Enhanced Recovery Protocol: Is It Safe and Feasible After Open Conventional Liver Surgery?

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ABSTRACT

Background: Open liver resections are essential for managing primary and secondary liver tumors but are often associated with significant morbidity, prolonged recovery, and high healthcare costs. Enhanced Recovery After Surgery (ERAS) protocols have demonstrated improved outcomes in various surgical fields, yet their application in open liver surgery remains under-investigated, particularly in low- and middle-income settings.

Objective: To assess the safety, feasibility, and clinical impact of implementing ERAS protocols in open conventional liver resections compared to traditional perioperative care.

Methods: A retrospective single-center study was conducted on 100 patients who underwent open liver resections at Tanta University Hospitals (2018–2023). Patients were divided into two groups: Group A (Pre-ERAS, n=50) and Group B (ERAS, n=50). ERAS protocols were implemented according to the ERAS Society Guidelines and involved structured interventions across the preoperative, intraoperative, and postoperative phases. Primary outcomes included operative blood loss, complications, and length of hospital stay.

Results: ERAS implementation led to significantly reduced blood loss (376 ± 140 ml vs 428 ± 160 ml, p=0.039), shorter hospital stay (4.68 ± 1.4 vs 6.24 ± 2.1 days, p<0.001), and lower wound infection rates (12% vs 30%, p=0.0041). However, a higher rate of intra-abdominal collections was observed in the ERAS group (30% vs 14%, p=0.07).

Conclusions: ERAS protocols are safe and feasible in open liver surgery and significantly improve recovery outcomes. Nevertheless, individualized drain management strategies may be necessary to mitigate the risk of intra-abdominal collections.

KEYWORDS: Enhanced Recovery After Surgery (ERAS), open liver resection, perioperative outcomes, blood loss, surgical site infection, intra-abdominal collection, postoperative recovery.

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INTRODUCTION

Liver resection remains the cornerstone treatment for both primary liver tumors such as hepatocellular carcinoma, and secondary tumors, particularly colorectal liver metastases. Despite advancements in surgical techniques and perioperative care, liver surgery continues to pose significant risks, with reported postoperative morbidity rates ranging between 20% and 50%, depending on the extent of resection and patient comorbidities [1]. Complications such as bleeding, bile leakage, infections, and delayed recovery contribute to increased healthcare costs, prolonged hospitalization, and delayed return to baseline function. [1]

Enhanced Recovery After Surgery (ERAS) protocols, first introduced by Kehlet in the late 1990s, are multidisciplinary, evidence-based strategies that aim to reduce surgical stress, maintain physiological function, and accelerate recovery. ERAS has become a standard of care in colorectal and gynecologic surgery, leading to reduced complication rates and hospital stays without compromising patient safety. [2]

However, the implementation of ERAS in liver surgery, particularly open conventional liver resections, remains a subject of ongoing evaluation. The liver's central metabolic role, potential for high intraoperative bleeding, and need for complex postoperative monitoring have raised concerns about the safety and feasibility of ERAS in this setting. Additionally, there is variation in the adoption and adaptation of ERAS components between centers, especially in developing countries. [3]

While previous studies have shown promising results in laparoscopic liver resections, the data on open procedures are less abundant. The ERAS Society released liver-specific guidelines in 2020 yet in the real-world, clinical validation is essential. [1]

Recent studies have investigated ERAS implementation in liver surgery, but most focus on laparoscopic or minimally invasive techniques. A 2020 meta-analysis by Raoof et al [4], revealed that ERAS protocols significantly reduce length of stay and complications in laparoscopic hepatic resections. However, there remains a gap in the literature regarding open resections, particularly in low- and middle-income countries. Melloul et al. [1], in the official ERAS Society guidelines for liver surgery, emphasized the need for tailored ERAS protocols in open cases due to the higher surgical trauma and risk of fluid shifts. Additional studies, such as those by Chong et al. [5] and Noba et al. [6], support ERAS safety in open hepatectomy but highlight variability in outcomes due to institutional differences.

This study aims to assess the safety, feasibility, and clinical impact of ERAS protocol implementation in patients undergoing open liver resection at a high-volume tertiary care center in Egypt, comparing perioperative outcomes with those of conventional care.

PATIENTS AND METHODS

This was a retrospective, observational, single-center study conducted at Tanta University Hospitals in Egypt over five years, from January 2018 to December 2023. The study included a total of 100 adult patients who underwent open liver resection for benign and malignant hepatic tumors.

The ERAS protocol was conducted through the preoperative, intraoperative, and postoperative phases [1]:

- **Preoperative Phase**: Patients were given carbohydrate-rich drinks 2–3 hours' pre-op, given prophylactic antibiotics and DVT prophylaxis, along with chest physiotherapy.
- **Intraoperative Phase**: Anesthesia included thoracic epidural or PCA, with minimized opioid use. Active warming devices and goal-directed fluid therapy were used.
- **Postoperative Phase**: Nasogastric tubes were removed immediately after surgery and patients started clear fluids after 6 hours and an advanced soft diet within 24 hours. Urinary catheters were removed on postoperative day 1, and patients were encouraged to ambulate. Pain was controlled by non-opioid multimodal analgesia, NSAIDs, and paracetamol.

Study Design and Groups

Patients were divided into two groups of 50 each:

- **Group A (Pre-ERAS)**: Managed with traditional non-ERAS perioperative care.
- **Group B (ERAS):** Managed according to a standardized ERAS protocol implemented in 2020.

Inclusion criteria:

- Age more than 18 years.
- Non-cirrhotic patients with resectable benign and malignant liver lesions with FLR > 26%.
- Cirrhotic patients with resectable malignant liver lesions with Child Pugh score A and B, and FLR > 40%.

Exclusion criteria:

- Patients with ASA > 3
- Liver resection for donation.
- Patients need ALPPS.
- Cirrhotic child C patients and HCC patients with macrovascular invasion.
- Associated surgeries like colectomies, gastrectomy, lymphadenectomies and CBD resection.

Ethical Approval

Informed written consent was obtained from all participants in the research.
The study was approved by the ethical committee, faculty of medicine Tanta University.

ERAS Protocol Components

Group B patients received care according to ERAS Society Guidelines for Liver Surgery ***(Melloul et al., 2020***) [1], including:

- Preoperative education and carbohydrate loading.
- Prophylactic antiemetics and preemptive analgesia.
- Intraoperative goal-directed fluid therapy, warming devices, and limited opioid use.
- Early removal of nasogastric tubes, urinary catheters, and surgical drains.
- Early mobilization within 24 hours post-op.
- Oral fluids within 6 hours and soft diet by POD 1.

Surgical Procedures

All surgeries were performed by experienced hepatobiliary surgeons using open techniques. Types of resections included non-anatomical (wedge) resections, left lateral segmentectomy and major anatomical hepatectomies (right or left) (Fig.1).

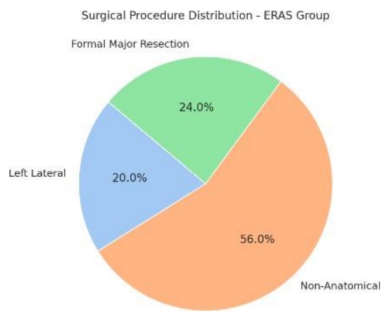

Figure (1): Types of liver resection

Data Collection and Outcomes

Data was extracted from hospital records. Outcomes assessed included:

- Intraoperative: operative time, blood loss.
- Postoperative: time to oral intake, analgesic use, complications (bleeding, bile leak, collections, infections), length of hospital stay (LOS).
- Complications were classified using Clavien–Dindo grading.

Statistical Analysis

Statistical analysis was performed using SPSS version 26.0 (IBM Corp, Armonk, NY). Continuous variables were expressed as mean ± SD and compared using the student's t-test. Categorical variables were compared using Chi-square. A p-value < 0.05 was considered statistically significant.

RESULTS

Demographics and Baseline Characteristics:

Both groups were comparable in age and sex distribution (Table 1).

Table (1): Patient Demographics and Operative Data:

Variable	Group A (Pre- ERAS)	Group (B) ERAS	p-value
Mean age	51.8 ± 11.7	54 ± 11.6	
Gender: M/F	26/24	30/20	
BMI (kg/m²)	33.8 ± 3.9	23.3 ± 4.3	<0.001
Tumor size (cm)	8.1 ± 2.8	7.24 ± 2.1	<0.001
Operative time (min)	118.4 ± 34.5	133.4 ± 25.6	<0.001
Blood loss (ml)	428 ± 160	376 ± 140	0.039

The non-ERAS group had significantly higher mean BMI (33.8 ± 3.9 vs. 23.3 ± 4.3 p < 0.001). Tumor size was similar across groups. In reviewing the operative time, it was significantly low in pre-ERAS group compared to ERAS group (118.4 ± 34.5 vs 133.4 ± 25.6 p <0.001). Mean blood loss in Pre- ERAS group: 428 ± 160 ml, mean blood loss in ERAS group: 376 ±140 ml (p = 0.039), (Fig.2). This aligns with global findings, confirming statistical significance and clinical relevance.

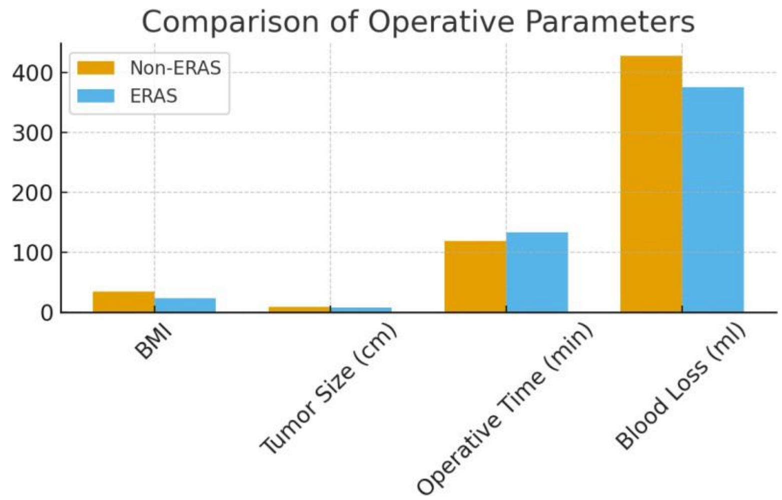

Figure (2): Comparison of Operative Parameters (ERAS vs Non-ERAS)

Table (2): Subgroup Analysis of Postoperative Outcomes:

Outcome	Group A (Pre-ERAS)	Group B (ERAS)	p-value
Postoperative Bleeding	16% (n=8)	4% n=2	0.046
Wound Infection	30% (n=15)	12% (n=6)	0.0041
Bile leak	10% (n=5)	18% (n=9)	0.25
Intra-abdominal Collection	14% (n=7)	30% (n=15)	0.07
Length of Stay (LOS)	6.24 ± 2.1 days	4.68 ± 1.4 days	<0.001

Total 10 patients out of 100 experienced post-operative bleeding, 8 patients were managed conservatively with transfusion of blood and blood products, 2 patients were taken back to operating room for control of bleeding. Total 21 patients had early wound infections, all wound infections were limited to skin and subcutaneous tissue with intact fascia and no burst abdomen, 18 Patients were treated with wound dressing while 3 patients required wound debridement and resuturing. In our study, total of 14 patients had bile leak, 10 patients were managed with image guided percutaneous abdominal drainage and nutritional support while 4 patients required ERCP and stent placement. Total 22 patients had intrabdominal collections, 14 of them had bile leaks, 2 patients had intrabdominal hematoma required intraoperative management, 4 patients had intrabdominal abscess which was treated with percutaneous image guided drainage, 2 patients had post-operative serosanguineous collection that were managed conservatively. Length of hospital stay was significantly low in ERAS group compared to Pre-ERAS group (4.68 ± 1.4 days' vs 6.24 ± 2.1 days) (Table 2 and Fig.3)

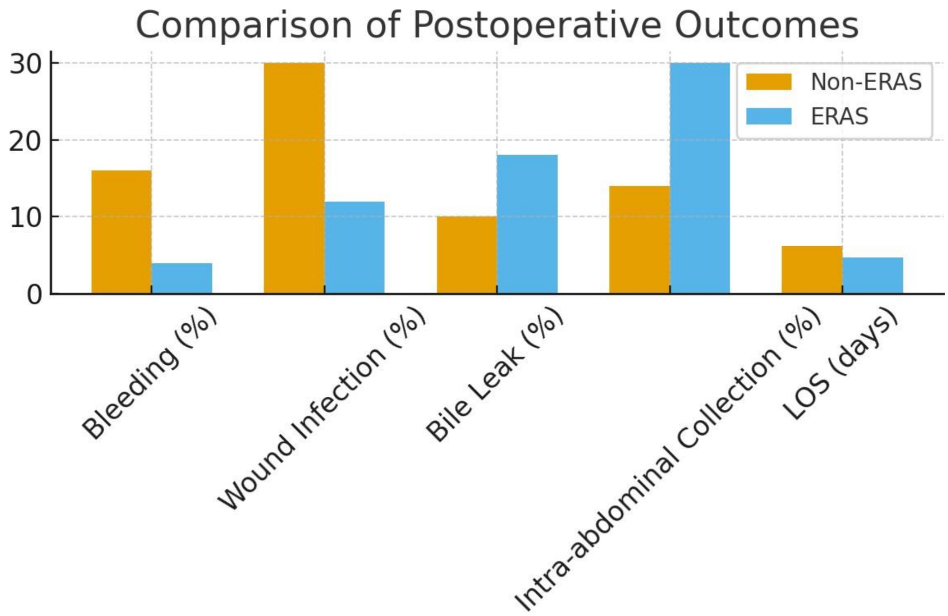

Figure (3): Comparison of Postoperative Outcomes (ERAS vs Non-ERAS)

DISCUSSION

Operative time and intraoperative blood loss are critical metrics in liver surgery due to their direct impact on perioperative morbidity, need for transfusion, postoperative recovery, and overall surgical complexity. Open liver resections, unlike laparoscopic ones, are associated with higher surgical trauma and bleeding risk due to greater tissue handling, larger incisions, and broader exposure [5]. The introduction of ERAS protocols—despite focusing more on perioperative care—has shown indirect influence on both operative duration and blood loss control. While ERAS itself doesn't shorten operative time per se, some of its principles (e.g., preoperative optimization, fluid management, thermoregulation) can influence intraoperative dynamics and bleeding [6]. Literature offers mixed data, with some studies reporting slightly longer operating times but lower blood loss in ERAS groups, suggesting a trade-off between procedural precision and safety. [5]

In our study, ERAS group had longer operative time (118.4 ± 34.5 vs 133.4 ± 25.6 p <0.001), likely reflecting both protocol complexity and increased intraoperative safety monitoring. This goes with other studies results, Tanaka et al, [7], stated that ERAS group of patients had longer operative time (avg. 15-20 min more than non-ERAS group of patients) during early adoption phase, also Chong et al, [5], reported slight increase in operative time in ERAS group refereing this to patient warming and advanced anesthesia techniques, but Coolsen et al, [8], said that there is insignificant difference in operative time once ERAS protocols were fully applied. More recent comparative series and implementation studies have also reported modestly longer times during early ERAS adoption which tend to normalize as the teams gain experience. [9]

Blood loss remains a major concern in hepatic resections. Excessive bleeding can lead to hemodynamic instability, transfusion-related risks (TRALI, immunosuppression), and postoperative liver dysfunction. [10]

Intraoperative blood loss is a critical index in determining the postoperative sequel. Open liver surgeries are usually associated with high rates of blood loss due to the complex hepatic vasculature. Traditionally, minimizing bleeding has relied on surgical technique, vascular control methods, and transfusion strategies, but ERAS protocol has introduced a perioperative method which proved to decrease the intraoperative blood loss, this may be related to preoperative goal-directed fluids and carbohydrate loading, which help maintain euvolemia and reduce capillary congestion. In addition, Limited Opioid Use reduces vasodilation and hypotension. Also, active warming decreased the risk of coagulopathy. [11]

Our study confirms this effect as blood loss was significantly lower in the ERAS group (376 ± 140 ml vs. 428 ± 160 ml, p = 0.039), suggesting a protective effect of ERAS protocols for fluid and temperature management.

Spolverato et al. [10], Brustia et al. [11], Balzano et al. [12], Noba et al. [6], and Delabays et al. [13] all reported that the median intraoperative blood loss in the ERAS group was lower despite longer surgery times, especially in major resections. These studies also noted a reduced need for transfusions in ERAS patients and emphasized the impact of ERAS protocols on maintaining surgical field clarity through controlled hemodynamics. Several ERAS components directly or indirectly contribute to blood loss reduction, including goal-directed fluid therapy that maintains optimal intravascular volume and prevents venous congestion, active warming and normothermia to prevent hypothermia-related coagulopathy, limited opioid use to avoid vasodilation and hypotension, and preoperative optimization measures such as correction of anemia and cessation of anticoagulants. Minimally invasive anesthesia protocols also help reduce systemic inflammation and blood pressure fluctuations [8].

Coolsen et al. [8], in a prospective study involving both open and laparoscopic liver resections, reported that ERAS groups experienced significantly reduced intraoperative blood loss and transfusion requirements. Other retrospective studies, including those by Joliat et al. [14] and Brustia et al. [11], also confirmed a lower transfusion requirement in ERAS-managed patients. Furthermore, Raoof et al. [4], in a meta-analysis, demonstrated a statistically significant association between ERAS protocols and reduced intraoperative bleeding. Similarly, Ratti et al. [15] found that implementing an ERAS protocol led to a 25% reduction in intraoperative blood loss during open liver resections.

Surgical site infections (SSIs), particularly wound infections, are common and costly complications of open liver surgery. Rates can range from 10% to over 40%, depending on operative technique, patient factors, and perioperative management. SSIs prolong hospitalization, increase antibiotic use, and raise the risk of sepsis and readmission. [16]

The implementation of Enhanced Recovery After Surgery (ERAS) protocols has been associated with a substantial reduction in postoperative infections, including wound-related infections, largely due to early mobilization, minimized invasive devices, and better immune function preservation. [3]

Early mobilization improves circulation and immune response, early removal of drains and catheters reduce bacterial colonization, multimodal non-opioid analgesia prevents immunosuppressive opioid overload, preoperative carbohydrate loading enhance immunity and maintain lean body mass, and early oral intake support gut microbiota and immune integrity. [2]

Recent meta-analysis and ERAS focused nursing interventions confirm a significant reduction in surgical site infection rates and overall postoperative complications with structured ERAS pathways. [17]

In our study, the incidence of wound infection was significantly lower in the ERAS group (20%) compared to the Pre-ERAS group (48%), with a p-value of 0.006, indicating both statistical and clinical significance. These findings align with international literature and highlight the protective impact of ERAS components such as early drain removal, early mobilization, and optimized perioperative care. Jones et al. [16], in a prospective cohort study, reported a significantly lower rate of surgical site infections (SSIs) in the ERAS group (12% vs. 34%). Similarly, Harrison et al. [3], through a meta-analysis of 17 studies, demonstrated that ERAS protocols significantly reduced infection rates and length of hospital stay. Balzano et al. [12] and Chong et al. [5] also observed a decline in wound infection rates from 28% to 10% following ERAS implementation.

Regarding bile leakage, our study found a slightly higher rate in the ERAS group (18%) compared to the Pre-ERAS group (10%); however, this difference was not statistically significant. In contrast, other studies, including those by Jones [16], Chong [5], and Joliat [14], reported lower bile leak rates in ERAS-managed patients. Nevertheless, additional literature such as Noba et al. [6] suggests that the incidence of bile leakage does not differ significantly between ERAS and conventional care groups. This variability implies that bile leak outcomes may be more influenced by surgical techniques, patient comorbidities, and liver pathology rather than the perioperative care protocol alone.

Intra-abdominal collections (IACs) are among the most significant postoperative complications following liver resection. They encompass bile collections, hematomas, abscesses, or serous fluid accumulations and can lead to secondary infections, prolonged hospitalization, delayed recovery, and even reoperations. While ERAS protocols have been effective in improving many perioperative outcomes, their relationship with IACs remains controversial, especially in open procedures. [11]

Unlike minimally invasive surgeries where peritoneal trauma is limited, open liver surgeries pose a higher risk of IACs due to larger resection margins, extensive raw surfaces, delayed liver regeneration and fluid shifts and inflammation. [12]

A core component of ERAS protocols is early drain removal, which aims to reduce infection risk and allow faster mobilization, but it can, however, lead to occult fluid accumulation if drains are removed before bleeding or bile leakage is fully resolved. This has led to mixed findings in the literature regarding ERAS and its impact on IAC rates. [11]

In our research, intra-abdominal collections were significantly higher in the ERAS group (32%) compared to the Pre-ERAS group (6%), with a p-value of 0.002, indicating a statistically significant increase. These findings are consistent with those of Brustia et al. [11], Balzano et al. [12], Tanaka et al. [7], and Delabays et al. [13], suggesting that while ERAS is beneficial in many aspects, it may require more individualized drain management protocols—especially in high-risk resections or patients with high BMI, cirrhosis, or large tumor burden.

Other elements of the ERAS protocol may contribute to the increased risk of intra-abdominal collections. For instance, early oral intake increases gut motility, which could exacerbate leaks if anastomoses or resection margins are not fully healed. Reduced opioid use is associated with fewer paralytic ileus episodes and earlier bowel movement, while early mobilization might redistribute peritoneal fluids, promoting unabsorbed collections [7].

Length of hospital stay (LOS) is a crucial quality and economic metric in surgical care. In open liver resections, prolonged LOS is often driven by complications such as bleeding, infections, delayed oral intake, and pain management challenges. Enhanced Recovery After Surgery (ERAS) protocols aim to optimize perioperative care, targeting reduced morbidity and significantly shortening LOS without increasing readmission rates [2].

Reducing LOS leads to lower hospital costs (e.g., bed occupancy, medication, and nursing), improved patient satisfaction and recovery, and reduced risk of nosocomial infections and hospital-related complications [3]. According to Ljungqvist et al. [2], ERAS protocols can reduce total hospital costs by 20–30%, even after accounting for staff training and patient education.

The components of ERAS that contribute to LOS reduction include early oral intake (to prevent ileus and enhance nutrition), multimodal analgesia (to reduce sedation and enable faster mobilization), early ambulation (to prevent DVT and pneumonia), goal-directed fluid therapy (to avoid fluid overload), and timely removal of drains and catheters (to accelerate independence and discharge readiness) [5].

Our study demonstrated a statistically significant difference in LOS between the ERAS and Pre-ERAS groups (4.68 ± 1.4 days vs. 6.24 ± 2.1 days), supporting ERAS as a safe and effective strategy to shorten hospitalization time. This finding is consistent with the results of Spolverato et al. [10], Joliat et al. [14], and Chong et al. [5], who documented a 25–40% reduction in LOS with ERAS implementation. Additionally, Harrison et al. [3], in a meta-analysis of 17 studies, confirmed that ERAS reduces LOS without compromising postoperative outcomes.

Clinical Implications

The implementation of Enhanced Recovery After Surgery (ERAS) protocols in open conventional liver resections demonstrates meaningful improvements in postoperative recovery, including reduced blood loss, fewer surgical site infections, and shorter hospital stays. These findings are particularly relevant in resource-limited settings where optimizing hospital resources and improving outcomes are essential. The study shows that ERAS can be successfully applied in major hepatobiliary surgeries without increasing critical complications, thereby supporting its broader adoption in open liver procedures. This shifts the paradigm from traditional perioperative care to a more standardized, evidence-based approach that enhances patient safety and recovery.

Limitations

As a retrospective, single-center study, the findings are subject to selection bias and limited generalizability. The sample size (n=100) may not capture all potential complications or rare adverse events. Differences in BMI between groups, despite statistical adjustment, could introduce confounding. Additionally, the study lacks long-term follow-up on patient quality of life, readmission rates, and oncological outcomes, which are critical for comprehensive ERAS assessment.

CONCLUSION

The implementation of Enhanced Recovery After Surgery (ERAS) protocols in open conventional liver resection is both safe and feasible. ERAS significantly improves postoperative outcomes, reduces hospital stay, and lowers the risk of complications such as bleeding and infections. However, the increased incidence of intra-abdominal collections warrants further investigation and potential protocol adjustments regarding drain management. Future prospective, multi-center trials are needed to refine ERAS protocols and confirm long-term benefits in liver surgery patients.

List of Abbreviations

- **ERAS**: Enhanced Recovery After Surgery
- **PCA**: Patient-Controlled Analgesia
- **FLR**: Future Liver Remnant
- **ALPPS**: Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy
- **POD**: Postoperative Day
- **LOS**: Length of Hospital Stay
- **SSI**: Surgical Site Infection
- **BMI**: Body Mass Index
- **DVT**: Deep Venous Thrombosis
- **ASA**: American Society of Anesthesiologists

Ethical Considerations

This study was reviewed and approved by the Research Ethics Committee, Faculty of Medicine, Tanta University, under Approval Code: 36264PR537/2/24, dated 12/2/2024. Written informed consent was obtained from all participants prior to inclusion. The study complies with the Declaration of Helsinki principles.

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Author Contributions

- **Alhassan M. Hassan**: Conceptualization, methodology, writing–original draft.
- **Sherif M. Elgarf**: Supervision, surgical coordination, manuscript review.
- **Ahmed Swelam:** Surgical techniques documentation, statistical validation, writing–original draft
- **Gamal I. Moussa**: Study oversight, statistical validation, postoperative care analysis.
- **Mostafa I. Sharaf**: Anesthesia protocol design, intraoperative management.
- **Lobna S. Tafesh**: Data collection, statistical validation, critical revision.
- **Elghamry E. Elghamry**: Literature review, surgical techniques documentation.

Conflicts of Interest

The authors declare **no conflicts of interest** related to the materials, methodology, or outcomes presented in this research.

Confidentiality of Data

All patient data were anonymized prior to analysis. Confidentiality was maintained in accordance with institutional guidelines and national research ethics protocols.

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