Short-term outcomes after minimally invasive oesophagectomy

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ABSTRACT

INTRODUCTION: Minimally invasive oesophagectomy (MIO) has gained increasing popularity. This study reports the results of the first patients operated using this technique at our department.

METHODS: All procedures were prospectively registered in a database. Patients were followed until death, two years after surgery or 1 January 2019.

RESULTS: A total of 150 procedures were performed (from 23 November 2015 to 27 February 2018). The median procedure time decreased from 350 minutes for the initial 75 patients to 320 minutes for the final 75 patients ($p < 0.05$). Blood loss decreased from 200 ml to 100 ml ($p < 0.05$), respectively. The conversion rate for the abdominal procedure was 7% for the initial 75 patients and 8% for the final 75 patients (not significant (NS)). For the thoracic procedure, the corresponding figures were 11% and 7% (NS), respectively. Anastomotic leakage was seen in 17% (initial patients) and 11% (final patients) (NS); however, less than 20% of the leakages needed surgical treatment. The median length of post-operative stay was nine days for both groups. For all 150 patients, pulmonary complications were observed in 18% and cardiac complications in 11%. The 30-day mortality rate was 2% and the one-year survival rate was 86% (124 registered patients).

CONCLUSIONS: MIO was introduced at our department with acceptable morbidity and mortality rates and the short-term oncological result was not compromised.

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TRIAL REGISTRATION: The study was approved as a quality project by the Region of Southern Denmark (18/37355).

Minimally invasive oesophagectomy (MIO) for oesophageal or gastro-oesophageal junction (GEJ) cancer has gained popularity across the world. A recently published meta-analysis demonstrated that MIO is associated with a reduced risk of cardio-pulmonary complications, less intraoperative blood loss and a shorter length of stay (LOS) [1]. However, the anastomotic leakage rate has been reported to be the same in MIO as in open technique. MIO is associated with a higher quality of life than open procedure one year after surgery [2], but data on the potential benefits of MIO on the long-term survival rate are limited. Only one randomised controlled study has been published. In this European multi-centre study with a total of 115 patients, the three-year survival rate was equal in both groups (50.5% (MIO) versus 40.4% (open group), $p = 0.21$) [3]. No difference in overall survival at a medium follow-up of 40 months was also a finding in a single-centre study comparing robot-assisted thoraco-/laparoscopy with open technique [4]. However, the primary end point of this study was overall surgery-related post-operative complications and not long-term survival.

MIO is technically challenging, and a considerable learning curve is often needed. Thus, an increased number of anastomotic leakages must be expected, especially in the introduction phase [5]. The aim of this study was to describe our initial experience with implementing MIO in our centre with a focus on the procedure, its complications and short-term survival.

METHODS

Implementation of minimally invasive oesophagectomy

The Department of Surgery, Odense University Hospital, is the tertiary referral centre for upper gastrointestinal malignancies in the Region of Southern Denmark with a catchment area of approximately 1.5 million inhabitants. Prior to implementing MIO, patients with resectable lower oesophageal or GEJ tumours underwent open Ivor-Lewis oesophagectomy at our institution. Based on the promising results with a lower risk of cardio-pulmonary complications and a shorter hospital stay following MIO, we decided to try to change our surgical strategy from open to minimally invasive technique. In September 2015, our team visited Helsinki University Central Hospital, Helsinki, Finland, which had extensive experience with MIO. After evaluating their setup, we decided to introduce MIO in our unit with some minor modifications. The first MIO was performed at our hospital on 23 November 2015. Initially, obese patients, patients with large tumours, patients who had pre-operative radiotherapy and patients with an oesophageal stent inserted prior to surgery were excluded from MIO in an attempt to minimise any technical difficulties. In addition, our capacity for MIO was only one case per week at the time. Thus, all remaining patients were offered conventional open

ORIGINAL ARTICLE

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oesophagectomy. In January 2016, the chief surgeon from Helsinki visited our department and assisted us with two cases. After his evaluation of our set-up and our technical skills, he recommended us to consider MIO as our standard operation technique regardless of co-morbidity, tumour size and preoperative treatment. Following a visit to Karolinska University Hospital, Stockholm, in January 2017, we changed the thoracic approach from left lateral to prone position because this enables double lung ventilation and provides better ergonomics for the surgeon. The dissection and anastomotic techniques remained unchanged.

The procedure

Essential steps of the abdominal part: The patient was placed in anti-Trendelenburg and in the so-called French position. Pneumoperitoneum (12 mmHg) was established with a 12 mm trocar to the left of the umbilicus, and an extra 15 mm trocar was placed in the right side. If laparoscopy in combination with laparoscopic ultrasound revealed no metastatic disease, the procedure was continued by placing an additional two 5 mm trocars and a 5 mm liver retractor in the upper abdominal part (**Figure 1**). The lesser omentum (station 3) was resected and the oesophagus mobilised in the hiatal region. The cardiac lymph nodes (stations 1 and 2) were dissected as were lymph nodes along the left side of the hepatoduodenal ligament (station 12) and the splenic and the hepatic arteries (station 11 and 8). The left gastric vessels were ligated and divided. The greater curvature of the stomach was then mobilised, preserving the left gastric epiploic vessels by starting from the corpus region towards the left crus of the diaphragm. A part of the greater omentum was left attached to the stomach for later use as an omental wrap covering the anastomosis. A stapler (Endo GIA with Tri-Staple (Covidien), 45 mm black magazine) was used approximately 5 cm proximally to the pylorus for the first step of the making of the gastric conduit. This was then subsequently completed with additional staplers (Endo GIA, 45 mm purple magazine). The diameter of the gastric conduit was intended to be approximately 4 cm. A bridge of stomach wall (around 4 cm) between the specimen and gastric conduit was kept for the later pull up into the thorax. Finally, a feeding catheter jejunostomy was placed 30 cm anally from the ligament of Treitz. The jejunum was fixed to the peritoneum with a purse-string suture around the catheter and with two additional fixating sutures.

Essential steps for the thoracic part: The patient was placed in prone position. Four trocars were inserted; one of these was used via a wound protector/retractor (Figure 1). The oesophagus was mobilised from the hiatus to above the tumour with the azygos vein being divided, if needed with a stapler (Endo GIA, vascular magazine). The level for transection of the oesophagus was based on the findings at the pre-operative gastroscopy and the per-operative thoracoscopy. The lymphatic tissue of the meso- and peri-oesophagus and of the bronchial arch was then removed. The oesophagus was divided using a stapler (Endo GIA, 60 mm black magazine), the stomach remnant was pulled into the thorax and divided, and the specimen was removed via the wound protector/retractor. A circular stapler anvil (EEA OrVil (Covidien)) was placed trans-orally in the oesophagus and pulled through the oesophagus by a central cut in the stapler line. The gastric conduit was opened in the distal end and a 25 mm circular stapler (EEA (Covidien)) was introduced. The anastomosis was performed near the greater curvature region of the straightened gastric conduit. The gastric conduit was closed using an Endo GIA (60 mm, purple magazine). The anastomosis was then secured with the omental wrap. Two drains (one close to the anastomosis and one in the pleural cavity) were placed. A naso-gastric tube was finally placed, guided by gastroscopy.

The procedures were performed by a team of consisting of two gastrointestinal and two thoracic surgeons. All had experience in laparoscopic and thoracoscopic procedures as well as in open oesophageal cancer surgery before MIO was introduced.

Quality control data

All patients who were operated with MIO due to oesophageal or GEJ cancer were registered prospectively in a database. The preoperative stage for all included patients was assessed by endoscopy, endoscopic ultrasonography and CT (plus positron emission tomography/CT for patients with squamous cell carcinoma). Prior to surgery, all patients were evaluated at the

FIGURE 1

Position of ports at minimally invasive oesophagectomy. A. Abdominal part. B + C. Thoracic part.

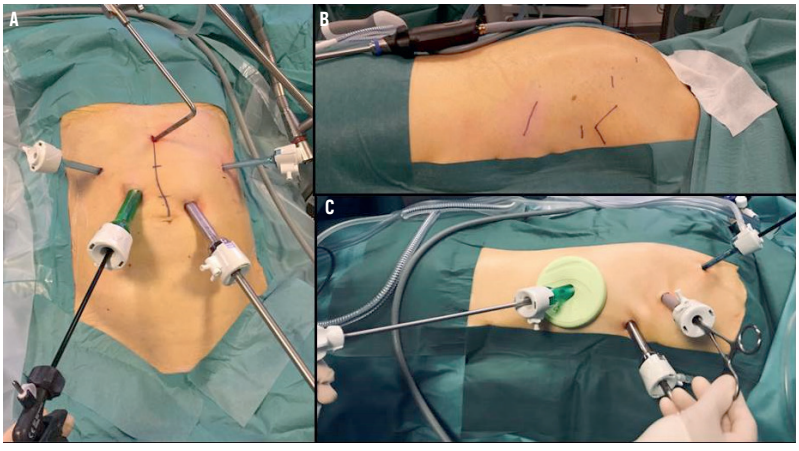

TABLE 1

Comparison of demographic data between the first 75 patients (Group 1) and the last 75 patients (Group 2) operated with minimally invasive oesophagectomy.

	Group 1	Group 2
Gender, n (%)		
Male	62 (83)	66 (88)
Female	13 (17)	9 (12)
Age, median (range), yrs	66 (33-81)	69 (46-84)
ASA score, n (%)		
1	5 (7)	7 (9)
2	48 (64)	50 (67)
3	22 (29)	18 (24)
Preoperative histology, n (%)		
Squamous cell carcinoma	9 (12)	5 (7)
Adenocarcinoma	66 (88)	69 (93)

ASA = American Society of Anesthesiologists.

TABLE 2

Comparison of quality of surgery between first 75 patients (group 1) and last 75 patients (group 2) operated with minimally invasive oesophagectomy.

	Group 1	Group 2	p-value
Total procedure time, median (range), min.	350 (240-480)	320 (200-540)	〈 0.05
Blood loss, median (range), ml	200 (20-1,350)	100 (20-2,600)	〈 0.05
Conversion to open surgery, n (%)			
Abdominal part	5 (7)	6 (8)	NS
Thoracic part	8 (11)	5 (7)	NS
Risk of anastomotic leakage, n (%)[a]			NS
Type I	8	3	
Type II	3	3	
Type III	2	2	
Total	13 (17)	8 (11)	
Lymph nodes removed, median (range), n	27 (12-54)	26 (11-63)	NS
Length of post-operative stay, median (range), days	9 (8-56)	9 (5-88)	NS

NS = not significant.

a) According to the Esophagectomy Complications Consensus Group: Leak with no change in therapy or treated medically (Type I), leak treated by radiology or endoscopy (Type II), leak treated by surgery (Type III).

TABLE 3

Comparison of complication severity[a] between first 75 patients (Group 1) and last 75 patients (Group 2) operated with minimally invasive oesophagectomy. The values are n (%).

	Group 1	Group 2	p-value
None	41 (55)	42 (56)	NS
Grade I	0	1 (1)	NS
Grade II	15 (20)	19 (25)	NS
Grade III	11 (15)	10 (14)	NS
Grade IV	6 (8)	3 (4)	NS
Grade V	2 (2)	0	NS

NS = not significant.

a) Compared according to [8]. Grade I: Any deviation from the normal post-operative course. Grade II: Requiring pharmacological treatment. Grade III: Requiring surgical, endoscopic or radiological intervention. Grade IV: Life-threatening complication requiring intensive care unit management. Grade V: Death.

multidisciplinary team conference and had preoperative chemo or chemo-radiation therapy according to the guidelines of the Danish Oesophageal-Cardiac-Stomach Cancer Group [6]. Age, gender, preoperative histology, American Society of Anesthesiologists (ASA) score, total procedure time, blood loss, conversion rate (abdominal and thoracic part registered separately), anastomotic leakage (according to the Esophagectomy Complications Consensus Group [7]), complications (according to Clavien Dindo [8]), number of removed lymph nodes, LOS, 30- and 90-day mortality rates, and the one-year survival rate were registered. In order establish if any changes had occurred in the post-operative outcome over time, the patients were divided into two equal groups: The initial 75 MIO-operated patients (Group 1) and the final 75 MIO-operated patients (Group 2). Two-sample Wilcoxon rank-sum test was used for comparison. Patients were followed until death, two years after surgery or until 3 January 2019 (a minimum observation time of nine months), whichever came first.

Trial registration: The study was approved by the Region of Southern Denmark (18/37355).

RESULTS

The 150 included patients underwent surgery from 23 November 2015 to 27 February 2018. During the study period, an additional 33 patients were admitted for treatment of oesophageal or GEJ cancer where MIO was not attempted for miscellaneous reasons (e.g., metastatic disease, planned open procedure or cervical anastomosis). Demographic data for the first 75 patients (Group 1) and the final 75 patients (Group 2) are shown in **Table 1**. There was no difference in gender, age, ASA score or preoperative histology between the two groups. Quality measures regarding surgery are listed in **Table 2**. A significant decrease in median total procedure time and median blood loss was observed between Group 1 and Group 2; the risk of conversion to open surgery, anastomotic leakage rate, median number of removed lymph and median LOS was the same. Complication severity is listed in **Table 3**. There was no difference between the two groups. In total, pulmonary complications were observed in 18% and cardiac complications in 11% of the patients. The in-hospital mortality rate for all 150 patients was 2% and the 30-day mortality rate was also 2%. The 90-day mortality rate

was 6% and the one-year survival rate was 86% (124 registered patients).

DISCUSSION

This study showed that the total median procedure time and median blood loss decreased significantly from the first 75 patients to the final 75 patients. This is probably explained by a learning curve and the shift from left lateral to prone position for the thoracic part of the procedure. The risk of anastomotic leakage decreased over time, but this trend was insignificant; in the final 75 patients, it remained above the 10% standard established by the Danish Oesophageal-Cardiac-Stomach Cancer Group [9]. In a study on the learning curve of MIO with 646 patients, it was observed that 119 cases were needed to reach a plateau in the leakage rate, and this decreased from 18.8% during the learning phase to 4.5% in the steady state phase [5]. Thus, hopefully, we have not yet reached our steady state level for leakages after the initial 150 patients presented in this study.

Another explanation for the relatively high percentage of leakages could be that already after three months of MIO experience, we chose this as our standard technique. Thus, all operations were initiated with minimally invasive technique irrespectively of whether the patient had a potentially high risk of leakage, e.g., due to smoking, oesophageal stent, preoperative radiotherapy or obesity. In a study from a Swedish institution, the transformation from 100% open to 100% minimally invasive technique took three years [10]. A selection of the "best" patients for MIO in the learning phase would be understandable in order to get familiar with the technique and keep a low risk of complications. However, the Swedish study showed a high complication rate with MIO in the learning phase during the time when open surgery was also performed as standard technique. The leakage rate was more than double the one observed in our study, and it took five years to reach a 10% leakage rate which, as mentioned, is considered the standard in Denmark. Other centres also have experienced high leakage rates during the introduction of MIO and a decline in these rates over time [11-13]. Thus, the time needed to reach an acceptable leakage rate is multifactorial, but one factor seems to be the annual number of performed operations.

Despite a relatively high number of leakages, the 30- and 90-day mortality rates and the one-year survival rate were in line with Danish standards [9]. It is known that anastomotic leakage after oesophagectomy decreases the five-year survival rate [14]. However, this observation is based on data from the open era. It is not known whether this also holds true for anastomotic leakage following MIO. Time will tell if the relatively high leakage rate in the introduction phase will have an impact on our five-year survival rate. As mentioned previously, only one randomised study has compared MIO with open technique on long-term survival, and this study showed no significant benefit of MIO [3]. Naturally, more studies are needed on this topic, but if MIO does, in fact, not increase the long-term survival rates of oesophageal and GEJ cancer compared with open technique, one benefit of MIO might be shorter hospitalisation. In our study, no difference was observed in LOS between the initial and the final patients, but this is because most patients followed our postoperative recovery principles from the open era. Recently, our department has introduced an enhanced recovery programme after MIO inspired by the principles of enhanced recovery [15]. We have no data on this yet, but our assumption is that patients are now discharged earlier and that they have had a faster recovery when seen in the out-patient clinic. Thus, even if MIO does offer better long-term oncological results, a shorter hospitalisation period and improved quality of life are arguments for introducing the technique despite the fact that MIO is cumbersome and might temporarily give a poorer outcome for patients during the introduction phase.

CONCLUSIONS

MIO was introduced at our department with acceptable morbidity and mortality rates without compromising the short-term oncological result.

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