Original Article

Morbidity and mortality in elderly patients after minimally invasive esophagectomy

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Background: Elderly patients undergoing gastrointestinal surgery run a higher risk of postoperative complications and mortality. Currently available literature on elderly patients undergoing an esophagectomy is inconclusive and dates from the time before minimally invasive techniques were widely implemented.

Methods: Length of hospital stay, 90-day morbidity and mortality were analyzed from patients undergoing minimally invasive esophagectomy (MIE) between 2014 and 2017 in a single center. Data from patients aged 76 years or older were compared to patients aged 71 to 75 years old.

Results: A total of 187 patients underwent MIE. Nineteen patients aged 76 years or older (group 1) were compared to 41 patients aged 71 to 75 years (group 2). Median age was 77 years (76–83 years) in group 1 and 72 years (71–75 years) in group 2 (P<0.05). There were no significant differences in sex, Charlson comorbidity score, number of patients undergoing neoadjuvant chemoradiation, histological tumor type, tumor stage, number of lymph nodes harvested and type of anastomosis. There were no significant differences in length of hospital stay, 90-day morbidity and mortality. The anastomotic leakage rate was 21.1% in group 1 and 14.6% in group 2 (P=0.535). Mortality rate was 10.5% and 4.9% respectively (P=0.415).

Conclusions: No significant difference was seen in morbidity and mortality after MIE comparing the eldest to younger old patients. Therefore, patient selection should not be based on calendar age alone.

Keywords: Complications; elderly; esophagectomy

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Introduction

Esophageal cancer is one of the leading causes of cancer-related deaths worldwide (1). The majority of esophageal cancer patients are older than 65 years. Forty-four percent of all newly diagnosed esophageal cancer patients are 70 years or older (Dutch cancer registration) and more than 33% of all patients are older than 75 years (2).

There is an increase in esophageal cancer in elderly patients due to the increase in average life expectancy and an overall increase in the incidence of esophageal cancer in the Western world (3). Therefore, an increase in elderly patients presenting for esophagectomy is observed (3).

Patients with esophageal cancer have more comorbidity than other cancer patients, especially cardiovascular comorbidity, making this group of patients more at risk for perioperative complications (4,5). Furthermore, esophagectomy in elderly patients is more challenging as elderly patients undergoing gastrointestinal surgery are at higher risk for postoperative complications and mortality (6).

Elderly patients are often excluded from clinical trials (7,8). Current literature is inconclusive regarding surgery related morbidity and mortality after esophagectomy in elderly patients and dates from the time before minimally invasive surgical techniques and enhanced recovery programs after

surgery (ERAS) were implemented (9,10).

Therefore, the results of previous trials are difficult to interpret and may not be applicable to current surgical practice in elderly patients. In this study we compared morbidity and mortality between elderly and younger-elderly patients undergoing minimally invasive esophagectomy (MIE) for esophageal cancer in a single high-volume center in The Netherlands.

Methods

Patients

Patients older than 70 years old with esophageal cancer undergoing MIE in the Elisabeth-Tweesteden Hospital in Tilburg, The Netherlands between September 2014 and December 2017 were identified from the consecutive cohort of patients. All cases were assessed in multi-disciplinary tumor board meeting for decision making about on neo-adjuvant treatment, using chemo- and radiation therapy according to the "CROSS-regimen" (11). Standard preoperative staging included esophagogastroscopy, endoscopic ultrasound, CT scans of the thorax and abdomen and PET scan when appropriate. All patients were assessed during an outpatient visit by one of the surgeons and a dedicated physician assistant as well as the medical oncologist and radiotherapist. MIE was planned 8–10 weeks after completion of chemoradiation therapy. Patients were assessed a second time by a surgeon in an outpatient visit 3 weeks before the planned operation to assure their condition before surgery.

Surgical procedure

All patients underwent a MIE with restoration of the gastrointestinal tract via either cervical esophagogastric anastomosis (McKeown) or intrathoracic esophagogastric anastomosis (Ivor-Lewis), depending on the type of location of the tumor (e.g., mid- or proximal esophageal cancers or distal esophageal cancers). A standardized two-field lymphadenectomy was performed, followed by creation of the gastric conduit and reconstruction with the gastric conduit placed in the posterior mediastinum. An omental wrap was performed after completion of the anastomosis. A Jackson-Pratt drain was left in proximity of the anastomosis and a pleural drain was inserted in the right pleural cavity. Furthermore, during the laparoscopic surgical phase a feeding jejunostomy was placed to ensure adequate enteral nutrition.

Postoperative care

All patients were monitored in surgical ICU for at least 1 day postoperatively. All patients received analgesia via an epidural for at least 3 days. During the first 5 days after surgery hemocytometry, serum C-reactive protein, and serum creatinine levels analysis were performed every day. Level of amylase was determined in the Jackson-Pratt drain daily as an early indicator for anastomotic leakage (12). The pleural drain was removed on postoperative day 1 or 2, depending on production (<400 cc/24 hours). The nasogastric tube was removed on postoperative day 3 if there were no signs of complications and patients were allowed to drink water after removal of the nasogastric tube. If there were no signs of anastomotic leakage patients were allowed to resume their normal oral diet on the fourth postoperative day. Jackson-Pratt drain was removed if amylases level in the drain was not elevated and if there were no signs of anastomotic leakage or chyle leakage after resuming oral diet. If there were signs of anastomotic leakage, a CT scan of the thorax and abdomen with oral contrast was performed. Anastomotic leakage was treated depending on the leakage severity: nil by mouth and nasogastric tube, antibiotics, by (radiological) drainage, stent (intrathoracic anastomosis) or bedside opening (cervical anastomosis).

Data collection

Data were retrospectively collected via patient medical files regarding age at time of surgery, gender, neo-adjuvant treatment, tumor regression score, clinical and pathological TNM score (13), tumor type, tumor location, and number of positive lymph nodes. Charlson comorbidity index was calculated with age factor (14). Operative details on type of anastomosis (e.g., McKeown or Ivor-Lewis) and conversion rates were collected. Tumor regression grade after neoadjuvant chemoradiation was scored using the Mandard classification (15). Postoperative outcomes included length of hospital stay (days), any 90-day morbidity and mortality. Textbook outcome was calculated for every patient (16). Anastomotic leakage was defined as Esophagectomy Complications Consensus Group (ECCG) type 2 or higher (17). Data on follow-up were also retrospectively collected via patient medical files. Medical ethics committee approval was not required for this study as all patient and hospital information was anonymous. All procedures

performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Statistical analysis

Data from patients aged 76 years or older and patients aged 71 to 75 years old were compared. Dichotomous or categorical variables are presented as absolute numbers and percentages. Continuous variables are shown as their absolute numbers. A Chi square test was performed to assess differences categorical data. A Mann-Whitney U test was performed for continuous variables. Statistical analyses were performed using SPSS version 25 (Armonk, NY: IBM Corp). A P value less than 0.05 was considered significant.

Results

Patient, tumor and treatment characteristics

Our cohort consisted of 187 patients who underwent MIE between 2014 and 2017. From this cohort two groups were selected: the eldest elderly (group 1, aged 76 years or older) and younger elderly (group 2, aged 71 to 75 years). Group 1 consisted of 19 patients with a median age of 77 years (76–83 years). In group 2, 41 patients had a median age 72 years (P<0.05). There were no significant differences in sex, Charlson comorbidity score, number of patients undergoing neoadjuvant chemoradiation, histological tumor type, tumor stage, number of lymph nodes harvested and type of anastomosis. An overview of patient characteristics can be found in *Table 1*.

Morbidity and mortality

There were no significant differences in length of hospital stay, 90-day morbidity and mortality. The overall incidence of complications was 57.5% in group 1 and 65.9% in group 2. The percentage of anastomotic leakage was 21.1% (n=4) in group 1 and 14.6% (n=6) in group 2 (P=0.535). Mortality rate was 10.5% (n=2) and 4.9% (n=2) respectively (P=0.415). The majority of complications were cardiovascular complications including atrial fibrillation and myocardial infarction. Incidence was 31.6% (n=6) in group 1 and 14.6% (n=6) in group 2 (P=0.127). Pulmonary complications included pneumonia and were seen in 26.3% (n=5) in group 1 and 34.1% (n=14) in group 2. Median length of hospital stay was 12 days (5–86 days) in group 1 and 11.5 days (1–102 days) in group 2 (P=0.858). In both groups one patient died because of myocardial infarction, shown by autopsy. And in both groups one patient died because of pneumonia after anastomotic leakage. An overview of surgery related morbidity and mortality is shown in *Table 2*. Detailed analysis of group 1 identified four octogenarians in which 90-day mortality was zero.

Long-term outcome

Data on 1-year follow-up was available for 21 out of 41 patients in group 2 and 13 out of 19 patients in group 1. With a mean follow-up of 10.0 months (0–24 months) in group 1 and 19.5 months (0–35 months) in group 2. A trend was seen towards better 1-year survival in group 2 (76.2%) compared to group 1 (46.2%), P=0.075. An overview of long-term outcome is shown in *Table 3*.

Discussion

In this single center cohort study, no significant difference was seen in morbidity and mortality after MIE comparing the eldest elderly to younger elderly patients. Neither was there a significant difference in long-term survival between the two groups. The anastomotic leakage rate was 21.1% in group 1 and 14.6% in group 2. The observed anastomotic leakage rate is in accordance with current literature, reporting rates up to 30% after MIE (18). More than 57.9% of patient aged 76 years or older had one or more complications. This rate is higher than in the general population, where the rate of major complications up to 32% (18). The number is also higher than for colorectal surgery, where complication rates in the eldest elderly are up to 41% (6). Most complications were cardiovascular or pulmonary complications, which is in accordance to elderly undergoing open esophagectomy and in elderly undergoing colorectal surgery (6,10). The 90-day mortality of 10.5% in group 1 compared to 4.9% in group 2 is high. Although the small number of patients might be limiting statistical power, this number is comparable to existing literature investigating larger number of patients where similar mortality ratios are seen, without significant difference between younger and elderly patients (19).

Median length of hospital stay was 12 days. In elderly undergoing open esophagectomy a mean length of hospital stay of 18 days was reported (10). Although our study is no

Table 1 Patient, tumor and treatment characteristics

Characteristics	Group 1 (aged 76 years or older) (N=19)	Group 2 (aged 71–75 years) (N=41)	P value
Age (years)	77 [76–83]	72 [71–75]	0.000
Gender			0.558
Male	13 (68.4)	31 (75.6)	
Female	6 (31.6)	10 (24.4)	
Charlson comorbidity score	4 [3–8]	4 [3–7]	0.935
Tumor regression score	2 [1–5]	2 [1–5]	0.936
cT			0.064
1	3 (17.6)	1 (2.7)	
2	6 (35.3)	7 (18.9)	
3	7 (41.2)	28 (75.7)	
4	1 (5.9)	1 (2.7)	
pT			0.676
0	7 (36.8)	14 (34.1)	
1	3 (15.8)	10 (24.4)	
2	6 (31.6)	8 (19.5)	
3	3 (15.8)	9 (22.0)	
Tumor type			0.83
Squamous cell carcinoma	5 (26.3)	8 (19.5)	
Adenocarcinoma	13 (68.4)	31 (75.6)	
Other	1 (5.3)	2 (4.9)	
Tumor location			0.331
Mid	1 (5.3)	6 (14.6)	
Lower	18 (94.7)	33 (80.5)	
Junction	0 (0)	2 (4.9)	
Neoadjuvant treatment			0.181
Yes	17 (89.5)	40 (97.6)	
No	2 (10.5)	1 (2.4)	
Transhiatal surgery			0.226
Yes	0 (0)	3 (7.3)	
No	19 (100.0)	38 (92.7)	
Conversion to laparotomy			0.492
Yes	0 (0)	1 (2.4)	
No	19 (100.0)	40 (97.6)	
Anastomosis			0.579
Cervical (McKeown)	3 (15.8)	9 (22.0)	
Intrathoracic (Ivor-Lewis)	16 (84.2)	32 (78.0)	
Lymph nodes with malignant cells	0 [0–8]	0 [0–7]	0.425
Lymph nodes harvested	16 [4–39]	17 [6–32]	0.312

Data are presented as N (percentage) or median [range].

Table 2 Ninety-day morbidity and mortality after minimally invasive esophagectomy

Variables	Group 1 (aged 76 years or older) (N=19)	Group 2 (aged 71–75 years) (N=41)	P value
Length of hospital stay (days)	12 [5–86]	11.5 [1–102]	0.858
90-day mortality	2 (10.5)	2 (4.9)	0.415
Complications	11 (57.9)	27 (65.9)	0.552
Number of complications	0 [0–3]	1 [0–5]	0.921
Anastomotic leakage	4 (21.1)	6 (14.6)	0.535
Pulmonary complications	5 (26.3)	14 (34.1)	0.544
Cardiovascular complications	6 (31.6)	6 (14.6)	0.127
Surgical site infections	3 (15.8)	5 (12.2)	0.703
Delirium	1 (5.3)	5 (12.2)	0.390
Other complications*	2 (10.5)	9 (22.0)	0.287
Reintervention	1 (5.3)	3 (7.3)	0.767
Length of stay on the ICU	1 [1–28]	1.5 [1–77]	0.729
Resume oral intake after surgery (days)	5 [3–76]	4 [1–75]	0.857
Textbook outcome	6 (31.6)	14 (34.1)	0.844

Data are presented as N (percentage) or median [range]. *, Other complications included decubitus, electrolyte disorders, urosepsis and chylothorax.

Table 3 Long-term follow-up after minimally invasive esophagectomy

Variables	Group 1 (aged 76 years or older) (N=19)	Group 2 (aged 71–75 years) (N=41)	P value
Follow-up (months)	10.0 [0–24]	19.5 [0–35]	0.227
1-year survival (%)	6/13 (46.2)	16/21 (76.2)	0.075

Data are presented as N (percentage) or median [range].

comparison between MIE versus open surgery, the results suggest that although complication rates are higher than in younger patients, elderly patients might benefit from minimally invasive techniques (20).

The retrospective nature of this study has several limitations. American Society of Anesthesiologist physical status classification was not systematically recorded. After surgical treatment most patients were referred back to their center of diagnosis after a short-term follow-up of 3 months to see for surgical complications. Therefore, data regarding long-term outcome were not available for all patients. However, the aim of this study was to investigate surgical related morbidity and mortality and not long-term outcome of disease. Furthermore, data were only available for patients managed operatively, thus preventing comparison of those who deemed unfit for surgery or who refrained themselves from surgery after counseling. Although the number of patients in this study is low, this is by our knowledge the largest series of a single center presenting outcome after MIE in elderly patients (10).

Being a single center study made it possible to investigate at individual patient level, instead of database research as is seen in previous studies on this topic (16,21). Our center is a large regional referral center for esophageal cancer treatment. Hospital volume is related to mortality and survival in patients after esophagectomy. Therefore, in The Netherlands esophageal surgery is only performed regionalized and centralized in high volume centers (>21/year) (22). These results are likely not only due to better surgery, but also to better staging, decision making and postoperative care due to improvement of the expertise of the health care professionals in the referral hospitals. In our hospital all

patients are assessed before treatment by the same team of surgeons, a dedicated physician assistant, medical oncologists and radiotherapists. Moreover, all patients diagnosed with esophageal cancer in our referral area are discussed in our experienced multi-disciplinary and multi-center tumor board meeting, making the variance in treatment strategy for all patients low. We did not used specified criteria for selecting elderly patients for MIE as well as younger patients. An important risk factor for postoperative complications is the presence of comorbidities (4). In our study the number of comorbidities and Carlson comorbidity score did not differ between the two groups. This is most likely a result of the selection process, emphasizing the importance of screening each candidate individually. Furthermore, some patients initially deemed fit for surgery had to drop-out or be postponed for surgery after neoadjuvant chemoradiation because of toxic side effects. We were unable to calculate the number of patients who had to drop-out. However, the number of drop-out after chemoradiation is generally low and is therefore unlikely to have influenced our results (11).

Efforts have been made to identify risk factors for morbidity and mortality after esophagectomy and to develop models for risk stratification (23). We suggest to include age as a significant but not the determent factor, as advanced age is not a contraindication for surgery (21). Furthermore, comparison to those who deemed unsuitable for MIE would be an interesting study subject, as the untreated group might have a poor long-term prognosis (24). Together with the results from our study, this knowledge can be of help in future shared decision making in elderly patients diagnosed with a potentially curable stage of esophageal cancer.

Conclusions

In this study there was no significant difference in morbidity and mortality after MIE for esophageal cancer comparing elderly to younger elderly patients. Therefore, curative MIE should not be denied on the basis of calendar age alone. Although diminished by careful patient selection and the use of minimally invasive surgical techniques, esophageal resection for cancer still comes with significant risks and patients need to be counseled thoroughly.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/aoe.2019.03.01). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Medical ethics committee approval was not required for this study as all patient and hospital information was anonymous. Individual informed consent was waived. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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