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REVIEW ARTICLE

Minimal Invasive Esophagectomy—a New Dawn of Esophageal Surgery

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Abstract
Surgery is the mainstay of esophageal cancer. However, esophagectomy is a major surgical trauma on a patient with high morbidity and mortality. The intent of minimally invasive esophagectomy (MIE) is to decrease the degree of surgical trauma and perioperative morbidity associated with open surgery, and provide faster recovery and shorter hospital stay with the equivalent oncological outcome. It also allows for lesser pulmonary morbidity, less blood loss, less pain, and a better quality of life. MIE is safe and effective but has a steep learning curve with high technical expertise. Recently, it is increasingly accepted and adopted all over the globe. In this article, we discuss the safety, efficacy, short-term, and oncological outcomes of thoracoscopic- and laparoscopic-assisted minimally invasive esophagectomy and robotic surgery compared with open esophagectomy with a special focus on the Indian perspective.

Keywords Minimal invasive esophagectomy · Esophageal surgery · Robotic surgery

Introduction

For localized esophageal cancer, radical esophagectomy remains the prime form of treatment. Esophagectomy is a highly invasive surgical procedure with associated morbidity ranging from 38 to 43% and a mortality of 8 to 10% [1]. Therefore, minimally invasive esophagectomy using the laparoscopic or thoracoscopic approach was developed to reduce surgical trauma and its associated morbidity.

Although several less invasive esophagectomy procedures have been described, the efficacy and safety of minimally invasive esophagectomy (MIE) are still under controversy. This review article attempts to clarify whether MIE has improved short-term outcomes compared with conventional open esophagectomy (OE) for esophageal cancer treatment. Besides, the differences between MIE and OE in the oncologic outcome are also reviewed. A special focus on the Indian perspective is also added.

Cuschieri et al. first reported on the video-assisted thoracoscopic mobilization of the esophagus along with laparotomy on five patients in 1992 [2]. This was soon followed by Azagra et al. [3], Collard et al. [4], and McAnena [5] reporting their experience using thoracoscopic resection and laparotomy on a small group of patients. DePaula et al., in 1995, described their experience on the first laparoscopic transhiatal esophagectomy procedure [6]. In 1996, Akaishi et al. [7] first reported thoracoscopic en bloc esophagectomy with radical mediastinal lymphadenectomy from Japan. Then, Watson et al. [8] described total endoscopic Ivor-Lewis esophagectomy in the year 1999. In the same year, Nguyen et al. [9] described the combined laparoscopic and thoracoscopic approach to esophagectomy. This was followed by Kernstine et al. [10] reporting their experience on robot-assisted thoracoscopic esophagectomy in 2004.

In 2003, Luketich et al. published their experience on a large series of 222 patients undergoing total MIE (thoracoscopy and laparoscopy) with a remarkable low surgical morbidity and mortality with a conversion rate of 7.2% [11]. Pneumonia and 30-day mortality rates were 7.7 and 1.4%. The same authors updated their results in 2012 with more than 1000 patients with an operative mortality of

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1.68% and median ICU and hospital stay of 2 and 8 days [12]. The traditional invasive vs. minimally invasive esophagectomy (TIME) trial [13] was the first randomized control trial comparing outcomes of minimally invasive transthoracic esophagectomy (TTE) against open TTE which was published in 2012 [14]. The trial showed MIE resulted in a lower incidence of pulmonary infections, a shorter hospital stay, a better quality of life, and short-term outcomes with equivalent nodal harvest and R0 resection [14].

Indian Perspective

Palanivelu et al. in 2006 reported the outcomes of thoraco-laparoscopic esophagectomy (TLE) for carcinoma of the esophagus for the first time in a prone position in 130 patients [15]. Patients were intubated with a single-lumen endotracheal tube with possible two-lung ventilation with pneumothorax of 6–8 mmHg. The authors demonstrated the feasibility of MIE in the prone position with better ergonomics, low postoperative morbidity, which gradually replaced conventional thoracoscopic mobilization of the esophagus in the left lateral decubitus position. Median ICU stay and hospital stay were 1 and 8 days. Perioperative mortality was 1.54%, and anastomotic leak rate 2.31%. Postoperative pulmonary complication rate was remarkably low (1.54%). The same authors shared their experience on laparoscopic esophago-gastrectomy without thoracic and cervical access for adenocarcinoma of the gastro-esophageal junction in a cohort of 32 patients. They found that the approach was associated with low morbidity and adequate oncological clearance while maintaining the benefits of minimally invasive surgery [16].

Puntambekar et al. in 2010 reported the outcomes of 112 patients undergoing thoracoscopic esophagectomy for carcinoma of the esophagus in the left lateral position. There were two conversions. The average thoracoscopic operating time was 85 min and blood loss of 200 ml. The mean mediastinal nodal yield was 20. Sixteen patients had postoperative morbidity, of which eight patients (7.27%) experienced pulmonary complications and three surgical mortality [17].

The same authors recently reported their 5-year experience on laparoscopic-assisted transhiatal esophagectomy on 81 cases, of which 94% had R0 resection [18]. Mean operating time and blood loss were 140 min and 80 ml. Mean postoperative ICU stay and hospital stay were impressively low (1 and 7 days). A total of 6.1% of cases had pulmonary infections, two (2.46%) temporary RLN palsy. There was no intraoperative or 30-day mortality. No anastomotic leaks were reported, but ten patients developed late anastomotic strictures. The mean nodal yield was 20, and the average survival was 28 months. Three patients had local recurrence, 18 regional recurrences, and 30 distant recurrences [18]. They also shared their experience of thoraco-laparoscopic esophagectomy in elderly patients (> 70 years) with carcinoma of the esophagus with remarkably low morbidity and mortality and suggested that age should not be a bar for undergoing surgery. Cardiac and respiratory complications were reported in 1.47% and 10.30% of patients. No conversions were required. Mean ICU stay and hospital stay were 4 and 13 days, respectively [19].

Parthasarathi et al. reviewed their experience of 143 cases of thoraco-laparoscopic Ivor-Lewis esophagectomy, 97% of which were performed for malignancy. The mean operative time was 458 min, blood loss 138 ml. The mean nodal yield was around 22 nodes. The average postoperative ICU stay and hospital stay were 5 and 13 days. The overall morbidity was 12.58% (RLN injury in 1.39%, pneumonia in 8.39%, chyle leak in 0.69%, anastomotic leak in 2.09%, anastomotic stricture in 12.58%). Overall, 30-day mortality was reported in 1 case (0.69%) [20].

Vageesh et al. reported the outcomes of laparoscopic-assisted transhiatal esophagectomy in a cohort of 26 patients. The median operative time, blood loss, and hospital stay were 300 min, 300 ml, and 11.5 days. Respiratory complications and anastomotic leak occurred in eight (30.7%) and three (11.5%) patients, respectively. The median nodal yield was 13. At a median follow-up of 19 months, five patients (19.23%) developed recurrence, of which three (11.5%) succumbed to disease [21].

Position

MIE was conventionally performed in the left lateral decubitus position (MIE-LP). However, MIE-LP required total lung collapse and retraction of the lung and is therefore met with severe pulmonary morbidity [22]. Cuschieri et al. first described thoracoscopic mobilization of the esophagus in the prone position in 1994 [23]. Later, Palanivelu et al. [15] reported MIE in the prone position in a large series of 130 patients. Their study showed that prone position is feasible, has lower respiratory complications, and a shorter operative time. The potential benefits of this position in comparison with the left lateral decubitus position were suggested by Fabian et al. [24]. Added to this, Noshiro et al. [25] reported that the prone position provides a better view of the surgical field around the left recurrent laryngeal nerve.

The short-term surgical results were studied in patients undergoing thoracoscopic esophagectomy in prone (TE-P) and lateral position (TE-L) by Kubo et al. [26] with two groups of 28 patients in lateral and 30 in the prone position. Blood loss, duration of systemic inflammatory response syndrome, and serum C-reactive protein levels on postoperative days 1 and 2 were significantly lower in prone group. Respiratory complications tended to be lower in the prone group. They concluded that esophagectomy in a prone position was feasible and safe. TE-P might be a substantially less invasive procedure than TE-L [26].

A systemic review showed that minimal invasive esophagectomy in the prone position has potential advantages of the shortened learning curve, better ergonomic position of surgical hands, and excellent exposure of the surgical field compared with MIE in lateral decubitus position [22]. Double-lung ventilation with a single endotracheal tube is more relevant in the prone position. In contrast, single-lung ventilation with double-lumen selective intubation is suitable and commonly used in the lateral position. Conversion to a traditional thoracotomy, if required urgently, will be an arduous task in the prone position.

Therefore, to circumvent this issue, esophagectomy is more commonly performed in a modified semi-prone position. It is recently becoming more popular globally and is safe, feasible, and at least comparable with MIE in terms of oncological clearance and postoperative complications [27]. Few authors have suggested a hybrid position approach for MIE [27]. The left lateral decubitus position is favored for the upper mediastinum procedure and the prone position for the middle and lower mediastinum procedure. The prone and left lateral decubitus position can be attained by just rotating the surgical table. This hybrid position enables to immediately convert from thoracoscopic to open surgery in the event of an emergency, which was a distinct disadvantage of the prone position [28].

Indian Perspective

Javed et al. studied MIE in the prone position (PP) and lateral decubitus position (LDP) in 25 and 23 cases and concluded that PP is an effective alternative to LDP. The incidences of postoperative pulmonary complications were 26.1% in the LDP group and 8% in the PP group. The excellent exposure achieved in prone position obviated the need for double-lumen endotracheal intubation and complete collapsing of the lung. A more meticulous dissection with a higher lymph nodal yield was achievable in PP [29].

Thakkar et al. published the results of the feasibility and safety of minimally invasive esophagectomy in a semi-prone position. Of 12 patients studied, one required conversion to thoracotomy, and there was one surgical mortality. Mean operating duration and blood loss of thoracoscopic part were 103 min and 110 ml, mean maximum end-tidal CO_2 38.5 mmHg. The mean nodal yield was 14, and all patients had R0 resection. The median ICU stay and hospital stay were 1 and 8 days [30].

Single-Lung Ventilation vs. Double-Lung Ventilation

Lin et al. studied the pros and cons of total lung ventilation (TLV) vs. one-lung ventilation (OLV). The apparent advantages of TLV like reliability and good exposure are marred by disadvantages, including a high incidence of hypoxemia, vocal cord paralysis, pulmonary shunting, atelectasis, bronchial injury, complicated intubation, and its maintenance. In contrast, OLV is fast, easy, and convenient with good oxygenation. The advantages of single lung endotracheal intubation (SLET) include convenient intubation, easy intraoperative management, and good oxygenation. Hemodynamic changes, circulation dysfunction, air embolism, acidosis, impaired coagulation, and probably increased tumor metastasis are its disadvantages. Current literature suggests that TLV with CO_2 pneumothorax is safe and feasible, and a good alternative of OLV in MIE [31].

Learning Process

Esophagectomy with mediastinal lymph node dissection is a complicated surgical procedure. It requires a lot of learning and experience, and minimally invasive surgery is a complex one that requires still more significant expertise and skills. The advantage and benefits of minimally invasive esophagectomy are proportionate to the number of cases experienced. Based on patient experience, Luketich et al. [11, 32, 33] concluded that minimally invasive esophagectomy was not beneficial for the first eight patients, of uncertain value for the next 77 patients, and beneficial for 222 patients. Osugi et al. [34] reported on the learning curve required and the efficacy of radical thoracoscopic esophagectomy done for thoracic esophagus cancer. The outcomes in the first 34 patients were compared with those of the last 46 patients. It was found that the duration of the thoracoscopic procedure, the incidence of postoperative pulmonary infection, and blood loss were significantly lesser, and the number of mediastinal nodes retrieved was higher in later 46 patients than in the first 34 cases performed. Multivariate analysis indicated that surgical experience predicted the risk of pulmonary infection.

Ninomiya et al. [35] were able to master complete thoracoscopic radical esophagectomies after performing 10 cases under the supervision of an experienced surgeon. Moreover, after 10 cases, the morbidity rates, incidence of recurrent laryngeal nerve palsy, blood loss, atelectasis, and postoperative pneumonia were lesser compared with cases done during the induction period. Although the surgeon had minimal experience with esophagectomy at the outset, guidance and supervision from another experienced surgeon made the surgeon master thoracoscopic radical esophagectomy safely and relatively quickly [35].

Indian Perspective

Somashekhar et al. reviewed their experience on 35 patients with histologically proven resectable carcinoma of the esophagus and underwent robot-assisted transthoracic and transperitoneal three-stage esophagectomy. In the first ten cases, total docking time, thoracic docking time, total operative time, thoracic-phase operative time, and blood loss were longer, which decreased significantly in the subsequent 25 cases [36].

Operative Time

The duration of surgery has been consistently shown longer for MIE compared with open esophagectomy (OE). The meta-analyses by Lv et al. [37], Guo et al. [38], and Nagpal et al. [39] reported a longer surgical duration for MIE. In line with the results of meta-analysis, the randomized controlled study TIME trial had shown the median operative time for MIE-TTE to be significantly longer than for open TTE (329 vs. 299 min) ($p = 0.002$) [14]. In contrast, a meta-analysis by Dantoc et al. did not find any significant difference between both the groups [40].

Blood Loss

The meta-analyses by Lv et al. [37], Yibulayin et al. [41], Nagpal et al. [39], Guo et al. [38], and Watanabe et al. [42] reported lesser blood loss in the MIE group than the OE group. The TIME trial also had significantly lesser blood loss in the MIE group compared with the OE group (200 vs. 475 ml) ($p < 0.001$) [14]. Excellent visualization of the operative field during MIE ensuring good hemostasis is attributed to decreasing blood loss.

ICU Stay and Hospital Stay

Yibulayin et al. found the duration of hospital stay, including ICU stay, to be significantly lower in the MIE group [41]. These findings were also confirmed by a meta-analysis by Nagpal et al. [39]. The TIME trial also reported the hospital stay to be significantly shorter in the MIE arm (14 vs. 11 days, $p = 0.044$), reflecting a faster postoperative recovery in the MIE arm [14]. A study analyzing the National Cancer Database of 4047 patients undergoing esophagectomy found MIE to be independently associated with a short hospital stay compared with OE with a mean reduction of 1.5 days [43].

Overall Morbidity

A meta-analysis by Yibulayin et al. [41], comprising thirty-five studies with 5991 cases, reported significantly lesser overall morbidity for the MIE group compared with the OE group (41.5 vs. 48.2%) (OR = 0.70, 95% CI = 0.626~0.781, $p < 0.05$). A meta-analysis by Guo et al. [38] and a nationwide study of 4047 patients undergoing esophagectomy for esophageal cancer [43] also asserted the above findings. Nagpal et al.'s meta-analysis showed significantly lower total complications in the MIE group than in the open group [39].

Anastomotic Location

The rate of anastomotic leak was found to be similar between MIE and open surgery. Yibulayin et al. [41] in their meta-analysis noted that there is no evidence of a reduced anastomotic leak in the MIE group (OR 1.023, 95% CI 0.870–1.202, p value = 0.785), in line with results of meta-analyses by Zhou et al. [44], Guo et al. [38], Lv et al. [37], and Nagpal et al. [39]. A meta-analysis by Zhou et al. [44] reported that there was a non-significant reduction of the cervical anastomotic leak of 14 cases per 1000 individuals treated with MIE when compared with OE. Both for hand-sewn and stapled cervical anastomosis, there was no significant reduction of the anastomotic leak for MIE-treated individuals. There was an insignificant absolute decrease of 24 patients per 1000 individuals treated with MIE compared with OE for stapled cervical anastomosis. For hand-sewn anastomosis, there was an insignificant reduction of 18 cases per 1000 individuals treated with MIE [44].

Anastomotic Stricture Rate

Lv et al.'s meta-analysis [37] showed that the anastomotic stricture rates were similar between the groups (OR = 1.76, 95% CI = 0.78–3.97, $p = 0.18$). In contrast, Sgourakis et al. [45] showed that MIE displayed a higher incidence of anastomotic strictures.

Indian Perspective

Mishra et al. found more anastomotic stricture rates in hand-sewn anastomosis than stapled anastomosis when an anastomotic leak occurs [46]. Kumar et al. compared 77 patients who underwent linear stapled ($n = 29$) and hand-sewn ($n = 48$) cervical anastomosis after esophagectomy. There was a significant reduction of anastomotic leak in the stapled group (7 vs. 27%) (p 0.03) [47]. Saluja et al. conducted a randomized trial comparing side-to-side stapled and hand-sewn esophagogastric anastomosis in the neck in a cohort of 174 patients undergoing esophagectomy for carcinoma of the esophagus [48]. There were no differences in the leak rates and postoperative outcomes between the two techniques. At a follow-up of 12 months, anastomotic strictures occurred less frequently following stapled anastomosis.

Wound Infection

The open group had significantly higher wound infection rates than the MIE group (RR 3.21; 95% CI 1.77–5.81; $p = 0.0001$) in a meta-analysis by Guo et al. [38].

Pulmonary Morbidity

The TIME trial reported that an overall in-hospital incidence of pulmonary infections was significantly lower in the MIE arm than the OE group (12 vs. 34%, $p = 0.005$), a finding similar to that reported in meta-analyses by Nagpal et al. [39], Guo et al. [38], and Watanabe et al. [42]. Similarly, Lv et al. [37] and Xiong et al. [49] in their meta-analyses showed that patients undergoing MIE had lesser respiratory complications than open surgery counterparts. Guo et al. [38] reported the open group had worse pulmonary complications, including pulmonary infection, acute respiratory distress syndrome, pulmonary embolism, and respiratory failure rate (RR 1.42; 95% CI 1.03–1.97; $p = 0.03$). Studies by Tsukada et al. [50] and Fukunaga et al. [51] have shown that thoracoscopic esophagectomy resulted in less cytokine production, interleukins, and granulocyte elastase in comparison with open transthoracic esophagectomy. It was associated with better respiratory kinetics with less surgical trauma. Thoracoscopic esophagectomy for esophageal cancer leads to better preservation of respiratory function and quality-of-life. Taguchi et al. [52] had shown that the pre-to-postoperative change in vital capacity was significantly lesser in MIE than OE.

Pulmonary Morbidity Concerning Position

A systematic review analyzed the literature between 2000 and 2015 for studies comparing MIE in the lateral decubitus (LD) or prone (PP) positions. A total of 387 cases were in the LD group and 336 in the PP group. The pooled analysis revealed that prone position MIE is superior to lateral decubitus MIE with decreased pulmonary complications, lesser estimated blood loss and increased mediastinal nodal yield [53].

Another similar systemic review by Koyanagi et al. found in contrast to the theoretical superiority of MIE-PP, individual reports from single institutions, with a smaller number of patients and shorter follow-up duration, failed to demonstrate the purported benefits and superior clinical outcome in MIE-PP groups against MIE-LD and OE groups. The incidences of short-term complications were similar for the MIE-PP and OE groups. The overall morbidity associated with MIE-PP was also comparable with that of OE [22]. Kuwabara et al. [54] found that the incidence of respiratory complications in the MIE-PP group was significantly lower than that of the MIE-LP group, while other studies did not show any difference [22]. Further larger clinical studies and randomized clinical trials are required to confirm these benefits of the MIE-PP group.

Cardiovascular Complications

Cardiovascular complications like acute myocardial infarction, heart failure, arrhythmia, pulmonary embolism, and deep vein thrombosis cause significant morbidity and mortality. Yibulayin et al. reported a very strong evidence of reduced cardiovascular complications in the MIE group (OR = 0.770, 95% CI = 0.681–0.872, $p < 0.05$) [41].

Recurrent Laryngeal Nerve Palsy

The incidence of vocal palsy ranges from 3.5 to 9.5% after esophagectomy [1]. Even though TIME trial [14] and Xiong et al. [49] showed a significantly lower rate of vocal cord palsies and recurrent laryngeal nerve injuries in the MIE group, meta-analyses conducted by Nagpal et al. [39], Guo et al. [38], Sgourakis et al. [45], and Yibulayin et al. [41] failed to show any difference.

Other Surgical Morbidities

Surgical technique–related complications such as tracheal laceration, splenic laceration, hemorrhage, and chylothorax were reported to be lesser in patients undergoing MIE [55], while Lv et al. [37] and Sgourakis et al. [45] showed no significant difference between MIE and OE in terms of reoperation rates, chylothorax, recurrent laryngeal nerve injury, fistulas, gastric conduit ischemia, and pleural effusions.

In-hospital Mortality

Yibulayin et al. [41] reported that the mortality risk was 3.8% in the MIE group vs. 4.5% in the OE group and a very strong evidence of reduced mortality in the MIE group (OR = 0.668, 95% CI = 0.539~0.827, $p < 0.05$), while Lv et al. [37] and Nagpal et al. [39] could not demonstrate reduced in-hospital mortality in favor of MIE (OR = 0.84, 95% CI = 0.60–1.19, $p = 0.33$). Parthasarathi et al. reported in a series of 143 cases of thoraco-laparoscopic Ivor-Lewis esophagectomies an impressively low 30-day mortality of 0.69% [20].

No. of Nodes Harvested

In their studies, Lv et al. [37] and Nagpal et al. [39] reported a similar harvest of lymph nodes in both groups. Similarly, these results were also confirmed in the randomized TIME trial [14]. In contrast, Dantoc et al. [40] and Watanabe et al. [42] found a significantly higher number of nodes harvested in the MIE group than the OE group (16 vs. 10) ($p = 0.02$) owing to magnified and better visualization of the surgical field. A population study also noted a higher number of lymph nodes harvested with MIE (15 vs. 13; $p = 0.016$) [43]. Yibulayin et al. [41] showed that there was no significant difference between the two groups. Parthasarathi et al. harvested an average of 22 nodes in their series of 143 cases of MIE Ivor-Lewis esophagectomy [20].

Margin Positivity

R0 resection rate was found to be 92% in MIE and 84% in OE in a systemic review by Wullstein et al. [56]. Burdall et al. [57] found a lower R1 resection rate of 6.1% in MIE patients compared with 15.6% in the open group. A meta-analysis by Lv et al. [37] reported similar R0 resection between the open and minimally invasive groups (RR = 1.03, 95% CI = 0.98–1.08, $p = 0.21$). The TIME trial [14] also reported that the number of retrieved lymph nodes and the completeness of resection (i.e., resection margin (R0)) were similar between both groups. Putmanbekar et al. had reported a R0 resection rate of 94% in their series of 81 patients undergoing laparoscopic-assisted THE [18].

Overall Survival

The meta-analysis by Lv et al. [37], which included only randomized trials and prospective studies, concluded that the MIE group had better overall survival than the open group (hazard ratio 0.54, 95% CI = 0.42–0.70, $p = 0.00001$). The authors concluded that this positive effect is probably due to the amplification effect of the minimally invasive surgery, with better delineation and dissection of tumor tissues and relevant lymph nodes. In a national-wide database of 18,673 esophagectomies performed in England over 12 years, Lazzarino et al. [58] found that patients undergoing MIE had better 1-year survival rates than patients receiving open esophagectomy (OR = 0.68, 95% CI = 0.46–1.01, $p = 0.058$). Guo et al. [38] indicated in their meta-analysis that combined thoracoscopic-laparoscopic esophagectomy did not compromise the 5-year overall survival rate. Given the long-term results, Osugi et al. [59] found similar 3-year survival rates following hybrid MIE and OE in patients undergoing 3-field lymph nodal dissection.

In their systematic review and meta-analysis, Dantoc et al. [40] found 1-, 2-, 3-, and 5-year survival better in favor of MIE but not significant. However, the TIME trial depicted no differences in disease-free and overall 3-year survival for open and MI esophagectomy [14]. Also, the updated review by Watanabe et al. [42] suggested that the oncologic outcomes of MIE were not inferior to those of OE. Puntambekar et al. reported a median OS of 28 months in laparoscopic THE in upfront operated cases [18].

East vs. West

Dantoc et al. [40] compared esophagectomies done in east vs. west centers. Western centers had statistically better nodal yield with open vs. MIE group, but the difference was not seen in eastern centers. Concerning survival, there was no statistically significant survival advantage for MIE between eastern and western centers.

Robot-Assisted Minimal Invasive Esophagectomy

Robot-assisted minimally invasive esophagectomy (RAMIE) was introduced in 2003 to overcome the technical restrictions of MIE [60]. Robotic surgery offers an excellent amplified three-dimensional view, providing a meticulous dissection with 7 degrees of freedom of movement [60].

The ROBOT trial [61] was a single-center randomized controlled trial from an expert robotic institute in Utrecht, Netherlands. One hundred twelve patients were randomly allocated to the RAMIE arm vs. open transthoracic esophagectomy (OE) arm. It was found that the RAMIE arm had a lower incidence of overall surgery-related complications (59 vs. 80%), with lower postoperative and cardiopulmonary morbidity with better short-term quality of life and short-term outcomes, lesser postoperative pain, and better short-term postoperative functional recovery compared with OE. At a median follow-up of 40 months, oncological outcomes were comparable between both the arms. In a matched comparative study by Weksler et al. [62], RAMIE was found to be equivalent to thoracoscopic MIE in terms of the short-term outcomes and without any clear additional advantages.

Yerokun et al. [63], using the National Cancer Database of 4600 patients who underwent resection of middle and distal esophageal cancers with clinical-stage T13N03M0, found the usage of a robotic approach in comparison with MIE without robotic assistance, was not associated with any significant differences in perioperative outcomes. However, MIE group survival was equivalent to open surgery. A meta-analysis by Jin et al. [64] found that RAMIE and MIE displayed similar feasibility and safety profile concerning conversion to open, R0 resection, postoperative complications, operation time, number of harvested lymph nodes, 30- and 90-day mortality rate, in-hospital mortality rate, and length of stay in hospitals.

In summary, RAMIE compared with open TTE is associated with significantly reduced perioperative complications with decreased blood loss, lower pulmonary and cardiac complications, lower postoperative pain, and better functional recovery and short-term quality of life. Oncologic outcomes, R0 resection rates, the number of harvested lymph nodes, and disease-free survival and overall survival were comparable between groups. In comparison with thoracoscopic MIE surgery, RAMIE does not give any added benefit.

Indian Perspective

Somashekhar et al. reviewed their experience on 35 cases of resectable carcinoma of the esophagus undergoing robot-assisted transthoracic and transperitoneal McKeown esophagectomy [36]. When compared with the first ten cases, total docking time, thoracic docking time, total operative time, thoracic-phase operative time, and blood loss decreased significantly in the subsequent 25 cases. The median numbers of lymph nodes dissected were 32. One case needed conversion. The median hospital stay was 8 days. All had R0 resection.

Puntambekar et al. reported on feasibility of robot-assisted thoracoscopic esophagectomy in a series of 83 cases of esophageal cancer [65]. They concluded that the procedure afforded precise en bloc dissection with mediastinal lymphadenectomy with reduced operative time, blood loss, and complications. The mean operative time and blood loss were 205 min and 87 ml. The mean number of nodes dissected were 18. There were no conversions. The mean ICU and hospital stay were 1 and 10.4 days, respectively. A total of 16 (19.28%) complications occurred.

Palanivelu et al. shared their experience of 15 patients undergoing RAMIE [66]. Patients with SCC underwent McKeown's procedure, and those with AC underwent the Ivor-Lewis procedure. Extended two-field with total mediastinal lymphadenectomy was done for all. The median operating time and blood loss were 558 min and 145 ml. There were no intraoperative adverse events and conversions. Recurrent laryngeal nerve paresis and pneumonia were the most common postoperative complications occurring in 3 (20%) and two patients (13.3%), respectively. The median hospital stay was 9 days.

Goud et al. described their experience of totally robotic esophagectomy for carcinoma of the esophagus on a large series of 162 patients [67]. The mean operating time was 292 min, and average blood loss 170 ml. The mean nodal harvest was 42. Five patients had postoperative respiratory complications, two anastomotic leaks, three chyle leaks, and four recurrent laryngeal nerve palsy. There was one in-hospital mortality; the mean ICU stay was 2.3 days. No conversions were reported. With a median follow-up period of 18 months, 145 (89.5%) patients were alive without any evidence of disease.

Hybrid Procedures

The MIRO trial, a multicentric, open-labeled randomized controlled trial from France, demonstrated hybrid minimally invasive esophagectomy in comparison with open esophagectomy resulted in reduced incidence of intraoperative and postoperative major complications (35.9 vs. 64.4%) (OR 0.31, 95% CI 0.18–0.55, $p = 0.0001$), specifically respiratory complications (17.7 vs. 30.1%), without compromising 3-year overall survival and disease-free survival [68]. Overall survival was 67% in the hybrid procedure group vs. 55% in the open procedure group at 3 years and 60 vs. 40% at 5 years (hazard ratio [HR] = 0.67, 95% CI = 0.44–1.01) in favor of the hybrid procedure. Disease-free survival was 57% vs. 48% at 3 years and 53% vs. 43% at 5 years (HR = 0.76, 95% CI = 0.52–1.11) favoring the hybrid procedure.

In further confirmation, the meta-analysis by Nagpal et al. [39] found decreased respiratory complications, lower anastomotic leak, lesser blood loss, and shorter ICU and length of stay in favor of hybrid MIE than open surgery. In contrast, cardiac complications, chyle leak, recurrent laryngeal nerve palsy, 30-day mortality, and total morbidity were similar in both groups.

Impact of Neoadjuvant Therapy

Only a few publications have evaluated minimally invasive esophagectomies, in conjunction with neoadjuvant therapy, to compare patients with surgery alone. The TIME trial, in which most of the patients received neoadjuvant chemoradiotherapy, found the rate of pulmonary infection and in the first 2 weeks; pulmonary infection in-hospital to be significantly lower in the minimally invasive group compared with the open group (29 vs. 9%) (12 vs. 34%) [14].

Spector et al. [69] found acceptable morbidity and low mortality with the three-hole minimal invasive esophagectomy after neoadjuvant chemoradiation compared with the open surgery group. Mungo et al. [70] found that neoadjuvant therapy for esophageal cancer does not increase the overall risk of postoperative complications or 30-day mortality after esophagectomy. Anand et al. found that the immediate postoperative outcome was not adversely affected after minimally invasive esophagectomy with thoracic duct resection. Moreover, after neoadjuvant chemoradiotherapy, resection of the thoracic duct does not increase nodal yield [71].

Quality of Life

The quality of life was better preserved in MIE than open surgery. After 6 weeks after surgery, all the questionnaires, the EORTC C30, the specific OES 18 questionnaires, and the SF 36, except for the mental component, were better in the MIE in the OE group. A systemic review by Taioli et al. evaluated the quality of life and found improved global health, emotional function, and social function more commonly after minimally invasive surgery than open surgery [72]. However, role function and physical function and symptoms, including eating problems, dysphagia, choking, and difficult saliva swallowing, declined for both surgery types.

Cost-effectiveness

The meta-analysis by Xiong et al. [49] found that MIE was less costly and more effective than OE; MIE was estimated to cost $1641 less than OE with an incremental gain in quality-adjusted life years of 0.022.

Future Research

The ROMIO trial, which has begun in the UK, has three arms: the MIE, the hybrid one, and the open [73]. In Japan, JCOG 1409, a non-inferiority trial, is comparing thoracoscopic esophagectomy vs. open esophagectomy for clinical stage I–III esophageal cancer in terms of overall survival [74]. The ICAN trial is an open randomized controlled multicenter superiority trial, comparing cervical esophagogastric anastomosis (CEA) with intrathoracic esophagogastric anastomosis (IEA) after MIE. The study hypothesizes that an IEA after MIE has a lower incidence of anastomotic leakage requiring reoperation or reintervention than a CEA. Secondary outcomes are the functional outcomes, quality of life, and cost-effectiveness [75].

Conclusions

Minimally invasive esophagectomy is associated with reduced pain postoperative pain, better quality of life indices, lower postoperative morbidity, and mortality comparable with open esophagectomy without any compromise of R0 resection rates, nodal harvest, and long-term oncological outcomes. The available evidence also suggests that MIE is a cost-effective tool than OE. There is still a paucity of data; the ongoing adequately powered randomized control trials should answer the queries regarding the complications, survival benefits, and long-term oncological outcomes of minimally invasive esophagectomy.

Authors' Contribution Syed Nusrath and Subramyeshwar Rao perceived the idea for the article, performed the literature search, and did data analysis. Syed Nusrath wrote the manuscript. All the authors equally contributed to drafting the manuscript and critically revising the work.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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