://onlinelibrary.wiley.com/doi/10.1002/art.34347
3. Eck JC, Hodges S, Humphreys SC. Minimally invasive lumbar spinal fusion. J Am Acad Orthop Surg. 2007;15(6):321–9.
4. Burns BH. an Operation for Spondylolisthesis. Lancet [Internet]. 1933 Jun;221(5728):1233. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673600857244

Corresponding author: Alaa Eldin Ezzat Mohammad, Mobile: 01067077405. Email: alaaeldeen@aswu.edu.eg

5. Pope JE, Mekhail N. Minimally invasive procedures for vertebral compression fractures. Anesth Spine Surg. 2012;(193):29–40.
6. Harms J, Rolinger H. A one-stage procedure in operative treatment of spondylolisthesis: Dorsal traction-reposition and anterior fusion. Z Orthop Ihre Grenzgeb [Internet]. 1982 Mar 18;120(3):343–7. Available from: http://www.thieme-connect.de/DOI/DOI?10.1055/s-2008-1051624
7. Mayer M. Minimally invasive lumbar fusion techniques. Oper Orthop Traumatol. 2020;32(3):179.
8. Patwardhan AG, Meade KP, Lee B. A Frontal Plane Model of the Lumbar Spine Subjected to a Follower Load: Implications for the Role of Muscles. J Biomech Eng [Internet]. 2001 Jun 1;123(3):212–7. Available from: https://asmedigitalcollection.asme.org/biomechanical/article/123/3/212/446743/A-Frontal-Plane-Model-of-the-Lumbar-Spine
9. Holly LT, Schwender JD, Rouben DP, Foley KT. Minimally invasive transforaminal lumbar interbody fusion: indications, technique, and complications. Neurosurg Focus [Internet]. 2006 Mar;20(3):1–5. Available from: https://thejns.org/view/journals/neurosurg-focus/20/3/foc.2006.20.3.7.xml
10. Garg B, Mehta N. Minimally invasive transforaminal lumbar interbody fusion (MI-TLIF): A review of indications, technique, results and complications. J Clin Orthop Trauma [Internet]. 2019;10:S156–62. Available from: https://doi.org/10.1016/j.jcot.2019.01.008
11. Davidson M, Keating JL. A Comparison of Five Low Back Disability Questionnaires: Reliability and Responsiveness. Phys Ther [Internet]. 2002 Jan 1;82(1):8–24. Available from: https://academic.oup.com/ptj/article/82/1/8/2836935
12. Cawley DT, Alexander M, Morris S. Multifidus innervation and muscle assessment post-spinal surgery. Eur Spine J [Internet]. 2014 Feb 22;23(2):320–7. Available from: http://link.springer.com/10.1007/s00586-013-2962-7
13. Fan S, Zhao X, Zhao F, Fang X. Minimally invasive transforaminal lumbar interbody fusion for the treatment of degenerative lumbar diseases. Spine (Phila Pa 1976) [Internet]. 2010 Aug;35(17):1615–20. Available from: http://journals.lww.com/00007632-201008010-00007
14. Brodano GB, Martikos K, Lolli F, Gasbarrini A, Cioni A, Bandiera S, et al. Transforaminal lumbar interbody fusion in degenerative disk disease and spondylolisthesis grade I: Minimally invasive versus open surgery. J Spinal Disord Tech [Internet]. 2015 Dec;28(10):E559–64. Available from: https://journals.lww.com/00024720-201512000-00012
15. Terman SW, Yee TJ, Lau D, Khan AA, La Marca F, Park P. Minimally invasive versus open transforaminal lumbar interbody fusion: Comparison of clinical outcomes among

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obese patients. Clinical article. J Neurosurg Spine [Internet]. 2014 Jun;20(6):644–52. Available from: https://thejns.org/view/journals/j-neurosurg-spine/20/6/article-p644.xml

16. Peng P, Chen K, Chen H, Zhang K, Sun J, Yang P, et al. Comparison of O-arm navigation and microscope-assisted minimally invasive transforaminal lumbar interbody fusion and conventional transforaminal lumbar interbody fusion for the treatment of lumbar isthmic spondylolisthesis. J Orthop Transl [Internet]. 2020 Jan;20:107–12. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2214031X1930213X
17. Aoki Y, Yamagata M, Ikeda Y, Nakajima F, Ohtori S, Nakagawa K, et al. A prospective randomized controlled study comparing transforaminal lumbar interbody fusion techniques for degenerative spondylolisthesis: Unilateral pedicle screw and 1 cage versus bilateral pedicle screws and 2 cages: Clinical article. J Neurosurg Spine [Internet]. 2012 Aug;17(2):153–9. Available from: https://thejns.org/view/journals/j-neurosurg-spine/17/2/article-p153.xml
18. Lo WL, Lin CM, Yeh YS, Su YK, Tseng YY, Yang ST, et al. Comparing miniopen and minimally invasive transforaminal interbody fusion in single-level lumbar degeneration. Biomed Res Int [Internet]. 2015;2015:1–5. Available from: http://www.hindawi.com/journals/bmri/2015/168384/
19. Chen K, Chen H, Zhang K, Yang P, Sun J, Mo J, et al. O-arm Navigation Combined with Microscope-assisted MIS-TLIF in the Treatment of Lumbar Degenerative Disease. Clin Spine Surg [Internet]. 2019 Jun;32(5):E235–40. Available from: https://journals.lww.com/01933606-201906000-00010
20. Peng CWB, Yue WM, Poh SY, Yeo W, Tan SB. Clinical and radiological outcomes of minimally invasive versus open transforaminal lumbar interbody fusion. Spine (Phila Pa 1976) [Internet]. 2009 Jun;34(13):1385–9. Available from: http://journals.lww.com/00007632-200906010-00009
21. Gu G, Zhang H, Fan G, He S, Cai X, Shen X, et al. Comparison of minimally invasive versus open transforaminal lumbar interbody fusion in two-level degenerative lumbar disease. Int Orthop [Internet]. 2014 Apr 17;38(4):817–24. Available from: http://link.springer.com/10.1007/s00264-013-2169-x
22. Lee KH, Yeo W, Soeharno H, Yue WM. Learning Curve of a Complex Surgical Technique. J Spinal Disord Tech [Internet]. 2014 Oct;27(7):E234–40. Available from: https://journals.lww.com/00024720-201410000-00010

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ORIGINAL ARTICLE

Predictors of Intention to Defend Cyberbullying Victims among Egyptian Adolescents: A Cross-Sectional Study

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ABSTRACT

Background and Aim: Cyberbullying is a major challenge for adolescents. The bystanders play a decisive role in either reinforcing or reducing harm. Empathy, sympathy, moral disengagement, and prior victimization may shape bystander intentions; however, little is known about these factors among Egyptian youth. This study examined predictors of adolescents' intention to defend cyberbullying victims in Aswan, Egypt, and tested for gender differences. **Methods:** A cross-sectional survey was conducted with 596 secondary schools' students, selected using multistage random sampling. Standardized instruments measured empathy, sympathy, moral disengagement, cybervictimization, and intention to defend. Analyses included Spearman's rho, Mann–Whitney U tests, and multiple linear regression with gender interactions. **Results:** In total, 40.6% of participants were male, and 42.4% reported experiencing cybervictimization. Sympathy ($B = 0.59$, $p < 0.001$) and cognitive empathy ($B = 0.48$, $p < 0.001$) were significant predictors of intention to defend. Moral disengagement correlated negatively with sympathy ($\rho = -0.16$, $p < 0.01$) but showed no direct effect on intention to defend. Neither prior victimization nor gender differences reached statistical significance, and interaction analyses confirmed that predictive results were stable across males and females. **Conclusion:** Sympathy and cognitive empathy are key drivers of adolescents' defending intentions in cyberbullying contexts. Enhancing these socio-emotional skills could strengthen prosocial bystander behaviour and support safer digital environments.

Keywords: Bystander; cybervictimization; Empathy; Sympathy; Moral disengagement.

INTRODUCTION

Cyberbullying, defined as intentional and repeated aggression through digital technologies (1), is a growing global concern with significant psychological, social, and academic consequences for young people (2). Adolescents frequently experience cyberbullying as bystanders rather than as victims or perpetrators (3), and their reactions can shape the incident's progression and impact (4). While many remain passive, others support the aggressor or intervene to defend the victim, highlighting the need to understand what drives these responses (4).

Bystander behavior in cyberbullying is shaped by contextual factors, such as social relationships, the environment, and incident characteristics, and personal factors, including empathy, moral disengagement, self-efficacy, and previous experiences with bullying either offline or online. Empathy and moral disengagement detected among the influential factors (5). Empathy consistently emerges as a key predictor of defending behavior across gender, age, and cultural contexts (6).

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Conversely, greater moral disengagement is linked to passive outsider behavior rather than active efforts to defend victims (7). Evidence regarding the role of previous cybervictimization is mixed, with some studies suggesting it promotes defending and others finding no significant association (4,8,9). Gender differences also appear inconsistent, though females generally show a greater tendency to defend compared to males, whose responses may lean toward passivity or supporting the aggressor (4,10). This gender pattern is complex and interacts with factors such as empathy, moral disengagement, and perceived severity of the incident (4,10).

In Egypt, adolescents' internet and social media use is rapidly increasing, exposing them to higher risk of cyberbullying (11). Despite this, there is a shortage of research examining bystander intentions in the Egyptian context.

Therefore, this study examines how empathy, sympathy, moral disengagement, and prior cybervictimization predict adolescents' intention to defend cyberbullying victims, and whether these relationships differ by gender, among secondary school students in Aswan, Egypt. Understanding these predictors in a non-Western setting can inform culturally relevant school and community interventions to promote prosocial online behavior.

PATIENTS AND METHODS

1.1.Study Design and Setting

A quantitative, cross-sectional study examined predictors of adolescents' intention to defend victims against cyberbullying. It was conducted in Aswan City, located in the Aswan Governorate in Southern Egypt, across a representative sample of general secondary schools serving students in grades 10 to 12 (ages 15–18).

1.2.Participants and Sampling

The target population consisted of all students enrolled in general secondary education in Aswan City (N = 8,179). Eligibility required access to both a mobile phone and the internet. The study analyzed a final sample of 596 students, drawn from the 644 invited, after excluding 42 for incomplete responses (response rate = 92.5). The dataset was originally collected for a thesis with cyberbullying prevalence as primary outcome but is also suitable for the present investigation of intention to defend. To assess statistical sensitivity, a post hoc power analysis for linear regression was conducted using G*Power 3.1. With N = 596, six predictors, $\alpha = 0.05$, and power = 0.80, the analysis indicated that the available sample provides sufficient sensitivity to detect small effects.
A multistage random cluster sampling procedure was used: ten schools were selected with probability proportional to enrolment size, and within each, two classes from different grade levels were randomly chosen. All students present in the selected classes during data collection were invited to participate.

1.3.Measures

2.3.a. Adolescents' Intention to Defend Cyberbullying Victims

Adolescents' intention to defend against cyberbullying was assessed using the method described by Schultze-Krumbholz et al. (2020) (12), based on the behavioral willingness framework developed by Gibbons et al. (1998) (13). Defending was measured with a single-item scale: *"Suppose you see that someone is being threatened, insulted, or made fun of in an online group or chatroom. All the group*

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or chat members dislike this person. How likely is it that you will intervene and try to defend this person?" Responses were rated on a seven-point Likert scale ranging from 1 (not at all likely) to 7 (very likely).

2.3.b. Cyberbullying Victimization

Participants' experiences with cyberbullying victimization were assessed using the European Cyberbullying Intervention Project Questionnaire (ECIPQ) (14). The ECIPQ is a validated 22-item instrument, of which 11 items measure cybervictimization. Participants reported the frequency of these behaviors over the past two months on a 5-point Likert scale (0 = "never" to 4 = "several times a week"). Participants were categorized as cyber-victims if they scored 2 or higher (at least once a month) on any cybervictimization item and 1 or lower (once or twice) on all cyberaggression items. The ECIPQ has demonstrated strong psychometric properties across cultural contexts (14).

2.3.c. Empathy and sympathy

Empathy and sympathy were assessed using the Adolescent Measure of Empathy and Sympathy (AMES) (15). The AMES was specifically developed for adolescents, making it well-suited for examining empathy in this age group. It consists of three four-item subscales measuring affective empathy (sharing others' feelings.), cognitive empathy (understanding others' feelings.), and sympathy (concern for others' suffering), each rated on a 5-point Likert scale (0 = never to 4 = always). Subscale scores are calculated as the mean score of the items, with higher mean values indicating stronger empathic or sympathetic tendencies.

2.3.d. Moral Disengagement

Cyberbullying-related moral disengagement was measured using the Cyberbullying Moral Disengagement Questionnaire (CBMDQ-15) (16), a 15-item tool grounded in Bandura's theory of moral disengagement (17). Responses were given on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). A mean score across all items was calculated, with higher values indicating higher levels of moral disengagement.

In the current sample, internal consistency was acceptable to good, with Cronbach's α ranging from 0.65 to 0.82 across measures.

1.4.Ethical Considerations

Ethical approval was granted by the Faculty of Medicine, Aswan University (IRB No. Asw.Uni./931/6/24) in June 2024. Approvals were additionally obtained from the Central Agency for Public Mobilization and Statistics (CAPMAS) and the Aswan Educational Directorate. Written informed consent from parents and assent from adolescents were obtained before starting data collection.

1.5.Questionnaire Development, Pilot Testing and data collection

The study questionnaire was assembled from previously validated instruments. Validated Arabic versions were used when available; otherwise, a forward–backward translation by bilingual experts

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was conducted to ensure cultural and accuracy. A pilot test with 20 students led to minor adjustments, improving clarity and suitability for the study population.
Data were collected in Aswan secondary schools between November 2024 and January 2025. Following ethical approvals, parental consents and adolescents' assents were obtained. Students completed the anonymous questionnaire during school hours in small groups under researcher supervision. The process took 20–30 minutes, and questionnaires were reviewed on-site for completeness.

1.6.Statistical analysis

All analyses were conducted using IBM SPSS Statistics, Version 26.0. Continuous variables with non-normal distributions were summarized using medians and interquartile ranges (IQRs), and categorical variables with frequencies and percentages.

Bivariate associations with intention to defend victims were assessed using Spearman's rho (ρ) for continuous predictors (empathy, sympathy, moral disengagement) and Mann–Whitney U tests for categorical predictors (gender, victimization).

Multiple linear regression was then performed, including gender, cyberbullying victimization, empathy (cognitive and affective), sympathy, and moral disengagement. Continuous predictors were mean-cantered before creating interaction terms with gender. Both the main model and Interaction term model were examined. Results are reported as unstandardized (B) and standardized (β) coefficients, 95% confidence intervals (CI), and p-values. Multicollinearity was checked using variance inflation factors (VIF). Statistical significance was set at p (probability value) < 0.05 (two-tailed).

RESULTS

The study included 596 secondary school students with a median age of 16 years (range 14–17). Males made up 40.6% of participants, and 42.4% reported cyberbullying victimization. Median scores were 3.2 (IQR: 2.8–3.8) for sympathy, 2.9 (IQR: 2.3–3.5) for cognitive empathy, 2.3 (IQR: 1.5–3.0) for affective empathy, 2.1 (IQR: 1.7–2.6) for moral disengagement, and 6 (IQR: 4–7) for intention to defend **(Table 1).**

Table 1. Sample characteristics of adolescents in Secondary schools, Aswan city, Egypt, 2024 (N = 596)

Variable	**N (%) or Median (IQR)**
Age (years) -Median (range)	16 (14-17)
Gender	
Male	242 (40.6)
Female	354 (59.4)
Cyberbullying victimization	

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Non-victimized	343 (57.6)
Victimized	253 (42.4)
Sympathy score-mean score (0-4)	3.2 (2.8-3.8)
Cognitive empathy-mean score (0-4)	2.9 (2.3-3.5)
Affective empathy-mean score (0-4)	2.3 (1.5-3)
Moral disengagement	2.1 (1.7-2.6)
Intention to defend	6 (4-7)

Continuous variables are presented as median (interquartile range); Categorical variables are presented as N (%).

When comparing groups, intention to defend cyberbullying victims scores were similar across gender. Both males and females had a median of 6 (IQR: 4–7), with no significant difference (p = 0.333). Scores were also identical between victimized and non-victimized adolescents, each with a median of 6 (IQR: 4–7), and the difference was not significant (p = 0.695) **(Table 2).**

Table 2. Bivariate associations between gender and cyberbullying victimization and intention to defend cyberbullying victims among Secondary schools students, Aswan city, Egypt, 2024 (N = 596)

Predictor	**Intention to defend Median (IQR)**	**P value**
Gender		
Male	6 (4-7)	0.333
Female	6 (4-7)	
Cyberbullying victimization		
Victimised	6 (4-7)	0.695
Not victimized	6 (4-7)	

Variables are presented as median (interquartile range); Mann–Whitney test was used

Regarding correlation analysis, Intention to defend showed positive correlations with sympathy (ρ = 0.29, p < 0.01), cognitive empathy (ρ = 0.29, p < 0.01), and affective empathy (ρ = 0.14, p < 0.01). Sympathy was also positively associated with cognitive empathy (ρ = 0.44, p < 0.01) and affective empathy (ρ = 0.49, p < 0.01), while cognitive and affective empathy correlated with each other (ρ = 0.36, p < 0.01). Moral disengagement correlated negatively with sympathy (ρ = –0.16, p < 0.01) and showed no other significant associations **(Table 3).**

Table 3. Correlation Matrix of study variables among Secondary schools students, Aswan city, Egypt, 2024 (N = 596)

Variable	**1**	**2**	**3**	**4**	**5**
1. Sympathy	1				
2. Cognitive empathy	0.44**	1			

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3. Affective empathy	0.49**	0.36**	1		
4. Moral disengagement	-0.16**	-0.04	-0.08	1	
5. Intention to defend	0.29**	0.29**	0.14**	-0.04	1

Values are Spearman's rho coefficients; ** significant P value < 0.01 (2-tailed).

Regression analysis indicated that sympathy (B = 0.59, 95% CI: 0.35–0.83, p < 0.001) and cognitive empathy (B = 0.48, 95% CI: 0.27–0.69, p < 0.001) predicted intention to defend. Gender, previous exposure to cyberbullying victimization affective empathy, and moral disengagement, were not significant predictors. The model explained 11.3% of the variance (Adjusted R^2 = 0.104, p < 0.001) **(Table 4).**

Table 4. Multiple linear regression predicting adolescents' intention to defend cyberbullying victims among Secondary schools students, Aswan city, Egypt, 2024 (pooled model, N = 596)

Predictor	B	95% CI for B	β	P value
Gender (Female)	-0.18	(-0.51, 0.14)	-0.05	0.268
Cyberbullying Victimization (Victimized)	-0.05	(-0.35, 0.25)	-0.01	0.733
Sympathy	0.59	(0.35, 0.83)	0.23	**< 0.001**
Cognitive empathy	0.48	(0.27, 0.69)	0.20	**< 0.001**
Affective empathy	-0.12	(-0.30, 0.06)	-0.06	0.197
Moral disengagement	-0.03	(-0.26, 0.20)	-0.01	0.784

B = unstandardized regression coefficient; β = standardized regression coefficient; 95% CI = 95% confidence interval); Reference categories: Gender = male, cyberbullying Victimization = not victimized.; Model statistics: R^2 =0.113, Adjusted R^2 = 0.104, F =12.46, p < 0.001.

Including gender interaction terms did not alter the pattern. None of the interaction effects reached significance. Sympathy (B = 0.53, 95% CI: 0.19–0.87, p = 0.001) and cognitive empathy (B = 0.41, 95% CI: 0.09–0.72, p = 0.001) remained significant predictors. The model explained 11.7% of the variance (Adjusted R^2 = 0.101, p < 0.001) **(Table 5).**

Table 5. Multiple linear regression testing gender interactions in predicting intention to defend among Secondary schools students, Aswan city, Egypt, 2024 (N = 596)

Predictor	B	95% CI for B	β	P value
Gender (Female)	-0.12	(-0.54, 0.30)	-0.03	0.57
Cyberbullying Victimization (Victimized)	-0.01	(-0.48, 0.46)	0.00	0.96
Sympathy	0.53	(0.19, 0.87)	0.21	**0.001**
Cognitive empathy	0.41	(0.09, 0.72)	0.17	**0.001**
Affective empathy	-0.16	(-0.43, 0.12)	-0.08	0.26
Moral disengagement	0.12	(-0.23, 0.47)	0.04	0.49
Gender × Victimization	-0.07	(-0.69, 0.54)	-0.02	0.82
Gender × Sympathy	0.11	(-0.37, 0.59)	0.03	0.65
Gender × Cognitive empathy	0.14	(-0.28, 0.56)	0.04	0.52
Gender × Affective empathy	0.06	(-0.31, 0.42)	0.02	0.77
Gender × Moral disengagement	-0.25	(-0.71, 0.21)	-0.07	0.28

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B = unstandardized regression coefficient; β = standardized regression coefficient; 95% CI = 95% confidence interval; Reference categories: Gender = male, cyberbullying Victimization = not victimized.; Model statistics: R^2 =0.117, Adjusted R^2 = 0.101, F =7.05, p < 0.001

DISCUSSION

This study examined factors shaping adolescents' intentions to defend cyber-victim. Sympathy and cognitive empathy predicted defending intentions, while other factors showed no significant effects. Overall, socio-emotional processes appear central to promoting prosocial bystander behaviour online.

Cybervictimization experience

Experiencing cybervictimization did not predict adolescents' willingness to defend victims. Adolescents who had been targeted were no more likely to act on behalf of others compared to those without such experiences. This result aligns with work showing that victimization does not reliably translate into bystander action (9).

In contrast, some evidence links victimization to increased intervention. Adolescents with prior cybervictimization sometimes report stronger readiness to defend, particularly girls, whereas boys tend to remain more passive (8). Other research connects victimization with higher empathy, which in turn promotes defending behaviour (18). Egyptian adolescents also show that empathy mediates the relationship between victimization and defending, with previously victimized youth more likely to intervene (19). The mixed findings suggest that victimization experience alone is not a consistent driver of defending. In some contexts, it might increase sensitivity to others' suffering and strengthens willingness to act, while in others it may evoke avoidance or indifference.

Empathy and sympathy

Sympathy and cognitive empathy were reliable predictors of defending intentions, whereas affective empathy was not. Adolescents who could adopt another's perspective and feel sympathetic concern for victims were more motivated to act, while simply sharing emotions with others appeared less influential. This distinction suggests that cognitive empathy and sympathy drive prosocial motivation, whereas affective arousal alone may not.

Prior studies also emphasize this pattern: defending rises when adolescents engage in perspective-taking, and the predictive role of empathy is generally stable (6,12). Egyptian adolescents also demonstrate that empathy is tightly linked to willingness to defend (19).

The role of sympathy is particularly notable. Although sympathy has been associated with defending in traditional bullying (20), evidence in the cyberbullying context remains limited. The present findings strengthen claims that sympathy promotes defending bystander behaviour online. Compassionate concern has also been linked to prosocial forms of defending, while empathic anger may encourage more aggressive interventions (21). These findings emphasize the need to differentiate between various emotional and motivational processes when designing prevention efforts. Strengthening sympathy and perspective-taking may be especially effective for fostering prosocial bystander roles.

Moral disengagement

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Prior research has linked lower moral disengagement with stronger tendencies to defend (22). In our study, however, moral disengagement did not directly predict defending intentions. However, it was negatively correlated with sympathy: adolescents who justified harmful behaviors or minimized their seriousness showed less concern for others' suffering. This pattern suggests that moral disengagement may decline defending intentions indirectly by weakening socio-emotional capacities rather than by independently suppressing prosocial action. Thus, the negative link with sympathy suggests that lowering moral disengagement may allow sympathy to flourish and, in turn, promote defending behavior.

Gender differences

Gender did not influence adolescents' intentions to defend in this study: males and females reported similar readiness to intervene. Moreover, gender neither predicted defending nor moderated the associations between sympathy, moral disengagement, or victimization and defending. This aligns with research reporting no significant gender differences (23), although other studies often find higher defending among girls (8,24). The absence of gender effects in our sample may reflect the characteristics of the online environment. As cyber contexts reduce the physical and social risks of intervention, thereby lowering barriers that often discourage adolescents from engaging. These findings suggest that cultural norms and situational contexts may shape gender differences in defending more than individual traits.

1.7. Limitations of the study

This study is constrained by several methodological limitations. First, its cross-sectional design prevents establishing causal relationships between the examined predictors and adolescents' intention to defend. Second, the intention to defend was measured using a single-item scale, which may limit the depth and reliability of this construct. Third, all measures relied on self-report, which may introduce social desirability and recall bias. Finally, despite using multistage random sampling, the study was limited to secondary schools in Aswan City, which may restrict generalizability to other regions in Egypt or to younger adolescents.

CONCLUSION

Sympathy and cognitive empathy were the strongest predictors of adolescents' intentions to defend victims of cyberbullying, underscoring the importance of socio-emotional skills in promoting constructive bystander behaviour online. Strengthening perspective-taking and sympathetic concern within school programs may enhance students' readiness to intervene and support victims. These findings suggest that policies promoting socio-emotional learning could contribute to safer and more supportive online environments.

List of Abbreviations

AMES — Adolescent Measure of Empathy and Sympathy

CAPMAS — Central Agency for Public Mobilization and Statistics

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CBMDQ-15 — Cyberbullying Moral Disengagement Questionnaire

CI — Confidence Interval

ECIPQ — European Cyberbullying Intervention Project Questionnaire

IQR — Interquartile Range

P — probability value

ρ — Spearman's rho coefficient

Conflict of Interest & Funding statement
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REFERENCES

1. Hinduja S, Patchin JW. Offline consequences of online victimization: School violence and delinquency. J. Sch. Violence. 2007;6(3):89–112. doi: 10.1300/J202v06n03_06

2. Zhu C, Huang S, Evans R, Zhang W. Cyberbullying Among Adolescents and Children: A Comprehensive Review of the Global Situation, Risk Factors, and Preventive Measures. Front Public Health. 2021 Mar 11;9. doi: 10.3389/fpubh.2021.634909

3. Antoniadou N, Kokkinos CM, Fanti KA. Traditional and cyber bullying/victimization among adolescents: Examining their psychosocial profile through latent profile analysis. Int. J. Bully. Prev. 2019;1(2):85–98. https://doi.org/10.1007/s42380-019-00010-04.

4. Polanco-Levicán K, Salvo-Garrido S. Bystander roles in cyberbullying: A mini-review of who, how many, and why. Front. Psychol. 2021;12:676787. doi: https://doi.org/10.3389/fpsyg.2021.676787

5. Domínguez-Hernández F, Bonell L, Martínez-González A. A systematic literature review of factors that moderate bystanders' actions in cyberbullying. Cyberpsychology. 2018;12(4). https://doi.org/10.5817/CP2018-4-1

6. Cai Y, Zhou Y. The association between empathy and cyberbullying bystander positive intervention: a meta-analysis. Curr. Psychol. 2024;43(47):36104–14. https://doi.org/10.1007/s12144-024-07073-3

7. Lo Cricchio MG, García-Poole C, Te Brinke LW, Bianchi D, Menesini E. Moral disengagement and cyberbullying involvement: A systematic review. Eur. J. Dev. Psychol. 2021;18(2):271–311. https://doi.org/10.1080/17405629.2020.1782186

8. Wang S, Kim KJ. Effects of victimization experience, gender, and empathic distress on bystanders' intervening behavior in cyberbullying. Soc. Sci. J. 2021;61(4):853–62. https://doi.org/10.1080/03623319.2020.1861826

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9. Zhao Y, Chu X, Rong K. Cyberbullying experience and bystander behavior in cyberbullying incidents: The serial mediating roles of perceived incident severity and empathy. Comput. Hum. Behav. 2023;138:107484. doi: https://doi.org/10.1016/j.chb.2022.107484

10. Jeyagobi S, Munusamy S, Kamaluddin MR, Ahmad Badayai AR, Kumar J. Factors influencing negative cyber-bystander behavior: A systematic literature review. Front. Public Health. 2022;10:965017. doi: https://doi.org/10.3389/fpubh.2022.965017

11. Ramadan OME, Alruwaili MM, Alruwaili AN, Elsharkawy NB, Abdelaziz EM, El Badawy Ezzat RES, et al. Digital Dilemma of Cyberbullying Victimization among High School Students: Prevalence, Risk Factors, and Associations with Stress and Mental Well-Being. Children. 2024 Jun;11(6):634. doi: 10.3390/children11060634

12. Schultze-Krumbholz A, Zagorscak P, Hess M, Scheithauer H. The Influence of School Climate and Empathy on Cyberbystanders' Intention to Assist or Defend in Cyberbullying. Int. J. Bully. Prev. 2020 Mar 1;2(1):16–28. doi: 10.1007/s42380-019-00040-8

13. Gibbons FX, Gerrard M, Blanton H, Russell DW. Reasoned action and social reaction: willingness and intention as independent predictors of health risk. J. Pers. Soc. Psychol. 1998;74(5):1164. doi: 10.1037//0022-3514.74.5.1164

14. Del Rey R, Casas JA, Ortega-Ruiz R, Schultze-Krumbholz A, Scheithauer H, Smith P, et al. Structural validation and cross-cultural robustness of the European Cyberbullying Intervention Project Questionnaire. Comput. Hum. Behav. 2015 Sep;50:141–7. doi: 10.1016/j.chb.2015.03.065

15. Vossen HGM, Piotrowski JT, Valkenburg PM. Development of the Adolescent Measure of Empathy and Sympathy (AMES). Pers. Individ. Differ. 2015 Feb;74:66–71. doi: 10.1016/j.paid.2014.09.040

16. DAY S, LAZURAS L. The Cyberbullying-specific Moral Disengagement Questionnaire (CBMDQ-15). [Internet]. (Unpublished); 2016 [cited 2025 Jan 8]. Available from: https://shura.shu.ac.uk/12890/1/CBMDQ%2015%20Overview.pdf. Access date: 2025 Sep 5

17. Bandura A, Barbaranelli C, Caprara GV, Pastorelli C. Mechanisms of moral disengagement in the exercise of moral agency. J. Pers. Soc. Psychol. 1996;71(2):364–74. doi: 10.1037/0022-3514.71.2.364

18. Van Cleemput K, Vandebosch H, Pabian S. Personal characteristics and contextual factors that determine "helping,""joining in," and "doing nothing" when witnessing cyberbullying. Aggress. Behav. 2014;40(5):383–96. doi: 10.1002/ab.21534

19. Hanna SE. Unraveling The Impact of Past Bullying Experiences on Bystander Intervention in Cyberbullying Incidents. 45–1:(29)2024;2024 .المجلة العلمية لبحوث الإذاعة والتلفزيون. doi: 10.21608/ejsrt.2024.379498

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20. Feng T, Wang X, Chen Q, Liu X, Yang L, Liu S, et al. Sympathy and active defending behaviors among Chinese adolescent bystanders: A moderated mediation model of attitude toward bullying and school connectedness. Psychol. Sch. 2022;59(9):1922–36. doi: https://doi.org/10.1002/pits.22736

21. Steinvik HR, Duffy AL, Zimmer-Gembeck MJ. Adolescents' Compassion is Distinctively Associated With More Prosocial and Less Aggressive Defending Against Bullying When Considering Empathic Emotions and Costs. J. Adolesc. 2025; doi: 10.1002/jad.12513

22. Song J, Oh I. Factors influencing bystanders' behavioral reactions in cyberbullying situations. Comput. Hum. Behav. 2018 Jan;78:273–82. doi: 10.1016/j.chb.2017.10.008

23. Jia Y, Wu Y, Jin T, Zhang L. How are bystanders involved in cyberbullying? A latent class analysis of the cyberbystander and their characteristics in different intervention stages. Int. J. Environ. Res. Public Health. 2022;19(23):16083. doi: https://doi.org/10.3390/ijerph192316083

24. Olenik-Shemesh D, Heiman T, Eden S. Bystanders' behavior in cyberbullying episodes: Active and passive patterns in the context of personal–socio-emotional factors. J. Interpers. Violence. 2015;32(1):23–48. doi: https://doi.org/10.1177/0886260515585531

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ORIGINAL ARTICLE

Study Of Thyroid Function in Male Infertility in Aswan

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ABSTRACT

Background: Hyperthyroidism increases sex hormone-binding globulin (SHBG), raising total testosterone but lowering free testosterone. Conversely, hypothyroidism reduces SHBG, decreasing total testosterone with normal or slightly reduced free testosterone. **Objectives**: To explore the relationship between thyroid function and male infertility in Aswan, considering environmental and genetic factors. The study assessed thyroid hormones (TSH, T3, T4), semen parameters (sperm count, motility, morphology), and fertility-related hormones (FSH, LH, prolactin, total and free testosterone, estradiol). It also aimed to determine the prevalence of thyroid dysfunction among infertile men. **Methodology:** A cross-sectional analytic study was conducted on 60 males (30 infertile, 30 fertile), aged 20–50, attending Aswan University Hospital's Endocrinology Clinics from October 2024 to March 2025. **Results:** Significant differences ($p < 0.05$) were found between fertile and infertile men in clinical and lifestyle factors. Strong positive correlations were observed between TSH, free testosterone, and prolactin, as well as between free T4, free testosterone, and prolactin. **Conclusion**: Male infertility is significantly associated with clinical, hormonal, and lifestyle factors. Early detection and management of thyroid dysfunction and related hormonal imbalances may improve fertility outcomes and support personalized treatment strategies.

Keywords: male, fertility, hyperthyroidism, hypothyroidism.

INTRODUCTION:

Male infertility is a significant reproductive health issue, affecting approximately 7% of men worldwide. Several factors contribute to it, including genetic, iodine deficiency and pollutants **[1].**

Thyroid dysfunction can significantly impact male fertility by disrupting the hormonal balance essential for spermatogenesis. The hypothalamic-pituitary-gonadal (HPG) axis regulates reproductive hormones, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, testosterone, and estradiol (E2). Thyroid hormones influence this axis, and any imbalance can adversely affect sperm production and overall fertility **[2].**

Hyperthyroidism is associated with elevated levels of sex hormone-binding globulin (SHBG), leading to increased total testosterone but decreased free testosterone levels. This imbalance can result in reduced sperm quality and motility, contributing to infertility **[3].**
Hypothyroidism can lead to decreased SHBG levels, resulting in lower total testosterone but normal or slightly reduced free testosterone levels.

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This condition may also cause elevated prolactin levels (hyperprolactinemia), which can suppress gonadotropin-releasing hormone (GnRH) secretion, subsequently reducing LH and FSH levels, and impairing testicular function **[4].**

OBJECTIVES (AIM):

To investigate the relationship between thyroid function and male infertility in Aswan, considering local environmental and genetic factors.
To assess thyroid hormone levels (TSH, T3, T4) in infertile men compared to fertile controls.
To evaluate the correlation between thyroid dysfunction and semen parameters (sperm count, motility, morphology) and other hormones affecting the fertility like (FSH, LH, prolactin, Total and free testosterone, Estradiol (E2).
To determine the prevalence of thyroid dysfunction in infertile males in Aswan.

SUBJECT AND METHODS

This cross-sectional analytic study included 60 adult males (30 infertile and 30 fertile controls) aged 20–50 years who attended the Outpatient Endocrinology Clinics of Aswan University Hospital over a 6-month period (October 2024 – March 2025). Participants' medical records were reviewed to determine eligibility.

Inclusion Criteria

- Adult men aged 20–50 years.
- Men diagnosed with secondary infertility, defined as the inability to achieve pregnancy despite previously fathering a biological child through natural conception **[5].**
- Fertile men with confirmed paternity served as the control group.

Exclusion Criteria

- Men with primary infertility, defined as failure to achieve pregnancy after ≥12 months of regular, unprotected intercourse, with no prior history of fathering a child **[6].**
- Patients with known genetic infertility syndromes.
- Those receiving thyroid-related or hormonal therapy.
- Men with systemic illnesses known to affect fertility.

Data Collection

Each participant underwent a comprehensive medical, surgical, reproductive, and sexual history assessment. Specific emphasis was placed on:

- Lifestyle and behavioral factors: smoking, alcohol consumption, recreational drug use, dietary patterns, and physical activity levels.
- Occupational and environmental exposures (e.g., toxins, high temperature).
- Psychosocial stress factors.

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A physical examination was conducted for all subjects, including evaluation of testicular size and secondary sexual characteristics.

Laboratory Investigations

1. Blood Sampling

Approximately 5–7 mL of venous blood was drawn aseptically from the antecubital vein using a sterile vacutainer. Samples were collected into serum separator tubes (SSTs) and allowed to clot for 30 minutes at room temperature, then centrifuged at 3,000 rpm for 10 minutes. Serum aliquots were stored at –20 °C until biochemical analysis.

2. Thyroid Function Tests (TFTs)

Serum thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) levels were quantified using electrochemiluminescence immunoassay (ECLIA) on a *Cobas e411 Analyzer* (Roche Diagnostics, Germany) **[7].**

3. Reproductive Hormone Profile

Serum total testosterone, free testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and estradiol (E2) were measured using enzyme-linked immunosorbent assay (ELISA) kits supplied by *Abbott Diagnostics* **[8].**

Semen Analysis

Participants were instructed to maintain 3–5 days of sexual abstinence prior to sample collection. Semen samples were obtained by masturbation in a private room at the clinic into a sterile, wide-mouth plastic container, kept at 37 °C until examination.

All semen analyses were performed according to the **World Health Organization (WHO) 2021 laboratory manual [9]**, assessing the following parameters:

- **Liquefaction Time:** Evaluated within 30–60 minutes at 37 °C.
- **Sperm Concentration:** Determined using a Neubauer hemocytometer after dilution with a standardized sperm-counting reagent.
- **Sperm Motility:** Categorized as progressive (≥ 30%), non-progressive (≈ 12%), or immotile (< 58%).
- **Morphology:** Examined via Papanicolaou staining under light microscopy, evaluating ≥ 200 sperm per slide.
- **Vitality:** Determined using Eosin–Nigrosin staining to differentiate live and dead spermatozoa **[9].**

ETHICAL CONSIDERATIONS:

The study was approved by the ethical committee of Faculty of Medicine, Aswan University, Egypt. and oral confirmed consent was taken from the participants caregivers. Privacy of the patients during history taking and examination was assured. Confidentiality of all data was assured.

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STATISTICAL ANALYSIS:

Data analyzed using SPSS software. Pearson correlation assessed relationships between thyroid hormones and semen parameters, while t-tests and ANOVA compared means between groups. A p-value < 0.05 considered statistically significant.

RESULTS:

60 adult males (30 infertile and 30 healthy ones) aged 20-50 years included in the study, the duration of the study was 6 months.

Table [1] The quantitative demographic characteristic of participates according to study groups

	Population of study	Mean± SD	T	P
Age	healthy adult	34.53±8.862	-.218	0.828
	infertile adult males	35.03±8.900		
duration of infertility	healthy adult	0.00±0.000	10.310	0.000
	infertile adult males	98.80±52.490		
Assessment of libido score (Male Sexual Quotient (MSQ) (sexual desire)	healthy adult	10.80±2.809	8.619	0.000
	infertile adult males	5.37±2.008		
frequency of sexual intercourse	healthy adult	2.00±1.203	6.185	0.000
	infertile adult males	0.47±0.629		

Table [1]: demonstrated that the association between quantitative demographic characteristic of participates and the outcome groups control and infertile adult males which in-relation to participate age there was insignificant difference between study groups (t=-0.218 , P=0.828). On other hand the other variables such as duration of infertility, assessment of libido (sexual desire), and frequency of sexual intercourse the association were significant differences which all P values < 0.05.

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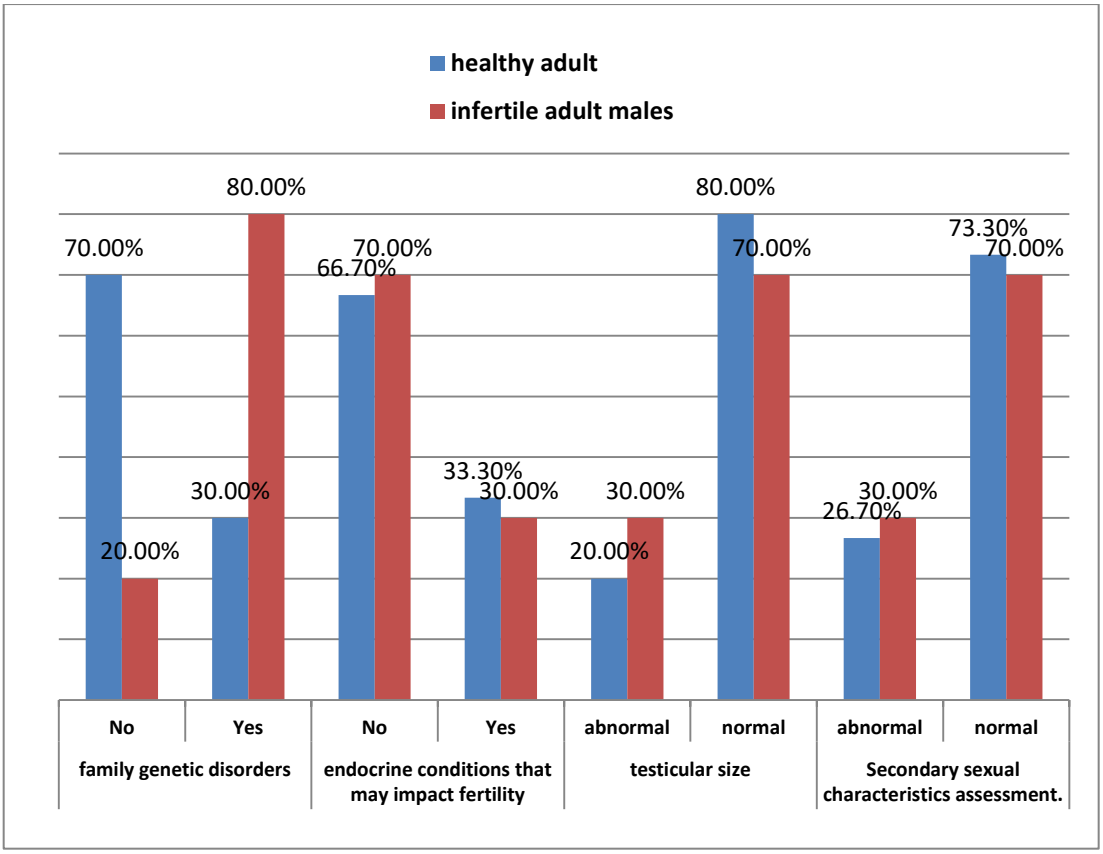

Figure [1] The qualitative demographic characteristic of participates according to study groups

Figure [1]: reported that the association between the qualitative demographic characteristic of participates and the outcome groups control and infertile adult males as regard to all non-modified risk factors were significant differences effect on occurred the infertile adult males. On other hand the associations were insignificant differences in-relation to endocrine conditions that may impact fertility, testicular size and Secondary sexual characteristics assessment.

Table [2] The association between thyroid function and reproductive parameters according to Study groups

Thyroid function		Study groups		Statistical tests	
		healthy adult	infertile adult males	X2	P
thyroid disorders	No	22(73.3%)	13(43.3%)	5.554a	0.018
	Yes	8(26.7%)	17(56.7%)		
thyroid disorders	No	22(73.3%)	13(43.3%)	12.381a	0.002
	Hypothyroidism	8(26.7%)	7(23.3%)		
	Hyperthyroidism	0(.0%)	10(33.3%)		
Motility Assessment	Immotile.	0(.0%)	12(40.0%)	46.050b	0.000
	non-progressively motile	3(10.0%)	17(56.7%)		
	progressively motile	15(50.0%)	1(3.3%)		
	rapidly progressive	12(40.0%)	0(.0%)		

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Morphology Assessment	less 200 sperm per slide	5(16.7%)	26(86.7%)	29.433a	0.000
	more 200 sperm per slide	25(83.3%)	4(13.3%)		
Vitality test:	dead sperm	1(3.3%)	26(86.7%)	42.088[a]	0.000
	live sperm	29(96.7%)	4(13.3%)		

Table [2]: showed that; the association between all thyroid function and all reproductive parameters were significant differences between study groups which the 56.7% of infertile adult males had thyroid disorders, and 33.3% of infertile adult males suffered from hyperthyroidism, which 86.7% of cases had less 200 sperm per slide with same percentage sperms were dead.

Table [3] The biochemical analysis according to study groups.

	Population of study	Mean± SD	t	p
TSH µIU/mL	healthy adult	1.9743±1.10677	-4.575-	.000
	infertile adult males	2.9811±0.47719		
Free T3 (FT3) pg/mL	healthy adult	2.587067±0.4401413	-11.347-	.000
	infertile adult males	3.855063±0.4253410		
Free T4 (FT4) ng/dL	healthy adult	1.285527±0.2899152	-7.417-	.000
	infertile adult males	1.73334±0.1591040		
Total Testosterone ng/dL	healthy adult	423.0623±185.45077	-4.821-	.000
	infertile adult males	710.8757±269.31269		
Free Testosterone pg/mL	healthy adult	17.646807±12.5799531	-1.597-	.116
	infertile adult males	24.166093±18.4891298		
Follicle-Stimulating Hormone FSH mIU/mL	healthy adult	4.5893±1.89426	-6.364-	.000
	infertile adult males	8.0932±2.34644		
Luteinizing Hormone LH mIU/mL	healthy adult	3.3403±1.22981	-7.856-	.000
	infertile adult males	6.0393±1.42419		
Prolactin ng/mL	healthy adult	8.9813±3.27922	-6.133-	.000
	infertile adult males	12.9173±1.26539		
Estradiol (E2) pg/mL	healthy adult	18.0844±5.08596	-6.773-	.000
	infertile adult males	28.5969±6.81209		
Liquefaction Time per minutes	healthy adult	25.97±13.810	15.501	.000
	infertile adult males	67.03±4.453		
Sperm Concentration million sperm per milliliter (mL) of semen	healthy adult	145.50±79.231	-9.581-	.000
	infertile adult males	6.73±3.999		

Table [3] shows that all biochemical parameters—including TSH, FT3, FT4, total testosterone, FSH, LH, prolactin, and estradiol—were significantly higher among infertile men compared with controls ($p < 0.05$). In contrast, sperm concentration was markedly lower in infertile males than in healthy controls (145.50 ± 79.231 vs. 6.73 ± 3.999 million/mL). The previously reported values (25.97 ± 13.810 vs. 67.03 ± 4.453) correspond to liquefaction time, not sperm

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concentration. Free testosterone was the only parameter that did not differ significantly between groups (p = 0.116).

Table [4] The correlation between the thyroid function TSH and reproductive parameters according to study groups.

Study groups			TSH µIU/mL
healthy adult	TSH µIU/mL	Pearson Correlation	1
		Sig. (2-tailed)	
	Total Testosterone ng/dL	Pearson Correlation	-.331-
		Sig. (2-tailed)	.074
	Free Testosterone pg/mL	Pearson Correlation	.876**
		Sig. (2-tailed)	.000
	Follicle-Stimulating Hormone FSH mIU/mL	Pearson Correlation	.309
		Sig. (2-tailed)	.097
	Luteinizing Hormone LH mIU/mL	Pearson Correlation	.036
		Sig. (2-tailed)	.851
	Prolactin ng/mL	Pearson Correlation	.934**
		Sig. (2-tailed)	.000
	Estradiol (E2) pg/mL	Pearson Correlation	.221
		Sig. (2-tailed)	.241
	Liquefaction Time per minutes	Pearson Correlation	.382*
		Sig. (2-tailed)	.037
	Sperm Concentration million sperm per milliliter (mL) of semen	Pearson Correlation	-.503**
		Sig. (2-tailed)	.005
infertile adult males	TSH µIU/mL	Pearson Correlation	1
		Sig. (2-tailed)	
	Total Testosterone ng/dL	Pearson Correlation	-.166-
		Sig. (2-tailed)	.381
	Free Testosterone pg/mL	Pearson Correlation	.636**
		Sig. (2-tailed)	.000
	Follicle-Stimulating Hormone FSH mIU/mL	Pearson Correlation	.339
		Sig. (2-tailed)	.066
	Luteinizing Hormone LH mIU/mL	Pearson Correlation	.097
		Sig. (2-tailed)	.612
	Prolactin ng/mL	Pearson Correlation	.766**
		Sig. (2-tailed)	.000
	Estradiol (E2) pg/mL	Pearson Correlation	.157
		Sig. (2-tailed)	.406
	Liquefaction Time per minutes	Pearson Correlation	-.039-
		Sig. (2-tailed)	.839
	Sperm Concentration million sperm per milliliter (mL) of semen	Pearson Correlation	.160
		Sig. (2-tailed)	.399
**. Correlation is significant at the 0.01 level (2-tailed).			
*. Correlation is significant at the 0.05 level (2-tailed).			

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Table [4]: showed that the correlation between the thyroid function TSH and reproductive parameters which in healthy control group, all correlation parameters were positive direct effect with highest strong r values as regard to Free Testosterone and Prolactin (r= 0.876 and 0.934, respectively), on other hand in-relation to Total Testosterone and Sperm Concentration million sperm per milliliter the correlation were negative indirect weak (r=-0.331 and -0.503, respectively). Furthermore, in relation to infertile adult males, also Total Testosterone correlation value was weak negative indirect r= -0.166, and Liquefaction Time r= -.039 on other hand the other parameters were positive direct correlation.

Table [5] The correlation between the thyroid function Free T4 and reproductive parameters

Population of study			Free T4 (FT4) ng/dL
healthy adult	Free T4 (FT4) ng/dL	Pearson Correlation	1
		Sig. (2-tailed)	
	Total Testosterone ng/dL	Pearson Correlation	-.208-
		Sig. (2-tailed)	.269
	Free Testosterone pg/mL	Pearson Correlation	.902**
		Sig. (2-tailed)	.000
	Follicle-Stimulating Hormone FSH mIU/mL	Pearson Correlation	.433*
		Sig. (2-tailed)	.017
	Luteinizing Hormone LH mIU/Ml	Pearson Correlation	.216
		Sig. (2-tailed)	.251
	Prolactin ng/mL	Pearson Correlation	.990**
		Sig. (2-tailed)	.000
	Estradiol (E2) pg/mL	Pearson Correlation	.406*
		Sig. (2-tailed)	.026
	Liquefaction Time per minutes	Pearson Correlation	.419*
		Sig. (2-tailed)	.021
	Sperm Concentration million sperm per milliliter (mL) of semen	Pearson Correlation	-.618**
		Sig. (2-tailed)	.000
infertile adult males	Free T4 (FT4) ng/dL	Pearson Correlation	1
		Sig. (2-tailed)	
	Total Testosterone ng/dL	Pearson Correlation	-.396*
		Sig. (2-tailed)	.030
	Free Testosterone pg/mL	Pearson Correlation	.785**
		Sig. (2-tailed)	.000
	Follicle-Stimulating Hormone FSH mIU/mL	Pearson Correlation	.058
		Sig. (2-tailed)	.760
	Luteinizing Hormone LH mIU/mL	Pearson Correlation	-.151-
		Sig. (2-tailed)	.426
	Prolactin ng/mL	Pearson Correlation	.819**
		Sig. (2-tailed)	.000
	Estradiol (E2) pg/mL	Pearson Correlation	-.106-
		Sig. (2-tailed)	.576
	Liquefaction Time per	Pearson Correlation	-.047-

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	minutes	Sig. (2-tailed)	.807
	Sperm Concentration million sperm per milliliter (mL) of semen	Pearson Correlation	.090
		Sig. (2-tailed)	.635
**. Correlation is significant at the 0.01 level (2-tailed).			
*. Correlation is significant at the 0.05 level (2-tailed).			

Table [5]: revealed that; the correlation between the thyroid function Free T4 and reproductive parameters which in healthy control group, all correlation parameters were positive direct effect with highest strong r values as regard to Free Testosterone and Prolactin (r= 0.902 and 0.990, respectively), on other hand in-relation to Total Testosterone and Sperm Concentration million sperm per milliliter the correlation were negative indirect weak (r=-0.208and -0.618, respectively). Furthermore, in relation to infertile adult males, also Total Testosterone correlation value was weak negative indirect r= -0.396, and Luteinizing Hormone LH r= -0.151and also in-relative to Estradiol and Liquefaction Time per minutes (r= -0.106 and-0.047, respectively). On other hand the other parameters were positive direct correlation.

DISCUSSION:

The present study identified significant associations between male infertility and several clinical, hormonal, and lifestyle parameters. Notably, more than half (56.7%) of infertile men exhibited thyroid dysfunction, with hyperthyroidism being the predominant form (33.3%). These findings support the hypothesis that alterations in thyroid function may negatively impact male reproductive performance through multifactorial hormonal mechanisms.

Non-modifiable demographic factors such as age and genetic background did not show a significant relationship with infertility in our cohort, which agrees with the non-significant age difference reported in Table 1 (P = 0.828). Likewise, age-related decline in semen quality has been well documented, particularly beyond the age of 40 years, where increased DNA fragmentation and reduced motility become evident **[10]**.

Although our results did not reveal a significant correlation between psychological stress and infertility, earlier studies have proposed that stress activates the hypothalamic–pituitary–adrenal axis and elevates cortisol, which may suppress gonadotropin secretion and impair sexual function. Kaltsas et al. **[11]** noted that such neuroendocrine activation also increases catecholamine release, resulting in vasoconstriction and reduced penile perfusion. The lack of significance in our data might be attributed to the small sample size or the transient nature of stress exposure among participants.

Similarly, diabetes did not show a statistically significant impact on fertility in our cohort. However, extensive literature has reported that poorly controlled or long-standing diabetes impairs Sertoli and Leydig cell functions, leading to reduced sperm count and motility **[12]**. The absence of this relationship in our findings may reflect effective glycemic control among diabetic participants or differences in disease duration.

Sexually transmitted infections were also not significantly associated with infertility in this study, differing from Dalal **[13]**, who emphasized that chronic epididymitis and orchitis can cause obstruction and antisperm antibody formation. This discrepancy could stem from underreporting or successful treatment of prior infections among our participants.

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Consistent with urological literature, our findings confirmed that testicular size alone is an unreliable marker of fertility when unaccompanied by hormonal or semen data **[14]**. This reinforces the necessity of comprehensive endocrine and seminal assessment in male fertility evaluation.

The high prevalence of thyroid dysfunction among infertile men in our cohort corresponds with findings by La Vignera and Vita **[15]**, who reported significant reductions in semen volume, motility, and morphology in both hyper- and hypothyroid men. Similarly, Hussein et al. **[16]** emphasized the essential role of thyroid hormones in spermatogenesis and sperm maturation. In our study, hyperthyroid patients demonstrated notably poor sperm motility and increased proportions of non-progressive or immotile spermatozoa, suggesting that excess thyroid hormone may induce oxidative stress, impair mitochondrial function, and disrupt sperm flagellar activity.

Biochemical analyses further supported these observations. Infertile men exhibited significantly elevated TSH, FT3, FT4, FSH, LH, prolactin, and estradiol (E2) levels compared with controls, whereas free testosterone levels did not differ significantly ($p = 0.116$). These hormonal patterns reflect a possible disruption of the hypothalamic–pituitary–gonadal axis secondary to thyroid imbalance. The absence of a significant difference in free testosterone could be explained by compensatory mechanisms maintaining bioavailable androgen despite altered SHBG levels. Comparable hormonal trends have been described in previous studies **[17]**.

Our findings regarding semen parameters corroborate those of Babatunde and Emokpae **[18]**, who demonstrated that both overt and subclinical thyroid dysfunction adversely affect sperm concentration, motility, and morphology through hormonal and oxidative mechanisms. Elevated FT3 and FT4 levels may enhance metabolic rate and reactive oxygen species generation, compromising sperm membrane integrity **[19]**. In our cohort, 86.7% of infertile men exhibited abnormal morphology (<200 sperm per slide) and similar proportions of non-viable sperm, reinforcing the adverse reproductive impact of thyroid dysregulation.

The strong positive correlations between TSH, FT4, and prolactin observed in our results highlight the intricate interplay between thyroid and pituitary functions. Hyperprolactinemia suppresses gonadotropin-releasing hormone (GnRH) secretion, thereby reducing LH and FSH output, which ultimately impairs spermatogenesis and testosterone production **[20]**. Elevated FSH and LH levels among infertile participants may also reflect compensatory pituitary stimulation secondary to testicular dysfunction **[21]**. Increased estradiol (E2) levels, as detected in our study, could be attributed to enhanced aromatase activity or obesity-related conversion of androgens to estrogens, a mechanism similarly described by Xu et al. **[22]**.

The observed decrease in libido and intercourse frequency among infertile participants is consistent with prior evidence linking infertility to psychological distress and sexual dysfunction. Agarwal et al. **[23]** reported that endocrine disturbances, particularly thyroid dysfunction, are commonly associated with reduced sexual desire and erectile performance. Similarly, Wischmann **[24]** highlighted that emotional burden and stress associated with infertility may lead to avoidance behavior and reduced coital frequency, which further limits conception chances.

Interestingly, our data showed significantly prolonged liquefaction time in infertile males (67 minutes vs. 25.9 minutes in controls). Delayed liquefaction is often associated with prostatic

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dysfunction or infection **[25]**, suggesting that accessory gland contribution to semen quality may also play a role in our infertile cohort.

The mean sperm concentration among healthy controls (145.5 × 10^6/mL) compared with infertile men (6.73 × 10^6/mL) was within the subfertile range defined by Guzick et al. **[26]**, who reported thresholds of <13.5 × 10^6/mL for sperm count and <32% for motility. This similarity strengthens the external validity of our findings.

Overall, the current results reinforce that thyroid dysfunction contributes to male infertility via multiple hormonal and metabolic pathways, influencing gonadotropin secretion, prolactin balance, sperm motility, and morphology. These findings emphasize the importance of routine thyroid screening in infertile men and early correction of thyroid abnormalities to optimize reproductive outcomes **[27]**.

CONCLUSION:

This study demonstrated a clear and statistically significant link between thyroid dysfunction and male infertility, highlighting the complex hormonal interplay between the thyroid, pituitary, and gonadal axes. More than half of the infertile men in our cohort exhibited abnormal thyroid function—predominantly hyperthyroidism—which was strongly associated with impaired semen quality, particularly reduced sperm motility, abnormal morphology, and decreased vitality.

The elevated levels of TSH, FT3, FT4, prolactin, FSH, LH, and estradiol observed in infertile males compared with controls underscore the pivotal influence of thyroid imbalance on reproductive hormones and spermatogenic efficiency. These findings reinforce that even subtle alterations in thyroid status can adversely affect male reproductive potential through hormonal dysregulation, oxidative stress, and impaired testicular function.

Clinically, our results advocate for routine evaluation of thyroid function as an integral part of the diagnostic workup in male infertility, especially in men presenting with unexplained or secondary infertility. Early detection and appropriate management of thyroid abnormalities may restore hormonal balance, improve semen parameters, and enhance fertility outcomes.

Future studies with larger sample sizes and longitudinal follow-up are warranted to further elucidate causal relationships and to determine whether targeted correction of thyroid dysfunction can significantly improve reproductive performance.

HUMAN ETHICS AND CONSENT TO PARTICIPATE

This study was reviewed and approved by the Institutional Ethics Committee of the Faculty of Medicine, Aswan University, under reference number Asw.Uni./1085/4/25. The approval was granted on April 7, 2025, for the research protocol titled “Study of Thyroid Function in Male Infertility in Aswan”.

All participants provided oral informed consent prior to inclusion in the study. The study was conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments.

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CONSENT FOR PUBLICATION

This manuscript does not contain any individual person's data in any form (including images, videos, or personal details). Therefore, consent for publication was not required.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and/or analyzed during the current study are not publicly available due to patient confidentiality and institutional policies but are available from the corresponding author on reasonable request.

CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest

FUNDING DECLARATION

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AUTHOR CONTRIBUTIONS STATEMENT

Mohamed A. Hassany conceptualized the study, collected clinical data, conducted the statistical analysis, and wrote the main manuscript text. Mariam A. Fawy contributed to the study design, literature review, and preparation of figures and tables. Both authors reviewed and approved the final manuscript.

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REFERENCES:

[1] Zimmermann MB, Boelaert K. Iodine deficiency and thyroid disorders. The lancet Diabetes & endocrinology. 2015 Apr 1;3(4):286-95.

[2] Sengupta P, Dutta S, Karkada IR, Chinni SV. Endocrinopathies and male infertility. Life. 2021 Dec 22;12(1):10.

[3] Mazzilli R, Medenica S, Di Tommaso AM, Fabozzi G, Zamponi V, Cimadomo D, Rienzi L, Ubaldi FM, Watanabe M, Faggiano A, La Vignera S. The role of thyroid function in female and male infertility: a narrative review. Journal of endocrinological investigation. 2023 Jan;46(1):15-26.

[4] AL-Humrany, E. K. A.. Effect of Hypothyroidism on Reproductive Hormones in Women (Doctoral dissertation, Ministry of Higher Education) (2019).

[5] Singh HD. Infertility in a crowded country: hiding reproduction in India. Indiana University Press; 2022 Dec 6.

[6] Garolla A, Pizzol D, Carosso AR, Borini A, Ubaldi FM, Calogero AE, Ferlin A, Lanzone A, Tomei F, Engl B, Rienzi L. Practical clinical and diagnostic pathway for the investigation of the infertile couple. Frontiers in endocrinology. 2021 Jan 19;11:591837.

[7] Abdi H, Faam B, Gharibzadeh S, Mehran L, Tohidi M, Azizi F, Amouzegar A. Determination of age and sex specific TSH and FT4 reference limits in overweight and obese individuals in an iodine-replete region: Tehran Thyroid Study (TTS). Endocrine Research. 2021 Jan 2;46(1):37-43.

[8] Omuse G, Maina D, Mwangi J, Wambua C, Radia K, Kanyua A, et al. Reference intervals for thyroid stimulating hormone and free thyroxine derived from neonates undergoing routine screening for congenital hypothyroidism at a university teaching hospital in Nairobi, Kenya: a cross sectional study. BMC Endocrine Disorders. 2016;16:21. doi:10.1186/s12902-017-0171-9

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Email: Mohamed.abass@aswu.edu.eg

[9] World Health Organization. WHO laboratory manual for the examination and processing of human semen. In Who laboratory manual for the examination and processing of human semen 2021.
[10] Zabihullah M, Kumar T, Jha K, Siddharth K, Ganguly A, Kumar Y, Mannan R, GANGULY A. The effect of age on semen quality among male partners of infertile couples: an observational study in a tertiary care center in eastern India. Cureus. 2023 Aug 3;15(8).
[11] Kaltsas A, Zikopoulos A, Dimitriadis F, Sheshi D, Politis M, Moustakli E, Symeonidis EN, Chrisofos M, Sofikitis N, Zachariou A. Oxidative stress and erectile dysfunction: pathophysiology, impacts, and potential treatments. Current Issues in Molecular Biology. 2024 Aug 14;46(8):8807-34.
[12] Maresch CC, Stute DC, Alves MG, Oliveira PF, de Kretser DM, Linn T. Diabetes-induced hyperglycemia impairs male reproductive function: a systematic review. Human reproduction update. 2018 Jan 1;24(1):86-105.
[13] Dalal R. Infection and Infertility. InGenital Infections and Infertility 2016 Jun 29. IntechOpen.
[14] Castle EP, Wolter CE, Woods ME. Campbell-Walsh urology (2021).
[15] La Vignera S, Vita R. Thyroid dysfunction and semen quality. International journal of immunopathology and pharmacology. 2018 May 5; 32:2058738418775241.
[16] Hussein RS. Thyroid Hormones and Their Role in Male Infertility: A Comprehensive Review. Journal of Biomedicine. 2024;14(2):231-4.

[17] Liu Q, Qiu Y, Jiang J, Long S, Zhu C, Chen G, Wen J. Causal association between thyroid function and the risk of infertility: a Mendelian randomization study. Frontiers in Endocrinology. 2024 Oct 4;15:1425639.
[18]Schlegel PN. Causes of azoospermia and their management. Reprod Fertil Dev. (2004); 16(5):561–572.

[19]Agarwal A, Parekh N, Selvam MK, Henkel R, Shah R, Homa ST, Ramasamy R, Ko E, Tremellen K, Esteves S, Majzoub A. Male oxidative stress infertility (MOSI): proposed terminology and clinical practice guidelines for management of idiopathic male infertility. World J Mens Health. (2019); 37(3):296–312.

[20]Wischmann T. Psychological impact of infertility and assisted reproduction. In: Handbook of Perinatal Clinical Psychology. Routledge; (2020). p. 61–81.

[21]Babatunde EM, Emokpae MA. A comprehensive review of thyroid dysfunction: hidden player in male infertility. Fertil Reprod. (2024); 6(4):166–175.

[22]Cannarella R, Condorelli RA, Mongioì LM, La Vignera S, Calogero AE. Molecular biology of spermatogenesis: novel targets of apparently idiopathic male infertility. Int J Mol Sci. (2020); 21(5):1728.

[23]Esteves SC, Zini A, Coward RM, Evenson DP, Gosálvez J, Lewis SE, Sharma R, Humaidan P. Sperm DNA fragmentation testing: summary evidence and clinical practice recommendations. Andrologia. (2021); 53(2):e13874.

[24]Rastrelli G, Corona G, Maggi M. The role of prolactin in andrology: what is new? Rev Endocr Metab Disord. (2015); 16(3):233–248.

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Email: Mohamed.abass@aswu.edu.eg

[25]Xu X, Sun M, Ye J, Luo D, Su X, Zheng D, Feng L, Gao L, Yu C, Guan Q. The effect of aromatase on the reproductive function of obese males. Horm Metab Res. (2017); 49(8):572–579.

[26]Mason MM, Schuppe K, Weber A, Gurayah A, Muthigi A, Ramasamy R. Ejaculation: the process and characteristics from start to finish. Curr Sex Health Rep. (2023); 15(1):1–9.

[27] Guzick DS, Overstreet JW, Factor-Litvak P, Brazil CK, Nakajima ST, Coutifaris C, Carson SA, Cisneros P, Steinkampf MP, Hill JA, Xu D. Sperm morphology, motility, and concentration in fertile and infertile men. N Engl J Med. (2001); 345(19):1388–1393.

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ORIGINAL ARTICLE

Complications of Laparoscopic Left Hemicolectomy in Left Colon Cancer

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ABSTRACT

Background: Colorectal cancer is a common malignancy worldwide. Laparoscopic colectomy offers less postoperative pain, faster recovery, and comparable oncological results but remains technically demanding with potential complications. **Aim**: To assess postoperative complications and short-term outcomes after laparoscopic left hemicolectomy in patients with left-sided colon cancer. **Patients and Methods:** A prospective study was conducted on 50 patients aged 35-75 years with histologically confirmed left colon adenocarcinoma who underwent laparoscopic left hemicolectomy at Aswan University Hospital between December 2022 and April 2025. Preoperative evaluation, operative data, pathology, and postoperative outcomes were analysed using SPSS version 26. **Results:** The mean age was 58.3 ‡ 9.6 years; 56% were male. Hypertension (38%) and diabetes (32%) were the main comorbidities. Conversion to open surgery occurred in 10%. Median lymph node yield was 19, and RO resection was achieved in 96%. Overall morbidity was 28%, major complications (Clavien-Dindo ≥ III) 8%, reoperation 6%, and mortality 2%. **Conclusion:** Laparoscopic left hemicolectomy is feasible and safe, with acceptable morbidity and satisfactory short-term oncological outcomes.

Key Words: Laparoscopic left hemicolectomy, colon cancer, complications, morbidity, Aswan University Hospital

INTRODUCTION

Globally, colorectal cancer ranks as the third most prevalent malignancy, with the left colon representing a common location for tumour development (1,2). Surgery continues to serve as the primary curative intervention, and laparoscopic approaches have gained increasing adoption owing to benefits including diminished postoperative pain, accelerated patient recovery, and equivalent oncological outcomes (3,4,5).

Nevertheless, performing laparoscopic left hemicolectomy demands sophisticated surgical expertise and presents potential complications including anastomotic leak, haemorrhage, ileus, and surgical site infection (6,7,8). Comprehending these complication profiles within specific patient populations is essential for enhancing clinical outcomes and informing surgical decision-making (5,9).

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The present prospective observational study sought to assess the complications and immediate postoperative outcomes of laparoscopic left hemicolectomy among left colon cancer patients treated at Aswan University Hospital.

PATIENTS AND METHODS

A prospective observational study conducted at Aswan University Hospital between December 2022 and April 2025.
Inclusion criteria: included patients aged 35-75 years with histologically confirmed left colon adenocarcinoma scheduled for laparoscopic left hemicolectomy.

Exclusion criteria: were emergency surgeries, synchronous tumors requiring extended resections, and patients unfit for general anesthesia.

All patients underwent full preoperative evaluation: demographic data, comorbidities, medical/surgical history, physical examination, routine labs (CBC, albumin, coagulation profile, renal/liver function, blood glucose, CEA), radiological workup with contrast-enhanced CT abdomen/pelvis, CT chest, and bone scan, and colonoscopy with biopsy. Surgery consisted of laparoscopic left hemicolectomy with oncological resection. Pathology included tumor type, grade, TNM stage, lymph node retrieval, and resection margins.

Data analysis was conducted utilizing SPSS version 26 software. Continuous data were reported as mean ±SD, whilst categorical data were presented as percentages.

Surgical methods: In the context of this study, radical left hemicolectomy is defined as complete excision of the primary tumour alongside removal of all associated lymph nodes, with the left colic artery ligated at its point of origin.

1. Patient Preparation & Positioning

- General anesthesia, endotracheal intubation.
- Supine position, legs apart (modified lithotomy).
- Tilt table to Trendelenburg with slight right tilt.
- Urinary catheter and nasogastric tube inserted.
- Prophylactic antibiotics, DVT prophylaxis.

2. Port Placement

- Pneumoperitoneum established (open/Hasson or Veress).
- Typical 4–5 ports:
    - 10–12 mm camera port (infra- or supra-umbilical).
    - 12 mm working port (right lower quadrant).
    - 5 mm assistant port(s) (right upper, suprapubic).
    - 5 mm left upper quadrant (for retraction, if needed) (Figure 1).

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Figure 1. Port placement configuration for laparoscopic left hemicolectomy showing typical 4-5 trocar positions

3. Exploration
   - Laparoscopic inspection to rule out peritoneal or liver metastases.
   - Confirm resectability.
4. Mobilization of Sigmoid & Descending Colon
   - Identify the inferior mesenteric vessels (IMA, IMV).
   - The peritoneum is incised along the white line of Toldt (positioned laterally to the descending colon).
   - The sigmoid and descending colon are mobilized in a medial direction (utilizing either medial-to-lateral or lateral-to-medial technique) (Figure 2).

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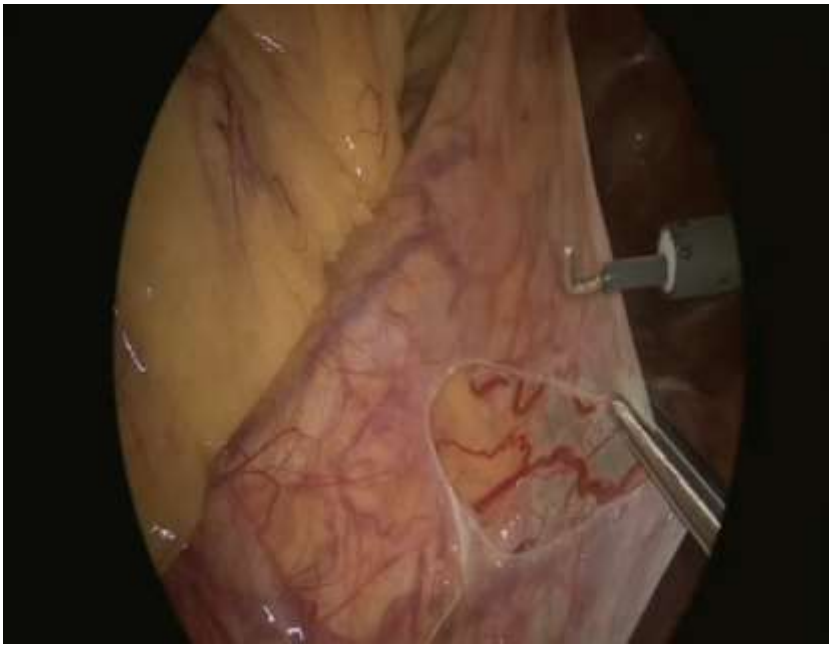

Figure 2. Laparoscopic view of mobilization of the sigmoid and descending colon along the line of Toldt

5. Vascular Control
   - The inferior mesenteric artery (IMA) is ligated either at its point of origin or distally to the left colic artery (adhering to oncological principles: high tie).
   - The inferior mesenteric vein (IMV) is transected and ligated in proximity to the ligament of Treitz.
   - Energy device or clips/stapler used (Figure 3-4).

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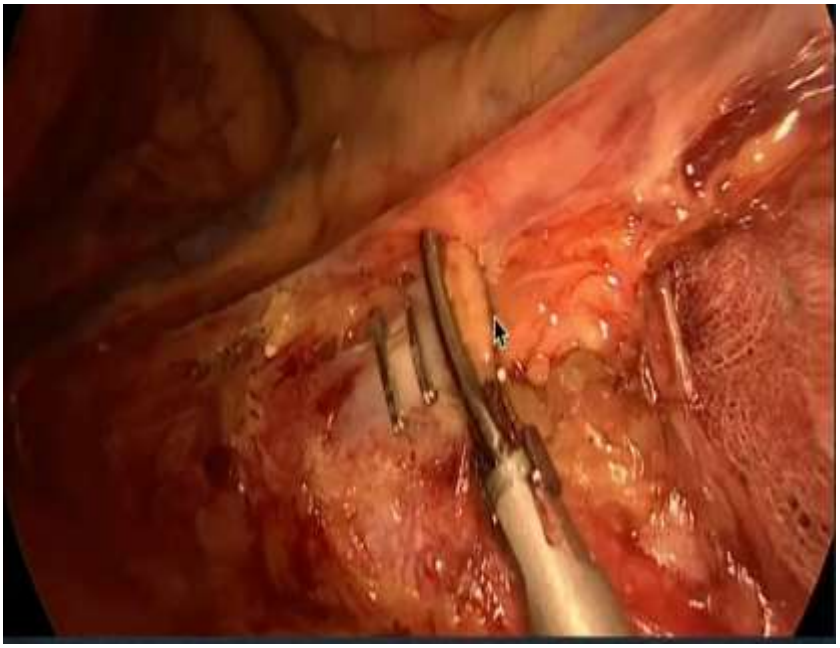

Figure 3. Intraoperative identification and isolation of the inferior mesenteric vessels prior to ligation

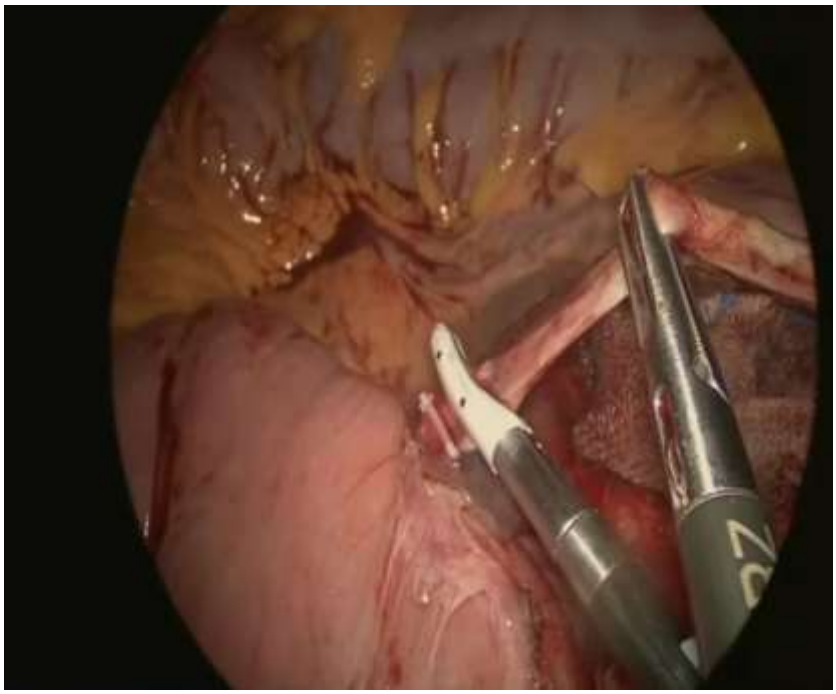

Figure 4. Vascular control showing ligation of the inferior mesenteric artery using energy device

6. Mobilization of Splenic Flexure (if needed)
   - Dissect along splenocolic ligament.
   - Divide attachments to pancreas and spleen (careful to avoid splenic injury).
   - Achieve tension-free anastomosis (Figure 5).

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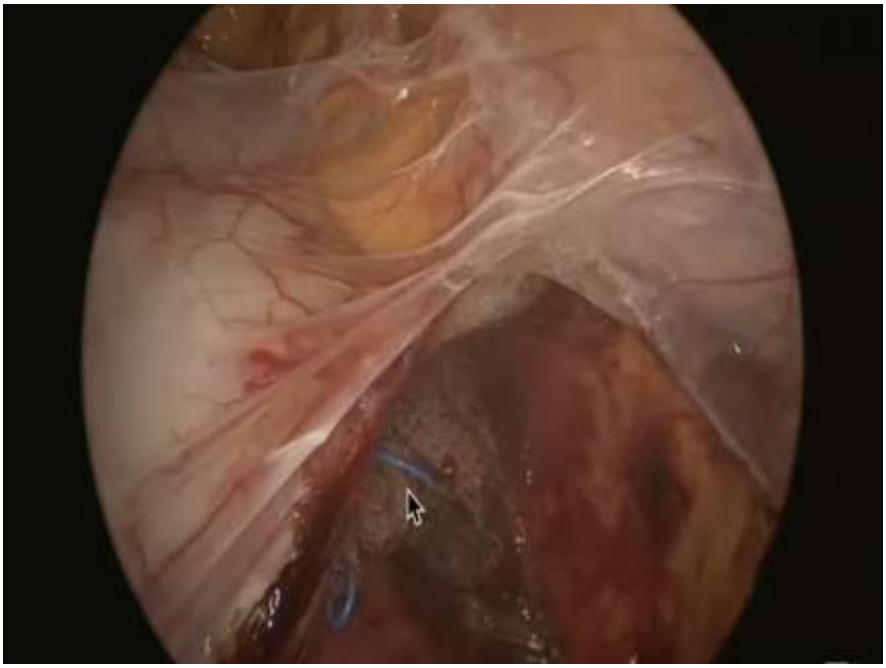

Figure 5. Mobilization of the splenic flexure with division of splenocolic attachments

7. Resection of Left Colon
   - Colon segment (usually from distal transverse colon to upper sigmoid) mobilized completely.
   - Mesocolon dissected to ensure adequate lymphadenectomy.
   - Divide bowel with laparoscopic linear stapler or exteriorize through a small incision (mini-laparotomy with wound protector) (Figure 6).

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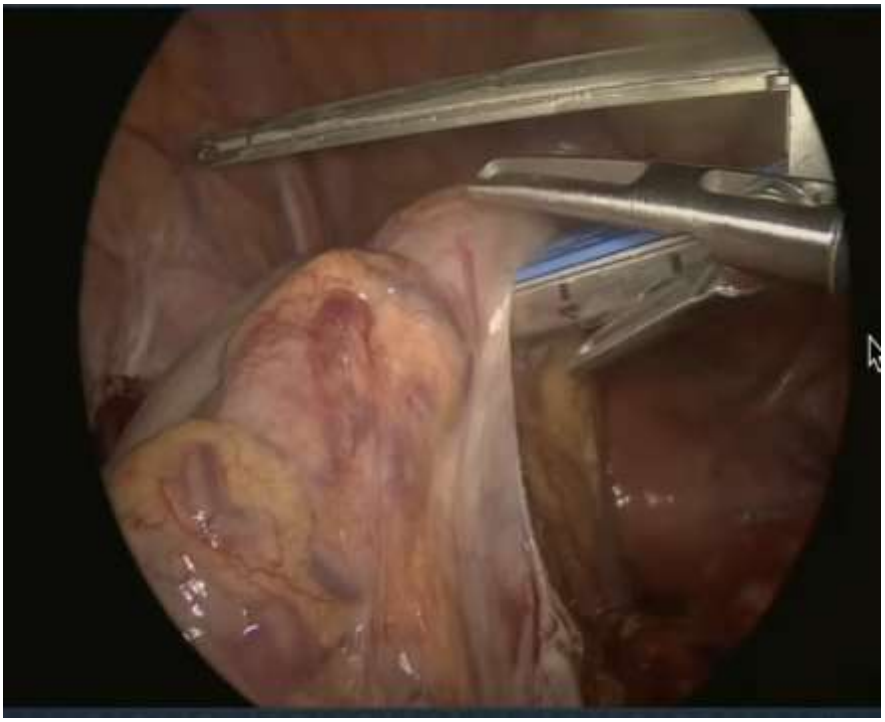

Figure 6. Division of the left colon using laparoscopic linear stapler during resection phase

8. Anastomosis
   - Extracorporeal or intracorporeal anastomosis:
     - Most commonly, colorectal stapled anastomosis (circular stapler per anus).
     - Ensure well-vascularized, tension-free ends.
     - Leak test (air or methylene blue) (Figure 7-8-9).

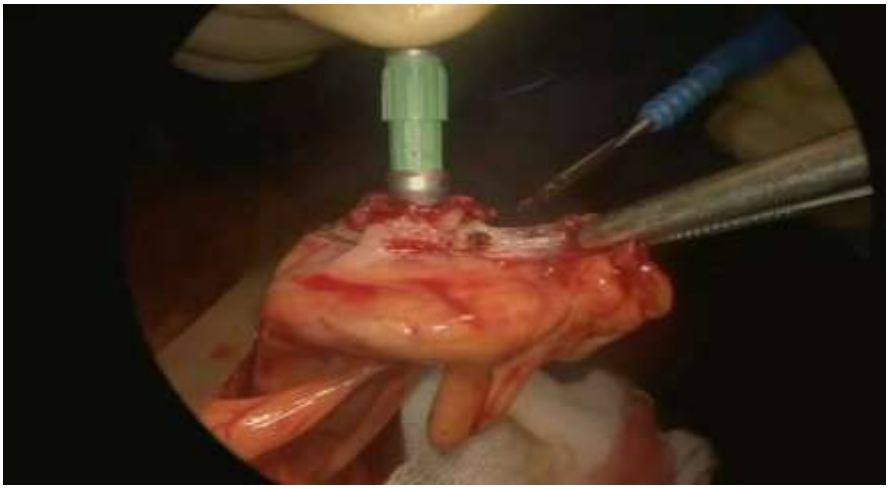

Figure 7. Exteriorized bowel preparation for colorectal anastomosis via mini-laparotomy

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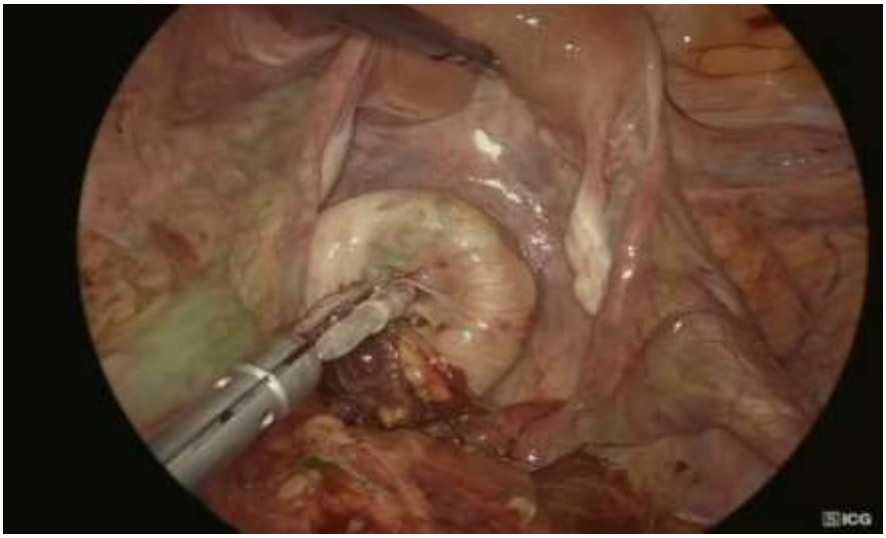

Figure 8. Intracorporeal view of circular stapled colorectal anastomosis formation

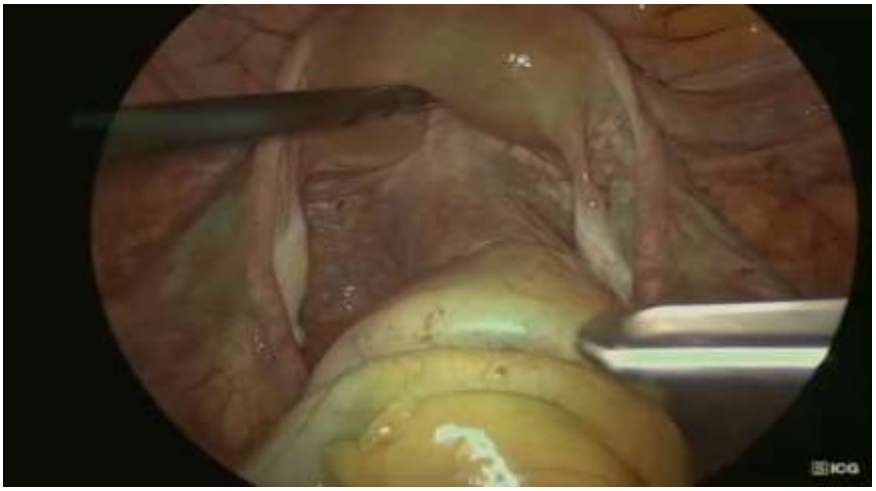

Figure 9. Leak test of completed anastomosis using methylene blue dye insufflation

RESULTS

Patient Characteristics

- Mean age: 58.3 ± 9.6 years
- Sex distribution: 28 males (56%), 22 females (44%)
- Comorbidities: hypertension 38%, diabetes mellitus 32%, coronary artery disease 10%, COPD 6%
- Hypoalbuminemia (<3.5 g/dL): 40%. **Table 1.**

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Table 1. Baseline demographic and clinical characteristics of patients undergoing laparoscopic left hemicolectomy (n=50)

Variable	Value
Number of the patient	50
Mean age	58.3±9
Sex	28 males(56%),22females(44%)
Hypertension	19(38%)
Diabetes mellitus	16(32%)
CAD	5(10%)
COPD	3(6%)
Hypoalbuminemia(<3.5 g/dl)	20(40%)

Operative Findings

- Mean operative time: 172 ± 35 min
- Conversion to open surgery: 5 cases (10%)

Pathology

- Histology: adenocarcinoma in all cases
- Tumor grade: well-differentiated 12%, moderately differentiated 62%, poorly differentiated 26%
- Tumor stage (T): T2 (10%), T3 (60%), T4 (30%)
- Nodal stage: N0 (56%), N1 (28%), N2 (16%)
- Median lymph node yield: 19 (IQR 15–23)
- R0 resection: 96%

Table 2. Histopathological characteristics and oncological outcomes of resected left colon cancer specimens

Parameter	Findings
Histology	Adenocarcinoma(100%)
Differentiation	Well 12%, moderate 62%, poor 26%
T stage	T2: 10%, T3: 60%, T4: 30%
Nodal stage	N0: 56%, N2: 28%N2:16%
Median lymph node yield 19	IQR 15-23
Resection margin	R0: 96%

Postoperative Complications

- Overall complications: 14 patients (28%)

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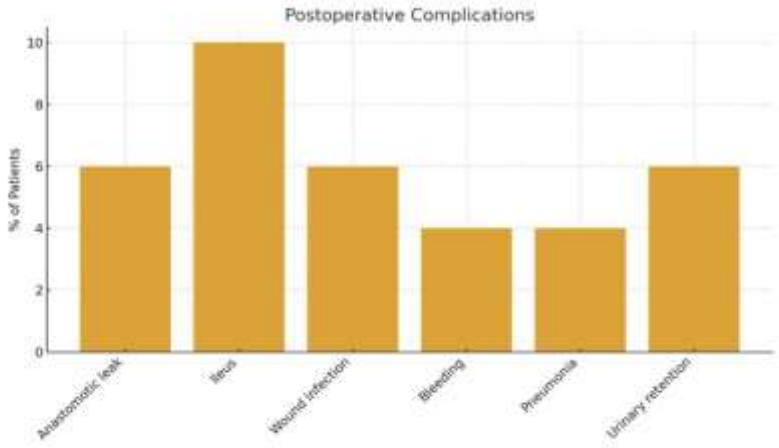
- Anastomotic leak: 3 (6%)
- Ileus: 5 (10%)
- Wound infection: 3 (6%)
- Bleeding requiring transfusion: 2 (4%)
- Pneumonia: 2 (4%)
- Urinary retention: 3 (6%)
- Major complications (CD ≥ III): 4 (8%)
- Reoperation: 3 (6%)
- Readmission: 5 (10%)
- 30-day mortality: 1 (2%)

Table 3. Incidence and distribution of postoperative complications following laparoscopic left hemicolectomy

Complication	Incidence
Overall complications	14% (28%)
Anastomotic leak	3 (6%)
Ileus	5% (10%)
Wound infection	3 (6%)
Bleeding	2 (4%)
Pneumonia	2 (4%)
Urinary retention	3 (6%)
Major complications (CD>III)	4 (8%)
Reoperation	3 (6%)
30 days mortalitiy	1 (2%)



DISCUSSION

The findings of this study indicate that laparoscopic left hemicolectomy performed for left-sided colon cancer yields acceptable morbidity rates and minimal mortality, confirming its status as a safe and efficacious surgical option for suitably selected patients. The postoperative complication rate observed in this cohort was 28%, aligning with internationally reported data wherein

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complication rates following laparoscopic colectomy generally range from 20% to 35%, influenced by factors including case complexity and institutional surgical expertise (4,5,7). The most frequent complications observed were anastomotic leak, wound infection, and postoperative ileus—findings that parallel the experiences reported in large multicenter trials and meta-analyses.

The anastomotic leak rate of 6% in our cohort falls within the expected range of 3–8% reported in previous laparoscopic colorectal series (6,10). Although anastomotic leakage remains one of the most feared complications due to its association with increased morbidity, prolonged hospitalization, and adverse oncologic outcomes, its rate in this study reflects adequate surgical technique, tension-free anastomosis, and careful patient selection. Early detection and prompt management of leaks were critical in minimizing their impact on recovery.

The conversion rate of 10% also compares favorably with global literature, where conversion rates range from 5% to 15% depending on tumor location, surgeon experience, and intraoperative difficulty (5,11). Conversion was primarily necessitated by dense adhesions, difficult splenic flexure mobilization, and locally advanced tumors. Conversion should not be regarded as a failure but rather as a safety measure to prevent intraoperative complications and ensure oncologic completeness(13,14)

Importantly, R0 resection was achieved in 96% of cases, confirming the oncologic adequacy of laparoscopic resection. The mean lymph node yield and negative resection margins in our study were comparable to international standards and randomized controlled trials (4,12). These findings affirm that laparoscopy provides equivalent oncologic clearance to open surgery when performed by experienced colorectal surgeons adhering to oncologic principles.

Regarding immediate postoperative results, the present findings reinforce the well-documented benefits of laparoscopic colectomy, such as diminished pain levels, earlier patient mobilization, and reduced length of hospitalization relative to traditional open surgical techniques, as evidenced in the COST, COLOR, and CLASICC trials. The minimal postoperative mortality and positive recovery outcomes documented in this cohort further underscore the advantages of minimally invasive surgery in managing colorectal cancer.

Certain limitations must nonetheless be admitted. This study was conducted at a single tertiary center with a small sample size (n = 50), which limits the generalizability of the findings to larger populations. Furthermore, oncologic long-term results including disease-free and overall survival were not reported in this paper, and further studies with longer follow-up would be required to assess such endpoints. The effect of the so-called “learning curve” for the surgeon, as well as operator experience, upon the rate of adverse events may present another confounding variable. The above limitations notwithstanding, this study does provide valuable information concerning the practical results of laparoscopic left hemicolectomy in the techniques of the surgeon in practice in a developing setting of regional health care, thus adding to the increasing body of evidence which does support its safety and efficacy.

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Future studies should include multicenter prospective studies with larger sample size, uniformity of perioperative management and prolonged oncologic follow-up period, to more adequately elucidate the generalizability and long-term effectiveness of the findings.

CONCLUSION

Laparoscopic left hemicolectomy treats left colon cancer effectively. The procedure produces positive immediate postoperative results with acceptable adverse event rates. Careful patient selection, optimization of comorbidities, and experienced surgical teams improve surgical outcomes.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2021: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–249.

2. Arnold M, Sierra MS, Laversanne M, et al. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683–691.

3. Lacy AM, García-Valdecasas JC, Delgado S, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet. 2002;359(9325):2224–2229.

4. Fleshman J, et al. Laparoscopic colectomy for cancer is not inferior to open surgery: long-term outcomes of the COST trial. Ann Surg. 2007;246(4):655–662.

5. Jayne DG, Guillou PJ, Thorpe H, et al. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC trial group. J Clin Oncol. 2007;25(21):3061–3068.

6. Braga M, et al. Complications after laparoscopic vs open resection for colorectal cancer. Arch Surg. 2002;137(2):127–132.

7. Veldkamp R, et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomized trial. Lancet Oncol. 2005;6(7):477–484.

8. Green BL, Marshall HC, Collinson F, et al. Long-term follow-up of the MRC CLASICC trial of conventional versus laparoscopically assisted resection in colorectal cancer. Br J Surg. 2013;100(1):75–82.

9. Martínez-Pérez A, Carra MC, Brunetti F, de'Angelis N. Short-term clinical outcomes of laparoscopic vs open colectomy for colon cancer: a systematic review and meta-analysis of randomized controlled trials. World J Gastroenterol. 2017;23(44):7896–7910.

10. Biondi A, Grosso G, Mistretta A, et al. Laparoscopic vs open approach for colorectal cancer: short- and long-term outcomes comparison. J Laparoendosc Adv Surg Tech A. 2016;26(8):695–702.

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11. Lujan J, Valero G, Hernandez Q, et al. Laparoscopic versus open colectomy for colorectal cancer: a prospective randomized trial. Br J Surg. 2002;89(9):1061–1065.

12. Kitano S, Inomata M, Mizusawa J, et al. Survival outcomes following laparoscopic versus open D3 dissection for stage II or III colon cancer. Lancet Gastroenterol Hepatol. 2017;2(4):261–268.

13. Negrut RL, et al. Systematic Review and Meta-Analysis of Laparoscopic Colorectal Surgery Outcomes — systematic review/meta-analysis concluding that conversion often reflects intraoperative challenges/unexpected anatomy and should not be viewed simply as a shortfall of the laparoscopic method. 2024.

14. Turkish Journal of Colorectal Disease — The Effect of Resection Methods on Outcomes in Colorectal Cancers: Does Conversion Matter? — recent review noting wide variation in conversion rates and emphasizing that conversion is often a necessary, safety-driven action rather than a complication. 2023–2024.

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ORIGINAL ARTICLE

Serum Interleukin 6 in Chronic Obstructive Pulmonary Disease patients and Its Relation to Severity and Acute Exacerbation

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ABSTRACT

Background: Globally, Chronic Obstructive Pulmonary Disease (COPD) represents a leading contributor to long-term illness and death. The inflammatory cytokine Interleukin-6 (IL-6) has been implicated in initiating and sustaining persistent inflammatory responses. Our objective was to evaluate circulating IL-6 concentrations in individuals with COPD and determine their association with disease severity and frequency of acute exacerbations. **Methods**: We performed a case-control investigation at a hospital setting, enrolling 50 COPD patients (age range: 40-80 years) alongside 50 healthy individuals matched for age and sex. Study participants completed comprehensive physical assessments and spirometric evaluations, including Forced Expiratory Volume in one second (FEV1), Forced Vital Capacity (FVC), Peak Expiratory Flow (PEF), and Forced Expiratory Flow between 25-75% of vital capacity (FEF25-75). Serum IL-6 concentrations were quantified using enzyme-linked immunosorbent assay (ELISA). **Results**: Among COPD patients, serum IL-6 concentrations demonstrated strong positive associations with both CAT and MMRC scoring systems, while exhibiting significant inverse relationships with FVC, FEV1, FEF25-75, and six-minute walking distance (all $p<0.001$). **Conclusions**: Circulating IL-6 levels demonstrate potential utility as a biomarker for monitoring COPD disease progression and predicting acute exacerbations, suggesting the need for additional research exploring its therapeutic applications.

Keywords: Serum biomarkers, Interleukin-6, Chronic Obstructive Pulmonary Disease, Acute Exacerbation.

INTRODUCTION

Worldwide, COPD stands as a significant source of chronic illness and premature death, affecting countless individuals who endure the condition for extended periods before experiencing fatal complication [1, 2]. A critical therapeutic objective involves minimizing exacerbation episodes; consequently, predicting exacerbation rates during the initial post-diagnosis year holds considerable clinical importance [3].

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Historically, COPD was viewed as a disease confined primarily to pulmonary tissue. However, contemporary understanding recognizes COPD as involving widespread systemic inflammatory processes.[3] Multiple inflammatory markers—encompassing tumor necrosis factor-alpha (TNF-α), C-reactive protein (CRP), fibrinogen, and activated white blood cells—have been documented in individuals with COPD, substantiating the systemic inflammatory component [4].

As a soluble pro-inflammatory cytokine, Interleukin-6 (IL-6) undergoes local synthesis at inflammation sites during initial immune responses before disseminating to target tissues [5]. This molecule serves essential functions in perpetuating chronic inflammatory states and contributing to pain pathway activation.

Elevated IL-6 production has been observed across numerous inflammatory and autoimmune conditions, spanning asthma, systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, and various pulmonary pathologies. Furthermore, IL-6 overexpression has demonstrated connections to inflammation-driven cancers, particularly pulmonary malignancies.[6, 7]

Accumulating scientific literature suggests a meaningful relationship between IL-6 concentrations and COPD pathophysiology. Therefore, our investigation sought to examine serum IL-6 levels in COPD patients and establish their correlation with disease severity and acute exacerbation patterns.

PATIENTS AND METHODS

According to GOLD 2023 guidelines, we classified acute exacerbation of COPD (AECOPD) as a sudden deterioration in respiratory manifestations necessitating therapeutic intervention beyond baseline management. Diagnostic confirmation relied on the presence of worsening breathlessness, increased sputum production, and/or changes in sputum characteristics (purulence), warranting treatment with antibiotics, systemic corticosteroids, or hospital admission. We documented exacerbation patterns during the 12-month period preceding enrollment through retrospective chart review and direct patient questioning, categorizing them as: zero exacerbations, a single moderate episode, two or more moderate episodes, or one or more events requiring inpatient care.

Our case-control investigation was performed at a hospital facility, encompassing 50 individuals diagnosed with COPD alongside 50 age- and gender-matched healthy controls between 2023 and 2024. COPD participants were enrolled during periods of clinical stability, characterized by an absence of acute deterioration necessitating medication adjustments or hospital admission during the prior four weeks, through the pulmonary outpatient clinic at Aswan University Hospital. Exacerbation history over the preceding year was gathered retrospectively via medical chart extraction and structured patient interviews. All study participants provided written informed consent. Institutional review board approval was secured from the Ethics Committees of both the Chest Department and Clinical Pathology Department at Aswan University Hospital.

Exclusion criteria We excluded individuals with documented histories of alternative respiratory conditions including asthma or allergic disorders, as well as those suffering from other chronic systemic diseases.

Comprehensive data collection included patient demographics, COPD disease duration, previous year's exacerbation record, CAT scores, mMRC ratings, COPD classification based on the 2023 Global Initiative for Chronic Obstructive Lung Disease (GOLD) framework, and current therapeutic

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regimens. Additionally, we assessed tobacco exposure history, biomass fuel exposure, and coexisting chronic medical conditions.

The COPD Assessment Test (CAT) represents a validated 8-item instrument evaluating how COPD affects patient health status. Scoring ranges from 0 to 5 for individual items, yielding a cumulative score between 0 and 40. Elevated scores reflect more substantial disease burden: 0-10 signifies minimal impact, 11-20 represents moderate impact, 21-30 denotes substantial impact, and 31-40 indicates severe impact.

The Modified Medical Research Council (mMRC) dyspnea scale comprises a 5-level grading system (0-4) for quantifying breathlessness intensity in relation to physical exertion triggers. Grade 0 reflects dyspnea occurring exclusively during vigorous physical activity, whereas Grade 4 characterizes breathlessness sufficiently severe to confine patients indoors or manifest during basic activities such as dressing and undressing.

Complete physical assessments and spirometric evaluations were administered to all study participants. Lung function measurements were obtained using a Jaeger MasterScreen PFT system (CareFusion/Vyaire, Germany) in accordance with American Thoracic Society/European Respiratory Society (ATS/ERS) standardized protocols. Each subject completed a minimum of three technically acceptable breathing maneuvers, with optimal values selected for analysis. Testing occurred with participants seated upright, and short-acting bronchodilator medications were discontinued at least 4 hours prior to evaluation. Measured spirometric indices included: Forced Expiratory Volume in one second (FEV_1), Forced Vital Capacity (FVC), Peak Expiratory Flow (PEF), and Forced Expiratory Flow between 25-75% of vital capacity ($FEF_{25–75}$%).

Six-Minute Walk Test (6MWT): We conducted the 6MWT following American Thoracic Society (ATS) standardized protocols along a level 30-meter corridor. Participants received instructions to ambulate maximally over a 6-minute period at self-selected speed, with uniform verbal encouragement delivered at 60-second intervals. Prior to testing, participants underwent a minimum 10-minute rest period while seated.

Our measurement protocol encompassed three phases:

Pre-test assessment: We documented baseline heart rate (HR), oxygen saturation (SpO_2), blood pressure, and dyspnea intensity using the modified Borg scale (ranging 0-10).

During-test monitoring: Continuous tracking of SpO_2 and HR occurred throughout the evaluation, with documentation of nadir SpO_2 values.

Post-test evaluation: Immediately following test completion, we recorded HR, SpO_2, blood pressure, dyspnea rating via the modified Borg scale, and total ambulation distance in meters.

The modified Borg dyspnea scale spans from 0 (representing no breathlessness) to 10 (indicating maximal breathlessness). Testing was discontinued if participants developed severe dyspnea, chest discomfort, lightheadedness, or demonstrated SpO_2 decline below 80%.

Laboratory Analysis:

Serum IL-6 quantification was performed utilizing a commercially available human IL-6 enzyme-linked immunosorbent assay (ELISA) kit (Bioassay Technology Laboratory, Shanghai, China) with a microplate ELISA reader (BioTek ELx800, BioTek Instruments Inc., USA) following manufacturer-specified protocols.

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Figure 1: GOLD 2023 COPD classification:

Group	Symptoms (CAT ≥10 or m MRC ≥2)	Exacerbation History
A	Low symptoms	0—1 exacerbation/year without hospitalization
B	High symptoms	0—1 exacerbation/year without hospitalization
E	Any symptom level	≥2 exacerbations/year or ≥1 with hospitalization

Figure 2: GOLD 2023 Spirometric staging of COPD:

GOLD Stage	Severity	FEV1 % predicted
GOLD 1	**Mild**	**≥80%**
GOLD 2	**Moderate**	**50—79%**
GOLD 3	**Severe**	**30—49%**
GOLD 4	**Very Severe**	**<30%**

RESULTS

Our investigation enrolled 100 subjects, stratified into two cohorts: Group A (COPD patients) and Group B (healthy controls).

Baseline demographic and clinical characteristics are displayed in Table [1]. Both groups demonstrated comparable demographic parameters with no statistically significant differences. Spirometric indices, encompassing Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV1), FEV1/FVC ratio, and Forced Expiratory Flow (FEF 25—75), demonstrated significantly reduced values in Group A relative to controls ($p < 0.001$). Circulating IL-6 concentrations exhibited significantly elevated values in COPD patients compared to controls (0.71 ± 0.27 vs. 0.20 ± 0.10, $p < 0.001$).

Table [1]:Demographic and clinical variables of the study population (n=100)

		Group A (n = 50)	Group B (n = 50)	P-value
Age (years)		58.74 ± 12.91	60.18 ± 12.59	0.574
Gender	**Male**	25 (50.0%)	30 (60.0%)	0.315
	Female	25 (50.0%)	20 (40.0%)	
Current Smoking		30 (60.0%)	26 (52.0%)	0.420
FVC		50.94 ± 9.15	104.74 ± 16.30	**0.000****
FEV1		32.40 ± 8.36	87.64 ± 15.26	**0.000****
FEV/FVC		0.64 ± 0.15	0.86 ± 0.21	**0.000****
FEF 25—75		13.72 ± 6.40	92.00 ± 10.04	**0.000****
IL-6		0.71 ± 0.27	0.20 ± 0.10	**0.000****

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*Data are presented as mean ± SD or frequency (%), FVC: Forced vital capacity, FEV1: Forced expiratory volume in one second, **: highly significant as P-value < 0.001.*

Table [2]: Clinical characteristics of Group A (COPD patients) are presented in Table [2]. Concerning exacerbation patterns, 52.0% (26/50) of participants reported one or more exacerbation episodes during the preceding year. Within this cohort, 34.0% (17/50) met criteria for frequent exacerbators (defined as either ≥2 moderate episodes or ≥1 episode necessitating hospital admission). The annual exacerbation rate per patient ranged between 0.6 and 1.04 based on categorical analysis. Mean symptom assessment scores included a COPD Assessment Test (CAT) value of 38.70 ± 5.14 and a Modified Medical Research Council (mMRC) dyspnea scale rating of 2.72 ± 0.56. When stratified using GOLD 2023 criteria, 20.0% of participants fell into Group B classification while 80.0% belonged to Group E. Spirometric severity distribution based on FEV_1 revealed: 40.0% classified as GOLD 2 (moderate severity), 36.0% as GOLD 3 (severe), and 24.0% as GOLD 4 (very severe).

Table [2]: Distribution of COPD patients [Group A] regarding the clinical variables (n=50)

Variable	**Group A** (n = 50)
Symptom Assessment Scores	
• CAT score (mean ± SD)	**38.70 ± 5.14**
• mMRC score (mean ± SD)	**2.72 ± 0.56**
Exacerbation Burden	
• Total patients with ≥1 exacerbation	**26 (52.0%)**
• Frequent exacerbators (≥2 moderate or hospitalization)	**17 (34.0%)**
• Estimated exacerbation rate per patient	**0.6 – 1.04/ year**
Exacerbation Category in the last year	
• **No exacerbation**	**24 (48.0%)**
• **1 moderate exacerbation**	**9 (18.0%)**
• **≥2 moderate exacerbations**	**4 (8.0%)**
• **≥1 leading to hospitalization**	**13 (26.0%)**
GOLD 2023 Classification	
• Group B	10 (20.0%)
• Group E	40 (80.0%)
GOLD 2023 Spirometric Grading (FEV_1-based)	
• GOLD 2 (Moderate, FEV_1 50—79%)	20 (40.0%)
• GOLD 3 (Severe, FEV_1 30—49%)	18 (36.0%)
• GOLD 4 (Very Severe, FEV_1 <30%)	12 (24.0%)

Values are expressed as mean ± SD or frequency (%). CAT: COPD assessment test; MMRC: Modified Medical Research Council.

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Table [3] Correlation analyses between IL-6 and various clinical and laboratory parameters within the COPD patient cohort are presented in Table [3]. A robust positive association was identified between IL-6 and mMRC score ($r = 0.605$, $p < 0.001$), alongside a moderate positive relationship with CAT score ($r = 0.588$, $p < 0.001$). Significant inverse correlations emerged with FVC ($r = -0.519$, $p < 0.001$), FEV1 ($r = -0.516$, $p < 0.001$), FEF 25—75 ($r = -0.563$, $p < 0.001$), and six-minute walking distance ($r = -0.546$, $p < 0.001$). Conversely, IL-6 demonstrated no statistically meaningful association with patient age ($r = -0.147$, $p = 0.309$) or FEV/FVC ratio ($r = -0.161$, $p = 0.264$).

Table [3]: Correlation between IL-6 with the diverse variables among group A (n=50)

Variable	**r**	**P-value**
Age	-0.147	0.309
FVC	-0.519**	0.000**
FEV1	-0.516**	0.000**
FEV/FVC	-0.161	0.264
FEF 25—75	-0.563**	0.000**
CAT score	0.588**	0.000**
MMRC	0.605**	0.000**
Six-minute walk test	-0.546**	0.000**

*Abbreviations: r represents correlation coefficient; FVC denotes Forced vital capacity; FEV1 represents Forced expiratory volume in one second; CAT indicates COPD assessment test; MMRC refers to Modified Medical Research Council. Statistical significance: * indicates P-value < 0.05; ** indicates P-value < 0.01.*

Table [4]: Relationship between serum IL-6 and exacerbation rate during the preceding year

	r	**P-value**
Frequency of exacerbation	0.54	<0.001

DISCUSSION

COPD, which is untreatable but tolerable, is a common condition with a significant socioeconomic impact, causing global morbidity and mortality. IL-6 represents a pleiotropic protein that triggers the acute phase response and exhibits pro-inflammatory properties, as well as demonstrated anti-inflammatory effects. While the airway epithelium is known to produce IL-6, T-cells and macrophages also secrete it within the lungs.

In this study, COPD patients [Group A] had an average IL-6 level of 0.71 ± 0.27, whereas those in Group B had 0.20 ± 0.10. This difference was statistically significant. These results were in accordance with several studies such as de Moraes et al[13] and Attaran et al [14] who revealed that COPD patients exhibited greater Serum IL-6 level than controls.Singh et al[1] also found COPD patient compared to healthy control individuals had substantially high blood level of IL6. Menon et al.

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[10]found greater IL-6 and hs-CRP levels in the experimental group compared to healthy controls, with statistical significance (P= 0.024 for IL-6 and < 0.01 for hs-CRP).
Within our COPD patient cohort, IL-6 exhibited a robust positive association with mMRC score (r = 0.605, p < 0.001) alongside a moderate positive relationship with CAT score (r = 0.588, p < 0.001). Moderate inverse associations were identified with FVC (r = -0.519, p < 0.001), FEV1 (r = -0.516, p < 0.001), FEF 25—75 (r = -0.563, p < 0.001), and six-minute walking distance (r = -0.546, p < 0.001). In accordance**, Huang et al** [3] revealed that FEV1 percent of the predicted and FEV1/FVC ratio were adversely linked with serum Il6.
Jorde et al. [11], reported that ΔFEV1 values of patients with a high-frequency exacerbation phenotype were significantly elevated, suggesting accelerated progression of bronchial obstruction .Similarly, Gan et al. (2004) [12]conducted a meta analysis and concluded that -6 was inversely associated with lung function, proposing IL-6 as a potential biomarker of disease progression.
In our study, COPD patients had a mean CAT score of 38.70 (range 25 to 47), an MMRC score ranging from 1.5 to 3.5 with a mean of 2.72, and a six-minute walk distance ranging from 80 to 489 meters, with a mean of 235.74. In our COPD patient group, IL-6 exhibited strong positive correlation with mMRC score (r = 0.605, p < 0.001) alongside moderate positive correlation with CAT score (r = 0.588, p < 0.001).Similarly, **Huang et al [3]** found that IL6 CAT score and mMRC score were all positively allied. Also **de Moraes et al**[13]found that patients with mMRC more than 2 exhibited greater serum Il6 than those with mMRC less than or equal to1. Moreover, the ECLIPSE study which also found a strong relationship between elevated systemic inflammatory markers (including IL-6) and decreased exercise tolerance and higher symptom burden in COPD[12].

We recommend that providing large-sample multicenter research is needed in future work to validate and generalize our results, and IL-6 may be an efficient diagnostic factor in patients with COPD.
However this study had several Limitations including: data collection occurred at a single institution. Additionally, the sample size remained relatively limited.

Conclusions:

Serum IL-6 may serve as a useful biomarker for assessing COPD progression and acute exacerbations, warranting further investigation into its therapeutic potential

List of Abbreviations:

AECOPD	Acute Exacerbations of COPD
CAT	COPD Assessment Test
COPD	Chronic Obstructive Pulmonary Disease
CRP	C-reactive protein
ECL	ElectroChemiLuminescence
FEF	Forced expiratory flow
FEV1	Forced Expiratory Volume in One Second
FVC	Forced Vital Capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
ELISA	Enzyme-Linked ImmunoSorbent Assay
hs-CRP	High-sensitivity C-reactive Protein

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IL-6	Interleukin-6
MMRC	Modified Medical Research Council
PaCO2	Partial Pressure of Carbon Dioxide
TGF	Transforming Growth Factor

Declarations

Ethics approval and consent to participate: Institutional ethics approval was obtained from the Faculty of Medicine, Chest Department ethics committee at Aswan University Hospital. All participants provided written informed consent.

Consent for publication: All authors consent to publication.

Availability of data and materials: Available from the corresponding author upon reasonable request.

Competing interests: None declared.

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Authors' contributions: SBA and SHM: study conception and supervision; OET and AAE: data collection; SHM and OET: data analysis and interpretation. All authors contributed to manuscript development and approved the final version.

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REFERENCES

1. Patel AR, Patel AR, Singh S, Singh S, Khawaja I. Global Initiative for Chronic Obstructive Lung Disease: The Changes Made. Cureus. 2019;11:e4985.
2. Guerreiro I, Soccal PM. [COPD and phenotypes]. Rev Med Suisse. 2019;15:2082-6.
3. Huang H, Huang X, Zeng K, Deng F, Lin C, Huang W. Interleukin-6 is a Strong Predictor of the Frequency of COPD Exacerbation Within 1 Year. Int J Chron Obstruct Pulmon Dis. 2021;16:2945-51.
4. Solleiro-Villavicencio H, Quintana-Carrillo R, Falfán-Valencia R, Vargas-Rojas MI. Chronic obstructive pulmonary disease induced by exposure to biomass smoke is associated with a Th2 cytokine production profile. Clin Immunol. 2015;161:150-5.
5. Tanaka T, Narazaki M, Kishimoto T. IL-6 in inflammation, immunity, and disease. Cold Spring Harbor perspectives in biology. 2014;6:a016295.
6. Ataie-Kachoie P, Pourgholami MH, Morris DL. Inhibition of the IL-6 signaling pathway: a strategy to combat chronic inflammatory diseases and cancer. Cytokine & growth factor reviews. 2013;24:163-73.
7. Rincon M, Irvin CG. Role of IL-6 in asthma and other inflammatory pulmonary diseases. International journal of biological sciences. 2012;8:1281.
8. Scheller J, Garbers C, Rose-John S, editors. Interleukin-6: from basic biology to selective blockade of pro-inflammatory activities. Seminars in immunology; 2014: Elsevier.
9. Hussein FGM, Mohammed RS, Khattab RA, Al-Sharawy LA. Serum interleukin-6 in chronic obstructive pulmonary disease patients and its relation to severity and acute exacerbation. The Egyptian Journal of Bronchology. 2022;16:10.

Corresponding Author: Sara Hamed Ahmed, **Phone numbers:** +20 112 365 3314
E-mail address: sarahamed1014@gmail.com

10. Menon B, Kaur C, Vardhan H, Gopi A, Md Yousoof D. Evaluation of Vitamin D, IL6 and Hs-CRP in Different Stages of Chronic Obstructive Pulmonary Disease and Their Correlation with Severity of Disease and Frequency of Exacerbations. Int J Aller Medications. 2016;2:20-7.
11. Jorde I, Stegemann-Koniszewski S, Papra K, Föllner S, Lux A, Schreiber J, et al. Association of serum vitamin D levels with disease severity, systemic inflammation, prior lung function loss and exacerbations in a cohort of patients with chronic obstructive pulmonary disease (COPD). Journal of Thoracic Disease. 2021;13:3597.
12. Gan WQ, Man SF, Senthilselvan A, Sin DD. Association between chronic obstructive pulmonary disease and systemic inflammation: a systematic review and a meta-analysis. Thorax. 2004;59:574-80.
13.de Moraes MR, da Costa AC, Correa KS, Junqueira-Kipnis AP, Rabahi MF. Interleukin-6 and interleukin-8 blood levels' poor association with the severity and clinical profile of ex-smokers with COPD. Int J Chron Obstruct Pulmon Dis. 2014;9:775-84.
14. Attaran D, Lari SM, Towhidi M, Maralani HG, Ayatollahi H, Khajehdaluee M, Ghanei M, Basiri R. Interleukin-6 and airflow limitation in chemical warfare patients with chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2010;5:335-40.
15- Disease GIfCOL. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2020 report. Available from: https://goldcopd.org/gold-reports/. Accessed November 9, 2019

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Vitamin D Receptor (VDR) Expression in Mammary Invasive Duct Carcinoma in Association with its Molecular Subtypes and Clinic-pathological Parameter

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ABSTRACT

Background: Vitamin D plays its rule through the vitamin D receptor (VDR), the expression of VDR is strongly related to size of breast cancer mass and presence metastasis in lymph nodes. **Purpose**: evaluate the association between intra-tumor VDR expression with molecular subtypes and clinic- pathological parameters in IDC of the breast. **Patients and Methods: Sixty** formalin-fixed paraffin-embedded tissue blocks of IDC of the breast were gathered from the Department of Pathology, Faculty of Medicine, Aswan University Hospital's archives between January 2023 and December 2023 for this retrospective investigation. Benign tumors, tumors from cases with a history of preoperative neoadjuvant therapy, tissue samples without complete clinic-pathological data, and tumors with significant necrosis were excluded from this study. Sixty breast carcinomas were eligible for inclusion based on sampling method and total mastectomy specimens. **Results:** A statistically significant association was found between VDR expression and both tumor size and lymph-node metastasis ($p < 0.001$). However, VDR expression showed no significant correlation with lymphovascular invasion (LVI), perineural invasion (PNI), luminal subtypes, patients' age , family history, tumor laterality, or the number of tumor masses. **Conclusion:** Due to its increased expression in cases of small tumor size and low stage, VDR is regarded as a good prognostic sign. Significantly positive nuclear VDR expression was seen in tumor cells in cases with positive ER and PR. Nuclear VDR expression was negative in those with elevated Ki67. Higher stage cancers showed decreased VDR expression.

Keywords: Vitamin D; Breast Invasive Duct Carcinoma; Breast Cancer

INTRODUCTION

Breast cancer is the most prevalent cancer globally and responsible for roughly 16% of cancer-related deaths and about 25% of all malignancy in women **[1].**

A diverse collection of tumors known as invasive ductal carcinoma (IDC) (also known as invasive carcinoma of no special type: ductal NST) lack the necessary features to be classified as a particular histological category. IDCs exhibit a broad range of histopathological features under the microscope. IDC can grow as isolated (single) cells, cables, well-defined nests, or diffuse sheets. Tubular distinction is typically either completely absent, hardly noticeable, or substantially developed **[2].**

Bone health and general physiological function depend on vitamin D, a fat-soluble vitamin. It is both a vitamin and a precursor to hormones because, in contrast to other vitamins, it can be cutaneous generated by exposure to ultraviolet B (UVB) radiation from sunshine. The two main

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forms of vitamin D are vitamin D2 (ergocalciferol), which obtained from plants, and vitamin D3 (cholecalciferol), which is made in the skin and is present in meals derived from animals. **[3]**
The nuclear receptor known as the vitamin D receptor (VDR), which is present in the lobule and ductal epithelial cells of healthy mammary glands, affects the transcription of target genes. It has been discovered that breast cancer lesions express more VDR than normal breast tissue. It is reasonable to anticipate that VDR expression in breast cancers is likewise linked to a better prognosis, since women with moderate versus low levels of vitamin D may have a higher survival after breast cancer **[4].**
Few studies have examined the relationship between breast cancer survival and tumor prognostic factors and VDR expression. The majority of these investigations examined a relatively small number of breast cancers, and their findings have been inconsistent **[5, 6].**
The biggest study to date found correlations with several prognostic markers associated to tumors, but not with survival **[6].**

PATIENTS AND METHODS

In this retrospective investigation, sixty formalin-fixed paraffin-embedded tissue blocks of IDC of the breast were gathered from the Department of Pathology, Faculty of Medicine, Aswan University Hospital archives between January and December of 2023. Benign tumors, tumors from cases with a history of preoperative neoadjuvant therapy, tissue samples without complete clinic-pathological data, and tumors with significant necrosis were excluded from this study. Sixty breast carcinomas were eligible for inclusion based on sampling method and total mastectomy specimens.

Histopathological Examination

According to Li et al., 2023 **[7],** tissue sections from every case under study were stained with hematoxylin and eosin (H&E) to record the diagnosis as well as a revision of their hormonal status and Ki67 level, with a cutoff limit of 14%. Tissue blocks embedded in paraffin and treated with 10% buffered formalin were used to create the specimens. The fifth version of the WHO Classification of Breast Tumors was used to classify the tumors histopathologically. The histopathological grading was done according to the Nottingham Histological Score System; modification of Scarff-Bloom- Richardson grading **system [8].** The eighth edition of the AJCC TNM staging system was used to stage the tumors **[9].**
The evaluation of HER2, PR, and ER expression was taken from already-existing medical information. At a cut-off of >10% positively stained nuclei, ER and PR were deemed positive. When available, HER2 status was determined using in situ hybridization (ISH) results. HER2 status was determined by immunohistochemistry (IHC) examination; HER2 was deemed positive when designated 3+ and negative when marked 0 or 1+. If ISH was not employed to corroborate the findings, IHC values of 2+ were classified as missing **[10].**

Immunohistochemical examination

Following labeling, it was discovered that breast cancer cells expressed VDR in a number of subcellular sites. Staining was seen in the cytoplasm, nuclear membrane, and nucleus. The nuclear stain was classified as positive over 11% of stained nuclei and negative below a cut-off of 10%. The cytoplasmic score was determined by multiplying the intensity scores of 0 (no stain), 1 (low intensity), 2 (moderate intensity), and 3 (high intensity) by the fraction values of 0 (0%), 1 (1-10%), 2 (11-50%), 3 (51-75%), and 4 (76-100%). Following that, cytoplasmic scores were separated into three categories: 0–6, 7–9, and 10–11 **[11].**

Statistical Analysis

IBM SPSS statistics for Windows version 18 was used to statistically evaluate the data. Means ±

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standard deviation (SD), median, and range were used to express quantitative data. Numbers and percentages were used to express qualitative data. The Shapiro-Wilk test was used to determine whether the data were normal. Several factors were assessed for statistical significance using the Chi-Square test and Fisher's Exact test; a p value of less than 0.05 was deemed statistically significant.

RESULTS

Evaluation of IHC expression of VDR:

All 60 (100%) of the IDC cases that were examined had varying degrees of VDR expression, which manifested as brownish nuclear and cytoplasmic staining. In 16 out of 60 instances (26.7%), nuclear VDR expression was positive; in 44 out of 60 cases (73.3%), it was negative. Of the 60 cases, 25 (41.7%) had low cytoplasmic VDR expression, 29 (48.4%) had moderate cytoplasmic VDR expression, and 6 (10%) had high cytoplasmic VDR expression. Figure 1, for instance:

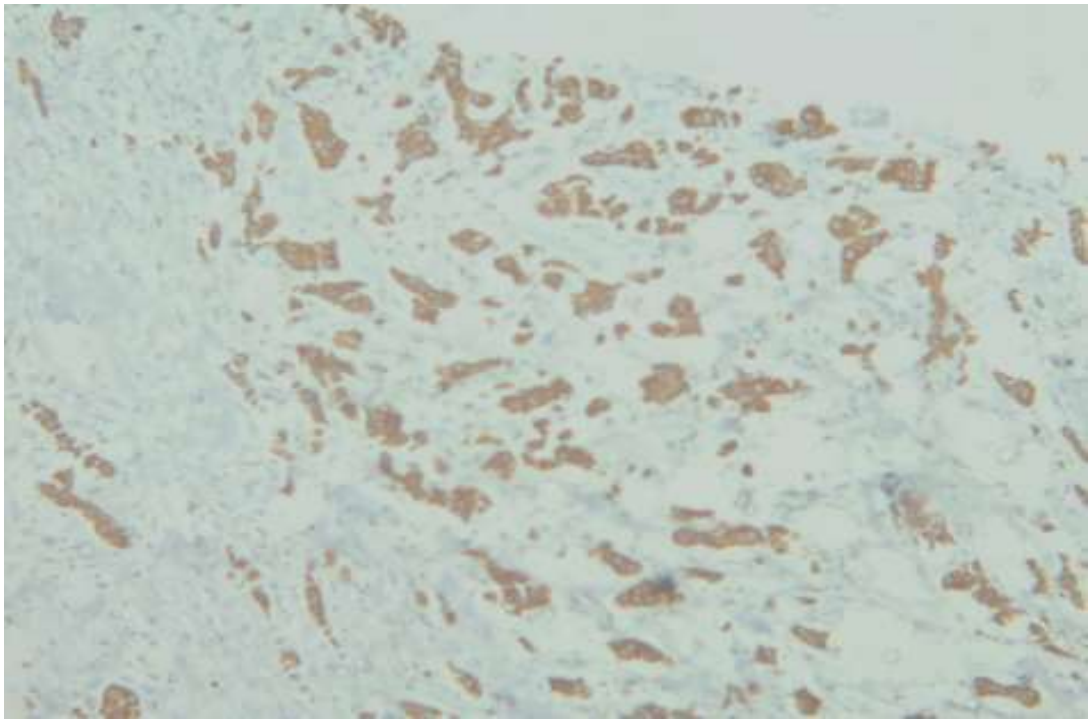

Figure 1: Tumor cells showed strong nuclear VDR score positivity (X100)

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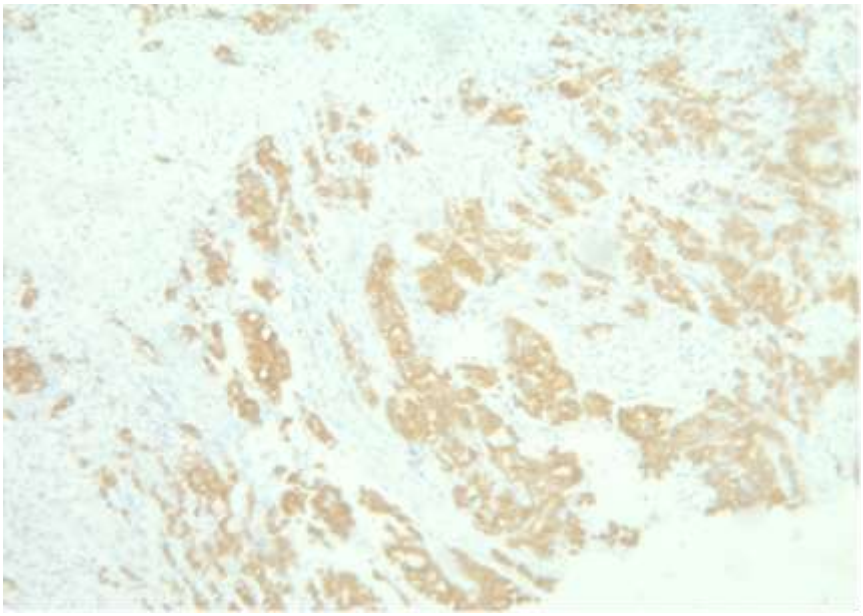

Figure 2: Tumor cells showed moderate cytoplasmic VDR score positivity (IHC X100).

Table 1: Nuclear and cytoplasmic VDR expression in the whole studied cases

Expression of VDR		**No**	**%**
Nuclear	Negative	44	73.3%
	Positive	16	26.7%
Cytoplasmic	Low intensity	25	41.7%
	Moderate intensity	29	48.3%
	High intensity	6	10.0%

Nuclear VDR expression and tumor size were statistically significantly correlated, whereas VDR expression did not significantly correlate with patients' age, family history, tumor side, or number of masses.

Table 2: Relationship between nuclear VDR expression and the demographic and clinical variables in the studied cases

Variable		**Nuclear VDR Expression**		**Test of Significance**	
		Negative	Positive	p-value	Sig.
Age (Mean ±SD)		50.82+9.4	51.56+13.45	0.84[T]	NS
Family history No (%)	No	24 (54.55%)	7 (43.75%)	0.459[C]	NS
	Yes	20 (45.45%)	9 (56.25%)		
Side No (%)	Right	22 (50%)	9 (56.25%)	0.668[C]	NS
	Left	22 (50%)	7 (43.75%)		
Number of masses No (%)	1	3 (6.8%)	11 (68.8%)	0.613[F]	NS
	2-3	28 (63.6%)	4 (25%)		
	>3	13 (29.5%)	1 (6.2%)		
Size of the tumor No (%)	≤2cm	2 (4.5%)	4 (25%)	0.038[F]	S
	>2cm	42 (95.5%)	12 (75%)		

[T] Student t-test of significance.

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(C) Chi-Square test of significance.
(F) Fisher's Exact test of significance.

There was a statistically significant correlation between VDR nuclear expression and ER, PR, and Ki67. Significantly positive nuclear VDR expression was seen in tumor cells in cases with positive ER and PR. Nuclear VDR expression was negative in cases with significant levels of positive Ki67.

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Table 3: Hormonal receptors (ER, PR), HER2 and Ki67 in relation to nuclear expression of VDR

Variable		**Nuclear expression of VDR**		**Fisher's Exact test**	
		Negative	Positive	p-value	Sig.
ER	Negative	42 (95.5%)	1 (6.2%)	<0.001	S
	Positive	2 (4.5%)	15 (93.8%)		
PR	Negative	40 (90.9%)	2 (12.5%)	<0.001	S
	Positive	4 (9.1%)	14 (87.5%)		
HER2	Negative	15 (34.1%)	3 (18.8%)	0.346	NS
	Positive	29 (65.9%)	13 (81.2%)		
KI67	Low level	5 (11.4%)	14 (87.5%)	<0.001	S
	High level	39 (88.6%)	2 (12.5%)		

In relation to the tumor grade of the cases under study, greater tumor grades showed decreased VDR expression. In 2/4 (50%) of Grade I, 14/50 (28%) of Grade II, and 0/6 (0%) of Grade III breast cancer patients, nuclear VDR was expressed. VDR demonstrated a statistically significant correlation with lymph node metastases among the factors under investigation ($p<0.001$).

Table 4: Relationship between tumor grade, stage, lymph node metastasis and the nuclear expression of VDR

		Nuclear score of VDR		**Test of significance**	
		Negative	Positive	p-value	Sig.
Grade No (%)	Grade 1	2 (50%)	2 (50%)	0.192(F)	NS
	Grade 2	36 (72%)	14 (28%)		
	Grade 3	6 (100%)	0 (0%)		
LN metastasis No (%)	N0	3 (6.8%)	10 (62.5%)	<0.001(F)	S
	N1	4 (9.1%)	5 (31.3%)		
	N2	10 (22.7%)	1 (6.3%)		
	N3	27 (61.4%)	0 (0%)		
T stage No (%)	T1	11 (25%)	3 (18.75%)	0.064(F)	NS
	T2	21 (47.73%)	13 (81.25%)		
	T3	10 (22.73%)	0 (0%)		
	T4	2 (4.55%)	0 (0%)		

(F) Fisher's Exact test of significance.
(M) Mann-Whitney test of significance.

Regarding the cytoplasmic expression: there was a statistically significant association between cytoplasmic VDR expression and tumor size together with hormonal receptors (ER, PR), HER2 and Ki67 in the studied cases (table 5&6).

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Table 5: Relationship between demographic data, tumor size and tumor masses and cytoplasmic VDR expression

		Cytoplasmic expression of VDR			Test of significance	
		Low intensity	Moderate intensity	Week intensity	p-value	Sig.
Age (mean±SD)		48.04+9.8	53.45+10.11	51.67+13.81	0.168(A)	NS
Family history No (%)	No	13 (52%)	16 (55.17%)	2 (33.33%)	0.702(F)	NS
	Yes	12 (48%)	13 (44.83%)	4 (66.67%)		
Tumor side No (%)	Right	14 (56%)	14 (48.28%)	3 (50%)	0.868(F)	NS
	Left	11 (44%)	15 (51.72%)	3 (50%)		
Number of masses No (%)	1	4 (16%)	6 (20.7%)	4 (66.7%)	0.489(F)	NS
	2-3	13 (52%)	18 (62.1%)	1 (16.7%)		
	>3	8 (32%)	5 (17.2%)	1 (16.7%)		
Tumor size					0.038(F)	S

(A) One Way ANOVA of significance.
(F) Fisher's Exact test of significance.

Table 6: Statistical relation between hormonal receptors (ER, PR), HER2 and Ki67 and VDR cytoplasmic expression in the studied cases

		Cytoplasmic VDR Expression			Fishers test	
		Low intensity	Moderate intensity	High intensity	p-value	Sig.
ER	Negative	21 (84%)	21 (72.4%)	1 (16.7%)	**0.008**	S
	Positive	4 (16%)	8 (27.6%)	5 (83.35)		
PR	Negative	21 (84%)	21 (72.4%)	0 (0%)	**<0.001**	S
	Positive	4 (16%)	8 (27.6%)	6 (100%)		
HER2	Negative	12 (48%)	6 (20.7%)	0 (0%)	**0.029**	S
	Positive	13 (52%)	23 (79.3%)	6 (100%)		
Ki67	Low level	6 (24%)	8 (27.6%)	5 (83.3%)	**0.025**	S
	High level	19 (76%)	21 (72.4%)	1 (16.7%)		

Higher tumor grades showed a discernible decrease in VDR cytoplasmic expression, however this was not statistically significant. In Grade I, 2/4 (50%) of the patients had low VDR expression, while the remaining 2/4 (50%) had strong VDR expression. VDR was low in 21/50 (42%), moderate in 25/50 (50%), and high in 4/50 (8%) of Grade II cases. VDR was low in 2/6 (33.3%) and moderate in 4/6 (66.6%) of instances of Grade III breast cancer. However, VDR and lymph node metastases had a significant statistical relationship ($p<0.001$) (table 7).

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Table 7: Statistical relation between tumor grade, lymph node metastasis, tumor stage and cytoplasmic expression of VDR

		Cytoplasmic VDR Expression			**Test of significance**	
		Low intensity	Moderate intensity	High intensity	P-value	Sig.
Grade No (%)	Grade I	2 (50%)	0 (0%)	2 (50%)	0.079(F)	NS
	Grade II	21 (42%)	25 (50%)	4 (8%)		
	Grade III	2 (33.3%)	4(66.6%)	0 (0%)		
LN metastasis No (%)	N0	4 (16%)	4 (13.8%)	5 (83.33%)	0.031(K)	S
	N1	3 (12%)	6 (20.7%)	0 (0%)		
	N2	5 (20%)	5 (17.2%)	1 (16.67%)		
	N3	13 (52%)	14 (48.3%)	0 (0%)		
T stage No (%)	T1	9 (36%)	5 (17.24%)	0 (0%)	0.181(F)	NS
	T2	11 (44%)	17(58.62%)	6 (100%)		
	T3	5 (20%)	5 (17.24%)	0 (0%)		
	T4	0 (0%)	2 (6.9%)	0 (0%)		

(F) Fisher's Exact test of significance.

(K) Kruskal Wallis test of significance.

*Post-hoc test was significant between: **(K1)** High intensity Vs. (Low intensity and moderate intens Statistical evaluation of both nuclear and cytoplasmic VDR score showed no significant relation with LVI, or PNI .

Both nuclear and cytoplasmic score of VDR, showed insignificant association, regarding luminal subtypes

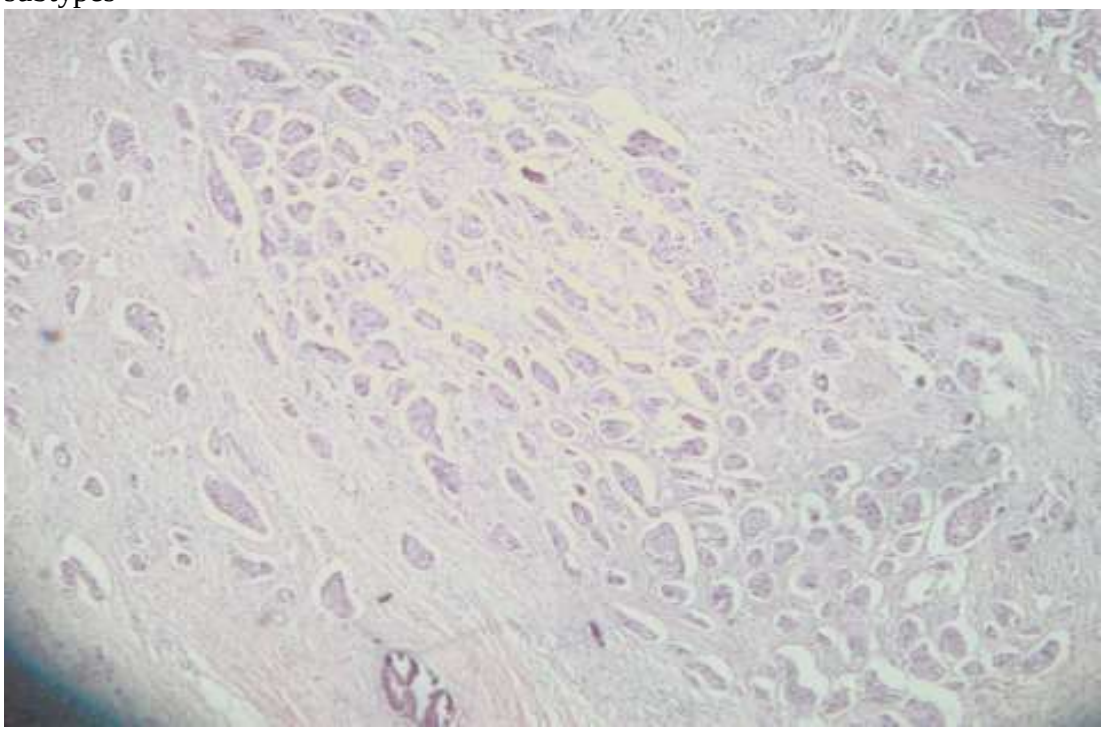
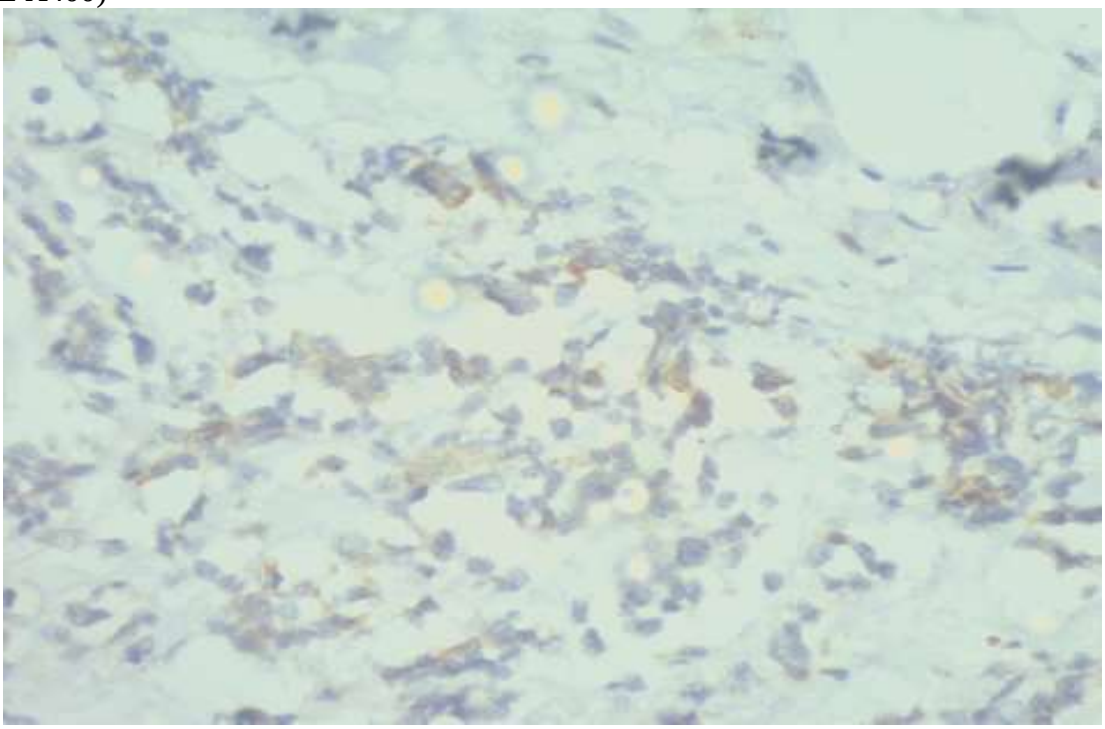


Figure 3: IDC of the breast (H&E X100)

Figure 4: IDC of the breast (note cellular atypia, pleomorphism and nuclear hyperchromatism) (H&E X400)



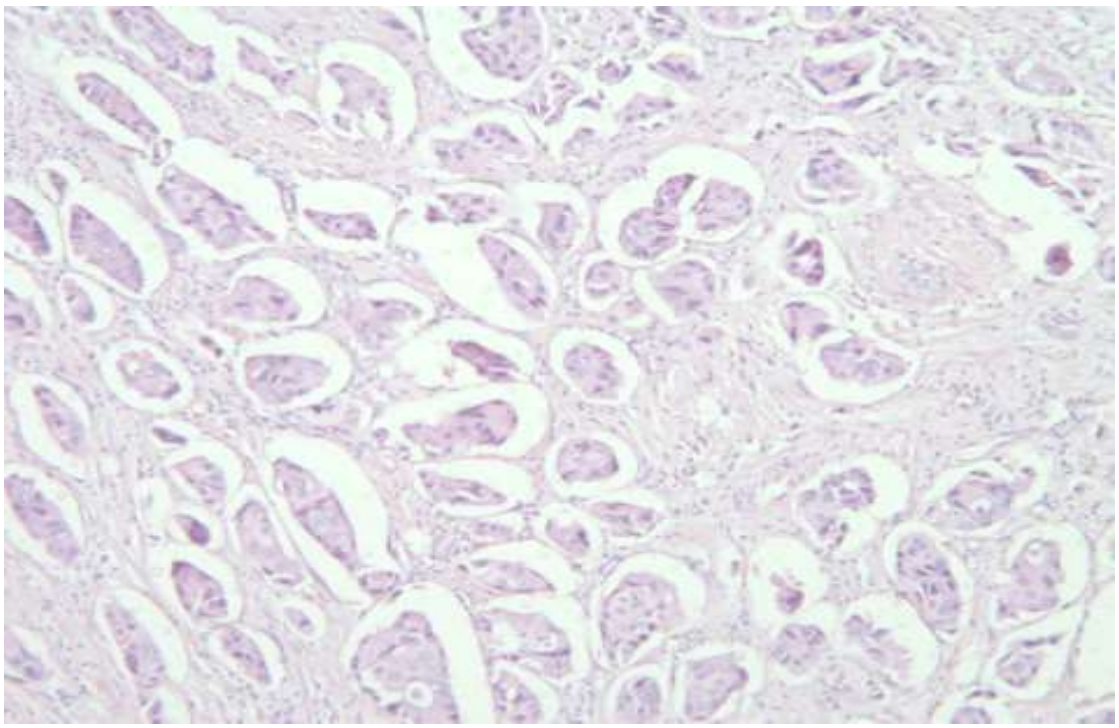


Figure 5: Tumor cells showed week cytoplasmicVDR score positivity (IHC X100)

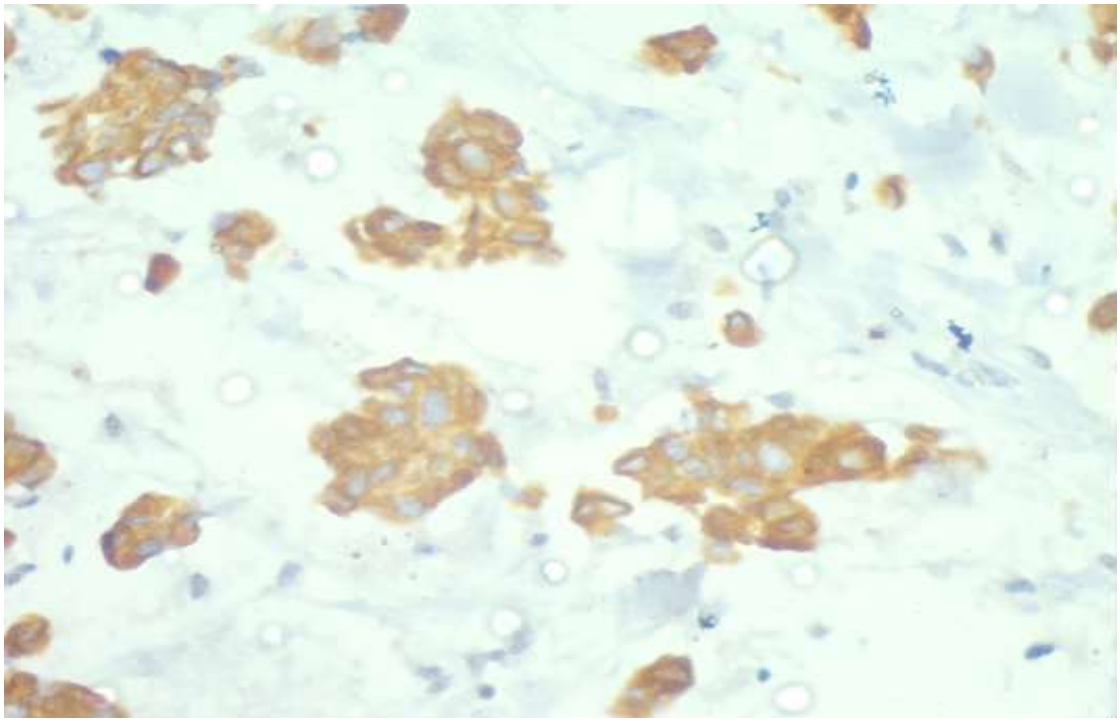


Figure 6: Tumor cells showed strong cytoplasmic VDR score positivity (IHC X400)

DISCUSSION

In both normal and breast cancer tissue, the VDR plays a role in cell proliferation and differentiation. The mammary gland's immunological, stromal, and epithelial cells all express VDR. During some hormonal stages like puberty and pregnancy, it is dynamically controlled in the epithelial compartment **[12,13].**

Therefore; This study examined the relationship between intra-tumor VDR expression, molecular subtypes, and clinic-pathological characteristics in breast IDC.

Since this is what the majority of earlier investigations have found, it was anticipated to find solely nuclear staining in relation to VDR **[14, 15].** Thus, it was unexpected to discover VDR staining throughout our TMA's cellular membrane, cytoplasm, and nuclear membrane. VDR was found in the cytoplasm of dividing cells, according to another recent study **[16].** Unliganded VDR can therefore be found elsewhere in the tumor cells, and at least one other study on breast cancer survival has found VDR not just in the nucleus but also in the cytoplasm **[5].** Therefore, we use both nuclear and cytoplasmic labeling in our study

According to Saleem et al**. [17],** the frequencies of positively expressed patients for ER and PR were 31% and 36.2%, respectively. In the current study, we discovered that there were 28.3% cases with positive ER and 30% with positive PR.

70% of the patients examined in this study tested positive for HER2. This outcome is almost identical to that of Eziagu et al. **[18],** who discovered that 68.3% of patients had positive HER2.

In 68.3% of the cases examined, this study found a high Ki67 index. The findings of Eziagu et al. **[18],** who discovered that Ki-67 was positive in 83.6% of cases, varied slightly from this one. Because the references for Ki67 in the two research differed, the reference for Ki67 in this study was 14%, but the reference for Ki67 in their study was 20%.

In line with Mahsa et al. **[19],** who demonstrated that Grade-II lesions were seen in a significant number of patients, and Zhou et al**. [20],** who demonstrated that grade II resembled (68.3%) of the total number of cases, this work demonstrated that grade II

represented (83.3%) of all analyzed cases.

Twenty percent of the cases under study had perineural invasion. PNI was found in 1384 (15.6%) of the 8864 breast cancer patients that Narayan et al. **[21]** examined. This discrepancy results from the study's large number of cases (8864).

According to our findings, VDR expression was expressed in 60 out of 60 cases, with low intensity in 25 out of 60 cases (41.7%), moderate intensity in 29 out of 60 cases (48.4%), and high intensity in 6 out of 10 cases. This is almost in line with the findings of Huss et al. **[11],** who reported that VDR was expressed in all cancer cell compartments. Cytoplasmic VDR was expressed in a high percentage in 816/878 (92.9%) of the malignancies. The intensity distribution was broader: no stain (62, 7.1%), low intensity (208, 23.7%), moderate intensity (496, 56.5%), and high intensity (112, 12.8%).The present investigation demonstrated a substantial relationship between VDR and hormone receptors (ER, PR). Positive VDR expression was seen in patients with positive ER and PR, whereas negative VDR expression was seen in cases with negative ER and PR. This outcome is consistent with the findings of Ordóñez-Mena et al. **[22],** who verified that ER/PR positivity and the presence of VDR were positively correlated.

A statistically significant relationship between VDR and Ki67 level was found in the current investigation. VDR expression and Ki67 level are inversely correlated. VDR expression was linked to good prognostic traits including low Ki67 levels, according to Huss et al. **[11].** This demonstrates how poor prognostic variables, such as elevated Ki67, exhibit low VDR expression.

According to the current investigation, there was no statistically significant correlation between HER2 and VDR expression. VDR expression was higher in the HER2-enriched breast cancer subtype (66.7%), according to Putri et al. [23]. The fact that our results were based on 60 cases while theirs were based on 2343 examples may be the reason for the discrepancy.

In the current investigation, VDR did not significantly correlate with either LVI or PNI. This was comparable to the findings of Bahador et al. **[24],** who showed no significant correlation between VDR expression and either LVI or PNI. According to Cheang et al. **[25],** there is a conflicting link between vitamin D and breast cancer prognostic markers like tumor size, grade, stage, lymph node involvement, and hormone receptor status.

Conclusion

Based on the findings of this study, VDR is thought to be a promising prognostic sign because it is more prevalent in low-grade and small tumor patients. Significantly positive nuclear VDR expression was seen in tumor cells in cases with positive ER and PR. Nuclear VDR expression was negative in those with elevated Ki67. Higher grade tumors had less VDR expression. In the near future, this could be utilized as a target for IDC and as a sign of a favorable prognosis.

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REFERENCES

1. Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians, 71(3), 209-249
2. Duggan, C., Dvaladze, A., Rositch, A. F., Ginsburg, O., Yip, C. H., Horton & Anderson, B.

O. (2020). The breast health global initiative 2018 global summit on improving breast healthcare through resource-stratified phased implementation: Methods and overview. Cancer, 126, 2339-2352
3. Holick, M. F. (2007). Vitamin D deficiency. *New England Journal of Medicine*, *357*(3), 266–281. https://doi.org/10.1056/NEJMra070553
4. Sharma, R. (2019). Breast cancer incidence, mortality and mortality- to-incidence ratio (MIR) are associated with human development, 1990–2016: evidence from Global Burden of Disease Study 2016. Breast Cancer, 26, 428-445
5. Ditsch, N., Toth, B., Mayr, D., Lenhard, M., Gallwas, J., Weissenbacher, T & Jeschke, U. (2012). The association between vitamin D receptor expression and prolonged overall survival in breast cancer. Journal of Histochemistry & Cytochemistry, 60(2), 121-129
6. Al-Azhri, J., Zhang, Y., Bshara, W., Zirpoli, G., McCann, S. E., Khoury, T& Yao, S. (2017). Tumor expression of vitamin D receptor and breast cancer histopathological characteristics and prognosis. Clinical Cancer Research, 23(1), 97-103
7. Li, W., Lu, N., Chen, C., & Lu, X. (2023). Identifying the optimal cutoff point of Ki-67 in breast cancer: a single-center experience. *Journal of International Medical Research*, *51*(8), 03000605231195468.
8. Elston, C. W., & Ellis, I. O. (1991). Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. *Histopathology*, *19*(5), 403-410
9. Byrd, D. R., Brookland, R. K., Washington, M. K., Gershenwald, J. E., Compton, C. C., Hess, K. R., ... & Meyer, L. R. (2017). *AJCC cancer staging manual* (Vol. 1024). M. B. Amin, S. B. Edge, & F. L. Greene (Eds.). New York: springer.
10. Elebro, K., Bendahl, P. O., Jernström, H., & Borgquist, S. (2017). Androgen receptor expression and breast cancer mortality in a population-based prospective cohort. Breast cancer research and treatment, 165(3), 645-657

11. Huss, L., Butt, S. T., Borgquist, S., Elebro, K., Sandsveden, M., Rosendahl, A., & Manjer, J. (2019). Vitamin D receptor expression in invasive breast tumors breast cancer survival. Breast Cancer Research, 21, 1-13.

12. Narbaitz, R., Sar, M., Stumpf, W. E., Huang, S., & DeLuca, H. F. (1981). 1, 25-Dihydroxyvitamin D3 target cells in rat mammary gland. Hormone Research in Paediatrics, 15(4), 263-269.

13. Berger, U., Wilson, P., McClelland, R. A., Colston, K., Haussler, M. R., Pike, J. W., & Coombes, R. C. (1987). Immunocytochemical detection of 1, 25-dihydroxyvitamin D3 receptor in breast cancer. *Cancer research*, *47*(24_Part_1), 6793-6799.

14. Cui, X., Pertile, R., & Eyles, D. W. (2018). The vitamin D receptor (VDR) binds to the nuclear matrix via its hinge domain: a potential mechanism for the reduction in VDR mediated transcription in mitotic cells. Molecular and cellular endocrinology, 472, 18-25.

15. Giordano, Spreafico, F. S., Cardoso-Filho, C., Cabello, C., Sarian, L. O., Zeferino, L. C., & Vale, D. B. (2020). Breast cancer in men: clinical and pathological analysis of 817 cases. American journal of men's health, 14(4), 1557988320908109.
16. Bidoli, E., Virdone, S., Hamdi-Cherif, M., Toffolutti, F., Taborelli, M., Panato, C., & Serraino, D. (2019). Worldwide age at onset of female breast cancer: a 25-year population-based cancer registry study. Scientific Reports, 9(1), 14111
17. Saleem, I., Said, M. S., Izharullah, Islam, M., Nadeem, H., Hayat Khan, A., & Mehmood

Hashmi, A. (2023). Clinical evaluation of patients suffering from breast cancer and determination of evolving treatment therapies and better strategies related to breast cancer. International Journal of Natural Medicine and Health Sciences, 2(3), 17–24
18. Eziagu, U. B., Ndukwe, C. O., Kudamnya, I., Peter, A. I., & Igiri, A. O. (2022). Immunohistochemical Survey of Invasive Ductal Carcinoma of the Breast, using ER, PR, HER2 and KI-67 biomarkers, in Uyo, Nigeria. Ibom Medical Journal, 15(3), 223-235
19. Mahsa A, M., Heibatollahi, M., & Zahedifard, S. (2020). Comparison of ER, PR, Ki67 and HER-2/neu Reactivity Pattern with Patients' Age, Histologic Grade, Tumor Size and Lymph Node Status in Invasive Ductal Breast Cancer. International Journal of Cancer Management, 13(6)
20. Zhou, B. Y., Wang, L. F., Yin, H. H., Wu, T. F., Ren, T. T., Peng, C., & Xu, H. X. (2021). Decoding the molecular subtypes of breast cancer seen on multimodal ultrasound images using an assembled convolutional neural network model: A prospective and multicentre study. EBioMedicine, 74
21. Narayan, P., Flynn, J., Zhang, Z., Gillespie, E. F., Mueller, B., Xu, A. J., & Braunstein, L. Z. (2021). Perineural invasion as a risk factor for locoregional recurrence of invasive breast cancer. Scientific reports, 11(1), 12781
22. Ordóñez-Mena, J. M. (2022). The association between vitamin D levels and caries experience in children and youth participating in National Health and Nutrition Examination Survey 2011-2016: A cross-sectional study. The Journal of the American Dental Association, 153(9), 848-858
23. Putri, S. D., Nanza, S. R. Y., Widodo, I., & Purnomosari, D. (2022). The Association of Intra-Tumoral and Stromal Vitamin D Receptor (VDR) Expressions with Molecular Subtypes and Clinicopathological Factors in Breast Carcinoma. Asian Pacific Journal of Cancer Prevention: APJCP, 23(4), 1169
24. Bahador, M., Saeedi Nejad, M., Dabiri, S., Larizadeh, M. H., & Soofiabadi, M. F. (2024). Investigating the level of vitamin D receptor gene expression in two tumoral and healthy breast tissues in breast cancer patients and its association with prognostic factors. Journal of the Egyptian National Cancer Institute, 36(1), 12
25. Cheang, E., Ha, R., Thornton, C. M., & Mango, V. L. (2018). Innovations in image-guided preoperative breast lesion localization. The British Journal of Radiology, 91(1085), 20170740

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ORIGINAL ARTICLE

PROGNOSTIC SIGNIFICANCE OF PLATELET MICROPARTICLES IN NEONATAL SEPSIS

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ABSTRACT

Background: Platelet microparticles (PMPs) play a role in inflammation and thrombosis during sepsis.**Aim of the work :** This study evaluated (PMPs) prognostic significance in neonatal sepsis (NS) and their relationship to clinical outcomes. **Methods**: This prospective case-control study included 85 neonates: 30 with NS, 30 with non-septic infections, and 25 healthy controls. PMP levels were measured using ELISA. Clinical and laboratory parameters were compared, and ROC curve analysis assessed the diagnostic performance of PMPs. **Results**: PMPs were significantly higher in NS compared to non-septic and control groups ($p<0.05$). ROC analysis revealed limited diagnostic power (cutoff $51\times10^3/\mu L$, sensitivity 73.3%, specificity 63.3%). No significant correlation was found between PMPs and CRP, CBC, or liver/kidney functions. However, higher PMP levels were associated with mortality in NS ($p<0.001$).**Conclusion**: Elevated PMPs may have prognostic significance in neonatal sepsis, though their diagnostic accuracy is limited. Further studies are warranted to explore their role as biomarkers.

Keywords: Platelet Microparticles, Neonatal Sepsis, Prognosis, Inflammation, Mortality.

INTRODUCTION

During the neonatal age ,serious morbidity and mortality are correlated to neonatal sepsis (NS). Subclinical infection to severe local or systemic infection are among the clinical presentations.[1]
NS is defined as a systemic infection of the bloodstream manifesting in neonates within the first 28 days postpartum and consists of a clinical syndrome characterized by systemic manifestations of infection, circulatory shock and potential multisystem organ failure.[2]

Neonatal sepsis (NS) remains a leading cause of neonatal morbidity and mortality globally, disproportionately affecting populations in developing countries [3].

Platelet microparticles (PMPs), small vesicles shed from activated or apoptotic platelets, have emerged as potential biomarkers of inflammation and thrombosis.[4]

Platelet micro-particles (PMPs) seem to play a key role in multi-organ dysfunction and septic shock through differential tissue expression of enzymes related to inflammation and oxidative stress .They may be of prognostic value in sepsis [5]

This study aims to analyze the prognostic relevance of PMPs in neonatal sepsis and their association with clinical outcomes.

MATERIALS AND METHODS

This prospective case-control study was conducted on 85 neonates (≤28 days old) admitted to Aswan University Hospital. Participants were categorized into three groups: Group A (30 neonates with sepsis confirmed by positive blood culture), Group B (30 with non-septic infections), and Group C (25 healthy controls).

Exclusion criteria were infants older than 1-month, congenital diseases and maternal transmitted diseases.

All enrolled neonates underwent detailed history taking, systematic clinical examination, and complete laboratory evaluation. including CBC, CRP, kidney and liver function tests, and PMP levels measured by ELISA.

The technique of ELISA (enzyme-linked immunosorbent assay) for PMP detection

Reagent preparation

Wash buffer (1x) -If crystallization is observed in the concentrate, equilibrate to room temperature and gently mix until complete dissolution of the crystals is achieved. To prepare 600 ml of (1x) wash buffer, dilute 20 ml of the (30x) concentrate in deionized or distilled water. To prepare the standard dilution, pipette 50 µl of the standard diluent into each tube, then add 100 µl of the standard solution>

A standard concentration of 54 IU/ml was prepared in the fifth tube. From this tube, 100 µl was transferred into the fourth tube, and 50 µl was pipetted into the third tube to generate a serial dilution series. The undiluted standard (54 IU/ml) served as the high standard, while the sample diluent functioned as the zero standard (blank well, 0 IU/ml).

Assay procedure:

We have prepared all reagent, working stander blank samples as direct in the previous sections. The number of wells required was determined from the assay layout sheet. Unused wells and the desiccant were returned to the pouch, sealed, and maintained at 4 °C."

Pipette stander 5o mic to a testing standard well, pipette sample diluent 40 mic to testing sample, then We have added testing sample 10 mic (sample final dilution in a 5– fold), pipette sample to wells, we have not touched the well wall as far as possible and have mixed gently.

The wells were covered using the supplied adhesive strip and incubated for 30 minutes at 37 °C. The wash buffer was subsequently prepared by diluting the concentrate 30-fold with distilled water.

The adhesive strip was removed, and the liquid contents were discarded. Wash buffer was pipetted into each well, allowed to stand for 30 seconds, and then drained. This washing step was repeated five times. Subsequently, 50 µl of HRP-conjugate reagent was added to each well, except the blank well. The plates were then incubated under the specified conditions, Incubation: operation with 4.

Washing: operation with 6. Fifty µl of chromogen solution B was added to each well, and the plates were incubated for 15 minutes at 37 °C in the dark. The reaction was terminated by adding 50 µl of stop solution A to each well, resulting in a color change from blue to yellow. The blank well was used as the zero reference.

Absorbance was measured at 450 nm within 15 minutes after the addition of the stop solution.

Statistical analyses were performed using SPSS v26; $p<0.05$ was considered significant. Qualitative data were summarized as frequencies and percentages. The distribution of numerical data was evaluated for normality employing the Kolmogorov–Smirnov test.

Group comparisons were carried out using the Kruskal–Wallis test for non-normally distributed variables followed by the Wilcoxon-signed ranks test for pairwise comparisons. The Receiver Operating Characteristic (ROC) curve (ROC) curve analysis was employed to determine the cut-off value of PMPs for differentiating NS from other infections.

A p-value < 0.05 was considered significant.

RESULTS

Group A demonstrated significantly higher CRP and PMP levels than Groups B and C ($p<0.05$). PMP levels showed no correlation with CRP, CBC, or kidney/liver function parameters. ROC analysis revealed limited discriminative ability of PMPs for NS (sensitivity 73.3%, specificity 63.3%). PMP levels were significantly higher among neonates who died versus survivors ($p<0.001$).

Table 1

Table 1: Comparison between the three groups regarding sex distribution, C-reactive protein level, kidney, liver function results and platelet microparticles levels in the studied groups

	Group A (n=30)	**Group B (n=30)**	**Group C (n=25)**	**Test value**	**P**
HB (gm/dL)	15.0	12.9	15.0	1.009**	0.604
WBCs count x10^3/mm^3	15.3	11.7	11.4	1.608**	0.447
Neutrophil count x10^3/mm^3	9.3	7.0	9.6	4.770**	0.092
Platelet count x10^3/mm^3	180	199	220	6.609**	0.037
CRP (mg/L)	23.28	26.22	0.9	53.213**	< 0.001
	A vs. B	A vs. C	B vs. C		
	0.010	0.013	< 0.001		
Kidney function results					
Blood Urea (mg/dL)	23.5(11-79)	27.5 910-104)	19.0(14-44)	2.502**	0.286
S. Creatinine (mg/dL)	0.77(0.44-91.69)	0.75(0.43-1.41)	0.56(90.41-1.13)	4.980**	0.083
Liver function					
ALT (U/L)	9(2-17)	6(2-16)	10(4-20)	2.515**	0.284
AST (U/L)	33.5(16-93)	27(8-104)	28(13-64)	1.401**	0.496
Platelet microparticles levels					
PMPs (x10^3/µl)	55.4±8.1	48.8±10.8	48.6±6.4	5.78**	0.002
Post-hoc p-values	**A vs. B**	**A vs. C**	**B vs. C**		
	0.004	0.020	1.000		

Data are presented as frequency (%) or median. *: Chi-square test. HB: Hemoglobin, CRP: C-reactive protein, WBCs: White blood cells ** Kruskal–Wallis's test, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase.

Diagnosis of neonates in group B were enumerated in **table 2.**

Table 2: Diagnosis of neonates in group B

	N%
RD	17(56.7%)
RD I	2(6.7%)
RD II	8(26.7%)
RD III	4(13.3%)
RD IV	3(10.0%)
Postoperative	2(6.7%)
Fever	2(6.7%)
Infant of diabetic mother	2(6.7%)
Low birth weight	2(6.7%)
heart defect	1(3.3%)
Jaundice	1(3.3%)
Low birth weight + RD II	1(3.3%)
Low birth weight + RD IV	1(3.3%)
Suspected meningitis	1(3.3%)

Data is presented as frequency (%), RD: Respiratory distress.

Blood culture outcomes among Group A cases were enumerated in **table 3**.

Table 3: Blood culture outcomes in group A cases

	N%
Klebsiella pneumoniae	12(40.0%)
Staphylococcus aureus	7(23.3%)
CoNS	(16.7%)
Acinetobacter baumannii	1(3.3%)
Enterobacter cloacae complex	1(3.3%)

Data is presented as frequency (%), CoNS: Coagulase-negative staphylococci.

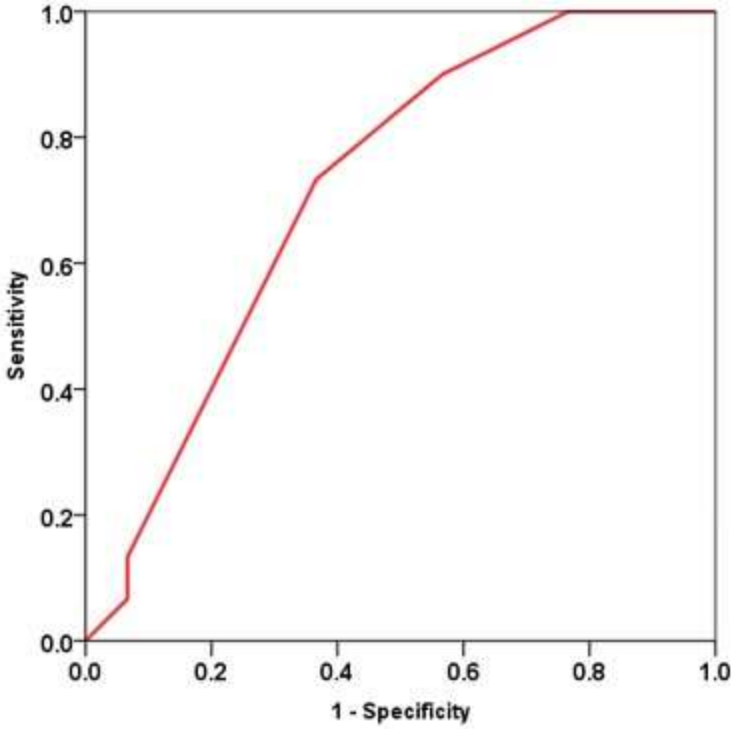

Figure 1: ROC curve of the predictive power of PMPs for differentiating NS from other infections

ROC curve analysis revealed a relatively weak predictive power of PMPs for differentiating NS from other infections, i.e. Group A from Group B. The sensitivity of PMPs at a cut-off of 51 x103/µl or more was 73.3% and the specificity was 63.3%. **Figure1**

Table 4: Correlation between platelet microparticles and CBC, CRP, and kidney and liver functions in groups A and B.

	Platelet microparticles			
	Group A		**Group B**	
	r	**p-value**	**r**	**p-value**
Hemoglobin	0.159	0.402	0.293	0.116
White blood cells	0.193	0.306	0.070	0.715
Neutrophils	0.206	0.275	0.093	0.627
Platelets	-0.029	0.879	-0.093	0.625
C-reactive protein	0.164	0.387	-0.211	0.263
Blood Urea	0.101	0.595	0.126	0.508

Serum Creatinine	-0.008	0.967	0.124	0.512
Alanine aminotransferase	-0.274	0.143	0.434	0.066
Aspartate aminotransferase	0.111	0.559	0.422	0.080

r: Correlation coefficient.

Table 5: Relation between platelet microparticles and type of organism in group A

Organism	**Platelet microparticles**
Klebsiella pneumoniae	57.4±10.1
Staphylococcus aureus	58.9±3.8
CoNS	50.9±4.4
Staphylococcus haemolyticus	56.3±11.7
Acinetobacter baumannii	54.0
Enterobacter cloacae complex	48.0
Staphylococcus epidermidis	44.5
Staphylococcus lentus	48.0
p-value*	0.049
K. pneumoniae vs. S. aureus	0.570
K. pneumoniae vs. CoNS	0.380
S. aureus vs. CoNS	0.043

* Kruskal-Walli's test comparing the three common organisms, CoNS: Coagulase-negative staphylococci.

PMPs in neonates infected with CoNS were significantly lower than those with S. aureus infection (p=0.043). However, no significant difference was found between Klebsiella pneumoniae and S. aureus infection (p=0.570) or CoNS (p=0.380). By the end of follow up 25 neonates (83.3%) of Group A (neonatal sepsis) and 7 (23.3%) of Group B died. The difference was statistically significant (p<0.001). **Table 5**

Table 6: Platelet microparticles levels in relation to neonatal death by the end of follow up

	Dead Neonates (n=32)	**Living Neonates (n=28)**
PMPs ($x10^3$/µl)	57.7±8.4	45.7±7.7
Test value*	102.000	
P-value	< 0 001	

Data were presented as mean ± SD, * Mann-Whitney Test.

The concentration of PMPs was significantly greater in non-surviving neonates than in surviving neonates. **Table 6**

The PMPs level was insignificantly different between both groups. **Table 7**

Table 7: Relation between platelet microparticles levels and prognosis of sepsis

	Living neonates (n=5)	**Dead neonates (n=25)**
PMPs ($x10^3$/µl)	50.1 ± 10.67	56.48 ± 7.27
Test value*	1.66	
P-value	0. .08	

Data were presented as mean ± SD.

Table 8: Kaplan Meier survival analysis of the studied groups

	Number of mortalities	**Mean**	**SE**	**95% CI for the mean**	**P value**
Group A	25 (83.33%)	0.8333	0.0681	0.700 – 0.967 (70.0%–96.7%)	**<0.001***
Group B	7 (23.33%)	0.2333	0.0765	0.084 – 0.383 (8.4%–38.3%)	
Group C	0 (0%)	0.0000	0.0000	0.000 – 0.100 (0%–10.0%)	

Mortality rate was significantly higher in (group A and group B) than group C (P <0.001). **Table 8**

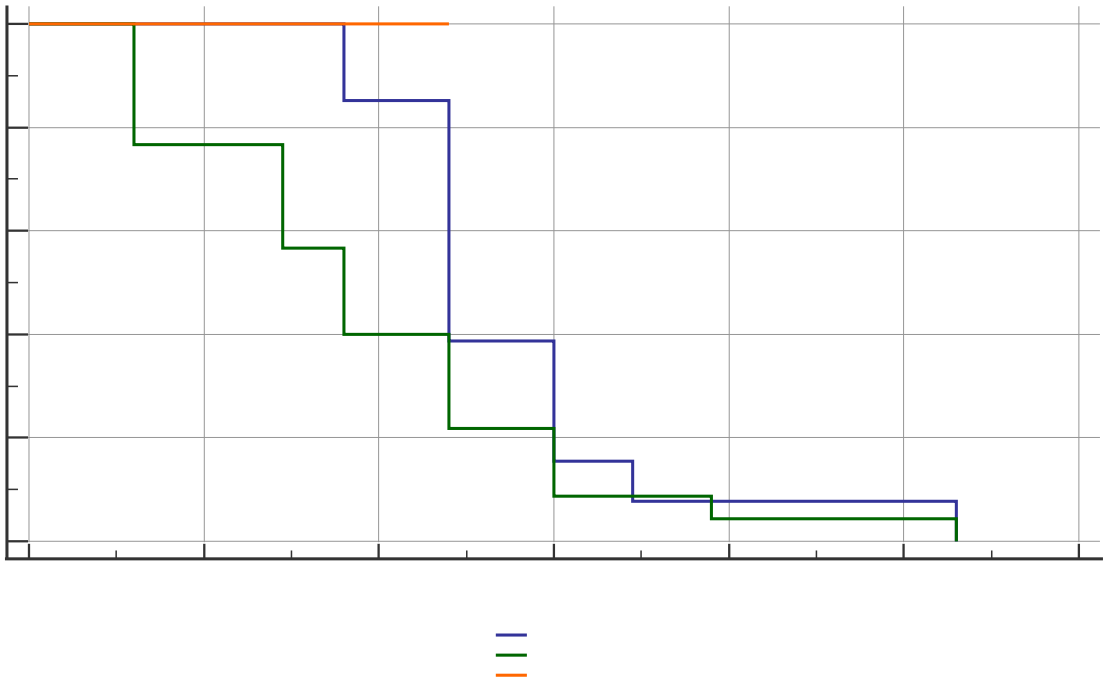

Figure 2: Kaplan Meier survival analysis of the studied groups

DISCUSSION

In the current study, PMPs were significantly higher in Group A (neonates with neonatal sepsis) compared to Group B (neonates with infections other than sepsis) (p=0.004) and Group C (healthy neonates) (p=0.005). However, no significant difference in PMPs was observed between Group B and Group C (p=0.937).

Furthermore, ROC curve analysis revealed a relatively weak predictive power of PMPs for differentiating neonatal sepsis from other infections At a cut-off value of 51 × 10^3/µl or more, the sensitivity of PMPs was 73.3%, while the specificity was 63.3%.

The absence of a significant difference between Groups B and C suggests that non-septic infections do not induce the same level of platelet activation. This reinforces the specificity of PMPs to septic conditions, likely due to the systemic inflammatory response in sepsis, which increases platelet activation and microparticle release.

These findings align with those of Bagchi [6] who assessed platelet indices as diagnostic markers for neonatal sepsis. Their study, involving 48 blood culture-proven sepsis cases and 48 healthy neonates as controls, demonstrated that thrombocytopenia, mean platelet volume (MPV), platelet large cell ratio (P-LCR), and the MPV-to-total platelet count ratio (MPV/TPC) were early markers for neonatal sepsis, with MPV/TPC showing the highest specificity (95.6%) and

predictive value (90.2%). They concluded that platelet indices are cost-effective and practical markers for neonatal sepsis diagnosis.

Additionally, our results are supported by Choudhary et al. [7] who investigated the importance of platelet indices as potential markers for neonatal sepsis. Their study demonstrated that neonates with sepsis exhibited significantly lower platelet counts and higher MPV and platelet distribution width values compared to controls ($p<0.0001$). Their results suggest that combining platelet indices with existing sepsis screening tools could enhance diagnostic accuracy and improve early identification of septic neonates.

Our results found that there was no statistically significant correlation between platelet microparticles and CBC, CRP, kidney functions, and liver functions in groups A and B. This finding suggests that while PMPs are elevated in neonatal sepsis. This finding contrasts with Ashour et al.[8] ,who assessed the pattern of systemic peripheral inflammatory response markers to explore their potential as early diagnostic predictors for the diagnosis of neonatal sepsis. The discrepancy between our findings and previous literature may be due to differences in study design, sample size, or the methodologies used for PMPs measurement.

Regarding the relationship between PMPs and the type of organism in Group A, we compared the three most common pathogens: Klebsiella pneumoniae, Staphylococcus aureus, and coagulase-negative staphylococci (CoNS). The analysis showed that PMPs levels in neonates infected with CoNS were significantly lower than those with S. aureus infection ($p=0.043$).

However, no significant difference was observed between Klebsiella pneumoniae and S. aureus ($p=0.570$) or between Klebsiella pneumoniae and CoNS ($p=0.380$).

Further studies is required to explore the mechanisms underlying these variations and their potential clinical implications.

Our findings are consistent with those of Bagchi,[6] who showed that Gram-negative bacteria were the most frequently isolated microorganisms in neonatal blood cultures. They suggested that most affected neonates likely acquired these pathogens during birth, leading to early-onset septicemia.

Furthermore, our study is in line with Choudhary et al.[7], who reported that Gram-negative bacteria were the predominant pathogens in neonatal sepsis cases, with Klebsiella pneumoniae being the most frequently isolated organism.

Based on our findings, it was observed that by the end of the follow-up period, mortality rates were significantly higher in Group A (neonatal sepsis), with 25 neonates (83.3%) not surviving, compared to 7 neonates (23.3%) in Group B ($p<0.001$).

Notably, PMPs levels were significantly higher in dead neonates compared to those who survived. This association suggests a potential prognostic value for PMPs in predicting disease severity and outcomes in neonatal sepsis.

Our findings align with previous studies highlighting the significant impact of neonatal sepsis on morbidity and mortality rates. for instance Stoll et al.[9] reported that neonatal sepsis is a major global health concern, contributing to high neonatal mortality. Similarly, their findings support our observation that sepsis is a critical determinant of neonatal outcomes.

Our findings demonstrate that platelet microparticles are elevated in neonatal sepsis compared with non-septic infections and healthy neonates. However, their diagnostic power remains limited. This aligns with previous studies highlighting PMP activation as part of sepsis pathology. The lack of correlation between PMPs and CRP suggests that PMPs may represent an independent inflammatory pathway. The observed association between elevated PMPs and mortality emphasizes their potential prognostic value. Larger multicenter studies are recommended to validate these findings.

CONCLUSION

Platelet microparticles are significantly elevated in neonatal sepsis and correlate with disease severity and outcome. PMPs levels did not show a significant correlation with systemic inflammatory markers or hematological parameters, suggesting a distinct role in sepsis pathology. Importantly, higher PMPs levels were associated with increased mortality in neonatal sepsis, suggesting a possible prognostic value. Despite limited diagnostic accuracy, they may serve as valuable prognostic markers for neonatal sepsis. Additional research is required to confirm their clinical utility.

REFERENCES

1. Odabasi IO, Bulbul A. Neonatal Sepsis. Sisli Etfal Hastan Tip Bul. 2020;54(2):142–58.
2. Ershad M, Mostafa A, Dela Cruz M, Vearrier D. Neonatal Sepsis. Curr Emerg Hosp Med Rep. 2019;7(3):83–90.
3. Hashem HE, Abdel Halim RM, El Masry SA, Mokhtar AM, Abdelaal NM. The utility of neutrophil CD64 and presepsin as biomarkers in neonatal sepsis. Int J Microbiol. 2020;2020:8814892.
4. Nomura S, Ozaki Y, Ikeda Y. Function and role of microparticles in various clinical settings. Thromb Res. 2008;123(1):8–23.
5. Reid VL, Webster NR. Role of microparticles in sepsis. Br J Anaesth. 2012;109(4):503-13.
6. Bagchi NR. Platelet parameters as early markers for neonatal sepsis. Int J Res Med Sci. 2023;11(4):1257–61
7. Choudhary RR, Makwana M, Mourya HK, Dabi J, Gulati K. Evaluation of platelet indices as markers of neonatal sepsis: a prospective case-control study. Int J Contemp Pediatr. 2018;5(5):1898–903.
8. Ashour R, Waael Z, Rashwan NI, Fayed HM. Systemic inflammatory markers response in neonatal sepsis. SVU Int J Med Sci. 2022;5(1):252–60.
9. Stoll BJ, Hansen N, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, et al. Late-onset sepsis in very low birth weight neonates. Pediatrics. 2002;110(2):285–91.

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ORIGINAL ARTICLE

CLINICAL OUTCOMES OF THE FISTULA BETWEEN MEDIAN CUBITAL VEIN AND BRACHIAL ARTERY

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ABSTRACT

Background: The brachial artery to median cubital vein arteriovenous fistula (BA-MCV AVF) is an alternative vascular access for hemodialysis, especially in the case of an inadequate distal vein. This study is to analyze the clinical results, patency and complication of BA-MCV AVF. **Methodology:** This was a prospective study of 50 patients with end-stage renal disease (ESRD) who were 18 years of age or older and needed hemodialysis access. Preoperative evaluations were based on the patients' demographics, comorbidities, laboratory results and detailed examination by duplex ultrasonography (DUS) of upper arm vessels. **Results**: Out of the total number of patients, males were 60% and females constituted 40% with the mean age of 52.34±10.12 years. The prevalence of diabetes and hypertension was 48 and 72%, respectively. Most fistulas (80%) were left sided. The average operative time was 56.8±4.20 min. Baseline vessel size measurements determined mean artery and vein diameters of 4.83±0.39 mm and 5.55±0.58 mm, respectively. Completion primary patency rates were 100% at 1 and 3 months and 86% at 6 months and 74% 1 year. Secondary patency was 100% throughout the entire observation period. Complications included stenosis of cephalic arch14%, central venous5%, hematoma14%, oedema18%, thrombosis/aneurysm10% and wound indfections6%. **Conclusion:** A-MCV AVF provides favorable early patency with acceptable complication rates, offering a viable option for hemodialysis access.

Keywords: arteriovenous fistula, brachial artery, median cubital vein, hemodialysis access, vascular complications

INTRODUCTION

Formation of a brachial artery to median cubital vein arteriovenous fistula (AVF) serves as an important access option for hemodialysis, especially when superficial venous anatomy is limited. There are several advantages to this configuration which may lead to successful maturation and good patency rates: Matching the vessel size; Shallow location for cannulation.

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Haddad et al. performed a systematic review of AVFs of the upper extremities and revealed that brachial-based fistulas tend to have favorable maturation rates when compared to grafts, emphasizing their importance as durable access (1). Nevertheless, patient selection and preoperative examination are still important to maximizing the outcome because anatomical variance and comorbid diseases influence significantly on the success of AVF formation (2).

Both anatomic and hemodynamic variables are associated with BrafMC AVF creation, with diameter reported to be the strongest predictor of success. Bahi showed that the fistula maturation and long-term patency is associated with the larger diameters of artery and vein (3). Similarly, Gomes et al. demonstrates the role of preoperative Doppler ultrasound screening in identifying vessels suitable for fistula formation as well as assist in operative planning and a decrease in early failure rates (4). This highlights the importance of a meticulous vascular mapping before surgery in order to select the appropriate vascular configuration for the patient (5).

Not without complication Brachial artery to median cubital vein AVFs have their limitations despite the benefits. The formation of steal syndrome, haematoma, and venous hypertension are other potential complications that may distress patient and compromise function. A study compared brachial-based autogenous AVFs with prosthetic grafts and higher risk for steal syndrome due to higher flow rates with brachial artery inflow (6). Moreover, Dukkipati et al. reported a case involving a fistula too close to major nerves that was associated with compression of the median nerve and complexity of the surgical anatomy of the antecubital fossa (7). These complications emphasize the necessity of a careful surgical and postoperative follow-up in order to minimize the risk (8).

Percutaneous methods are progressing, and alternative methods other than surgery are appearing in the creation of AVFs, such as brachial artery to median cubital vein fistulas. Nelson et al. highlighted the developing application of percutaneous arteriovenous fistula creation, which enables reduced procedure time and potentially less wound complications (4). A recent study by Montelongo reported succesful results of endovascular fistulas versus surgical method in the short term (9). Although the percutaneous approach appears to be promising, the importance of patient selection, in terms of both vessel depth and caliber, which may preclude it in some circumstances, should be strongly emphasized (10,11).

Long-term patency is a key issue in hemodialysis vascular access. Shahverdyan et al. showed excellent long-term results for both percutaneous and surgical brachial-based AVFs when individual patient factors are taken into account (8). Similarly, Bhatti et al. found one-year patency rates of >75% for brachial artery-based fistulas suggesting durable patency with adequate follow up (12). With close follow-up, early management of stenosis and individualized care, the brachial artery to the median cubital vein AVF results in a long standing reliable access (13).

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Brachial artery to median cubital vein AVFs constitute a useful access alternative, specifically in the presence of unfavourable forearm veins. Favorable results rely on diligent preoperative assessment, competent performance of the surgery, and close postoperative monitoring for early identification and treatment of complications. With new technology such as endovascular AVF creation, comparative studies are necessary to clarify long-term effect in comparison to surgical techniques (14-15). Individualized patient-centered strategies continue to be the focus of securing optimal hemodialysis vascular access (16).

The purpose of this study is to review the clinical results and patency rates of brachial artery (BA) to median cubital vein (MCV) arteriovenous (AV) fistulas in patients in need of hemodialysis access. The research also aims to reveal standard complications and success factors of fistulas.

PATIENTS AND METHODS:

This was a prospective trail done on 50 (cases > = 18 years of age, both gender), ESRD patients for hemodialysis. Inaccessible vein distal to cubital fossa and had distal radial artery, occluded distal radiocephalic AVF and the diameter of median cubital vein was at least 2.5cm. Before commencement of the study, Ethical Committee of Aswan University Hospital approved the study. There was a written informed consent of the person. Exclusive criteria were pediatric patients, those with antecubital vascular access operation history and young patients with cephalic vein >2.5 cm. All patients underwent the following: Demographic data (age, age at diagnosis of OSA, sex, occupation and residence), social history (smoking and alcohol intake), other comorbidities and complications, if present, general examination, vital signs, including BMI and blood pressure, clinical (hypertension, DM and first degree relative status) and laboratory data and liver function tests (albumin, total and direct bilirubin, INR, AST, ALT, and alkaline phosphatase), HCV Ab and HBsAg) and renal function tests (blood urea and serum creatinine), HbA1c, fasting blood sugar and lipid profile.

Preoperative assessment

A tourniquet was placed near the axilla for duplex ultrasound (DUS) of upper arm (compulsorily, we examine the cephalic, the basilic and the brachial veins, from ACV to at least 1cm beyond the cranial face of the arm). Stenosis or occlusion are also tested by tracing the appropriate diameters of the vein into the subclavian vein and examining the latter by means of direct, non-compressive examination and compression. Evaluation of draining veins: Compression and visual inspection were utilized at serial visits to review all draining veins for stenosis/thrombosis as they developed. Indirect central venous evaluation: Jugular and subclavian veins Adiagnostic afections of indirect signs of central venous stenosis were evaluated by using Doppler waveforms. The respiratory phasicity and cardiac pulsatility are two clues for stenosis or obstruction of the SVC and/or the non-visualized BC vein.

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Venography content pending.

A. Postoperative assessment:

The identification of complications and patency was mainly performed with duplex ultrasound with one year follow-up. At this time, venography is pending content. Potential complications are: immaturity(0%), outflow stenosis(an outflow velocity 400 cm/s or greater has been correlated with five percent of cases), hematoma, perigraft fluid, aneurysm, pseudoaneurysm, thrombosis/occlusion, and pseudoaneurysm.

Follow-up: Follow up will occur at 1, 3, and 12 months.

Sample Size Calculation

We use Steven K. Thompson equation to calculate the sample size, from the next formule[1]

$$n = \frac{N \cdot P(1-P)}{\left(\frac{(N-1)\cdot d^2}{Z^2}\right) + P(1-P)}$$

Where:

n: Sample Size, N: Population Size, Z: 95% level of confidence, d: Error Proportion, P: Probability,

Statistical analysis

Statistical tests were conducted using SPSS v26 (IBM Corp., Armonk, NY). Quantitative variables were demonstrated by standard deviation (SD) and mean (IQR). Qualitative variables were presented as frequency and percentage (%). The Shapiro-Wilk test was used to check if the data was normally distributed. A two-tailed $P < 0.05$ was considered a significant result.

RESULTS

Demographics The gender distribution in the study population is fairly even with a slightly higher percentage of males (60%) than females (40%). The average age of the patients was 52.34 years (ranging from 33 to 74), that means an age range of middle aged and older persons which is common for vascular access interventions. The burden of comorbidities was considerable, with nearly half of the cohort having diabetes (48%) and nearly three-fourths having hypertension (72%). Cardiovascular disease was also present in 16%, and such a high risk population is frequently encountered in vascular interventions, where multiple comorbidities can alter both operative risk and long term vascular access patency.

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Table 1: Demographic data and associated comorbidities of study subjects

	Total subjects	
n=50		
Age (years)	Mean ± SD	52.34 ± 10.12
	Median (Min-Max)	53.00 (33.00-74.00)
Gender	Female	20 (40.0%)
	Male	30 (60.0%)
Diabetes	n (%)	24 (48.0%)
Hypertension	n (%)	36 (72.0%)
Cardiovascular Disease	n (%)	8 (16.0%)

The operative features reflect a significant left-side procedure favoritism (80%) and likely represent either anatomical or practice patterns relating to operator or center preference for left-side access relating to vessel caliber or prior access difficulty characteristics. In 30% of the cases, the right side was employed. History of failed access was previously reported in 10% of patients, representing a difficult subset of patients for vascular access that may serve to confound future interventions. The average time of operation was 56.8 min and the standard deviation was low which shows the reliability of the operative duration and provides evidence of alignment of operative technique among the surgeons.

Table 2: Operation related data among study subjects

	Total subjects	
n=50		
Side	Left	40 (80.0%)
	Right	10 (20.0%)
Previous Access Failure	n (%)	5 (10.0%)
Mean Operative Time (minutes)	Mean ± SD	56.80 ± 4.20

Baseline arteriovenous (AV) measurements are informative of the vascular anatomy of the study population. Average arterial size was 4.83 mm while venous size was 5.55 mm, both sizes being in a range that would support AV access creation. The average anastomosis size was 10.42 mm, suggestive of appropriately sized surgical production of the AV shunt. The uniformly small ranges of vessel sizes indicate the cohort was more homogenous in their vascular caliber, a factor that could lead to more consistent results after upfront access orifice creation and be advantageous for long-term access patency.

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Table 3: Baseline AV measurements in study subjects

	Total subjects	
n=50		
Artery Size (mm)	Mean ± SD	4.83 ± 0.39
	Median (Min-Max)	4.80 (3.60-5.60)
Vein Size (mm)	Mean ± SD	5.55 ± 0.58
	Median (Min-Max)	5.60 (4.30-7.10)
Anastomosis Size (mm)	Mean ± SD	10.42 ± 0.95
	Median (Min-Max)	10.50 (8.80-12.60)

The complications database is a listing of a range of conditions present after surgery. The most common treated complication was cephalic arch stenosis, which was treated with percutaneous transluminal angioplasty (14%) or surgical bypass (10%) but occasionally required a more invasive resection with end-to-end anastomosis (6%). Central venous stenosis was treated by PTA (6%) and jugular bypass (6%), suggesting the need for both endovascular and surgical techniques in certain patients. Steal syndrome was reported in a minority of cases, treated conservatively or surgically. Minor complications, including hematoma (14%), edema (18%), thrombosis and aneurysm (10%), and wound infections (6%) occurred and are similar to the reported complication profile seen with AV access procedures. These results emphasize the necessity to be vigilant in the post-operative course and to personalize management.

Table 4: Complications Among Study Subjects

Complication	**Type**	**n (%)**
Cephalic Arch Stenosis	PTA	7 (14.0%)
	Surgical Bypass	5 (10.0%)
	Resection with End-to-End Anastomosis	3 (6.0%)
Central Venous Stenosis	PTA	3 (6.0%)
	Jugular Bypass	3 (6.0%)
Steal Syndrome	Conservative	2 (4.0%)
	Distal Revascularization	1 (2.0%)
	Anastomosis Reduction	1 (2.0%)
Hematoma		7 (14.0%)
Edema		9 (18.0%)
Thrombosis and Aneurysm		5 (10.0%)
Wound Infections		3 (6.0%)

Comparison data of patency rates of follow-up shows very good early results, with 1 month and 3 months patency rates being 100%. However, it tapered off a bit with the primary patency at 6 months and 1 year being 86% and 74% respectively, which brings to the fore the chronic nature of AV access dysfunction over age. Second ary patency, however, remained 100% at follow-up,^

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sug gesting that patency was excellent in the long term when reintervention was possible, although some patients required inter vention for access to continue to function. This highlights the need for surveillance and routine readiness for attempts to protect patency of access.

Table 5: Patency rate during follow-up period

Total subjects, n=50	**1m**	**3m**	**6m**	**1y**
Primary patency	50 (100%)	50 (100%)	43 (86%)	37 (74%)
Secondary patency	50 (100%)	50 (100%)	50 (100%)	50 (100%)

DISCUSSION

The present study population is representative of a standard hemodialysis cohort, being middle-aged to elderly, predominantly male, and having a high prevalence of diabetes and hypertension. This is in line with other literature, where comorbidity has a major impact on AV Feng outcome. Robinson et al. stressed that there is wide variation across Canadian centers in AVF use and comorbid patient characteristics, with older patients and comorbid patients disfavored variability in access might be related to patient-specific factors statics like age and comorbid responses which might tend to preclude access patients; Fistulas continue to produce better long-term results in the face of early higher rates of non-maturation of fistulas (17). In our study, in the presence of these comorbidities, median cubital vein-based AVFs exhibited an acceptable maturation and patency rates, pointing out the fact that meticulous preoperative mapping might be able to override many of the patient-related risk factors.

The overwhelming preference for left-sided fistula creation (80%) in our series is likely due to anatomic convenience as well as surgeon preference; the left side may afford superior vein caliber and the greater accessibility. Similar findings were reported by Vergara-Pérez et al., who also underscored the necessity of vessel selection in both surgical and endovascular AVF formation (18). The preoperative duplex evaluation carried out in our study was crucial in selecting suitable vessels, which contributed to limiting poor early results and to homogenize operative times (mean 56 min).

Vascular assessment in our patients showed good caliber arteries and veins and this for sure accounts for the very high technical success of fistula construction. Correct vessel diameter is a known predictor for maturing AVF. Janeckova et al. stated that providing suitable vessel diameter minimizes aneurysmal degeneration, which is a potential long-term complication of brachial-based fistulas (19). Sizes of our measured vessels were within ideal dimensions and may have accounted for the lack of early aneurysm development over the first year of follow-up.

The complication rate in this series was similar to previously published data, with cephalic arch stenosis as the predominant problem requiring intervention. Mishra compared the anatomical characteristics and outcomes of distal and proximal AVFs, and reported that although proximal

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AVFs with high flow rate, such as in the brachial-median cubital relationship, predicted an increased frequency of outflow stenosis and its related problems, with outflow stenosis found in more than half of the cases, which is higher than in distal AVFs, ranging from 7 to 27% (20). Steal syndrome, hematoma, thrombosis, and wound infection in our series are within the normal distribution for this type of high-flow fistula. Patwari et al. also demonstrated comparable rates of that support the need for long-term monitoring for early detection and treatment (21).

The patency rates at first 1 and 3 months (100%, respectively) decrease to 86% and 74% at 6 and 12-months, respectively, in our study population and are similar with other studies. Sungur et al. showed that the decrease of the PP rates with time could be offset by secondary interventions, which might keep long-term access open, as proven by our unaltered SP rate of 100% during follow-up (22). The consistent secondary patency corroborates the importance of early intervention in extending fistula function, a key objective in hemodialysis access surveillance.

The importance of Doppler ultrasonography in the preoperative evaluation and postoperative follow-up is also critical for the prevention and early management of complications as well for predicting AVF maturation. Suraj et al. reported that frequent Doppler monitoring can significantly increase the rates of maturation and treatment of complications in flow through grafts (23). Detailed duplex protocols in our study are probably responsible for early detection of stenosis and timely interventions, with excellent long-term results. Furthermore, comparisons with other types of fistulas, as well those presented by Kazemlou et al., suggest that the brachial artery to median cubital vein type may achieve as good, or better, outcomes in properly selected patients (24).

Although ruptumption could not be detected by our one-year follow up data, Peng et al. presented a case of pediatric patients with developed aneurysm of brachial AVF that was treated by coil embolization (25). This underscores the need for strict long-term follow-up beyond the first year in order to capture late complications.

Increasing interest in percutaneous AVF formation has resulted in alternative methods that may reduce insult to vessels without compromising access function. Hull et al. showed that percutaneously created devices with ultrasound guidance can produce patency rates similar to that of surgical AVFs, but long-term outcome comparisons are still lacking (26). Our study adds to the evidence that surgically constructed BA-MCV fistulas continue to be extremely durable, although new technology may give alternative options in selected patients.

It is the specifics of technical consideration at the time of AVF creation that are critically important in terms of long term outcome. It was stressed that meticulous surgical technique, including ideal 90-degree anastomotic configuration and intra-operative evaluation of the vessels, can significantly reduce failure rates (27). In our series, the stable average duration of surgical procedure and the low early failure rate point to uniform performance of the procedure and overall good early results.

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Lastly, the choice of anesthesia can be another perioperative factor that may impact the outcome. Regional anesthesia may also favor better outcomes since it improves an intraoperative vasodilatation, which might have beneficial effects on vessel handling and vessel patency, as described by Macfarlane et al. (28). That consideration may be important for future protocols which are looking to improve fistula success, although it was not evaluated in our study.

CONCLUSION

In conclusion, BACMV-AVF showed high early patency rates and acceptable complications, and could be effective as a durable access for hemodialysis in properly selected patients. Judicious preoperative assessment, specifically with duplex ultrasonography, standardized surgical technique combined with close follow-up, led to superior outcomes of primary and secondary patency. Although some potential complications, such as cephalic arch stenosis, hematoma, and steal syndrome, were noted, they were also manageable after intervention, respectively. These results lend support to continued use of BA-MCV AVF as a reliable access site, although the routine practice should always include individualisation of care, vigilance during follow up and consideration of emerging minimally invasive alternatives to further promote long-term vascular access patency.

REFERENCES

1. Haddad, D. J., Jasty, V. S., Mohan, B., Hsu, C. H., Chong, C. C., Zhou, W., & Tan, T. W. (2022). Comparing outcomes of upper extremity brachiobasilic arteriovenous fistulas and arteriovenous grafts: a systematic review and meta-analysis. *The Journal of Vascular Access*, *23*(1), 32-41.

2. Bahi, M. (2022). Effect of artery diameter and velocity and vein diameter on upper limb arteriovenous fistula outcomes. The Scientific World Journal, 2022(1), 2158013.

3. Kim, H., Ahn, S., Kim, M., Chung, C. T. Y., Choi, K. W., Ko, H., ... & Ha, J. (2022). Comparison between autogenous brachial–brachial upper-arm elevated direct arteriovenous fistulas and prosthetic brachial-antecubital indirect forearm arteriovenous grafts. The Journal of Vascular Access, 23(6), 936-945.

4. Nelson, P. R., Mallios, A., Randel, M., & Jennings, W. C. (2021, December). Percutaneous arteriovenous fistula creation. In Seminars in Vascular Surgery (Vol. 34, No. 4, pp. 195-204). WB Saunders.

5. Meguro, T., Tada, Y., Taniguchi, M., Hamauchi, S., Fukuhara, T., Miyoshi, Y., & Ono, S. (2024). Dural Arteriovenous Fistula Treated with Transvenous Embolization via the Upper Limb Cutaneous Vein. Journal of Neuroendovascular Therapy, 18(5), 142-148.

6. Kim, H., Nelson, P. R., Mushtaq, N., Mallios, A., Kempe, K., Zamor, K., ... & Jennings, W. C. (2023). Creating reverse flow arteriovenous fistulas with a forearm cannulation target. The Journal of Vascular Access, 24(4), 552-558.

Corresponding author: Kareem Diaa Ahmed, Tel: +201069492745; e-mail: kareemdiaa133@gmail.com

7. Dukkipati, R., Richler, A., Shah, A., & de Virgilio, C. (2022). Median nerve and ulnar nerve entrapment with cubital tunnel syndrome in a hemodialysis patient following creation of an arteriovenous fistula. Case Reports in Nephrology and Dialysis, 11(3), 275-280.
8. Shahverdyan, R., Mehta, T. I., Inston, N., Konner, K., & Vartanian, S. (2025). Long term results of a comparative study of percutaneous and surgically created proximal forearm arteriovenous fistulae. European Journal of Vascular and Endovascular Surgery.
9. Montelongo, S., Brooks, D. E., Klopfenstein, J., & Peden, E. K. (2022). Surgical creation of upper extremity arteriovenous fistula and grafts: a narrative review. Cardiovascular Diagnosis and Therapy, 13(1), 147.
10. Gomes, A. P., Germano, A., Sousa, M., Martins, R., Coelho, C., Ferreira, M. J., ... & Nunes, V. (2021). Preoperative color Doppler ultrasound parameters for surgical decision-making in upper arm arteriovenous fistula maturation. Journal of Vascular Surgery, 73(3), 1022-1030.
11. Vergara-Pérez, H., Diaitz-Usetxi Laplaza, R., Baliño Remiro, P., Pérez Alba, A., Rius Peris, A., Garcia Bello, Á., ... & Reque, J. (2025). Comparative outcomes of surgical versus percutaneous arteriovenous fistulas: a prospective study. Clinical Kidney Journal, 18(4), sfaf063.
12. Bhatti, M. S., Khuhro, A. Q., Brohi, I. B., Memon, M. A., & Manzoor, S. (2022). Arteriovenous fistula outcomes in terms of one year patency rate and complications. The Professional Medical Journal, 29(02), 188-192.
13. Liebetrau, D., Zerwes, S., Kerndl, H., Schaal, J., & Hyhlik-Dürr, A. (2023). Technical aspects of percutaneous endovascular arteriovenous fistula creation with the Ellipsys® Vascular Access System. Preliminary results after 16 patients. Langenbeck's Archives of Surgery, 408(1), 91.
14. Mallios, A., Kempe, K., & Jennings, W. C. (2024). Proximal Radial Artery Arteriovenous Fistulae. In Principles of Dialysis Access (pp. 157-165). Cham: Springer Nature Switzerland.
15. Cornman-Homonoff, J., Razdan, R., & Lozada, J. C. P. (2025, March). Anatomy of Endovascular Arteriovenous Fistula Creation. In Seminars in Interventional Radiology. Thieme Medical Publishers, Inc..
16. Mallios, A., Bourquelot, P., Harika, G., Boura, B., & Jennings, W. C. (2021). Percutaneous creation of proximal radio-radial arteriovenous hemodialysis fistula before secondary brachial vein elevation. The Journal of Vascular Access, 22(2), 238-242.
17. Robinson, T., Geary, R. L., Davis, R. P., Hurie, J. B., Williams, T. K., Velazquez-Ramirez, G., ... & Murea, M. (2021). Arteriovenous fistula versus graft access strategy in older adults receiving hemodialysis: a pilot randomized trial. Kidney Medicine, 3(2), 248-256.
18. Vergara-Pérez, H., Diaitz-Usetxi Laplaza, R., Pérez Alba, A., Baliño Remiro, P., Rius Peris, A., Fenollosa Segarra, M. Á., ... & Reque, J. (2025). Is endovascular arteriovenous fistula a feasible alternative for hemodialysis patients?. Blood Purification, 54(1), 37-43.
19. Janeckova, J., Bachleda, P., Koleckova, M., & Utikal, P. (2023). Brachial artery aneurysm as a late complication of arteriovenous fistula. The Journal of Vascular Access, 24(5), 926-932.
20. Mishra, B. (2021). Comparison of distal radiocephalic fistula vs proximal radiocephalic fistula. Journal of Family Medicine and Primary Care, 10(1), 132-137.

Corresponding author: Kareem Diaa Ahmed, Tel: +201069492745; e-mail: kareemdiaa133@gmail.com

21. Patwari, S. S., Dikle, S., Dube, S., Husain, S., & Patil, B. (2025). Short Term Arteriovenous Fistula Short Term Patency Rates at Tertiary Care Center. European Journal of Cardiovascular Medicine, 15, 734-736.
22. Sungur, M. A., Karaca, O. G., & Ecevit, A. N. (2021). Cost-effectiveness analysis of radiobasilic and brachiobasilic arteriovenous fistulas in hemodialysis patients. Therapeutic Apheresis and Dialysis, 25(5), 628-635.
23. Suraj, H. S., Kumar, S. A., Rachegowda, N., Rajeswari, G. T., Ullas, L. Y., Revanth, R. B., ... & Nagegowda, R. (2024). Role of Doppler Evaluation in Assessing the Maturation of the Arteriovenous Fistula for Hemodialysis: An Observational Study. Cureus, 16(3).
24. Kazemlou, H., Khaleghian, M., Motaghi, P., & Khavaninzadeh, M. (2022). Comparing the outcomes of proximal radial artery arteriovenous fistula and brachio-cephalic arteriovenous fistula for hemodialysis vascular access. Journal of Surgery and Trauma, 10(1), 4-10.
25. Peng, H. Y., & Liu, C. A. (2024). Successful treatment by coil embolization for pediatric brachial arteriovenous fistula: A case report. Radiology Case Reports, 19(9), 3599-3604.
26. Hull, J. E., Jennings, W. C., Cooper, R. I., Narayan, R., Mawla, N., & Decker, M. D. (2022). Long-term results from the pivotal multicenter trial of ultrasound-guided percutaneous arteriovenous fistula creation for hemodialysis access. Journal of Vascular and Interventional Radiology, 33(10), 1143-1150.
27. Sahasrabudhe, P., & Bindu, A. (2021). Nuances of arteriovenous fistula creation for vascular access in hemodialysis. Indian Journal of Plastic Surgery, 54(03), 257-263.

28. Macfarlane, A. J., Kearns, R. J., Clancy, M. J., Kingsmore, D., Stevenson, K., Jackson, A., ... & Aitken, E. (2021). Anaesthesia Choice for Creation of Arteriovenous Fistula (ACCess) study protocol: a randomised controlled trial comparing primary unassisted patency at 1 year of primary arteriovenous fistulae created under regional compared to local anaesthesia. BMJ open, 11(12), e052188.

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