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ORIGINAL ARTICLE

Long-term outcomes after robotic-assisted Ivor Lewis esophagectomy

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Abstract
Robotic assistance has gained acceptance in thoracic procedures, including esophagectomy. There is a paucity of data regarding long-term outcomes for robotic esophagectomy. We previously reported our initial series of robot-assisted Ivor Lewis (RAIL) esophagectomy. We report long-term outcomes to assess the efficacy of the procedure. We performed a retrospective review of 112 consecutive patients who underwent a RAIL. Patient demographics, diagnosis, pathology, operative characteristics, post-operative complications, and long-term outcomes were documented. Descriptive statistical analysis was performed for all the variables. Primary endpoints were mortality and disease-free survival. Overall survival (OS) and disease-free survival (DFS) were calculated using the Kaplan–Meier method. Of the 112 patients, 106 had a diagnosis of cancer, with adenocarcinoma the dominant histology (87.5%). Of these 106 patients, 81 (76.4%) received neo-adjuvant chemoradiation. The 30-, 60-, and 90-day mortality was 1 (0.9%), 3 (2.7%), and 4 (3.6%), respectively. There were 9 anastomotic leaks (8%) and 18 (16.1%) patients had a stricture requiring dilation. All-patient OS at 1, 3, and 5 years was 81.4%, 60.5%, and 51.0%, respectively. For cancer patients, the 1-, 3-, and 5-year OS was 81.3%, 59.2%, and 49.4%, respectively, and the DFS was 75.3%, 42.3%, and 44.0%. We have shown that long-term outcomes after RAIL esophagectomy are similar to other non-robotic esophagectomies. Given the potential advantages of robotic assistance, our results are crucial to demonstrate that RAIL does not result in inferior outcomes.

Keywords Survival · Esophageal cancer · Esophagectomy · Robotic · Ivor Lewis

Introduction

Esophageal cancer is the sixth leading cause of cancer-related deaths worldwide [1]. Surgery remains the mainstay of treatment. There are different types of surgery offered to patients, and each with its own set of advantages and disadvantages [2, 3]. One technique is the Ivor Lewis esophagectomy, the most commonly employed technique for esophagectomy.

Minimally invasive esophagectomy (MIE) has gained widespread acceptance. In fact, there was a threefold increase in the preference of MIE among surgeons between 2007 and 2014 [4]. Initially, MIE was performed using thoracoscopy, but the use of robotic assistance has been increasing [5]. Robotic assistance offers several advantages over thoracoscopic or open approaches, including better visualization and increased degrees of freedom [6]. Short-term studies have shown that robotic-assisted Ivor Lewis (RAIL) has similar outcomes to open and thoracoscopic esophagectomies [7]. A recent randomized controlled trial showed better post-operative outcomes with a robotic approach compared to an open approach, with comparable oncologic results [8]. Notably, the surgical approach in their series was the McKeon or three port technique. However, long-term outcomes of RAIL esophagectomy are lacking.

In an attempt to elucidate the long-term outcomes of RAIL, we examined our own series of patients. We examined both short- and long-term outcomes, with particular emphasis on long-term survival after RAIL esophagectomy.

Methods

After institutional approval, a retrospective chart review of patients who underwent a RAIL esophagectomy between 2011 and 2018 was performed. Demographic information

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including age, sex, body mass index (BMI), and co-morbidities was collected. Procedure information collected included operative time and estimated blood loss. Oncologic variables gathered included tumor type, tumor stage, administration of neoadjuvant therapy, margins after resection, number of nodes collected, and number of positive nodes.

The details of the surgical operation were described previously [9]. All surgeries were performed by a single surgeon (ZTH who has performed greater than 500 robotic procedures). In brief, we perform laparoscopic gastric mobilization and creation of the gastric conduit. Most patients underwent laparoscopic injection of 200 units of botulinum toxin into the pylorus. This is followed by robotic transthoracic esophagectomy with an intrathoracic anastomosis above the level of the azygous vein. Robotic surgery was performed using the DaVinci system Si and Xi (Intuitive Surgical, Inc. Sunnyvale, CA). Our anastomotic technique utilizes a linear stapler for the posterior wall while the front wall is manually sutured using a combination of 3-0 Vicryl and 3-0 Stratafix suture in two layers (Ethicon, Inc., Somerville NJ). In all cases, we utilize indocyanine green to assess conduit and esophageal perfusion using the robotic Firefly technology.

Patients are extubated in the operating room at the conclusion of the surgery. Feeds through a jejunostomy tube are initiated within 24–48 h after surgery. We perform esophagram on post-operative day 5 or 6. If this is without evidence of anastomotic leak, we remove the nasogastric tube and oral intake is initiated. Patients are discharged on average 7–10 days after surgery.

Post-operative complications were documented. These included arrhythmias, anastomotic leaks, myocardial infarction, pneumonia, ventilator-dependent respiratory failure, reintubation, acute renal failure, surgical-site infection, pleural effusion, chylothorax, deep vein thrombosis, and stroke. Longer-term complications, such as anastomotic stricture requiring dilation and delayed gastric emptying at 12 months, were documented as well. All-cause mortality, cancer-specific mortality, and disease-free survival were examined for all patients.

Descriptive analysis was performed for all variables. Continuous variables are described by mean and categorical variables described by proportions. Survival curves were calculated using the Kaplan–Meier Method. All statistical analyses were performed using R, version 3.5.1.

Results

Between 2011 and 2018, all patients who are candidates for an Ivor Lewis esophagectomy were approached with RAIL (112 total patients). Indication for surgery was cancer in 106 (94.6%) patients. Patient characteristics are summarized in Table 1. The mean age was 64.1 [SD 9.3] years. Eighty-nine (84.0%) patients were male. Most had a history of smoking (79.2%), and a majority had a history of hypertension (54.7%). Other co-morbidities included coronary artery disease (17.0%), diabetes (30.2%), GERD (50.9%), and COPD (17.0%). Most patients (76.4%) reported pre-operative dysphagia. Eighty-one (76.4%) received neoadjuvant chemoradiotherapy, and 18 (16.9%) had either a pre-operative gastrostomy or jejunostomy. Tumor characteristics are summarized in Table 2.

Table 1 Patient demographics

Patient characteristic	Number of patients	%
Age (Mean [SD])	64.1 [9.3]	
Male	89	84.0
BMI (Mean [SD])	27.4 [5.6]	
Neoadjuvant therapy	81	76.4
Smoking history	84	79.2
Pre-operative albumin (Mean [SD])	3.68 [0.46]	
Hypertension	58	54.7
Coronary artery disease	18	17.0
Diabetes	32	30.2
Gastroesophageal reflux disease	54	50.9
COPD	18	17.0
Pre-operative J feeding tube	15	14.2
Pre-operative G feeding tube	3	2.7
Pre-operative dysphagia	81	76.4

Table 2 Tumor type

Histologic type	Number of patients	%
Adenocarcinoma	98	87.5
Squamous cell carcinoma	3	2.68
High grade dysplasia	2	1.79
Other	9	8.04

The mean operative time was 357 min (range 256–582). As expected, operative times decreased over time, with a mean time of 346 min over the last 30 cases, compared to a mean of 364 min for the cases prior. The average blood loss was 64.6 ml. The mean number of nodes harvested was 19 (range 2–48). The median number of positive nodes was 0 (range 0–16). All patients had an R0 resection. The clinical and pathologic staging of the cancer patients is summarized in Table 3. Nineteen (19.8%) patients had pathologic complete response (pCR) and one patient (1.0%) had M1 disease.

Table 4 describes postoperative complications (with Clavien–Dindo grade). The most common complication was arrhythmia (28.3%). Pneumonia occurred in 11 (10.4%) patients, 14 (13.2%) patients required reintubation, and 14 (13.2%) had a pleural effusion. Nine (8.5%)

Table 3 Staging of cancer patients

Pathology	Number of patients	%
Clinical staging		
T1 N0	8	8.4
T2 N0	5	5.3
T3 N0	23	24.2
T1 N1	1	1.1
T2 N1	6	6.3
T3 N1	38	40.0
T2 N2	2	2.1
T3 N2	3	3.2
T2 Nx	2	2.1
T3 Nx	4	4.2
T4 Nx	1	1.1
M1	2	2.1
Pathologic staging		
pCR	19	19.8
T0 N1	1	1.0
T0 N2	1	1.0
T1 N0	24	25.0
T2 N0	12	12.5
T3 N0	13	13.5
T1 N1	6	6.3
T2 N1	2	2.1
T3 N1	6	6.3
T3 N2	6	6.3
T4 N2	1	1.0
T2 N3	1	1.0
T3 N3	3	3.1
T3 N0 M1	1	1.0

Table 4 Postoperative complications

Postoperative complication	Number of patients	%	Clavien-Dindo grade
Arrythmia	30	28.3	2
Anastomotic leak	9	8.5	3
Stricture	17	16.0	
Myocardial infarction	0	0.0	
Pneumonia	11	10.4	2
Vent dependent respiratory failure	10	9.4	4a
Reintubation	14	13.2	
Acute renal failure	5	4.7	4a
Surgical site infection	4	3.8	1
Pleural effusion	14	13.2	1
Chylothorax	2	1.9	1
Deep vein thrombosis	3	2.8	2
Stroke	0	0.0	
Delayed gastric emptying—6 months[a]	7	6.6	
Delayed gastric emptying—12 months[a]	3	2.8	
30-day mortality	1	0.9	5

[a]Rate among surviving patients

patients experienced an anastomotic leak, one of whom required re-operation. The remaining 8 patients were managed by endoscopically placed covered esophageal stents and all recovered uneventfully, with stent removal approximately 3 weeks after initial placement. Seventeen (16.0%) patients experienced an esophageal stricture that required dilation on long-term follow-up. Seven patients (6.6%) had delayed gastric emptying at 6 months (based on clinical and/or radiographic evidence), and 3 patients (2.8%) had delayed gastric emptying at 12 months.

The 30-, 60-, and 90-day mortality was 1 (0.9%), 3 (2.8%), and 4 (3.8%), respectively. Overall survival of all patients at 1, 3, and 5 years was 81.4%, 60.5%, and 51.0%, respectively. Figure 1 shows the overall and disease-free survival of the 106 cancer patients. For these patients, the 1-, 3-, and 5-year overall survival was 81.3%, 59.2%, and 49.4%, respectively, and the disease-free survival was 75.3%, 42.3%, and 44.0%.

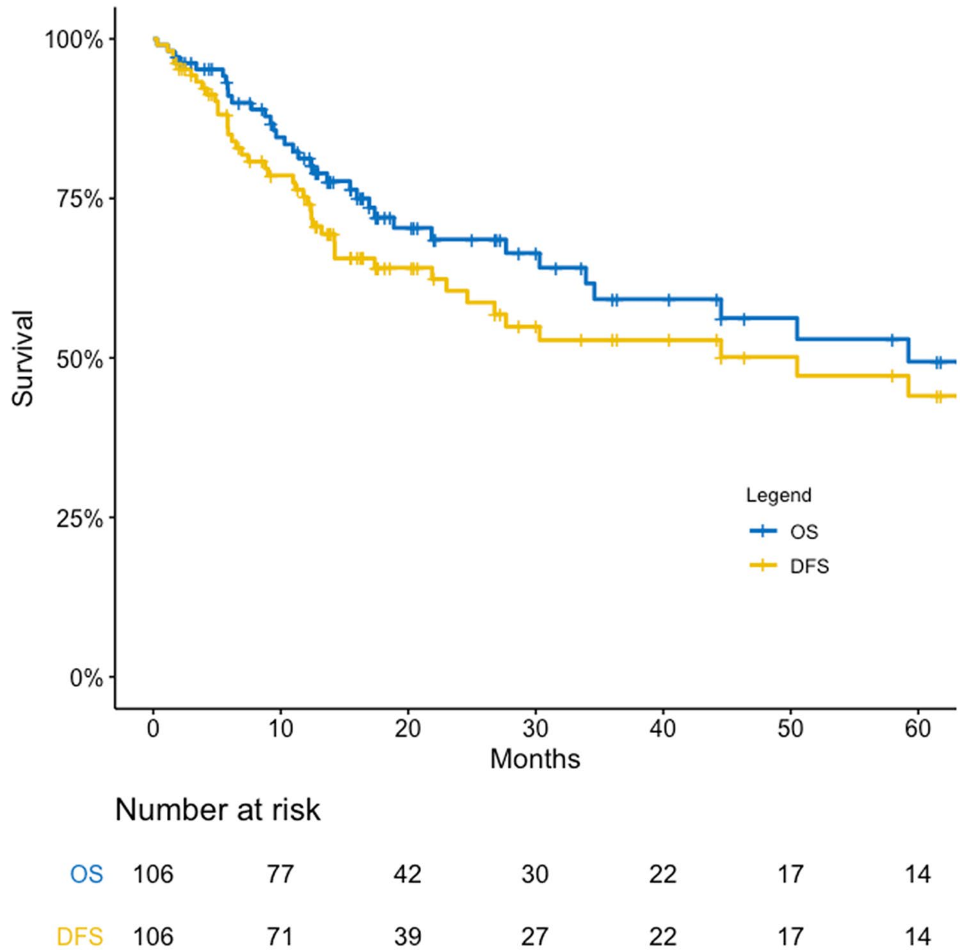
Discussion

The use of robotic assistance in a wide variety of surgical procedures has steadily increased and been widely accepted. While there have been multiple reports of short-term efficacy and safety, there is a paucity of data regarding long-term outcomes of robotic-assisted surgery. This is particularly true in RAIL esophagectomy. We sought to assess the long-term outcomes of RAIL esophagectomy performed at our institution to determine whether robotic assistance is equivalent to other techniques, particularly with respect to oncologic outcomes. To our knowledge, this is the largest such series reported, with 112 consecutive cases performed in a single institution. Of these, 106 were performed for a diagnosis of cancer. Not surprisingly, the majority of these patients had adenocarcinoma. Also, consistent with current practice, the majority of our cancer patients presented with locally advanced disease and received neo-adjuvant chemoradiation therapy.

Oncologic outcomes are an important measure of oncologic surgery, and RAIL is no exception. We collected a mean of 19 lymph nodes throughout our series (range of 2–48), consistent with other reports in the literature [10–14]. All patients in our series had an R0 resection. At minimum, this indicates that robotic assistance did not result in any compromise of surgical margin. No patient in this series incurred a local recurrence of their cancer.

Operative time and estimated blood loss are often used as a metric when comparing surgical approaches. Weksler

Fig. 1 Overall and disease-free survival of cancer patients. *OS* overall survival, *DFS* disease-free survival



OS: Overall Survival; DFS: Disease-Free Survival

et al. found no significant difference in the average operative time between MIE and a robotic-assisted esophagectomy [7]. Shridhar et al. studied 89 patients that underwent a RAIL esophagectomy and compared differences between patients that received neoadjuvant radiation and those that did not and found similar operative time and blood loss between the two groups [15]. In our series, the average operative time was 357 min and the average estimated blood loss was 64.6 ml. Our lower operative time may be secondary to utilizing the robot only for the intrathoracic portion of the surgery. We believe that the operative time would increase significantly if we were to utilize the robot for both portions, as the docking and undocking multiple times requires additional time. This is further supported by the findings of Puntambekar et al., who also utilize the robot for the intrathoracic portion, and use a laparoscopic approach for the intraabdominal portion of the surgery [16]. Kernstine et al. reported eight cases utilizing the robot for the entire procedure with a mean operative time of 11.1 h [17].

Another important measure of long-term outcome in esophagectomy is the development of anastomotic stricture. Strictures can be detrimental as they can lead to a decrease in the quality of life [18]. In our series, 16% of patients developed a stricture that required at least one dilation. This is considerably lower than the 23–42% of stricture rates reported in literature after an open esophagectomy [19, 20]. The rates of anastomotic strictures vary substantially after a robotic-assisted esophagectomy and can be between 10 and 68% [13, 21]. We believe our anastomotic technique described previously results in a lower stricture rate compared to the more common end to end anastomosis (EEA). However, we fully acknowledge that we do not have comparative data for this claim.

Delayed gastric emptying is a functional outcome of particular interest as it can increase the risk of aspiration and morbidity as well as decrease quality of life [22]. In our study, we found rates of 6.6% and 2.8% for delayed gastric emptying at 6 and 12 months, respectively. After an open esophagectomy, the rate of delayed gastric emptying can be as high as 40% [23]. Glatz et al. performed a matched case analysis comparing minimally invasive esophagectomies to open procedures [24]. In the immediate post-operative setting, they found an overall rate of 17% for delayed gastric emptying. Interestingly, they found an increased incidence of delayed gastric emptying in the minimally invasive group (23% vs 10%, $p = 0.042$) [24]. Zhang et al. found a delayed gastric emptying rate of 18.2%, and about 15% [25]. Our results indicate that a RAIL esophagectomy is comparable to open or MIE in rates of delayed gastric emptying. It is important to note, however, that direct comparisons are difficult due to wide practice variations with regard to drainage procedures. Our practice has moved away from pyloroplasty as we did not note a decrease in gastric emptying issues in our patients (data not shown).

Recent studies have shown perioperative mortality after an esophagectomy can be lower than 2% [26]. Fuchs et al. demonstrated that high hospital volume for the procedure led to lower mortality [26]. Luketich et al. examined 30-day mortality in a review of over 1000 patients after MIE and found a rate of 1.68% [27]. Seesing et al. performed a propensity matched analysis comparing mortality between open and minimally invasive esophagectomies, and found no difference in the rates of 30-day mortality (3.0% vs 4.7%, $p = 0.209$) [28]. These results indicate that perioperative mortality after an MIE is comparable to open esophagectomies. Espinoza-Mercado et al. compared open, minimally invasive, and robotic approaches and found no significant difference in 30-day mortality [29]. He et al. showed a 0% 90-day mortality after a robotic-assisted esophagectomy while a matched analysis showed no difference in mortality when compared to a thoracoscopic approach [30]. In our study, the 30-day mortality rate was 0.9% and a 90-day mortality of 3.8%, figures consistent with other reports.

Arguably, the most important outcome of any procedure performed for a diagnosis of cancer is long-term survival, both overall as well as disease-free survival. Incorporation of surgery into the treatment of localized esophageal cancer leads to improved survival [31]. This benefit is further enhanced with the addition of neoadjuvant therapy. The CROSS trial found a significant increase in the rates of R0 resection with the addition of neoadjuvant therapy (92% vs 69%, $p < 0.001$) [32]. A long-term analysis of the CROSS trial found a significant increase in overall survival at 5 years (33% vs 47%) with the addition of neoadjuvant therapy [33]. We have shown a 5-year overall survival of 49.4% and a 5-year disease-free survival of 44.0%. These findings are similar to those of others [10]. In addition, our survival rates are comparable to thoracoscopic MIE data. Woodard et al. reported a 5-year overall survival rate of 53.9% after a hybrid minimally invasive Ivor Lewis esophagectomy [34]. Lubbers et al. found a 5-year overall survival and disease-free survival rates of 51% and 55%, respectively, after a totally minimally invasive esophagectomy after neoadjuvant chemoradiotherapy [35]. Tapias et al. compared open and minimally invasive Ivor Lewis esophagectomy after neoadjuvant therapy and found no significant difference in survival between the two approaches [36].

Our study has several limitations. It is a retrospective study from a single institution. There was no selection process for the procedure and all patients brought to surgery were approached in the same manner. However, we made the decision to present consecutive patients, as no patients in the series were converted to any other procedure. Furthermore, it is difficult to perform any sub-group analyses given the size of our study. Similar to other case series, we do not have a control group. We also did not examine financial data to determine whether robotic assistance results in additional cost. While cost is an important consideration, it was not the aim of our study. Most, if not all, of the limitations of our study can be overcome in future studies by performing large multi-institution randomized controlled trials. However, we are fully aware of the difficulties in conducting such a trial. Finally, we do not have a direct comparison to our own thoracoscopic or open approaches as the number of patients undergoing these approaches is very small in our experience.

Conclusion

In conclusion, we continue to demonstrate the feasibility and safety of a RAIL esophagectomy through examination of long-term outcomes, including oncologic outcomes. Though we do not offer a direct comparison with more conventional approaches, we do believe that the RAIL esophagectomy is a valid alternative. However, large multi-center randomized controlled trials are warranted to measure the differences, if any, between approaches to an esophagectomy.

Declarations

Conflicts of interest Author P. Kandagatla, author A. Ghandour, author A. Amro, and author A. Popoff declare that they have no conflict of interest.

Disclosures Dr. Zane Hammoud is a proctor for Intuitive Surgical, Inc. and a consultant for Ethicon, Inc.

Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was waived by our Institutional Review Board due to the retrospective nature of the work (no patients were contacted for this study).

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