

# Minimally Invasive Esophagectomy for Cancer: Single Center Experience after 44 Consecutive Cases

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## SUMMARY

**Introduction** At the Department of Minimally Invasive Upper Digestive Surgery of the Hospital for Digestive Surgery in Belgrade, hybrid minimally invasive esophagectomy (hMIE) has been a standard of care for patients with resectable esophageal cancer since 2009. As a next and final step in the change management, from January 2015 we utilized total minimally invasive esophagectomy (tMIE) as a standard of care.

**Objective** The aim of the study was to report initial experiences in hMIE (laparoscopic approach) for cancer and analyze surgical technique, major morbidity and 30-day mortality.

**Methods** A retrospective cohort study included 44 patients who underwent elective hMIE for esophageal cancer at the Department for Minimally Invasive Upper Digestive Surgery, Hospital for Digestive Surgery, Clinical Center of Serbia in Belgrade from April 2009 to December 2014.

**Results** There were 16 (36%) middle thoracic esophagus tumors and 28 (64%) tumors of distal thoracic esophagus. Mean duration of the operation was 319 minutes (approximately five hours and 20 minutes). The average blood loss was 173.6 ml. A total of 12 (27%) of patients had postoperative complications and mean intensive care unit stay was 2.8 days. Mean hospital stay after surgery was 16 days. The average number of harvested lymph nodes during surgery was 31.9. The overall 30-day mortality rate within 30 days after surgery was 2%.

**Conclusion** As long as MIE is an oncological equivalent to open esophagectomy (OE), better relation between cost savings and potentially increased effectiveness will make MIE the preferred approach in high-volume esophageal centers that are experienced in minimally invasive procedures.

**Keywords:** esophageal cancer; surgery; minimally invasive esophagectomy; laparoscopy; outcome

## INTRODUCTION

Each year 462,000 people are diagnosed with esophageal cancer worldwide and 386,000 people die from it [1, 2]. Although the patients' satisfaction with surgery is lower comparing with other treatment options, probably due to its aggressiveness, surgical treatment remains the primary treatment for localized resectable esophageal cancer. Open transthoracic esophagectomy (OE) as a radical procedure has been the procedure of choice in the treatment of resectable esophageal cancer. It is an extensive and traumatic procedure with morbidity rate ranging between 30% and 50%. [3]. Transhiatal esophagectomy has been designed to decrease operative trauma in comparison to the transthoracic approach, but it is palliative in origin because it is not feasible to perform lymphadenectomy of the middle and upper mediastinum. Minimally invasive esophagectomy (MIE) results in a significant decrease of surgical trauma and could provide a proper visualization and exposure of the posterior mediastinum and adequate lymph node dissection [4-7]. In the majority of cases MIE is performed as a total MIE (tMIE) or hybrid MIE (hMIE) [8]. In change management from OE to tMIE, hMIE (laparoscopic or thoracoscopic procedure) is an intermediate but also a very large step. In

1992 Sir Alfred Cuschieri et al. [7] published a paper about thoracoscopic mobilization of the esophagus. The first large series (48 patients) using MIE with transhiatal approach was published by the Brazilian surgeon DePaula et al. [9]. To our knowledge, the largest personal series of MIE is the series of Luketich et al. [10] with more than 1,000 operated patients.

Hybrid MIE has been routinely performed by the team of the Department for Minimally Invasive Upper Digestive Surgery, Hospital for Digestive Surgery, Clinical Center of Serbia, since 2009 [11]. As a next and final step in the change management, from 2015 we utilized the total MIE as a standard of care.

## OBJECTIVE

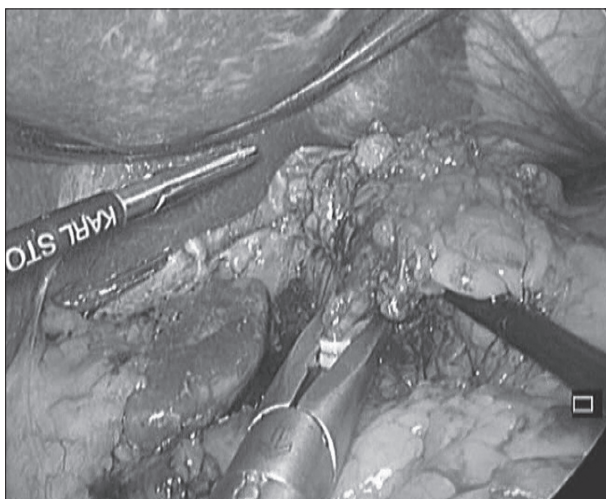
In this article, we report initial experience after 44 consecutive cases of hMIE (laparoscopic approach) for cancer and analyze surgical technique, major morbidity and 30-day mortality.

## METHODS

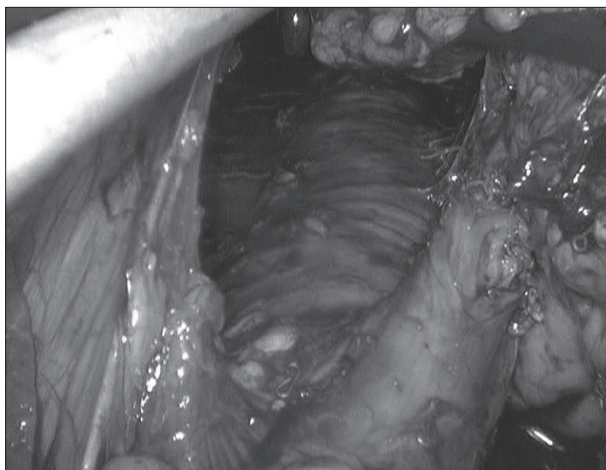
A retrospective cohort study included 44 patients who underwent elective hMIE for esophageal cancer at the Department for Minimally

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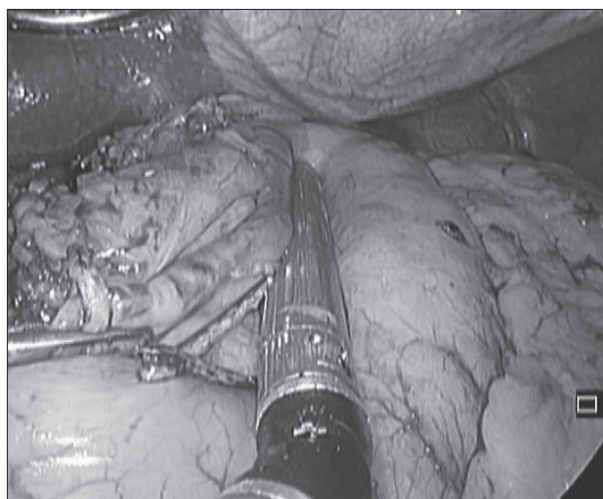
**Figure 1.** Isolation of the left gastric artery and lymph node dissection in the celiac region



**Figure 2.** Laparoscopic dissection of the lymph nodes in the lower mediastinum

Invasive Upper Digestive Surgery, Hospital for Digestive Surgery, Clinical Center of Serbia in Belgrade from April 2009 to December 2014. The standard preoperative work-up included symptoms evaluation, barium swallow radiography, upper flexible endoscopy with biopsy, computed tomography of thorax and abdomen and broncho-pulmonary evaluation (flexible bronchoscopy and pulmonary function tests).

All patients underwent antibiotic and deep veins thrombosis prophylaxis. The standard surgical technique for hMIE is described in detail in further text. Control barium test through a nasogastric tube (NG) was performed on the second postoperative day, followed by NG tube extraction in cases of normal pylorus transit. All patients received pulmonary physiotherapy and early mobilization. Control barium radiography was routinely performed on the seventh postoperative day followed by the clear liquid diet. Data regarding demographic characteristic, preoperative work-up evaluation, intraoperative data (duration of operation, intraoperative blood loss, etc.) and postoperative course details were all analyzed. In addition, postoperative complications were analyzed separately and graded according to the Dindo–Clavien classification [12].



**Figure 3.** Gastric tubulization with endoscopic staplers

After hospital discharge, the first check-up was performed a month after surgery and then periodically according to the European Society for Medical Oncology [13]. The standard postoperative annual check-up included symptoms evaluation, control barium radiography, computed tomography of the thorax and abdomen and upper flexible endoscopy.

## Surgical technique

### Laparoscopic part

Positions of the patient and trocars were adopted from Luketich et al. [4]. The laparoscopic part commenced with the exploration of the liver, peritoneal surfaces and integrity of the epiploic arcade. Afterwards, the transection of the gastrocolic ligament is performed, keeping in mind that the aim of that part is to preserve the integrity of the arcade as it will be the only blood vessel left to supply the gastric tube. The left gastroepiploic vessels are isolated, clipped and cut. After that, shot gastric vessels should be sealed and cut all the way from the left epiploic vessels to the angle of Hiss. Then, the transection of the gastrocolic ligament is continued backward to meet the pylorus. Pyloromyotomy or pyloroplasty was performed routinely in the majority of cases. However, it seems that this step is not necessary in all patients, especially after narrow gastric tube formation. Subsequently, left gastric vessels are isolated, clipped and transected. In case of squamous cell carcinoma, the left gastric vessels are ligated at the origin and lifted along with lymph nodes around the left gastric artery (Figure 1). In case of adenocarcinoma, dissection along the hepatic and splenic artery is routinely performed. Dissection of the lower mediastinum should be a part of the laparoscopic procedure. It is easier to do it laparoscopically than via thoracotomy or thoracoscopy (Figure 2). After sealing and cutting of the gastric arcade on the lesser curvature of the stomach we proceed with gastric tube formation. On average three to four articulating endoscopic linear staplers are used in creating the gastric tube (Figure 3).

## Open thoracic part

The patient is repositioned in the left lateral decubitus, and open thoracotomy is performed. In case of distal thoracic cancer, a typical two-field standard lymph node dissection is performed. When middle thoracic carcinoma is present, a two-field total lymph node dissection should be performed. After subtotal esophagectomy and gastric pull-up, mechanical esophago-gastric anastomosis is performed in the upper mediastinum and wrapped with the part of the omentum preserved along the greater curvature of the stomach. An NG tube is placed under the direct control and the gastric stump is closed with a linear stapler. The stomach is fixed in place with a couple of stitches to the surrounding pleura, and the thorax is closed after an insertion of a chest tube.

## RESULTS

The outcomes of 44 consecutive hMIEs (laparoscopic approach) for esophageal cancer from April 2009 to December 2014 were included. Male patients were more prevalent (84% male and 16% female patients); mean age was 61.4 years. The average Karnofski and ASA scores were 79.8 and 2.3, respectively. The average body mass index was 22.8 kg/m<sup>2</sup>. There were 16 (36%) middle thoracic esophagus tumors and 28 (64%) tumors of the distal thoracic esophagus. Analyzing tumor histology, there were 23 (52%) squamous cell carcinoma, 21 (48%) adenocarcinoma. Mean duration of operation was 319 minutes (approximately five hours and 20 minutes). In 42 patients (96%) pyloromyotomy or pyloroplasty was performed. All patients underwent stapled intrathoracic esophago-gastric anastomosis. Additional surgical procedures included atypical lung resections in two patients (5%). The average blood loss was 173.6 mL. Conversion rate was zero. Mean hospital stay was 16 days. The average number of harvested lymph nodes was 31.9. These data are summarized in Table 1.

The total of 12 patients (27%) had postoperative complications, while the mean intensive care unit (ICU) stay was 2.8 days. Postoperative complications mainly included major pulmonary complications, such as: atelectasis in one patient (2%), ARDS in one patient (2%) and pneumonia in six patients (14%). Other significant postoperative complications included anastomotic leakage, herniation of the transverse colon into the thorax, hemothorax needed operation, wound infection with dehiscence and bile leak in the case of severe adhesions after previous surgery in one patient each.

In addition, all postoperative complications were analyzed according to the Dindo–Clavien classification (Table 2). Overall, the 30-day mortality rate was 2%.

## DISCUSSION

In the literature, under the term of MIE many different procedures can be found (Table 3), and all of these procedures could be performed in the left lateral decubitus or

**Table 1.** Demographic characteristics, preoperative, intraoperative and postoperative course details

Feature	Value*	
Gender	Male	37 (84%)
	Female	7 (16%)
Mean age (years)	61.4 (30–81)	
Karnofski score	79.8 (60–90)	
ASA score	2.3 (1–3)	
BMI (kg/m <sup>2</sup> )	22.8 (15.2–33.2)	
Localization of the tumor	Middle thoracic	16 (36%)
	Distal thoracic and cardia	28 (64%)
Pathohistology	Squamous cell carcinoma	23 (52%)
	Adenocarcinoma	21 (48%)
Intraoperative details	Duration of operation (min)	319 (255–375)
	Pyloroplasty	42 (96%)
	Additional procedures /lung resection	2 (5%)
	Conversion	0
Postoperative course details	ICU stay (days)	2.8 (1–16)
	Transfusion (mL)	173.6 (0–1500)
	Hospital stay (days)	16.1 (5–45)
	30-day mortality	1 (2%)
	Harvested lymph nodes	31.9 (15–59)
p-Stage	0	1 (2%)
	I	8 (18%)
	Ila	6 (14%)
	IIb	0
	III	29 (66%)

\*The values are presented as the number of patients (with percentage), or as mean value (with range) of the feature.

ASA – classification and peri-operative risk according to the American Society of Anesthesiologists; BMI – body mass index; ICU – intensive care unit; p-Stage – pathologic stage according to UICC Classification (Union for International Cancer Control)

**Table 2.** Postoperative complications

Feature	Number	
Total number of postoperative complications	13	
Major pulmonary complications	Atelectasis	1 (2%)
	Pneumonia	6 (14%)
	Respiratory insufficiency	0
	ARDS	1 (2%)
Anastomotic leakage	1 (2%)	
Thoracic complications without anastomotic leakage*	2 (5%)	
Other**	2 (5%)	
Number of patients with complications	12 (27%)	
Dindo–Clavien classification	II	7 (16%)
	III	4 (9%)
	IV	0
	V	1 (2%)

\*Thoracic complications without anastomotic leakage were hiatal hernia and hemothorax needing operation.

\*\* Other complications were wound infection and dehiscence and bile leak in the case of severe adhesions after previous surgery.

ARDS – acute respiratory distress syndrome; Dindo–Clavien classification – classification of the postoperative course

**Table 3.** Variations of minimally invasive esophagectomy (MIE) [8]

Total MIE – thoracoscopic and laparoscopic esophagectomy
Hybrid MIE – either thoracoscopic or laparoscopic approach
Laparoscopic-assisted transhiatal esophagectomy
Video-assisted mediastinoscopic transhiatal esophagectomy
Robot-assisted MIE

prone position. In addition, the procedures could differ in respect to the extent of lymph node dissection and the position of anastomosis [8]. tMIE refers to a combined thoracoscopic and laparoscopic approach. hMIE is esophagectomy using either the thoracoscopic or laparoscopic approach. Although transhiatal esophagectomy can be performed using laparoscopy alone, the transcervical mediastinoscopic approach is added in some institutions to ensure mediastinal dissection. Robot-assisted MIE using the DaVinci system has only been introduced in a limited number of institutions [14, 15]. According to the systematic review of MIE cases published in the English language up to June 2012, tMIE is the most common procedure (58%), followed by hMIE (29%). hMIE with the thoracoscopic approach has been performed in 17% of patients and hMIE with laparoscopic approach in 12% [16].

With so many different procedures it is difficult to compare postoperative outcomes of MIE with more or less standard OE. A possible solution of the problem is to do a meta-analysis. To our knowledge, there are three meta-analyses comparing MIE with OE published by Biere et al. [17], Sgourakis et al. [18] and Nagpal et al. [19]. In addition, there are at least two well-designed randomized controlled trials (RCTs) comparing outcomes after MIE and OE. One is the TIME trial conducted in the Netherlands by Biere et al. [20]. The trial was designed to compare tMIE and OE with 115 patients enrolled and with a primary endpoint of 14-day pulmonary infection. The second trial is the MIRO trial conducted in France by Briez et al. [21]. The trial was designed to compare OE and hMIE (laparoscopic approach) in 280 patients enrolled and with a primary endpoint of major postoperative pulmonary complications. When duration of MIE is discussed, most agree that the duration of MIE is longer than that of OE. However, Nguyen et al. [22] have reported that MIE does not last significantly longer than OE if performed by experienced surgeons. In our series, the average duration of the operation was 319 minutes, which is comparable to results published by other authors [5, 23]. Gaining experience with MIE may reduce the operating time as it significantly depends on surgical experience. The average intraoperative blood loss in our series was 173.6 mL. Biere et al. [20] in their series reported average blood loss of 200 mL which is similar to our series. Also, Biere et al. [20] concluded that there was statistically significant difference in the intraoperative blood loss between MIE and OE, favoring MIE. Similar results were obtained in all three meta-analyses [17, 18, 19].

The overall morbidity in our series was 27%, which is similar to results published by Luketich et al. [4] and significantly lower compared to OE series [21]. While Biere et al. [17] and Sgourakis et al. [18] found no significant difference in the pulmonary complications, in the meta-analysis performed by Nagpal et al. [19] a significant improvement of pulmonary morbidity rates was observed in four studies, whereas no significant difference in the frequency of pulmonary complication was reported in 10 studies. The rates of major pulmonary complications in

our series do not differ significantly from those published by Briez et al. [21] with an exception of respiratory insufficiency rates, probably due to the larger number of patients in their series. In the RCTs, both Biere et al. [20] and Briez et al. [21] found significantly lower prevalence of pulmonary complications and concluded that lower prevalence of pulmonary complications provided evidence for the short-term benefits of MIE compared with OE for patients with resectable esophageal cancer.

Length of hospital stay and stay in the ICU were reduced in tMIE and thoracoscopic-assisted groups when compared to open surgery group, suggesting early recovery in the case of MIE [17]. Our experience has demonstrated that MIE could be performed safely, with overall 30-days mortality of 2%, mean ICU stay of 2.8 days and average hospital stay of 16 days, which correlates with results published by Yamamoto et al. [24] and Smithers et al. [25]. Oncologic result of different procedures could be compared in respect to the number of harvested lymph nodes and survival rates. In our series, average number of harvested lymph nodes was 31.9, which is similar to results published by Taguchi et al. [26] and even higher compared to the best OE series. Other authors have found that oncologic outcomes of MIE are not inferior to those of OE [17, 25, 27, 28]. On the contrary, the number of retrieved lymph nodes is higher in MIE than in OE. Magnifying the view of the surgical field might contribute to the increase in retrieved nodes.

In terms of overall survival, many authors believe that there is no difference in three-year and five-year survival rates between minimally invasive and open surgical approach [25].

In the past decade MIE has been increasingly performed to treat resectable esophageal cancer. In the UK, there has been a steady increase in the uptake of MIE, with 24.7% of esophageal cancer resections in 2009 being performed using a hybrid or completely minimally invasive approach [29]. This fact expresses attitude in favor of the acceptance and distribution of minimally invasive procedures for esophageal carcinoma treatment worldwide. Finally, Lee et al. [30] reported that MIE is cost-effective compared to OE in the management of patients with resectable esophageal cancer.

## CONCLUSION

As long as MIE is oncologically equivalent to OE, cost savings and potential increased effectiveness associated with MIE should make it the preferred approach in high-volume esophageal centers that are experienced in minimally invasive procedures. Indeed, at the Department of Minimally Invasive Upper Digestive Surgery in the Hospital for Digestive Surgery in Belgrade, hMIE (laparoscopic approach) was the standard of care for patients with resectable esophageal cancer in the period between 2009 and 2014. As a next and final step in the change management, from January 2015 we utilized tMIE as the standard of care.

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## Минимално инвазивна езофагектомија у лечењу карцинома једњака: искуство након 44 операције

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**Увод** У Одељењу за минимално инвазивну хирургију горњег дигестивног тракта Клинике за дигестивну хирургију Клиничког центра Србије у Београду хибридна минимално инвазивна езофагектомија (МИЕ) је стандардна терапијска опција од 2009. године. Као завршни корак у управљању променом, од јануара 2015. године уведен је концепт тоталне МИЕ.

**Циљ рада** Циљ рада је био да се анализира искуство у лечењу карцинома једњака хибридном МИЕ из перспективе анализе хируршке технике, те морбидитета и морталитета болесника.

**Методе рада** Ретроспективном кохортном студијом обухваћена су 44 болесника која су подвргнута елективној хибридној МИЕ ради лечења карцинома једњака између априла 2009. и децембра 2014. године у Одељењу за минимално инвазивну хирургију горњег дигестивног тракта Клинике за дигестивну хирургију Клиничког центра Србије у Београду.

**Резултати** Од укупног броја болесника, код 16 (36%) је утврђен тумор средњег торакалног једњака, а код 28 (64%) тумор дисталног торакалног једњака. Операција је у просеку трајала 319 минута (око пет сати и двадесет минута). Просечан губитак крви је био 173,6 милилитара. Постоперационе компликације су забележене код 12 болесника (27%), а просечно време проведено у јединици интензивне неге било је 2,8 дана. После операције болесници су у болници остајали у просеку 16 дана. Током операције уклоњено је просечно 31,9 лимфних жлезда. Укупна стопа смртност током 30 дана од операције била је 2%.

**Закључак** Док год је МИЕ онколошки еквивалентна отвореној езофагектомији, бољи однос трошкова и ефеката МИЕ чини је процедуром избора у центрима са искуством у лечењу болести једњака и центрима који имају значајно искуство у минимално инвазивној хирургији.

**Кључне речи:** карцином једњака; хирургија; минимално инвазивна езофагектомија; лапароскопија; исход

Примљен • Received: 04/05/2015

Прихваћен • Accepted: 29/05/2015