Open or Minimally Invasive Resection for Oesophageal Cancer?

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Abstract

Oesophagectomy is one of the most challenging surgical operations. Potential for morbidity and mortality is high. Minimally invasive techniques have been introduced in an attempt to reduce postoperative complications and recovery times. Debate continues over whether these techniques decrease morbidity and whether the quality of the oncological resection is compromised. Globally, minimally invasive oesophagectomy (MIO) has been shown to be feasible and safe, with outcomes similar to open oesophagectomy. There are no controlled trials comparing the outcomes of MIO with open techniques, just a few comparative studies and many single institution series from which assessments of the current role of MIO have been made. The reported improvements of MIO include reduced blood loss, shortened time in high dependency care and decreased length of hospital stay. In comparative studies there is no clear reduction in respiratory complications, although larger series suggest that MIO may have a benefit. Although MIO approaches report less lymph node retrieval compared with open extended lymphadenectomy, MIO cancer outcomes are comparable. MIO will be a major component of the future oesophageal surgeons' armamentarium, but should continue to be carefully assessed.

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Randomized trials comparing MIO versus open resection in oesophageal cancer are urgently needed: two phase III trials are recruiting, the TIME and the MIRO trials.

Contents

1 Introduction

With increasing experience and skills at performing laparoscopic and thoracoscopic surgery in the past decade, minimally invasive oesophagectomy (MIO) is increasingly being used for surgical management of oesophageal cancer (OC). By the early 1990s, some surgeons had developed and used protocols for thoracoscopic oesophagectomy, initially restricting its use to T1 and T2 OC without neoadjuvant chemoradiation (Akaishi et al. 1996; Gossot et al. 1993). However, with time, indications for thoracoscopic oesophagectomy were expanded to include more advanced OC, irrespective of neoadjuvant treatment. The techniques in MIO vary from totally minimally invasive to hybrid procedures where one stage of the operation is performed either by thoracoscopy or laparoscopy. Unlike other minimally invasive procedures, to date, MIO has not been broadly adopted. It is still considered one of the most complex gastrointestinal surgical operations, and many questions remain unanswered as to the real advantages of applying minimally invasive techniques, particularly in a disease which is frequently locally advanced and highly lethal. Mortality, morbidity, oncological radicality, reproducibility and the cost of the procedure are some of the topics under debate. Recent reviews (Butler et al. 2011; Gemmill and McCulloch 2007; Nagpal et al. 2010; Sgourakis et al. 2010) focusing on the role of MIO have emphasized that the benefits of this approach are controversial due to the complexity involved. Several comparative studies have been conducted between MIO and open oesophagectomy, but uncertainty about the advantages of one technique over the other persists due to the absence of published randomized trials. The question about the best approach for oesophagectomy in OC is consequently still to be resolved.

Table 1.1 Minimally invasive oesophagectomy techniques for oesophageal cancer

With thoracoscopic approach	
Thoracoscopic/laparoscopic oesophagectomy with cervical anastomosis	MIO
Thoracoscopic/laparoscopic oesophagectomy with thoracic anastomosis	MIO
Thoracoscopic oesophageal mobilization with laparotomy and cervical anatomosis (hybrid)	Hybrid
Without thoracoscopic approach	
Laparoscopic gastric mobilization with thoracotomy and intrathoracic anastomosis (hybrid)	Hybrid
Total laparoscopic transhiatal oesophagectomy	MIO

2 MIO Techniques

As there has never been a consensus regarding the superiority of any of the various open oesophagectomy techniques, it is not surprising that there is no agreement on the best MIO approach either. Minimally invasive adapatations of every conceivable approach to oesophageal resection have been reported (Table 1.1).

Transhiatal MIO utilizes laparoscopic abdominal dissection and preparation of the gastric conduit followed by a cervical anastomosis created via a traditional open approach in the neck. Mediastinal dissection of perioesophageal lymph nodes, including those in the subcarinal station, can be assessed through the hiatus using the lighting and magnifications afforded by the laparoscopic technology (Swanstrom and Hansen 1997). The oesophageal specimen can be removed through the neck incision. Some surgeons prefer to combine the laparoscopic tranhiatal approach with a mini-laparotomy to facilitate gastric tube creation as well as to remove the specimen. Finally, the oesophagus can be also removed from the mediastinum via an inversion technique with or without division of the vagus nerve (Jobe et al. 2004; Peyre et al. 2007).

Many surgeons prefer a thoracoscopic approach, typically performed through the right chest, with patients positioned in lateral decubitus or prone positions (Dapri et al. 2008; Fabian et al. 2008). Thoracoscopy can be used as a part of a 3 stage MIO, where the procedure begins in the chest and ends with laparoscopy and a cervical anastomosis, or as part of the Ivor- Lewis oesophagectomy where the oesophagogastric anastomosis resides in the chest. In this procedure the specimen is removed through a mini-thoracotomy, and the anastomosis is created at the apex of the chest (Bonavina et al. 2003).

Combinations of open and minimally invasive techniques are also an option, such as laparoscopy with thoracotomy (Briez et al. 2012) or thoracoscopy with laparotomy. These so-called hybrid techniques are applied for a variety of reasons, such as an oncological requirement, prior surgery in either cavity, surgeon experience, comfort level or surgeon preference.

Although the goal of MIO is to perform an equivalent operation to the open procedure without omitting any critical steps, some aspects considered as routine for open oesophagectomy have fallen out of favour, such as the performance of a pyloroplasty, jejunostomy placement or removal of the azygos vein.

3 Results

The primary goal of MIO is to decrease surgical morbidity associated with the open approach. No direct comparative trials have been published so far between open and MIO, but results for the TIME (Biere et al. 2011) and the MIRO (Briez et al. 2011) trials are urgently awaited. At present, the data shows that mortality rates and the incidence of complications reported are essentially equivalent for both techniques (Table 1.2). It is likely that any benefit of MIO is overshadowed by the persistent rate of complications independent of the approach, such as anastomotic leaks. It seems conceivable that, in the absence of such complications, patients with a minimal access approach enjoy quicker recovery, quicker return to normal activities and decreased long-term pain when compared to patients with similarly uncomplicated open procedures. This, however, has yet to be proven. MIO has been demonstrated as feasible for OC resection, but the oncologic value and safety is often questioned especially following neoadjuvant chemoradiation. The debate over the optimal surgical approach for OC, regardless of the technique, continues despite accumulating evidence in support of radical lymphadenectomy (Mariette and Piessen 2012). Few MIO series report lymph node retrieval and long-term results (Table 1.3).

Results coming from 3 meta-analyses published, based on non randomized comparative data, are contradictory. Two did not find significant differences between the MIO and the open approaches (Biere et al. 2009; Sgourakis et al. 2010). The third suggests that patients undergoing MIO had better operative and postoperative outcomes with no compromise in oncological outcomes (as assessed by lymph node retrieval) (Nagpal et al. 2010). Patients receiving MIO had significantly lower blood loss, and shorter postoperative ICU and hospital stay. There was a 50 % decrease in total morbidity in MIO group. Subgroup analysis of comorbidities demonstrated significantly lower incidence of respiratory complications after MIO; however, other postoperative outcomes such as anastomotic leak, anastomotic stricture, gastric conduit ischemia, chyle leak, vocal cord palsy, and 30 days mortality were comparable between the two techniques. The benefit of even one endoscopic stage in hybrid MIO (thoracoscopy with laparotomy or laparoscopy with thoracotomy) was noted, and blood loss and respiratory complications were still found to be lower, consistent with open versus totally MIO analysis, thus highlighting the advantage of applying a minimally invasive approach to oesophagectomy. It should be noted that few studies were matched for tumour stage, location or perioperative treatments. This fact could have introduced some bias, as for example patients with more advanced stages may have undergone open surgery.

Table 1.2 Postoperative surgical outcomes after minimally invasive oesophagectomy compared to open resections: literature study results

Authors Year	n	Approaches	Mortality (%)	Overall morbidity (%)	Pneumonia (%)	Cardiac arrhythmia (%)	Anastomotic leak (%)	Graft ischemia (%)	Chylothorax (%)
Law et al. (1997)	22	MIO (TSO)	0	18 (81.8 %)	3 (13.6 %)	3 (13.6 %)	0	NR	NS
	63	Open	0	63 (100 %)	11 (17.5 %)	14 (22.2 %)	2 (3.2 %)	NR	NS
Nguyen et al. (2000)	18	MIO (TLSO)	0	7 (38.9 %)	2 (11.1 %)	NR	2	0	0
	36	Open	0	19 (52.8 %)	6 (16.7 %)	NR	(11.1 %) 4 (11.1 %)	1 (2.8 %)	1 (2.8 %)
Nguyen et al. (2000)	77	MIO (VATS)	0	31 (40.3 %)	12 (15.6 %)	1 (1.3 %)	1 (1.3 %)	0	3 (3.9 %)
	72	Open	0	32 (44.4 %)	14 (19.4 %)	3 (4.2 %)	2 (2.8 %)	0	0
Kunisaki et al. (2004)	15	MIO (VATS + HALS)	0	NR	0	NR	2 (13.3 %)	NR	NS
	30	Open	0	NR	1 (3.3 %)	NR	1 (3.3 %)	NR	NS
Van den Broek et al. (2004)	25	MIO (THO)	0	14 (70 %)	2 (8 %)	NR	2 (8 %)	0	2 (8 %)
	20	Open	0	18 (72 %)	2 (10 %)	NR	3 (15 %)	0	0
Bresadola et al. (2006)	14	MIO (THO and TLSO)	0	8 (57.1 %)	1 (7.1 %)	NR	1 (7.1 %)	NR	0
	14	Open	0	6 (42.9 %)	2 (14.2 %)	NR	2 (14.2 %)	NR	0
Bernabe et al. (2005)	17	MIO (THO)	0	NR	NR	NR	NR	NR	NS
	14	Open	0	NR	NR	NR	NR	NR	NS
Shiraishi et al. (2006)	116	MIO (TLSO)	3 (2.6 %)	NR	25 (21.6 %)	3 (2.6 %)	13 (11.2 %)	NR	NS
	37	Open	3 (8.1 %)	NR	12 (32.4 %)	4 (10.8 %)	9 (24.3 %)	NR	NS

(continued)

Table 1.2 (continued)

Authors Year	n	Approaches	Mortality (%)	Overall morbidity (%)	Pneumonia (%)	Cardiac arrhythmia (%)	Anastomotic leak (%)	Graft ischemia (%)	Chylothorax (%)
Braghetto et al. (2006)	47	MIO (VATS/ LSO)	3 (6.3 %)	18 (38.2 %)	7 (14.8 %)	NR	3 (6.4 %)	0	1 (2.1 %)
	119	Open	13 (10.9 %)	72 (60.5 %)	22 (18.5 %)	NR	17 (14.3 %)	1 (0.8 %)	0
Smithers et al. (2007)	332	MIO (TLSO)	7 (2.1 %)	207 (62.3 %)	87 (26.2 %)	55 (16.6 %)	18 (5.4 %)	5 (1.5 %)	17 (5.1 %)
	114	Open	3 (2.6 %)	76 (66.7 %)	35 (27.8 %)	21 (18.4 %)	10 (8.7 %)	2 (1.7 %)	7 (6.1 %)
Fabian et al. (2008)	22	MIO (TLSE)	1 (4.5 %)	15 (68.2 %)	1 (4.5 %)	4 (18.2 %)	3 (13.6 %)	1 (4.5 %)	0
	43	Open	4 (9.8 %)	31 (72.1 %)	10 (23.3 %)	8 (18.6 %)	3 (7.0 %)	0	2 (4.7 %)
Zingg et al. (2009)	56	MIO (TLSO)	2 (3.6 %)	19 (34.5 %)	17 (30.9 %)	NR	NR	NR	NR
	98	Open	6 (6.1 %)	20 (23.5 %)	33 (38.8 %)	NR	NR	NR	NR
Perry et al. (2009)	21	MIO (LIO)	0 1	13	1 (5 %)2	4	4 (19 %)	NR	NR
	21	Open	(5 %)	(62 %) 17 (81 %)	(10 %)	(19 %) 7 (33 %)	6 (29 %)	NR	NR
Parameswaran et al. (2009)	50	MIO (TLSO)	1 (2 %)	24 (48 %)	4 (8 %)	NR	4 (8 %)	5 (16 %)	3 (6 %)
	30	Open	1 (3 %)	15 (50 %)	2 (7 %)	NR	1 (3 %)	2 (10 %)	1 (3 %)
Pham et al. (2010)	44	MIO (TLSO)	3 (6.8 %)	NR	11 (25 %)	NR	4 (9 %)	1 (2 %)	NS
	46	Open	2 (4.3 %)	NR	7 (15 %)	NR	5 (11 %)	1 (2 %)	NS
Schoppmann et al. (2010)	31	MIO (TLSO)	0	11 (35.5 %)	2 (6.2 %)	NR	1 (3.2 %)	0	2 (6.4 %)
	31	Open	0	23 (74.2 %)	11 (35.5 %)	NR	8 (25.8 %)	1 (3.2 %)	1 (3.2 %)

(continued)

Table 1.2 (continued)

AuthorsYear	n	Approaches	Mortality (%)	Overall morbidity (%)	Pneumonia (%)	Cardiac arrhythmia (%)	Anastomotic leak (%)	Graft ischemia (%)	Chylothorax (%)
Singh et al. (2011)	33	MIO (TLSO)	Values NR	Values NR	NR	NR	NR	NR	NR
	31	Open	$p = 0.34$	$P = 0.06$	NR	NR	NR	NR	NR
Mamidanna et al. (2012)	1155	MIO (TLSO,,HMIO)	46 (4.0 %)	NR	230 (19.9 %)	102 (8.8 %)	NR	NR	NR
	6347	Open	274 (4.3 %)	NR	1181 (18.6 %)	611 (9.6 %)	NR	NR	NR
Ben-David et al. (2012)	100	MIO (TLSO)	1 (1 %)	NR	9 (9 %)	8 (8 %)	5 (5 %)	NR	3 (3 %)
	32	Open	2 (5 %)	NR	5 (15.6 %)	R	4 (12.5 %)	NR	NR
Briez et al. (2012)		MIO (HMIO)	2.1	35.7	15.7	NR	5.7	0.7	NR
		Open	12.9	59.3	42.9	NR	4.3	0.0	NR

MIO minimally invasive oesophagectomy; *VATS* video-assisted thoracoscopic oesophagectomy; *HMIO* hybrid MIO; *HALS* hand-assited laparoscopic oesophagectomy; *TSO* thoracoscopic –assisted oesophagectomy; *TLSO* thoracolaparoscopic oesophagectomy; *LIO* laparoscopic inversion oesophagectomy; *LSO* laparoscopic oesophagectomy; *NR* not reported

Table 1.3 Oncological outcomes after minimally invasive oesophagectomy compared to open resections: literature study results

Authors (Year)	n	Approaches	Number of lymph nodes retrieved (median)	R0 resection rate (%)	3-year survival (%)
Law et al. (1997)	22	MIO (TSO)	7 (2–13)	10	62 (2 years)
	63	Open	13 (5–34)	NR	63 (2years)
Nguyen et al. (2000)	18	MIO (TLSO)	10.8 ± 8.4	18	NR
	36	Open	6.6 ± 5.8	NR	NR
Osugi et al. 2003 (2003)	77	MIO (VATS)	33.9 ± 12	NR	70
	72	Open	32.8 ± 14	NR	60
Kunisaki et al. 2004 (2004)	15	MIO (VATS + HALS)	24.5 ± 10	NR	NR
	30	Open	26.6 ± 10.4	NR	NR
Van den Broek et al. (2004)	25	MIO (THO)	7 ± 4.9	21 (84 %)	60 % (f/u 17 ± 11 months)
	20	Open	6.5 ± 4.9	18 (90 %)	50 % (f/u 54 ± 16 months)
Bresadola et al. (2006)	14	MIO (THO/ TLSO)	22.2 ± 12	NR	NR
	14	Open	18.6 ± 13.4	NR	NR
Bernabe et al. (2005)	17	MIO (THO)	9.8 (NR)	NR	NR
	14	Open	8.7 (NR)	NR	NR
Shiraishi et al. (2006)	116	MIO (TLSO)	31.8 (NR)	NR	NR
	37	Open	30.1 (NR)	NR	NR
Braghetto et al. (2006)	47	MIO (VATS/ LSO)	NS	NR	45.5 %
	119	Open	NS	NR	32.5 %
Smithers et al. (2007)	332	MIO (TLSO)	17 (9–33)	263	42 %
	114	Open	16 (1–44)	90	30 %
Fabian et al. (2008)	22	MIO (TLSE)	15 ± 6	22 (100 %)	NR
	43	Open	8 ± 7	NR	NR
Zingg et al. (2009)	56	MIO (TLSO)	5.7 ± 0.4	NR	Median survival—35 months MIO and 29 months open
	98	Open	6.7 ± 0.5	NR	
Perry et al. (2009)	21	MIO (LIO)	10 (4–12)	NR	NR
	21	Open	3 (0–7)	NR	NR

(continued)

Table 1.3 (continued)

Authors (Year)	n	Approaches	Number of lymph nodes retrieved (median)	R0 resection rate (%)	3-year survival (%)
Parameswaran et al. (2009)	50	MIO (TLSO)	23 (7–49)	NR	74 % (2 year survival)
	30	Open	10 (2–23)	NR	58 % (2 year survival)
Pham et al. (2010)	44	MIO (TLSO)	13 (9–15)	NR	NR
	46	Open	8 (3–14)	NR	NR
Schoppman et al. (2010)	31	MIO (TLSO)	17.9 ± 7.7	29 (93.5 %)	64 %
	31	Open	20.5 ± 12.6	30 (96.8 %)	46 %
Singh et al. (2011)	33	MIO (TLSO)	14 (6–16)	30	55 % (2 year survival)
	31	Open	8 (3–14)	30	32 % (2 year survival)
Mamidanna et al. (2012)	1155	MIO (TLSO/ HMIO)	NR	NR	NR
	6347	Open	NR	NR	NR
Ben-David et al. (2012)	100 32	MIO (to be detailed)	NR	1 (1 %)	NR
		Open	NR	0	NR
Briez et al. (2012)		MIO (HMIO)	22 (8–53)	85.7	58 (2 year survival)
		Open	22 (6–56)	87.9	57 (2 year survival)

MIO minimally invasive oesophagectomy; *VATS* video-assisted thoracoscopic oesophagectomy; *HMIO* hybrid MIO; *HALS* hand-assited laparoscopic oesophagectomy; *TSO* thoracoscopic – assisted oesophagectomy; *TLSO* thoracolaparoscopic oesophagectomy; *LIO* laparoscopic inversion oesophagectomy; *LSO* laparoscopic oesophagectomy; *f/u* follow up; *NR* not reported

From a technical and biological standpoint, the outcomes of open and MIO for cancer should be equivalent. Improved lighting and visibility, along with the magnification afforded by minimally invasive equipment, may prove superior for meticulous dissection and lymph node harvest. However, until large series report long-term survival by stage or results of large randomized trials are published, the true oncologic value of MIO will remain controversial.

4 MIO Learning Curve

As with all procedures, there are inherent technical challenges faced when applying a new technique. Oesophagectomy is a complex, technically challenging procedure fraught with potential pitfalls in nearly every step of the procedure. Many of the largest open series discuss the fact that morbidity and mortality decrease with experience (Hofstetter et al. 2002; Mariette et al. 2004). Technical complication rates have also been shown to negatively impact cancer specific survival (Rizk et al. 2004). As such, oesophagectomy has been designated an operation best left in the hands of experts at high-volume centers. Little is written regarding the learning for MIO directly, but is has been suggested that it may be more than 50 procedures (Bizekis et al. 2006; Decker et al. 2009). It appears that a hybrid procedures, especially using a laparoscopic and open thoracic approach may have a short learning curve and less oncological drawbacks (Briez et al. 2012).

Ideally, MIO should be performed by surgeons experienced in both advanced laparoscopy/thoracoscopy and surgical oncology for OC. Dedication to mastery of several MIO techniques allows the operation to be tailored to the individual patient using the less invasive approach matched to the pathology at hand. Certainly the extent of the oncologic resection should be based on the tumour, not the technique, and should be the primary goal.

5 Comments and Future

Open oesophagectomy remains the most effective treatment for OC with 5 year survival rates of approximatively 50 % being reported in several selected series, especially in combination with neoadjuvant chemoradiation (Bonavina et al. 2003; Mariette et al. 2008; Portale et al. 2006). This is a dramatic improvement, with survival rates several decades ago being consistently less than 20 %. Whereas endoscopic mucosal resection or radiofrequency ablation can cure OC that have not penetrated the muscularis mucosa, open oesophagectomy remains the gold standard treatment for the disease (Mariette et al. 2011). Improvements in chemoradiation protocols have been reported as effective adjuncts in surgical therapy (Mariette et al. 2007). Today, a multimodality approach to OC is common and preferred for tumours extending beyond the submucosa or with suspected lymph node involvement.

MIO has been gaining popularity since the first reports nearly two decades ago. Similar to open surgery, several techniques exist including totally laparoscopic transhiatal or transthoracic resection, as well as combinations, or hybrid techniques. Much as with open OC surgery, no consensus has been reached regarding the superiority of any particular MIO adaptation. Currently, no significant decrease in operative morbidity has been proven for MIO compared to its open counterpart, even if some large comparative studies suggest a significantly better postoperative course without compromising oncological outcomes (Briez et al. 2012; Osugi et al. 2003; Shiraishi et al. 2006; Smithers et al. 2007). Most reports of MIO for locally advanced cancers include a thoracic dissection. The role for MIO in these cancer stages is controversial but will become more defined as the procedures mature beyond their steep learning curves and long-term outcome data becomes available.

Randomized trials may be difficult due to the wide variety of techniques available, the heterogeneity in surgeons' preferences, the relative low number of procedures performed, the complexity of such surgery, and the variety of postoperative complications after oesophagectomy. Even if no direct comparative trials have been published so far between open and MIO, results of two well-known randomized trials, the TIME (Biere et al. 2011) and the MIRO (Briez et al. 2011) trials are keenly awaited. The TIME trial aims at comparing over 120 patients, the approach to the MIO includes a right thoracosocpy and laparoscopy. The primary endpoint are postoperative respiratory complications within the first two postoperative weeks, whereas secondary endpoints are duration of the operation, blood loss, conversion to the open procedure, morbidity, quality of life and hospital stay. The MIRO trial will test, in over 200 patients randomised, the impact of laparoscopic gastric conduit creation with open thoracotomy (hybrid procedure) on major 30-day postoperative morbidity, especially on pulmonary complications. Secondary objectives are to assess the overall 30-day morbidity, 30-day mortality, disease-free and overall survival, quality of life and medico-economic analysis. It is hypothetized that hybrid MIO would decrease major postoperative morbidity without compromising oncological outcomes through an easily reproducible surgical procedure.

To conclude, there are many variations of MIO with combinations of thoracoscopic and laparoscopic approaches with and without open approaches to the abdomen or chest. Data coming from non randomized studies suggest MIO is safe, with similar outcomes to open resection for both the surgical and the oncological outcomes. Data from meta-analyses suggest that MIO may show improvement with less blood loss, less time in ICU, less pulmonary complications and shorter hospital stay. However, the effect of MIO on quality of life and return to normal activity has not been assessed. Medico-economic analyses are required. Results from two randomized trials (Biere et al. 2011; Briez et al. 2011) will soon be published to offer higher level evidence of this highly debated procedure.

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