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The Influence Of Enhanced Recovery After Surgery (Eras) Protocol On Recovery After Gastroesophageal Junction (Gej) Tumour Resection – A Review.

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Abstract:
Background*: This review paper examines the influence of Enhanced Recovery After Surgery (ERAS) protocol on recovery after Gastroesophageal Junction (GEJ) tumor resection. The ERAS protocol has emerged as an effective alternative to conventional protocols, offering substitutes that expedite patient recovery, thereby reducing the length of hospital stays.*
The conventional protocol for postoperative care often involves prolonged fasting, bed rest, and the use of nasogastric tubes. However, the ERAS protocol challenges these practices by implementing a multidisciplinary approach emphasizing early mobilization, optimized pain management, and oral intake. This review paper aims to assess the impact of these ERAS interventions on the recovery of patients undergoing GEJ tumor resection.
Numerous studies have demonstrated the benefits of the ERAS protocol in enhancing postoperative recovery. By minimizing the physiological stress response to surgery, ERAS facilitates a faster return of gastrointestinal function, reduces complications, and ultimately leads to shorter hospital stays. The ERAS protocol achieves these outcomes through evidence-based interventions, including preoperative counseling, preoperative carbohydrate loading, minimally invasive surgical techniques, optimized fluid management, and early removal of urinary catheters.
Furthermore, the ERAS protocol also addresses patients' psychological and emotional needs, promoting their active involvement in their recovery process. By empowering patients and providing them with education and support, ERAS ensures a holistic approach to postoperative care.
In conclusion, the ERAS protocol has proven to be an effective alternative to conventional protocols for patients undergoing GEJ tumor resection. It has challenged traditional practices and introduced interventions that expedite recovery, reduce complications, and decrease the length of hospital stays. The multidisciplinary nature of the ERAS protocol underscores its success, as it integrates evidence-based interventions to address both physiological and psychological aspects of patient care. However a standardized ERAS protocol for GEJ tumor resection has is yet to be implemented. Implementing the ERAS protocol is crucial in optimizing patient outcomes and enhancing the overall quality of care in GEJ tumor resection surgery.

Key Word*:Gastroesophageal junction tumor; enhanced recovery after surgery; fast-track recovery,recovery; length of hospital stay; perioperative care; multidisciplinary approach; patient education; ERAS guidelines; postoperative care; nutritional support; early mobilization; and pain management.*

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I. Introduction

Gastroesophageal junction tumor surgery is major surgery and the main curative intervention for GEJ tumors; the type of surgery used for GEJ tumor surgery (resection and reconstruction) varies depending on the generally accepted classification of GEJ tumor (Siewert classification). However, the ideal surgical resection for GEJ tumor resection is still unestablished, especially for Siewert type II gastroesophageal junction tumor; this challenge stems from the fact that GEJ tumor classifications refer to the origin of the tumor without factoring

the extent of infiltration of the tumor both proximally and distally[1]. GEJ tumor surgery consists of esophagectomy and gastrectomy, with radical lymphadenectomy followed by reconstruction of the resected part of the gastric tract. Surgeons commonly opt for esophagectomy for type I GEJ tumors with gastrectomy for type II (cardia) and type III GEJ tumors[2]. The general surgical options to select from are esophagectomy or gastrectomy, although diverse approaches can be explored][3],The high morbidity and mortality rate from the general surgical choices stated above are a cause for concern as it has not shown any significant change (decrease) over the years, global reviews have shown esophagectomy to have morbidity of 59% and 30-day mortality of 2.4%[4], gastrectomy has a reported morbidity and mortality of 23.3% and 3.3% respectively[5,6], with the reported morbidity and mortality outcomes, it is important for us to create means to decrease complications and ways to handle postoperative snags at the same time aggrandizing early recovery. One stratagem that has shown great prospects in positively influencing surgical outcomes is the Enhanced Recovery After Surgery (ERAS) protocol.

Since the conceptualization of the ERAS protocol, it has shown great strives and remarkable advancement; Henrik Kehlet first illustrated this concept in 1997 in the milieu of colorectal surgery[6,7]. The advancement of the protocol is evident in the evolution of the disciplines involved in the protocol. It is now implemented as a multidisciplinary protocol that comprises surgeons, anesthesiologists, critical care physicians, physiotherapists, nutritionists, nurses, and patients (including relatives or caregivers) in the perioperative care of the patient and integrating evidence-based protocols into clinical practice. The ERAS protocol, aka fast-track protocol, has remarkably reduced; the length of hospital stay, surgical stress response, and morbidity; it also accelerates postop recovery[8]. ERAS society was pioneered in 2010, and since then, different guidelines for the protocol have been published. Each tailored to a surgical specialty or surgical approach (colorectal, bariatric surgery, gastrectomy, liver surgery, and gynecologic oncology). Perpetration of ERAS protocols has shown evidence-based results in curtailing treatment costs without jeopardizing surgical[9].

There are insufficient published evidence-based studies on ERAS protocol being incorporated into GEJ tumor resection, one of the reasons why this is so is due to the complexity of GEJ tumor resection (GEJ tumor surgery consisting of esophagectomy and gastrectomy, with radical lymphadenectomy followed by reconstruction of the resected part of the gastric tract), also because of the position of the GEJ tumor it requires both thoracic and general surgical expertise, even though general surgery as a specialty has made great strife with ERAS protocol especially in colorectal surgery, thoracic surgery only occupies a minuscule portion of enhanced recovery literature.

Due to the absence of a standardized guideline of ERAS protocol at the moment tailored specifically for GEJ tumor resection, institutions are using the non-standardized guideline for GEJ tumor resection, utilizing the standard ERAS guidelines for esophagectomy and gastrectomy (being the generalized components of GEJ tumor resection), or the generalized ERAS protocol for upper gastrointestinal tract (esophagus, stomach, and duodenum) surgery.

Studies addressing the practicality and advantageousness of ERAS after esophagectomy explored a variety of strategies consisting of different components due to the lack of criterion protocol prior to 2018; studies of esophagectomy done with ERAS protocol prior to the availability of a standard guideline have shown promising outcomes, a systemic review that stood out and played a role in generating ERAS protocol for esophagectomy is Findlay et al. 2014. This coherent retrospective study reported positive primary outcome (morbidity, mortality, and length of hospital stay). However, it reported weak and incomplete evidence owing to the lack of a comprehensive guidelines[10]. An ensuing meta-analysis by Pisarska et al. [11] compares two groups, the ERAS group versus the conventional group, reported positive outcomes disclosing fewer non-surgical and pulmonary complications and shorter periods of hospitalization in the ERAS group, without significant influence on morbidity and mortality. A further meta-analysis by Markar SR et al. pinpointed elements that could be the key components of ERAS for esophagectomy[12]. Current standard guidelines of ERAS for esophagectomy was published by the ERAS society in 2018 to specifically better the surgical outcome of esophagectomy[13].

Gastrectomy is one of the procedures that handsomely contributed to the number of ERAS literatures available, with early influence in bariatric surgery. DP Lemanu et al.[14] performed a randomized clinical trial where two groups were formed (ERAS group and conventional group) and compared to a historical group that had the same procedure, the outcome of the clinical trial showed the ERAS protocol in the context of bariatric surgery reduces the length of hospitalization, economical without negatively affecting the surgical outcome. In 2014 K. Mortensen et al.[15] provided an evidence-based framework for ERAS guidelines recommended by the ERAS society covering perioperative care for patients undergoing gastrectomy. The framework is made up of two parts "procedure-specific" and "Generalized (not procedure-specific) elements." The procedure-specific framework is used with the ERAS guidelines for pancreaticoduodenectomy. The procedure-specific framework of consensus guidelines for enhanced recovery after gastrectomy consists of 8 elements; Preoperative nutrition, Preoperative oral pharmaconutrition, Access (of gastrectomy), Wound catheters, and transversus abdominis

plane block, Nasogastric/Nasojejunal decompression, Perianastomotic drains, Early postoperative diet and artificial nutrition, and Audit. The Yagamata et al.[16] review further focused on some of the procedure-specific elements; Preoperative nutrition/ pharmaconutrition, Access of gastrectomy, Nasogastric decompression, Perianastomotic drains, and Early postoperative diet and artificial nutrition, considering that these elements are of great interest to surgeons.

As earlier stated, we will be focusing on the ERAS guideline for both esophagectomy and gastrectomy since GEJ tumors position affects both the esophagus and the stomach, and resection of the tumor also affects both depending on the type.

COMPONENTS OF ERAS PROTOCOL

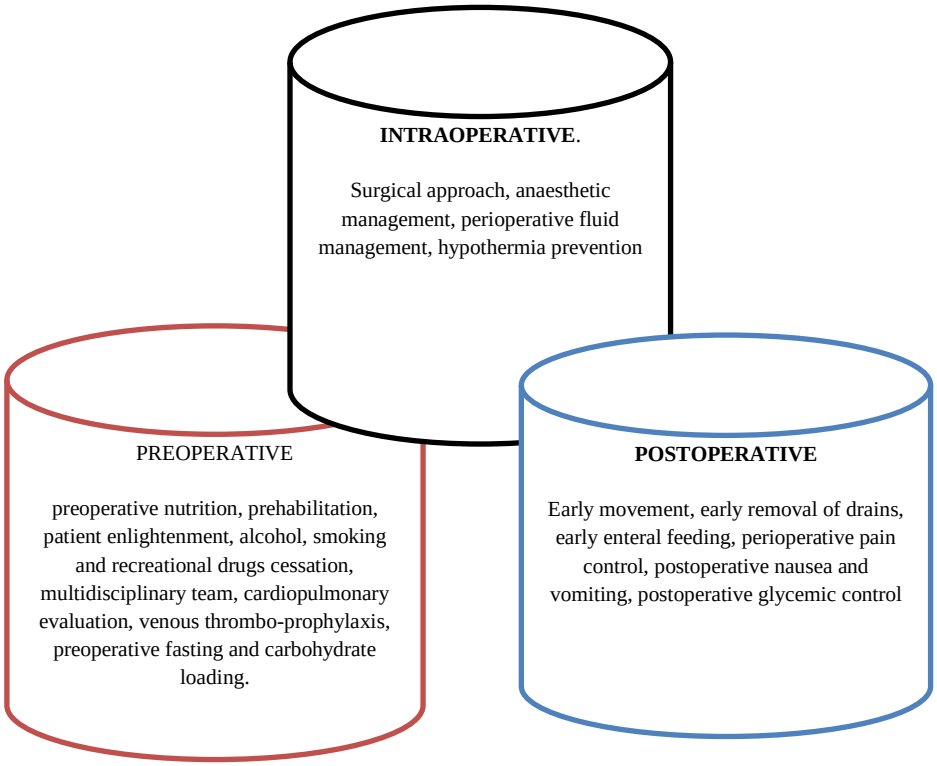

Figure 1; components of ERAS protocol.

The components of Enhanced Recovery After Surgery (ERAS) can be classified into three overlapping phases; preoperative phase (ERAS elements implemented before the surgery), intraoperative phase (ERAS elements implemented during the surgery), and postoperative phase (ERAS elements implemented after the surgery). It is important to note that these phases are not clearly demarcated, as the concept of ERAS works in continuum, and functions as a whole.

Enhanced Recovery After Surgery Guidelines For Gastroesophageal Junction Tumor Resesction.

Enhanced recovery after surgery guidelines for the resection of GEJ tumor resection is unique and varies based on the type of GEJ tumor (using Siewert's classification; type I, II, and II) considering the expertise of the surgeons (thoracic surgeons and general surgeons) and the surgical intervention(esophagectomy and gastrectomy) all depends on the GEJ tumor type in question.

Classification of GEJ tumor

There is contention regarding the molecular origin and anatomical position of GEJ tumors; this has been ongoing for decades-long. This contention has immensely contributed to the absence of a unison approach for an efficient medical intervention for those with GEJ tumors. The classification of GEJ tumors based on an anatomical approach by Siewert and Stein to expedite research leading to treatment posed a strategy where the tumor is divided into 3 types based on the epicenter of the tumor; Type I, Type II, and Type III[17].

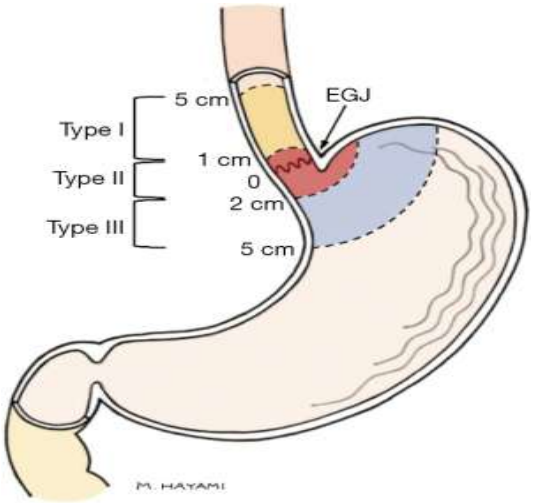

FIGURE 2: GEJ tumour Siewert's Classification[18]

Guidelines for ERAS after GEJ tumor resection base on types.

Thoracic surgery and general surgery are associated with a significant level of surgical stress; these are surgical specialties involved in GEJ tumor resection, Enhanced recovery after surgery protocol has substantially contributed to the reduction of surgical stress by trying to revolutionize physiological and psychological responses to major surgery like GEJ tumor resection[19]. ERAS guidelines address the two main components of stress response: neuroendocrine–metabolic and inflammatory–immune[20]. Surgical approach preference is usually based on the tumor type and the target of obtaining complete R0 (microscopic) and R1 (macroscopic) tumor resection.

Surgeons widely utilize Siewert's classification to treat patients with GEJ tumors optimally. The classification categorized GEJ tumors into three; type I, type II, and type III.

Type I, between 1 and 5 cm above the GEJ; type II, between 1 cm above and 2 cm below the GEJ; type III, between 2 and 5 cm below the GEJ [21]. Type I is considered a disease of the esophagus; on the other hand, type III is considered a disease of the gastric, and type two still stands as a grey area and is debatable[22].

GEJ tumor is a controversial topic because of its anatomical position, histological composition, and its unique lymphatic drainage pathways, which include both the mediastinal and abdominal fields,[23,24]by extension so is its optimal treatment choice. The controversies surrounding it have immensely contributed to the individualized approach to treatment for each type. Curative surgical resection of GEJ tumors generally involves esophagectomy and gastrectomy; this is the bases of different ERAS guidelines for GEJ tumor resection.

The general components guidelines for ERAS after GEJ tumor resection are divided into 3 subgroups, putting the implementation time of the components in perspective: PRE-operative, INTRA-operative, and POST-operative.

Table 1. Key Components of ERAS Protocol.

PRE-operative	INTRA-operative	POST-operative
-preoperative nutrition (assessment and intervention) - prehabilitation -patient enlightenment - alcohol, smoking and recreational drugs cessation. -multidisciplinary team - cardiopulmonary evaluation -venous thrombo-prophylaxis, -preoperative fasting and carbohydrate loading.	-Surgical approach -anaesthetic management - perioperative fluid management, -hypothermia prevention.	-Early movement -early removal of drains -early enteral feeding -perioperative pain control - postoperative nausea and vomiting, -postoperative glycemic control

Guidelines for ERAS after type I GEJ Tumor resection.

GEJ type I tumor is anatomically positioned between 1 and 5cm above the GEJ; it may invade the GEJ from its proximal part. It normally emerges from Barrett's esophagus; that is to say, it is normally a result of the advancement of Barrett's disease. GEJ type one is conventionally considered a disease of the esophagus[25]. A typical type I GEJ tumor resection procedure is a radical trans mediastinal or transthoracic en bloc esophagectomy with resection of the proximal stomach[26]. The ERAS guideline for GEJ type I tumor resection is for esophagectomy, as earlier stated, with components that include the 3 generalized subdivisions of the ERAS framework (pre-operative, intra-operative, and post-operative).

PRE-operative protocol

Pre-operative nutritional status (assessment and intervention/correction)

Precedent to diagnosis, esophageal cancer ranks first in median weight loss among all malignant tumors stemming from malnutrition. Severe malnutrition in esophageal cancer patients is an aftermath of difficulty swallowing, prolonged loss of appetite, and malignant tumor cachexia (excess cytokines leading to severe muscle wasting). The prevalence of severe emaciation and undernourishment in GEJ cancer affects up to 80% of patients putting them at risk of prolonged hospitalization due to complications [27,28]. Age-associated muscle wasting and generalized weakness from cancer cachexia affect both surgical outcome and convalescence of patients[29].

At an initial consultation, A dietician (stakeholder in the ERAS team) assesses in regards to the nutritional status of the patient, using the European Society for Clinical Nutrition and Metabolism (ESPEN) criteria [30]; this assessment comes after diagnosis has been made.

Table 2: Nutritional risk assessment and intervention table [31]

NUTRITIONAL RISK	SYMPTOM	INTERVENTION
Low risk	Normal intake Minimal weight loss	Dietary advice
Moderate risk	Anorexia/dysphagia Unintentional weight loss 5-9%	Protein and energy supplements
High risk	Severe dysphagia Unintentional weight loss>10% Body mass index <18kg/m^2	

Patients with esophageal malignant tumors often present anemic, which may necessitate transfusion that negatively affects morbidity[32]. Preoperative pharmaconutrition is the administration of nutrients that mainly contain arginine, omega-3 unsaturated fat, and nucleotides prior to surgery. Zhang Y et al. substantiated the contribution of pharmaco-nutrition in decreasing surgery-induced stress and inflammatory response, which reduces morbidity and enhances recovery, in a study on gastrointestinal cancer[33]. Postsurgical immuno-nutrition is still debatable; two systemic reviews have opposite views on the influence of immuno-nutrition post-esophagectomy[34,35]. A randomized clinical trial by Sultan et al. concluded that early feeding after surgery with immuno-nutrition supplements is not advantageous over normal enteral feeding[36].

Prehabilitation

Prehabilitation is a pre-surgical program to improve surgical outcomes, tailored into the ERAS program to fast-track the return to normal post-surgery. The need to enhance attaining a functional state postoperation stems from the fact that it is a major problem associated with postop complications [37]. Prehabilitation has different components, including supplementation of nutrients, mental health counseling, medical optimization, and customized training depending on the patient's state, combining aerobics and strengthening routines [38]. Taking deep breaths with spirometry and inspiratory muscle exercise to optimize respiration reduces pulmonary complications, which is common in thoracotomy [39]. Studies by Carli et al. demonstrated that prehabilitation significantly boosts quality of life by decreasing anxiety, melancholic episodes, and lethargy[40]. The initial result from Minnella et al. study on the effect of prehabilitation on esophageal surgery showed significant improvement in postsurgical functional capacity[41]. The RCT by Gillis et al. proposed that a minimum of four weeks of prehabilitation before surgery positively influences postoperative outcomes compared to postoperative rehabilitation[42]. Esophagectomy is a major surgery; prehabilitation increases the physiological reserve of the patient prior to the surgery, thereby increasing the chances of a better surgical outcome.

Patient enlightenment

Preoperative enlightenment or education of the patient deals with the patient's mental state, handling and processing any form of fear and anxiety. It mentally prepares the patient for the treatment; the patient is usually informed about the advantage of the procedure, the peril, and the aftereffects[43].

Pre-esophagectomy enlightenment is integrated into many ERAS guidelines, with online resources available to the patient[44]. Studies by Goodman et al. concluded that proper patient enlightenment can decrease the length of hospital stay[45], patient enlightenment also reduces postsurgical pain[46], and studies have shown that elimination of anxiety increases the chances of a patient retaining information with proper patient enlightenment[47]. Patient enlightenment makes patients feel at ease and gives them a sense of belonging to the team. Helping fast-track their recovery, which is what ERAS protocol is all about.

Cessation of smoking, alcohol, and recreational drugs consumption

During pre-surgical counseling, patients and caregivers are informed about the importance of smoking, alcohol, and recreational drug cessation. The need for cessation of smoking, alcohol, and recreational drugs cannot be over-emphasized to optimize postop recovery. Two typical and vital risk factors that significantly increase postop complications are; smoking and perilous drinking; the complications they bring can lead to organic dysfunction. Restraint from using these can decrease serious postop complications like; infections, cardiopulmonary complications, and wound healing. Lindström D et al. and Yoshida et al. [48,49,50]. studies demonstrated that complete abstinence from smoking and drinking for up to 4 weeks prior to surgery significantly decreases complications, particularly wound infections and pulmonary complications.

The use of recreational drugs, especially psycho-stimulants like cocaine and methamphetamines, before surgery, can lead to serious postop complications[51]. Acute use of cocaine before surgery exposes patients to cardiac-related postop complications. Chronic cocaine users' analgesic dosage may be higher because of their tolerance. Non-toxic users do not need dosage adjustment during surgery[52].

Multidisciplinary team (MDT)

Taylor et al.'s review that posed a question about evidence of the usefulness of a multidisciplinary team reported that it aids better decision-making concerning the patient and helps specialists make an informed decision and collectively create a customized treatment plan for the patient[53]. Treatment plans created following the MDT format have been shown to drastically increase the standard of patient care, offering effective plans and a more organized journey through all the phases of ERAS. Evidence-based data concerning patient contribution needs to be improved. However, Stephens et al.'s esophageal cancer study showed that MDT management plays an important role in improving a patient's treatment, outcome, and journey[54].

An MDT is also beneficial to the clinician and wider population, as it allows the clinician to be aware of the protocol in place and the personnel in charge of each step, have complete access to consultation notes, and be aware of changes in treatment plan[55].

Cardiopulmonary assessment

Cardiopulmonary assessment (CPA) is the process of evaluating a patient's heart and lungs; this is usually done before any major medical procedure is done. This does not reduce the risk of postop complications but identifies patients that may need to improve the state of their health in other to have better surgical outcomes. CPA deals with the pulmonary and cardiac assessment, which is done separately; it includes echocardiography, spirometry, and stress ECG test[56]. Cardiopulmonary exercise testing (CPET) is an outstanding and grounded test because it is a composite approach to evaluating multiple systems (respiratory, cardiac, vascular, musculoskeletal, and hematopoietic). It is not invasive and safe. The main benefit of CPET is its ability to evaluate the patient's systems under stress which helps to predict the body's reaction to stress after the surgery[57]. There is still a big research gap and unanswered questions regarding using CPET to ascertain cardiopulmonary function prior to esophagectomy to improve surgical outcomes. A less superlative assessment tool that is frequently utilized in place of CPET is the incremental shuttle walk test (ISWT) and the 6-minute walk distance (6 WMD)[58,59]. Although Murray et al.'s study concluded that the shuttle walk test is a sensitive indicator of postop complications[60], the data, and research available to support less superlative tests in comparison to CPET are limited.

Venous thrombo-prophylaxis

Esophagectomy is the curative treatment for all esophageal cancers. However, it is not void of risk, and venous thromboembolism (VTE) is one of the postop complications of esophagectomy; it accounts for up to 5-7%, with a mortality rate that is twice the complication rate[61]. Kato et al. asserted that there is an increased risk for VTE after surgery when the surgery in question includes the dissection of cervical lymph-node dissection (due to its close proximity to major blood vessels like; internal jugular vein and subclavian vein)[62], Tsutsumi et al.'s study supported this assertion[63]. The best way to obviate VTE is to amalgamate mechanical (compression stockings and intermittent pneumatic device) and drug (Heparin with low molecular weight or unfractionated heparin) intervention for patients with a high chance of having VTE; the American College of Chest Physicians

proposed this protocol as prophylaxis, they also proposed that the administration of drugs should be done 2-12hrs prior to surgery and incessant till 4 weeks postop [64,65].

Preoperative fasting and carbohydrate loading.

The American Society of Anesthesiologists' proposed preoperative fasting and carbohydrate loading (CHL) protocol has been adopted into the ERAS guideline. They proposed that solids can be taken in 6hrs prior to surgery and liquid (carbohydrate loading) 2hr prior to surgery[66]. These proposed guidelines have led to good postop outcomes after many studies disapproved of the conventional 12hr fasting dogma and showed they could have negative side effects[67]. In the case of esophagectomy, it is paramount that the guideline is customized for each patient considering the risk of obstruction by the tumour and difficulty in swallowing due to the GEJ tumour. There is no generally agreed upon drink for carbohydrate loading, as such common drinks can be used [68].

Intra-operative Protocol

The intra-operative protocol includes; surgical approach, anaesthetic management, perioperative fluid management, hypothermia prevention.

Surgical approach

Timing of esophagectomy

Treatment to shrink GEJ tumour prior to curative treatment (surgery) is usually given (neoadjuvant therapy); however, the right time to perform esophagectomy is not known; various studies have been done to determine the right time for surgery post-neoadjuvant therapy, considering that both chemotherapy and radiotherapy significantly suppress the immune system causing delayed healing[69]. The FLOT 4 trial used a 4weeks interval between the final dosage of chemotherapy and surgery[70], while the CROSS trial proposed 4-6 weeks from the final day of radiotherapy administration[71]. An advanced curative treatment of GEJ tumour and esophagal tumour consists of neoadjuvant chemoradiotherapy (nCRT) with the operation[72] although the historical interval between the last day of nCRT and surgery that has been used over the years is the one proposed by the CROSS trial (4-6weeks), an observational study in the Netherlands has proposed surgery 8weeks after the last dose of nCRT this study is based on the observation of the results of CROSS cohort study[73]. The patient's health status, the level of shrinkage, and the patient's inflammatory response at the time of surgery greatly influence the surgical outcome[74,75]. These factors can vary with time, so timing regarding esophagectomy or any surgery after nCRT is important. The ERAS society guideline recommended surgery after the last dose of chemotherapy and radiotherapy separately, 3-6 weeks and 6-8weeks, respectively, as the best time range for surgery[76].

Surgical Access

Some factors are put into consideration when choosing what type of surgery is suitable for a patient that needs GEJ tumour resection; the extent of infiltration of the tumour determine with endoscopy, Axial imaging, and histological analysis; another important factor is the physiological state or reserve of the patient. A meta-analysis that has an ensuing subgroup analysis by Hulscher et al. and Omoloo et al., respectively, demonstrated in the meta-analysis that there is a decrease in the rate of respiratory complications after transhiatal esophagectomy compared to trans-transthoracic esophagectomy whose analysis is indicative of improved survival rate, the sub-group analysis was base on loco-regional of the primary tumour, it demonstrated a survival for patients that had transthoracic resection with few positive lymphnodes[77,78]. Many centres opt for transthoracic resection since it has a higher survival rate, favours the patient and the surgeon regarding the surgical field, and access to obtain negative margin(RO resection), correct staging, and removal of affected lymph nodes. Transhiatal resection is considered if the patient's pulmonary system is already compromised due to fibrosis or infection to avoid pulmonary postop complications[79].

Type of surgery; Minimally invasive or open esophagectomy

Esophagectomy as a surgical procedure has evolved significantly over the years, and each stage has tremendous benefits; however, the emergence of a new esophagectomy technique does not extinct other types. Esophagectomy can be performed by; open esophagectomy (OE) or minimally invasive esophagectomy (VAT; video-assisted thoracoscopic surgery).

Open esophagectomy has the benefit of complete resection of lymph nodes; however, the mode of surgical access increases the risk of respiratory complications. A study by

Guo et al. recorded a noticeable decrease in respiratory function of up to 30% due to the thoracoscopy, lung injury, and soreness in the early days of postop[80].

The ERAS society generally approves minimally invasive surgeries as part of the guideline as they play a major role in improving surgical outcomes and generally have fewer postop complications. A subsequent study of the TIME trial, which is a three years follow-up on the randomized study of minimally invasive versus open esophageal resection, demonstrated that minimally invasive esophagectomy is advantageous in the sense that there is less blood loss, no or fewer respiratory complications, shorter length of hospitalization and life expectancy[81]. Mariette et al. trial (MIRO trial) demonstrated better outcomes without jeopardizing the surgery[82]. Studies like that of Wang et al. and Li et al. have demonstrated that MIE is a better option for esophagectomy than OE because of less pulmonary risk as postop complication[83]. A meta-analysis by Jingwen et al. concluded that even though MIE protects respiratory function more than OE, a larger randomized control trial[84] is needed. The benefits of MIE align with the fundamentals of ERAS; hence, ERAS society proposes it as a surgical choice; however, the surgeon is expected to tailor the choice that will be more beneficial to the patient.

Degree of lymphadenectomy

GEJ tumours have a high level of involvement of lymph nodes, as they easily metastases. The dissection of the lymph node station has been a debatable topic among surgeons, as some take a radical approach while others use a conservative approach[85]. The study by Altorki et al. reported an improved survival rate for Three-field dissection(dissecting the upper abdominal, superior and inferior mediastinal and cervical nodes) with unobserved records in cases with five or more positive lymphnodes[86]. The histology of the tumour influences the lymphadenectomy; the ERAS Society proposed two-field lymphadenectomy(removing the bilateral mediastinal nodes in addition to the lymphadenectomy) for T1b-T3/4 GEJ adenocarcinoma without removing the recurrent laryngeal nerve node, and three-field lymphadenectomy for early-stage GEJ squamous cell carcinoma[87]. The ERAS recommendation does not favour any lymphadenectomy but utilized both, considering both two-field and three-field lymphadenectomy have complications as most studies have demonstrated similar postsurgical mortality complications for both types[88,89]. Surgeons speculate that the ongoing clinical trial NCT00193817 will demonstrate more than the available studies have to choose preference or mend current guidelines for selection. A review by Ashok et al.[74] proposes that oncological principles should be prioritized over ERAS when selecting the type of lymphadenectomy.

Conduit preference

Selecting and using the right conduit (as a substitute for the esophagus) during esophagectomy is vital; choices to explore include the stomach, jejunum, colon and gastric tube[90]. All these choices have advantages and disadvantages. After analyzing the pros and cons of each option, the options are chosen, fully considering the patient's overall health state. The stomach is commonly used because it can easily be repositioned with a single anastomosis; its abundant vasculature is both an advantage (abundant blood supply) and a disadvantage (sensitivity if the vessels prune to rapturing) in the reconstruction process. Other disadvantages are; the possibility of slow emptying of the stomach, backflow of bile, loss of gastric storage ability, and risk of leaking at an anastomotic site[91]. Tie Patients who have undergone gastric resection before the esophagectomy or with a tumour that has greatly infiltrated the stomach cannot utilize this option[92]. Colon is used as a second choice if the stomach cannot be utilized because of a tumour or in young patients for reconstruction during esophagectomy[93]; its length, great vascular supply and low tolerance to acid are advantageous. The disadvantages are; the need for prior assessment (colonoscopy), prolonged surgical time, and three anastomoses required[94]. The length of the jejunum poses a limitation for it to be used even though the risk of leakage is substantially low. A review by Irino et al. reported the severity of difficulty in swallowing and reflux as quite low from a study[95]. Gastric tubes can be utilized in most cases, especially when the integrity of the stomach is compromised; it has the advantage of decreased chance of leakage and decreased gastric voiding[91]. ERAS society recommended that all options are viable; none is a perfect fit for all cases, so surgeons' choices should be tailored to the patient's needs.

Importance of Pyloroplasty

It is a common drainage procedure used when the gastric is used as a conduit for reconstruction after esophageal resection; in the case of GEJ tumour resection, this procedure is done as it involves esophgectomy[96]. It is generally connected with the denervation of the vagus nerve (vagotomy), which causes pylorospasm and blockage of the gastric outflow with the possibility of raising the chances of; an inability for proper nutrient oral intake, decreased integrity of anastomosis causing leakage and aspiration[97]. The importance of pyloroplasty is debatable and different surgeons have conflicting views about it; this controversy is fostered by the absence of comprehensive research with conclusive findings. A review by Orman et al. concluded that pyloroplasty reduces gastric symptoms from vagotomy (gastric outlet blockage and delayed gastric emptying. Side effects from this procedure are limited, but significant impacts on outcomes like; mortality and nutrition were inconclusive[98]. It also has no recorded positive influence on pulmonary complications. Because gastric reconstruction is the most

common conduit used, its complications can be improved by injecting botulinum poison into the pylorus, and the dilation of the pylorus[97] ERAS society has not given any recommendation for this procedure due to low evidence level.

Ligation of thoracic duct as preventive measure

This preventive measure is performed in anticipation of chylothorax (accumulation of digestive lymph in the thoracic region). Chylothorax is a rare but fatal complication from damage to the thoracic duct or lymphatic vessels; its occurrence rate is 0.4% to 4%[99]. The chronic loss of chyle causes malnourishment, suppressed immunity, and fluid volume depletion, all of which negatively impact prognosis following esophagectomy[100]. The management of this postop complication has been debatable as some recommend a cautious approach to management, while others recommend that another surgery should be performed to decrease mortality[101]. A review and meta-analysis by Crucitti et al.[102]showed that the chances of bile spreading in the thoracic cavity were reduced substantially in patients that have all structures within the bounds of the aorta and azygous vein ligated during esophagectomy. Other studies suggested that the thoracic duct should be ligated only if damaged during surgical procedures.

Nasogastric decompression

This process involves passing down a nasogastric tube (NG tube) through the nose down to the stomach to reduce pressure postoperatively. In the case of esophagectomy, the tube is positioned in the reconstructed esophagus (mostly gastric conduit if the stomach is used as a conduit option) over the anastomosis to decrease the pressure within the conduit postoperatively. It was initially speculated that nasogastric decompression has benefits such as reducing the rate of gastric and pulmonary complications and reducing pressure within the conduit used, which aids in maintaining the integrity of the anastomosis; over time, studies were done that suggested otherwise[103]. Other studies suggested that NG decompression raises the risk of anastomotic site compromise, causing leakage and increasing respiratory complications[104].

Two studies comparing early and late removal of the decompression tube by Mistry et al. and Shackcloth et al. demonstrated that early removal of the NG tube could significantly decrease respiratory complications and leakage; this finding struck a balance for many esophageal surgeons[105,106].ERAS society suggested that the NG tube can be placed during esophagectomy but has to be removed early, preferably postoperative day 2 (POD 2), without a peculiar need to keep it.

Feeding access

Two viable feeding options generally utilized post-esophagectomy are enteral and parenteral. So far, research data available for enteral feeding are propitious compared to parenteral. Fong et al. and Mazaki et al. showed that enteral feeding significantly decreases the compromise of the anastomosis's integrity and decreases surgical stress response[107]. The preference for enteral feeding over parenteral feeding by surgeons after esophagectomy is supported by 3 randomized studies comparing enteral feeding versus total parenteral feeding that showed no postop complications that are not related to catheter for enteral feedings[108,109,110] Enteral feeding can be done using jejunostomy or nasojejunal tubes both of which, the insertion of jejunal tube (J-tube) operatively to deliver food to the jejunum directly is feasible but has complications such as displacement of the tube, contamination of the insertion point, and trickling of nutrients. In contrast, nasojejunal feeding has the main disadvantage of being uncomfortable and having fewer complications than jejunostomy[111]. ERAS society stressed the importance of enteral feeding and recommended it; however, the decision on which type of feeding to choose depends on the surgeons' opinion of what the patient in question needs and tolerance of the feeding.

Anaesthesia management

Anaesthetic management majorly involves the administration and monitoring of anaesthesia and ventilation intra-operatively. Whether or not gaseous or intravenous analgesics are used for sedation during esophagectomy does not significantly affect major complications in esophagectomy, such as pulmonary complication[112].

Ventilation technique

Ventilation is important during esophagectomy, as the patient undergoing this procedure has a high chance of respiratory complication with morbidity of up to 25%[113], which doubles in patients older than 70 years[114]. Two randomized clinical trials by Shen et al. and Michelet et al. demonstrated that ventilation that protects the lungs intra-operatively decreases respiratory complications and inflammations[115], allowing for early extubation. The evidence of clinical research available supports the use of two-lung protective ventilation (TLV), also referred to as low tidal volume ventilation (TLV) in abdominal surgery[116], single lung ventilation is standard during thoracic surgery and also utilized to isolate infected lug from the other[117]; however limited

resources are demonstrating its benefits compared to TLV. The advantage of positive end-expiratory pressure (PEEP) at a high level (>2cm H20) is quite ambiguous at the moment[118]. ERAS society strongly recommends lung protective ventilation and states that gaseous and intravenous anaesthesia can be effectively used[13].

Perioperative fluid management

Managing fluid in every surgery is very important as it can wildly affect morbidity and mortality rates; the importance of striking a balance when it comes to fluid administration and monitoring should be emphasized. Exorbitant fluid administration during Esophagectomy can cause acute lung injury (ALI)[119]. A meta-analysis by Glatz et al.[120] concluded that excessive fluid administration during and after Esophagectomy significantly raises morbidity rate, and cumulative fluid balance before and after surgery can be used as a predictive tool to assess the likelihood of poor surgical outcomes[121]. Patients with low albumin before surgery are severely affected by fluid overload[122].

For patients undergoing Esophagectomy, the focus during the procedure should be on "balance" as they can be affected by both restrictive and fluid overload. When fluid administration is restricted, it can lead to hypovolemia due to blood loss intraoperatively, evaporation of fluid, and its involvement with the third space further heightens fluid loss; fluid restriction also depends on vasopressors which can affect perfusion of reconstructed conduit[123]. A meta-analysis by Varadhan et al. comparing restrictive and free fluid administration showed that none has a significant advantage over the other; however, comparing balanced and imbalanced fluid administration, they concluded that balanced fluid therapy has the advantage of up to 59% lesser complications and shortens hospital stay[124]. ERAS society recommends focusing on fluid administration to maintain physiological balance using crystalloids to avoid adding more than 2kg/day[13].

Hypothermia

Hypothermia is a major risk factor in all surgical procedures that involve exposing anatomical cavities for a long period; Esophagectomy is one such procedure; it takes a long period and involves two cavities. Hypothermia begins to manifest when the core temperature drops to 36 degrees Celsius; it is important to pay attention to hypothermia when a patient is managed with enhanced recovery after surgery protocol, as its manifestation can neutralize what ERAS stands to achieve. Studies and analysis have shown that hypothermia during surgery is associated with certain complications such as; prolonged healing of wound due to infection, which can increase the length of hospital stay (LOS)[125], bleeding mainly due to flawed adhesion of platelets leading to transfusion, heart-related complications[126,127], it is one of the factors that significantly influence recovery from anaesthesia as the breakdown of all the drugs administered intra-operatively is altered, another symptom of hypothermia is shivering which increases oxygen utilization[124], RAS highly recommended that core temperature should be closely monitored and regulated above 36 degrees Celsius intra-operatively, this can be achieved by warming fluid before administrating it, using warming blankets, forced air mattress and or circulating-water blankets to sustain normothermic[13].

Intensive care unit (ICU)

The ICU is the first stop after surgery, where recovery begins. Patients are monitored closely as they recover from anaesthesia and are placed on a pain relief regimen. Patients are also extubated here; in the case of Esophagectomy, extubation is done almost immediately after surgery. This is feasible with the help of less invasive surgical techniques and effective pain relief regimens. Admitting patients into ICU postoperatively is financially demanding, which contradicts two factors ERAS protocol aims to influence; financial implication and length of hospital stay; the benefits of ICU admission have been debated on[128]. ERAS society recommends that the need for ICU admission depends on the patient's condition. Otherwise, other options should be explored, like progressive care unit (PCU)[13].

Post-operative strategies

Early movement and thoracic exercise

Early movement postoperatively has drawn surgeons' attention over the years with an increase in evidenced based studies that shows the adverse effect of postop bed rest on a fast recovery. Early organized movement is one of the major postop components of ERAS. The initiation of movement of postop is a preventive measure against complications that can arise due to immobility, such as; frailty, insulin resistance, blood clot formation, pulmonary complication and muscular dystrophy[129]. Early mobilization has also shown a positive impact on patients psychologically[130]. Since early mobilization benefits all the systems, it is important to be intentional about it[131]; patients and caregivers should be enlightened about the benefits before surgery and motivated to move as early as the day of surgery, considering the state of the patient's health. The movement should be organized and monitored. The progress made each day can be used to structure the movement of the subsequent day. The provision of written and pictorial illustrations around surgical wards is very helpful and

informative, and respiratory exercises are also encouraged to post Esophagectomy to optimize the function of the respiratory system. ERAS society recommended commencing movement on the day of surgery by setting daily goals and keeping records of movement[13].

Early removal of tubes and drains

The placement of peri-anastomotic drains to detect leakages in surgeries involving the neck and thoracic region has not been irrefutably demonstrated. As a result, it is not a standard protocol to insert a drain during the surgical procedure[132]. To descry chyle (chylothorax), air, bleeding and anastomotic leakage and ensure the proper function of the lungs chest drain is usually situated during Esophagectomy; however, it is a source of discomfort to the patient in terms of pain and inability to move freely[133]. The output of chest drain and lung expansion are the major factors determining when a chest drain is removed. Many institutes remove the drain when its output is between 100ml/day and 150ml/day; no evidence exists to support this[134]. ERAS Society recommends that one chest drain should be used instead of two to reduce pain and allow for easy mobility; chest drains should be removed as soon as possible in the absence of any complications meant to be detected[13].

Patients with Esophagectomy usually have multiple tubes and drains inserted to monitor the output and input of fluids and deliver required nutrients and medications post-surgically. As much as these tubes and drains are inserted for a purpose, prolonged usage can cause complications and delay recovery. Immediately after an esophagectomy procedure, the patient should routinely have; chest tube(s), epidural catheter, urinary catheter, a nasogastric tube (NG tube), either a nasojejunal or jejunostomy tube, arterial line, intravenous catheter, and a urinary catheter, these contribute ton postop pain and discomfort.

Post-operation day 2 (POD 2) is a golden time frame in postop recovery; it is suitable for removing most drains and tubes after due diligence, enhancing recovery. Chest drains can be removed post-x-ray if there is no need for it; the general recommendation is at post-operation day 2 (POD 2)[13], urinary catheters are also removed at POD 2[135] when the diuretic phase has been attained except in a situation where the epidural catheter is still inserted, it is important to wait to avoid complications, especially in elderly men[136]. Also, NG tubes are removed POD 2 in the absence of inflation of the gastric tube[108]. The removal of the arterial line and intravenous catheter is tailored to the patients need for them based on the surgeon's and nurse's discretion.

Early enteral feeding

Enteral feeding post-esophagectomy plays a significant role in restoring optimal physiological function (being the first choice of post-Esophagectomy feeding)[137], thereby reducing the impact of surgical stress. Patients with esophageal cancer are always disadvantaged regarding nutritional status due to dysphagia prior to diagnosis and malignant tumour cachexia. If enteral feeding is introduced at the right time, the effort to optimize the nutritional status before surgery will be well-spent. Regardless of the delivery method of enteral feeding (jejunostomy or nasojejunal tube), it should commence as soon as possible. It is recommended that enteral feeding should begin POD 1. It is important to pay attention to the patient's tolerance to the nutrient as continuity and increment to meet the physiological demand by POD 3[13].

Oral feeding

Commencement of oral feeding is a major post-esophagectomy milestone, and it is one of the most important elements of ERAS. The common reason for hesitancy in oral feeding is the consciousness of the reconstructed oesophagus and its tendency to increase the chances of the anastomotic site(s) to leak[138]. A study by Madhuri et al. proposed that oral feeding's cost is not significantly different from enteral feeding; however, it decreases the need for home care assistance[139]. Early commencement of oral feeding was demonstrated by Lassen et al.[140] to be connected with decreasing the length of hospital stay (LOS); studies demonstrating its connection with leaking at anastomotic sites are still unclear. The anastomotic site can be monitored using imaging like computed tomography scan, swallowing contrast, and endoscopy. The choice of which option to work with depends on the availability of the examination instruments in an institution and the surgeon's discretion. A systemic review and meta-analysis by Hao et al.[141]. demonstrated that early oral feeding (EOF) significantly enhances immunity postoperatively, reduces LOS, and aids in reducing pulmonary complications compared to traditional oral feeding (TOF). EOF has also been shown to improve the quality of life (short term) and fast-track the recovery of gastrointestinal function[142]. In a situation where the patient has postop complications such as damage of the recurrent laryngeal and a high tendency to aspirate food, it is recommended that the patient is closely monitored by inspecting the integrity of the conduit and the anastomotic sites using endoscopy before oral feeding is introduced[143]. It is vital to have rehabilitation strategies in place, and the patient and caregivers are informed of this during the pre-surgical counselling.

Perioperative analgesia

Several studies have demonstrated that administering Thoracic epidural analgesia (TEA) decreases respiratory morbidity in crucial surgeries. Consequently, Esophagectomy utilizes TEA as analgesia, and it has been demonstrated that it significantly reduces the main complication that comes with Esophagectomy; respiratory complications[144]. An RCT by Li et al.[145]. Demonstrated that TEA potentially minimizes stress reaction, enhances surgical recovery, and decreases hospital stay and expenditures in Esophagectomy; these conclusions align with what ERAS protocol is meant to achieve. TEA involves the appropriate positioning of one or two lines that administer the analgesia that numbs both the thoracic and abdominal region (this is of great benefit to Esophagectomy, as the procedure involves both the thoracic and abdominal region). The utilization of epidurogram can enhance the effectiveness of analgesia[146]. TEA is most effective when the patient's body fluid volume is normal. If the patient is hypovolemic, vasopressors may be administered, which counters some TEA benefits like enhancement of blood flow to the reconstructed gastric conduit in esopahgetomy[147]. However, the restoration of MAP in patients with normal volume using vasopressors while administering TEA has been shown to improve blood supply to conduit and proper oxygenation. The utilization of TEA as the first choice for managing pain postoperatively was highlighted by the principles for the management of pain after thoracotomy[148]. Experienced anesthesiologists can provide TEA safely to these patients, with a low rate of major side effects, despite the dangers and problems of the procedure being widely documented[149]. Another alternative analgesic technique that can be used is a paravertebral blockade for post-thoracotomy pain as it has fewer complications and does not negatively affect blood volume on administration compared to TEA; as a result, many surgeons tend to favour it[150]. For main management, other drugs as adjuncts are also administered, such as; acetaminophen is administered 6 hourly, not >4g within 24 hours (as an anti-inflammatory, analgesic and antipyretic), NSAIDS in the absence of renal dysfunction, Gabepentinoids have the potential to reduce the use of opioids in thoracotomy[151], ketamine, magnesium[152], and lidocaine. Different institutes administer adjunct drugs differently depending on their protocol and the patient's health status. ERAS Society recommends TEA as a first-line analgesic and paravertebral analgesia as an alternative[13].

Guidelines for ERAS after type II and III GEJ Tumor resection.

The general framework of guidelines for Enhanced Recovery after surgery is the same. However, the details and recommendations vary based on the surgical procedure and the system/region involved. Even though surgical intervention is the recommended curative treatment for gastroesophageal junction tumors before metastasizing, the surgical specialty and the procedure involved in the various types differ. Studies have shown that the unique surgical strategy of each type of GEJ tumor is paramount to resection success. Type II Siewert is considered the true cardiac carcinoma, and type III Siewert is a subcardia gastric tumor.

The best surgical option for GEJ type one still needs to be determined; the options are esophagectomy, gastrectomy, and left thoracoabdominal esophago-gastrectomy. All three surgical techniques can be used to resect GEJ type II. If esophagectomy is the surgical choice, then the ERAS protocol for GEJ type (esophagectomy protocol) can be used; if gastrectomy is the surgical choice, then the ERAS protocol for gastrectomy will be used, and if left thoracoabdominal esophago-gestrectomy is the surgical choice a blended ERAS protocol is used (combining both esophagectomy and gastrectomy ERAS protocol.

Studies have shown that the surgical approach for type II and III GEJ tumors should be tailored to individual patients using surgical technique options[153]. Other studies have suggested that they should be treated as gastric cancers just like GEJ type l has been proposed to be considered as type esophageal cancer[154]. A study by Kamarajah et al.[155] concluded that esophagectomy has more prognostic value than gastrectomy, although more evidence-based research is still needed.

Enhanced Recovery After Surgery Protocol For Gastrectomy (GEJ Type II And III)

Gastrectomy is a surgical procedure involving resectioning the part (partial) or the whole stomach. This procedure is often done to resect tumors; the choice of complete or partial gastrectomy depends on the cancer's infiltration level. It is a complicated surgery that has risk factors such as Age, patient comorbidities, hemoglobin levels, albumin levels, type of gastrectomy, and multi-visceral resection which have been identified as risk factors for postoperative morbidity and mortality after gastrectomy; it's major complication is leakage from the anastomotic site[156]. A guideline for enhanced recovery after surgery for gastrectomy was published in 2014[157]; this was much needed considering the impact it had on colorectal surgery, and since then, its impact has been quite substantial because the prevalence of gastric tumors has been on the rise[158]. Surgical intervention is the best kind of treatment before metastasis.

The ERAS protocol guideline for gastrectomy is the procedure-specific guideline, which includes 8 components; preoperative nutrition, preoperative oral pharmaco-nutrition, access, wound catheters, transverse abdominis plane block, nasogastric/nasojejunal decompression, perianastomotic drains, early postoperative diet and artificial nutrition, and audit.

It also has general components that include; patient enlightenment, alcohol, and smoking cessation, oral bowel preparation, pre-surgical fasting and pre-surgical carbohydrate loading, pre-surgical anesthesia administration, antithrombotic prophylaxis, anti-microbial prophylaxis, and skin preparation, epidural analgesia, intravenous analgesia, anesthetic management, post-surgical nausea and vomiting, prevention of hypothermia, post-surgical glycaemic control, fluid balance, urinary drainage, bowel movement stimulation, and early scheduled mobilization[159].

Preoperative nutrition/pharmaconutrition

The guideline stated that the administration of a special diet prior to gastrectomy is not important in patients with good nutritional status after nutritional risk evaluation using the European Society for Clinical Nutrition and Metabolism (ESPEN) criteria[30]; patients with moderate to high risk should follow the ESPEN recommendation. A famous study that has drawn attention to preoperative nutrition is the study by Zheng et al., which demonstrated the impact of nutrition on gastric cancer patients immediately (incision site infection) and after 3 years (survival rate)[160]. In regards to preoperative immuno-nutrition (arginine-and omega 3 fatty acid supplements, glutamine, enteral immuno-nutrition), some RCTs have shown promising results while others have contradicted; however, the recently published meta-analysis and reviews have demonstrated that proper nutrients intake like preoperative nutrition with or without immuno-nutrition enhances recovery[161,162.]

Access and surgery type (for GEJ tumor type ll and III)

ERAS protocol highly recommends minimally invasive procedures as they greatly influence recovery time, reduce; the use of opioids and risk of wound infection, and aid early mobility. As stated earlier, the surgical options are esophagectomy, esophago-gastrectomy, or gastrectomy. The surgical access for esophagectomy is either transhaital resection or transthoracic resection, a highly recommended caveat of pre-surgical pulmonary complications. Recommended access for gastrectomy is generally transabdominal surgery for proper access and extensive lymph node dissection[163].

Regarding surgical technique choice, laparoscopic gastrectomy is the first choice after considering oncological protocol. Irrespective of the choice of procedure (esophagectomy, gastrectomy, or esophago-gastrectomy) for GEJ type III and III tumor resection, the ERAS Society strongly recommends a minimally invasive approach after an oncological review[164]. Laparoscopic gastrectomy has shown both long and short-term promise[165,166]. The studies that demonstrated the benefits of laparoscopic gastrectomy also highlighted its challenges in terms of technical limitations.

In terms of effectiveness and safety, a study by Ming-zhe et al. concluded that Enhanced recovery after surgery greatly influences laparoscopic radical gastrectomy[167].

Wound Catheters and transversus abdominis plane block

Placing catheters at wound sites to administer analgesic (TAP) is a surgical practice with some prospects. This requires the insertion of the catheter at the surgical site and infusing the wound TAP to reduce postop pain. It is used in place of epidural analgesics, achieving a controlled pain level for patients post-surgically without exposing them to complications like low blood pressure, nerve damage, headache, and infections, that arise from using epidural analgesics. As this is not a conventional practice, there has been resistance to adopting it; however, some studies have been done to demonstrate its effectiveness for abdominal surgeries[168,169]. A study by Zheng et al. concluded that continuous wound infusion with analgesic after open gastrectomy reduced morphine usage and enhanced recovery within 48hrs postop[170]. It also reduces post-surgical emesis and nausea and substantially decreases the length of hospital stay (LOS)[171]. The utilization of wound catheters favors what the ERAS protocol stands to achieve, hence why it has been adopted into the protocol, even though presences can influence mobilization. In the case of resection of GEJ tumor type II and III, this can be utilized to cocktail the use of morphine postop, decrease nausea and vomiting, and overall fast-tracking the recovery. ERAS society recommends it, emphasizing the need for more studies as available resources are limited[157].

Nasogastric/nasojejunal decompression

Using a nasogastric/nasojejunal decompression tube depends on the GEJ type II or III procedure. The insertion of a nasogastric decompression tube was once considered a necessity to improve surgical outcomes for esophagectomy procedure; however, this has been disputed by recent studies[106]; this implies that if the surgical procedure for the GEJ tumor resection is esophagectomy decompression tubes are not recommended except there is an indication after careful analysis of the patient by the surgeon. Pacelli et al. concluded in their studies that using an NG/NJ decompression tube for gastrectomy is also not necessary[172], as it does not significantly influence the recovery of the patient[157] or indicates the presence of postop complications. Even though some surgeons still use it due to established conventional protocol.

Perianastomotic drains

The use of perianastomotic drains is a conventional routine; few studies support the use of perianastootic drains. The placement of perianastomotic drains to detect leakages in surgeries involving the neck and thoracic region has not been irrefutably demonstrated; as a result, it is not a standard protocol to insert a drain during the surgical procedure[132]. To descry chyle (chylothorax), air, bleeding, and anastomotic leakage and ensure the proper function of the lungs chest drain is usually situated during esophagectomy; however, it is a source of discomfort to the patient in terms of pain and inability to move freely[133]. Several studies have demonstrated that the placement of

perinastomotic drain in gastrectomy does not significantly enhance recovery in terms of shortening the length of hospital stay, the early passage of flatus, early commencement of feeding[173,174], postoperative pulmonary complication, abscess within the abdomen, and mortality. A meta-analysis by Liu et al. showed that patients without the drain have fewer postop complications than those with drain placement y[175]. ERAS society recommends that the use of drains should be avoided as it will drastically reduce the chances of postop complications arising from using drains.

Early post-surgical nutrition and artificial nutrition

Commencement of nutrition postoperatively is essential; it is an important milestone. However, the exact time to commence nutrition has been a bone of contention for a while. Patients undergoing GEJ tumor resection are at high risk of malnourishment and cachexia, which is detrimental to their recovery and postop tolerance of chemotherapy, radiotherapy, or both.

The conventional protocol has been nil-per-os (npo or NPO); patients abstain from taking food and medication orally for some days[176]; some studies have challenged this conventional practice. Still, they are not specific to patients that had GEJ tumor resection[177]. Some studies support the commencement of oral feeding from POD 2, which at that moment was a breakthrough from the conventional protocol[178]. A systemic review and meta-analysis by Hao et al.[141] demonstrated that early oral feeding (EOF) significantly enhances immunity postoperatively, reduces LOS, and aids in the reduction of pulmonary complications compared to traditional oral feeding (TOF) in esophagectomy, another meta-analysis by He et al.[179] concluded that early oral feeding post gastrectomy is associated with enhanced recovery by shortening hospitalization time, and decreases expenses without compromising the integrity of anastomosis. Early oral feeding post gastrectomy has shown great potential, demonstrating its merits, viability, and safety[180]. Nutritional intervention with artificial nutrition, preferably taking high-energy drinks at intervals or using tubes, commences in some patients on POD 6 if they have not attained up to threescore (60%) of the desired percentage[181]. ERAS Society recommends oral feeding commences from POD 1; feeding should be monitored and increased strategically to avoid intolerance[157].

Audit

Routine analysis of the surgical outcome of patients that utilized the protocol should be done to ascertain the feasibility of the application of the components of the protocol for both the medical team and the patient; it also allows tailoring some components to fit the facility depending on the infrastructures available, and also to suit the community (considering beliefs, traditions, and racial influences). An audit has proven to be a vital part of ERAS protocol regardless of the type of surgical procedure performed, as it enhances medical outcomes through feedback[182].

The audit is particularly important in GEJ tumor resection because various real-time graphical techniques are currently available to track surgical treatment results following gastro-oesophageal surgery[183]. ERAS society strongly recommends audit[157].

Non-procedure specific components

Pre-surgical patient enlightenment

Over the years, enlightening patients before a procedure has greatly improved fast-tracking recovery. Patients are more cooperative, and caregivers or relatives are usually less resistant to implementing set protocols. Providing exhaustive information to patients before surgery helps buffer anxiety, reducing morphine intake and length of hospital stay[184]. Studies have shown a link between psychological factors and enhanced surgical recovery[185]. Explaining daily milestones that need to be attained postop motivates patients to strive and invest more in the recovery strategy; it also influences complication rates. A study by Edward et al. demonstrated that websites can be used to arm the patient with the right answers that can help buffer the patient's anxiety[186]. These tremendous benefits are why pre-surgical patient enlightenment is incorporated into the ERAS protocol.

The above benefits of patient enlightenment apply to all surgical procedures, including resecting GEJ tumors type II and III. ERAS II Society recommends that patient enlightenment be done routinely before any surgical procedure[157].

Pre-surgical smoking and alcohol cessation

High level of alcohol consumption has shown to be detrimental to positive surgical outcomes[187], and abusive alcohol intake prior to surgery increases morbidity rate after surgery188; this goes to show that proper clerking of the patient to determine the level of alcohol intake before surgery and enlightenment can change postop comes. Intensive perioperative management is required for patients that are considered alcohol abusers; this is because both alcohol abuse (AA) and alcohol withdrawal (AW) are detrimental[189]. Studies by Tonnesen et al.[190]. have shown that postop outcomes of patients that have up 5 or more bottles of alcohol daily and abstain for a month prior to surgery have better postop outcomes.

Daily smoking also influences post-surgical outcomes negatively; cessation of it has proven to be beneficial to recovery and shorten the length of hospital stay[191]. One month of smoking cessation prior to surgery significantly improves outcomes[192].

Persistent alcohol consumption and smoking prior to GEJ tumor resection is to the peril of the patient, as poor prognosis is inevitable, there will be poor wound healing, and an increase of pulmonary risk complications, which is the most common complication with the procedure of GEJ resection leading to increase morbidity and longer hospitalization period. ERAS society recommends cessation of both alcohol and smoking cessation before the surgery, and pulmonary pre-habilitation is advised[157].

Oral bowel preparation

Mechanical bowel preparation (MPB) is a traditional preoperative practice intended to rid the big bowel of feces to decrease postop complications and easy intraoperative maneuvering[193]. Studies have shown that it has serious physiological consequences that might be linked to dehydration[194]. This shows that conventional practices are not necessarily the best; implementing this practice does not enhance recovery[191].ERAS society does not recommend this practice[157].

Pre-surgical fasting and carbohydrate loading

Contrary to popular opinion, withholding oral intake from patients from midnight is not advantageous to the patient; it can increase insulin resistance and elevate organic stress response[195]. This is not to say that patients should not fast prior to surgery, as it lowers the risk of aspiration after anesthesia administration. Food consumption is advised for up to 6 hours before administration of anesthesia, and a clear carbohydrate-loaded fluid can be taken up to 2 hours prior to anesthesia administration[157]; this decreases starvation and thirst and improves the mental state of the patient, as drink high in carbohydrates reduces hunger and thirst more efficiently than intravenous glucose infusion[196]. ERAS society recommends pre-surgical fasting for up to 2 hours and 6 hours for fluid and solid, respectively, caveat of diabetic patients.

Preanesthetic medication

This is the administration of analgesics prior to anesthesia to reduce postoperative pain. Some medications do not show any results, while others show desirable results for a short period postop[197]. It is recommended that patients that are on analgesics for a long-term condition should continue before surgery. Minimal sedation can be administered using anxiolytic before anesthesia as severe anxiety can make pain management harder postoperatively; an RCT by Caumo et al. concluded that administration of anxiolytic (melatonin or clonidine) prior to surgery significantly reduces postop pains and morphine use compared to placebo[198]. Evidence has shown that carbohydrate drinks ERAS society recommends short-acting anxiolytics; however, long-acting is not recommended because of limited data supporting their viability[157]. Based on the recommendation, short-acting can be routinely administered. In contrast, long-acting should not be routinely administered for GEJ tumor resection, irrespective of the type of GEJ tumor being resected.

Antithrombotic prophylaxis

Venous thromboembolism (VTE) is one of the major postop complications; it is the presence of blood clots in the vein, a serious medical condition with high morbidity and mortality rate. This condition can be brought about by factors related to GEJ tumors, such as; cancer treatment, major surgical procedures, decubitus state, tumor size or load, etc. The administration of antithrombotic before surgery significantly reduces the chances of such complications. Heparin is often utilized as a prophylaxis, and low molecular weight heparin is commonly administered[199]. Administration can begin between 2 to 12 hours before surgery; other studies have shown that thromboprophylaxis that begins earlier before hospitalization is more effective. In individuals with an elevated risk of VTE, mechanical methods (intermittent pneumatic leg compression and elastic stockings) may offer additional advantages in terms of prevention[200]. Pharmacological thromboprophylaxis is recommended over mechanical thromboprophylaxis[193]. ERAS Society recommends using LMWH as prophylaxis for patients at high risk of VTE and continuing dosage up to 4 weeks postop; the use of mechanical prophylaxis should also be explored.

Skin disinfection and Antimicrobial prophylaxis

Surgical site infections (SSIs) lead to very poor surgical outcomes and complications; pathogens from the skin are the major source of SSIs hence the reason why skin preparation is very important before any surgical procedure, compounds comprising iodophors or chlorhexidine gluconate are currently among the most widely used for skin preparation[201]. Chlorhexidine-alcohol preoperative scrubbing of the patient's skin is more effective than povidone-iodine scrubbing in decreasing SSIs[202].

Administration of antimicrobial treatment prior to and during surgery to cocktail infections has been demonstrated to be effective in surgeries involving the gastrointestinal system[203]; the prophylaxis can be administered once (an hour before the surgery) and 3-4hours during the surgery, depending on the half-life of the drug administered[204]. ERAS society recommends skin preparation and antimicrobial administration preoperatively[157].

Epidural analgesia

Epidural analgesia has several well-established benefits in gastrectomy; excellent analgesic effect can be attained postoperatively with proper administration and control of epidurals; it relieves patients from pain while at rest and during early movement. It Significantly reduces the body's stress response due to surgery that causes postop complications, reducing cardiac, respiratory, and gastrointestinal complications[205]. ERAS Society recommends using epidural analgesia as part of the protocol because of its influence in reducing postop complications157.

Intravenous analgesia

Intravenous infusion of analgesia or PCA serves as an alternative if epidural analgesia cannot be administered. A study by Zhu Zhenxin et al.[206] .

demonstrated the efficacy of patient-controlled epidural analgesia versus patient-controlled intravenous analgesia, concluding that patient-controlled epidural analgesia is more efficient in pain control; however, it also showed enough benefits that qualify patient-controlled intravenous analgesia as an alternative during gastrectomy. A double-blind randomized control trial (RCT)[207] also showed diminished use of fentanyl postoperatively in patients that had lidocaine injections before and during laparoscopic gastrectomy. ERAS society recommends using it as an alternative[157].

Anesthetic Management

Proper anesthetic management plays an important role in enhancing the patient's recovery and reducing postop morbidity; the patient's assessment by the anesthetic team determines the anesthesia regimen administered during surgery. The existence of comorbidities influences the management of each patient. Commonly used anesthesias are short-acting such as propofol and dexmedetomidine[208], and opioids, such as sufentanil and remifentanil, combined with short-acting relaxants. The deep neuromuscular block is utilized for laparoscopic procedures to ensure proper surgical space and diminish immediate postop pain[209]. It is important that the right amount of anesthetic agents are administered to avoid deeper sedation than necessary- this can be attained using the Bispectral index (BIS)[209]. Patients at medium or high risk of respiratory complications can benefit from using low-tidal volume ventilation. All the above have benefits that enhance patients' recovery. The ERAS society recommends that management be utilized[157].

Post-surgical nausea and vomiting

Patients with a laparoscopic gastrectomy procedure may have post-surgical nausea and vomiting afterward (PONV). Diverse prophylactic regimens have been explored to curtail it, reduce patient discomfort, and enhance recovery. A randomized double-blind trial[210]concluded that a combination of Haloperidol, Dexamethasone, and Ondansetron is effective in Prevention of Postoperative Nausea and vomiting. There is reservation as regards the use of steroids because of the hypothesis that it may increase the risk of anastomotic bleeding post-gastrectomy. ERAS society recommends[157] that a multimodal approach towards preventing PONV should be implemented as part of the protocol before, during, and after surgical procedures.

Prevention of hypothermia

It has been initially speculated that laparoscopic procedures will prevent inadvertent perioperative hypothermia (IPH); however, this notion has been proven wrong by a recent research[211] that concluded that the carbon dioxide released during laparoscopic procedures contributes to hypothermia. Maintaining normothermia during surgical procedures in the abdominal region decreases postop complications like infections at surgical incision sites usually caused by low oxygenation of the tissue[212]. It also decreases cardiac complications, decreases the effect of anesthetic agents after surgery, and decreases patients' post-anesthetic distress (cold shivers)[213]. Some research[214] has suggested that; warming should begin 2hrs prior to the procedure, effective

warming strategies should be explored and utilized, especially in surgeries that take a long period, fluid administered during the surgery should be done with warm fluids, and set guidelines should be observed[215]. ERAS Society recommends avoiding hypothermia by utilizing warm air and warm water garment system.

Post-surgical glycemic control

Insulin resistance and increased glucose that, as a result of surgical stress, tangibly influences morbidity and mortality post gastrectomy, the administration of carbohydrate liquid (carbohydrate loading) before the procedure (gastrectomy) substantially decreases the negative influence it has on recovery[216]. Hence the reason why carbohydrate loading is an essential part of ERAS protocol because it decreases insulin resistance lowering hyperglycemia, other ERAS protocol component that plays a part in reducing glucose resistance are those that effectively reduces surgical stress like Epidural analgesia, proper fluid balance, opioid-sparing, and utilization of less invasive access during the surgery. Pre-surgical preventive measures towards reducing surgical stress, which decreases post-surgical insulin resistance, are recommended for proper glycemic control without the risk of the patient becoming hypoglycemic after administering insulin to control hyperglycemia. The ERAS society recommended that all possible measures be taken to decrease the risk of insulin resistance and hyperglycemia post-gastrectomy procedure[157].

Fluid balance

Stress response as a result of surgical procedures with common sources from the endocrine and inflammatory origin[217] affects the body's fluid balance (hypovolemia, water, and salt surfeits), leading to postop complications involving the cardiac, respiratory, and gastrointestinal systems. Fluid management is an important routine perioperatively; perioperative fluid homeostasis plays an important role in enhancing patients' recovery of patients, hence an important component of the ERAS protocol. Fluid depletion is considered in the balancing of fluid as administration of EDA is part of the ERAS protocol (vasodilation effect leading to hypotension). The utilization of observatory tools like cardiac monitors has not been précised in determining whether the patient is hyper or hypo perfused. To achieve proper fluid management, other components of the ERAS protocol, like avoidance of fasting and bowel preparation(avoiding dehydration) and intake of clear carbohydrate drinks (favors hydration) between 2-3 hours before gastrectomy, help sustain fluid balance[218]. It is important to avoid dehydration and over-hydration during perioperatively as both are associated with an increased risk of complications. ERAS society also recommends that fluid management be customized to the patients' need to attain homeostasis (Goal-directed fluid therapy).

Urinary drainage

Transurethral catheterization is the conventional practice of draining urine during and after surgical procedures; however, suprapubic urinary drainage has been explored in the last few years, especially for abdominal surgery, as it significantly decreases microbial infections-urinary tract infections (UTIs)[219]. For postop recovery to be enhanced, factors such as; reinsertion, infection, discomfort, and ability to drain urine are considered before urinary drainage removal. It has been shown that early removal of drainage is considerably beneficial (POD 1) compared to removal at POD 3-4[220].ERAS Society recommends that suprapubic catheterization be used if urinary drainage has to go on for up to 4 days; otherwise, transurethral catheterization should be used for urinary drainage and removed at POD 1-2157 for the gastrectomy procedure.

Bowel movement stimulation

Postoperative ileus is a gastrectomy postop complication that increases both morbidity and mortality. Over the years, surgeons have tried to avoid that pitfall. The components of ERAS, like proper fluid management, early mobilization, and analgesia[221,222,223,] aid in early intestinal peristalsis. A recent study has shown that chewing gum after surgery leads to the secretion of gastrointestinal hormones that stimulate peristalsis[224]. ERAS Society recommends that attention be given to fluid balance, anesthesia, and laxative administration as they can facilitate intestinal peristalsis[157].

Early scheduled mobilization

Bed rest after gastrointestinal surgery is a dogma that has been proven to be disadvantageous towards enhanced recovery after gastrectomy, as it negatively influences the restoration of the body to an optimal physiological state by improving respiratory, cardiovascular, and gastrointestinal functions. It is vital that the movement is planned and supervised[225] to avoid accidents and take note of progress. It may influence the patient's psychological state and shortens the length of hospital stay (reducing financial implication)[226]. ERAS Society recommends that the patient progressively commence mobility from POD 1 with proper documentation[157].

Our institution's protocol

Our institution's ERAS protocol is implemented in non-emergency GEJ tumor resection, utilizing our multidisciplinary team (MDT), which includes; surgeons, nurses, an anesthesiologist, a nutritionist, a physiotherapist, an oncologist, a radiologist, a pathologist, and a psychologist. Each team member is familiar with the institution's ERAS protocol, and a meeting is held to revise the protocol for certain patients.

All patients are enlightened about the procedure and the protocol; this has proven to improve the level of cooperation in the implementation of the elements of the ERAS protocol; the dietician confirms the nutritional status of the patient, the radiologist examines the patient to re-access the extend of infiltration and choose the best procedure base on the type of GEJ tumor. Prehabilitation is done to optimize the respiratory, cardiac, and musculoskeletal systems. Neoadjuvant therapy is usually administered for all GEJ tumor patients 4-8 weeks before the surgical procedure. Antithrombotic prophylaxis is administered before the procedure and continued afterward by administering low molecular weight heparin, and we also utilize intermittent pneumatic compression devices after surgery.

We utilize multimodal analgesia (reduced opioid use), including multimodal analgesia (Intravenous injection of COX-2 receptor inhibitor(Parecoxib 40mg IV)； TAP（transversus abdominis plane）, PCA (patient-controlled analgesia)
Intravenous injection of low-dose hormones on the day of surgery and the first day after surgery).

As regards to commencement of the diet, a drink is offered after the patient regains consciousness,

Half-flow diet after ventilation: including rice porridge, oral enteral nutrition preparation, etc. (Ideal goal: oral EN target amount of 8-10 kcal / kg on POD 1, 5-10 kcal/kg per day, gradually increasing to 25-30 kcal per kg).

The utilization of gastric tubes and catheter management is common. The conventional indwelling gastric tube is only placed in special cases (POVN, bloating)

Urinary catheters are removed within 24 hours of GEJ tumor resection.

Early mobilization is planned and implemented postoperatively.

Ideal target amount: awake and active in bed on the day of surgery; on the POD 1, 100 meters of movement should be performed. On POD 2, the patient should get out of bed and walk up to 250 meters. On POD 3 and 4, the patient should walk up to 300-500 meters.

The infusion of a patient is carefully monitored perioperatively.

Oral carbohydrate is administered before the operation: 400 ml of 12.5% glucose solution should be consumed 2 hours before the surgical procedure.

Preoperative bowel preparation: Low-fiber diets (Medsupcln or soybean) are normally given orally three days before surgery, and intestinal lavage powder is given orally one day before surgery. Food and liquid are offered but not mandated from POD 1; the intake is monitored and encouraged to increase after analyzing tolerance. Postoperative fluid infusion is

Most procedures are minimally invasive, except if a complication requires open surgery.

The MDT team members of the ERAS team have an audit meeting at intervals to review the cases that used the ERAS protocol to improve the protocol.

II. Conclusion

The ERAS protocol has proven to be an effective protocol, that has over time challenged the conventional protocol and provides substitutes that have fast-track the recovery of patients, reducing the length of hospitalization and the cost. However, controversial surgical procedures like the resection of GEJ tumors needs a standardized protocol to effectively decrease the controversies surrounding it, which can positively influence morbidity and mortality rates. Unifying the ERAS protocols presented in this review by the ERAS society indicating the specific procedure beneficial for the different types of GEJ tumor based on Siewert's classification will help medical professionals to effectively select a protocol base on the type of GEJ tumor.

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