

# Propensity Score–Matched Analysis Comparing Minimally Invasive Ivor Lewis Versus Minimally Invasive McKeown Esophagectomy

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**Introduction:** Totally minimally invasive esophagectomy (TMIE) is increasingly used in treatment of patients with esophageal carcinoma. However, it is currently unknown if McKeown TMIE or Ivor Lewis TMIE should be preferred for patients in whom both procedures are oncologically feasible.

**Methods:** The study was performed in 4 high-volume Dutch esophageal cancer centers between November 2009 and April 2017. Prospectively collected data from consecutive patients with esophageal cancer localized in the distal esophagus or gastroesophageal junction undergoing McKeown TMIE or Ivor Lewis TMIE were included. Patients were propensity score matched for age, body mass index, sex, American Society of Anesthesiologists classification, Charlson Comorbidity Index, tumor type, tumor location, clinical stage, neoadjuvant treatment, and the hospital of surgery. The primary outcome parameter was anastomotic leakage requiring reintervention or reoperation. Secondary outcome parameters were operation characteristics, pathology results, complications, reinterventions, reoperations, length of stay, and mortality.

**Results:** Of all 787 included patients, 420 remained after matching. The incidence of anastomotic leakage requiring reintervention or reoperation was 23.3% after McKeown TMIE versus 12.4% after Ivor Lewis TMIE ( $P = 0.003$ ). Ivor Lewis TMIE was significantly associated with a lower incidence of pulmonary complications (46.7% vs 31.9%), recurrent laryngeal nerve palsy (9.5% vs 0.5%), reoperations (18.6% vs 11.0%), 90-day mortality (7.1% vs 2.9%), shorter median intensive care unit length of stay (2 days vs 1 day) and shorter median hospital length of stay (12 vs 11 days) (all  $P < 0.05$ ). R0 resection rate was similar between the groups. The median number of examined lymph nodes was 21 after McKeown TMIE and 25 after Ivor Lewis TMIE ( $P < 0.001$ ).

**Conclusions:** Ivor Lewis TMIE is associated with a lower incidence of anastomotic leakage, 90-day mortality and other postoperative morbidity compared to McKeown TMIE in patients in whom both procedures are oncologically feasible.

**Keywords:** cervical anastomosis, intrathoracic anastomosis, Ivor Lewis esophagectomy, McKeown esophagectomy, minimally invasive esophagectomy, transthoracic esophagectomy

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Totally minimally invasive esophagectomy (TMIE) is increasingly used in treatment of patients with esophageal carcinoma.<sup>1</sup> TMIE has been shown to reduce pulmonary complications, postoperative pain and hospital length of stay compared to open esophagectomy,<sup>2</sup> without compromising oncologic safety.<sup>3</sup> There are several surgical approaches for TMIE: the Orringer procedure (laparoscopic transhiatal with cervical anastomosis),<sup>4</sup> the McKeown procedure (thoracoscopic with cervical anastomosis)<sup>5</sup> and the Ivor Lewis procedure (thoracoscopic with intrathoracic anastomosis).<sup>6</sup> Transhiatal TMIE is currently not favored,<sup>1</sup> because no adequate thoracic lymph node dissection can be performed which might compromise survival in selected patients.<sup>7</sup> For patients with resectable esophageal carcinoma between the level of the carina and the gastroesophageal junction, both a McKeown TMIE as an Ivor Lewis TMIE esophagectomy are considered feasible and oncologically appropriate.

It is, however, currently unknown whether McKeown TMIE or Ivor Lewis TMIE is associated with lower postoperative morbidity. A recent review and meta-analysis concluded that no randomized controlled trials and only 5 comparative cohort studies have been published comparing McKeown TMIE with Ivor Lewis TMIE.<sup>8</sup> In addition, these 5 studies were single center studies, included a limited number of patients, all studies were retrospective and none of the studies corrected for case-mix parameters. Therefore, the aim of the present study was to compare postoperative morbidity in patients undergoing McKeown TMIE or Ivor Lewis TMIE in patients with distal esophageal or gastroesophageal junction carcinoma with case-mix correction by propensity score matching in a multicenter setting.

## METHODS

### Study Setting

This retrospective cohort study with prospectively collected data included patients undergoing McKeown TMIE and Ivor Lewis TMIE in 4 Dutch hospitals. All centers are regional referral centers for esophageal cancer surgery and perform at least 40 TMIE per year. In addition, all centers experienced a transition from McKeown TMIE to Ivor Lewis TMIE as the preferred surgical procedure for patients with esophageal cancer during the study period. In all hospitals, perioperative care pathways were implemented before the start of this study. In 3 out of 4 hospitals, all operated patients went to the intensive care unit (ICU) for at least 1 day and in 1 of the hospitals, patients were only transferred to the ICU on indication.

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### Patients

Consecutive patients with malignant tumors of the esophagus or gastroesophageal junction (cT1b-4a N0-3 M0) undergoing elective, curative TMIE were included between November 2009 and April 2017. All patients with carcinoma of the proximal or middle esophagus and patients with carcinoma of the gastric cardia were excluded, to ensure that only patients in whom both McKeown TMIE and Ivor Lewis TMIE were feasible were included. Curative resection after neoadjuvant chemoradiotherapy according to the CROSS scheme<sup>9</sup> was the standard treatment in the Netherlands during the study period. In selected cases, neoadjuvant chemotherapy was administered. Patients receiving definitive chemoradiation therapy and a subsequent salvage procedure were excluded from this analysis.

### Surgeons and Operative Technique

All patients were operated by a dedicated esophageal surgical team. Most procedures were performed by 2 surgeons. All patients underwent TMIE including a laparoscopic lymph node dissection in supine position and thoracoscopic lymph node dissection in prone position. Anastomotic techniques in the Ivor Lewis TMIE group were fully mechanical circular end-to-side anastomosis or semi-mechanical linear side-to-side (S-S) anastomosis. In the McKeown TMIE group, anastomotic technique was handsewn end-to-end, end-to-side, or S-S, semimechanical S-S<sup>10</sup> or stapled S-S.<sup>11</sup> Pyloric drainage procedures were not routinely performed.

### Casemix and Outcome Parameters

Casemix parameters were patient sex, age, body mass index, American Society of Anesthesiologists score, Charlson Comorbidity Index, clinical tumor stage, tumor location, tumor histology, and neoadjuvant treatment.

Primary outcome parameter was anastomotic leakage requiring reintervention or reoperation. The Esophagectomy Complications Consensus Group definition of anastomotic leakage was used, and it was defined as a full thickness gastrointestinal defect involving the esophagus, anastomosis, staple line, or conduit.<sup>12</sup> Anastomotic leakage was diagnosed by contrast computed tomography scan, endoscopy, drainage of ingested materials or gastric content into chest tubes or signs of anastomotic leakage during reoperation or autopsy. Anastomotic leakage was graded according to the Esophagectomy Complications Consensus Group into type I (no reintervention or reoperation required), type II (reintervention but no reoperation), and type III (requiring reoperation).<sup>12</sup>

Secondary outcome parameters were conversion rate; operative time; chyle leakage; pulmonary complications; pneumonia; cardiac complications; jejunostomy-related complications; overall complications (defined as the combined incidence of all complications); hospital length of stay; ICU length of stay; readmissions within 30 days; and 30-day, 90-day, and in-hospital mortality and textbook outcome. Outcome parameters are described in more detail in online appendix I. In addition, R0 resection rate and the number of examined lymph nodes were recorded. Textbook outcome, a composite outcome parameter of an “ideal outcome” in a patient, was used and this was scored if the outcome in a patient met the following criteria: radical (R0) resection, 15 or more resected lymph nodes, no perioperative complications, no reinterventions or reoperations, no complications of Clavien-Dindo grade 3 or more,<sup>13</sup> no ICU readmission, no hospital length of stay of more than 21 days, no hospital readmission less than 30 days, and no mortality of less than 30 days and no in hospital mortality.<sup>14</sup> Reinterventions were subdivided into radiologic and endoscopic reinterventions. Endoscopic reinterventions were defined as any endoscopic procedure used to treat anastomotic leakage.

### Analysis

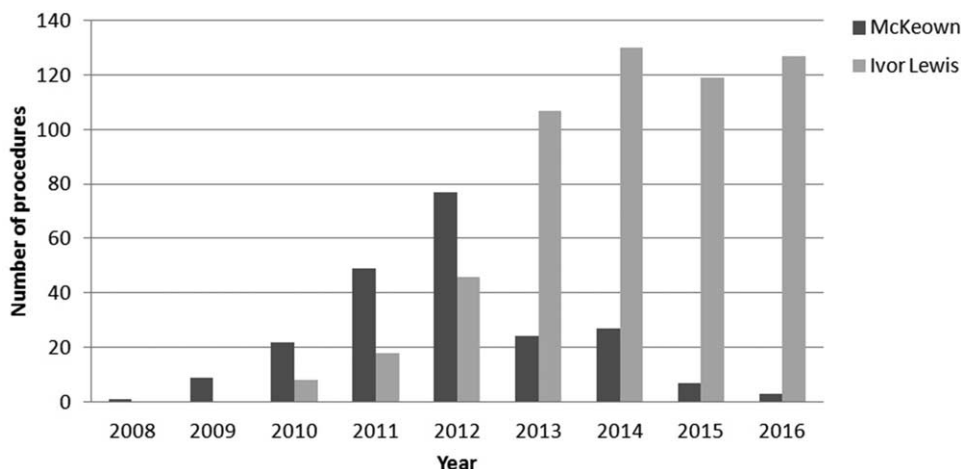
A propensity score–matched analysis was performed to minimize selection bias. Propensity scores were calculated using logistic regression. All casemix factors and the hospital of surgery were entered in the regression model with the operative technique (McKeown TMIE or Ivor Lewis TMIE) as dependent variable. The cases were matched for their propensity scores using a matching ratio of 1:1, nearest neighbor matching protocol, with a caliper of 0.2. Cases were not reusable after matching.<sup>15</sup>

Outcome parameters were analyzed using IBM SPSS for Windows (version 22.0, Armonk, NY). The chi-square test or Fisher exact test was used when appropriate to evaluate whether differences in binomial variables were statistically significant. For continuous variables that did not display a normal distribution, the Mann-Whitney *U* test was used. Differences were considered statistically significant when the *P* value was less than 0.05.

## RESULTS

### Patient Characteristics

Data from 787 consecutive patients were analyzed. The use of TMIE increased over time and a substantially higher proportion of patients underwent Ivor Lewis TMIE during later periods (Fig. 1).



**FIGURE 1.** Number of totally minimally invasive esophagectomies performed, per type of procedure, per year.

Before matching, significant differences between patients undergoing McKeown TMIE and Ivor Lewis TMIE were present for tumor type, tumor location, clinical stage, Charlson Comorbidity Index, and the hospital of surgery. After propensity score matching, 420 patients remained to be evaluated (210 in each group). After matching, only tumor type remained significantly different between the McKeown TMIE and Ivor Lewis TMIE groups, although the difference between the groups was reduced by the matching procedure. Details of patient characteristics before and after matching are shown in Table 1.

### Postoperative Complications

Unmatched and matched outcome parameters are shown in Table 2. After matching, the incidence of anastomotic leakage requiring reintervention or reoperation was 23.3% in the McKeown TMIE group and 12.4% in the Ivor Lewis TMIE group ( $P = 0.003$ ).

No association between tumor type and anastomotic leakage requiring reintervention or reoperation was observed. The difference in anastomotic leakage between the groups persisted in a post-hoc binary logistic regression analysis that corrected for tumor type ( $P = 0.004$ ). An additional post-hoc binary regression analysis showed that the difference in anastomotic leakage requiring reintervention or reoperation persisted after correcting for year of surgery ( $P = 0.018$ ). The total incidence of anastomotic leakage was 28.1% after McKeown TMIE and 13.8% after Ivor Lewis TMIE ( $P < 0.001$ ).

The incidence of pulmonary complications was 46.7% after McKeown TMIE and 31.9% after Ivor Lewis TMIE ( $P = 0.002$ ). Atrial fibrillation occurred in 25.7% in the McKeown TMIE group and in 16.7% in the Ivor Lewis TMIE group ( $P = 0.023$ ). The incidence of recurrent laryngeal nerve palsy was 9.5% after McKeown TMIE and 0.5% after Ivor Lewis TMIE ( $P < 0.001$ ) (Table 2).

**TABLE 1.** Comparison of Casemix Characteristics in the Overall Population, and Undergoing McKeown TMIE Versus Ivor Lewis TMIE, Before and After Propensity Score Matching

Variables	All Patients (n = 787)	Before Matching			After Matching		
		McKeown (n = 226)	Ivor Lewis (n = 561)	P	McKeown (n = 210)	Ivor Lewis (n = 210)	P
Hospital							
Hospital 1	185 (23.5%)	16 (7.1%)	169 (30.1%)	<b>&lt;0.001</b>	16 (7.6%)	15 (7.1%)	0.974
Hospital 2	107 (13.6%)	40 (17.7%)	67 (11.9%)		39 (18.6%)	41 (19.5%)	
Hospital 3	177 (22.5%)	18 (8.0%)	159 (28.3%)		18 (8.6%)	20 (9.5%)	
Hospital 4	318 (40.4%)	152 (67.3%)	166 (29.6%)		137 (65.2%)	134 (63.8%)	
Age							
Median/IQR	65.0 (12.4)	64.4 (13.6)	65.0 (12.2)	0.359	64.5 (13.7)	64.9 (12.9)	0.696
BMI							
Median/IQR	25.5 (5.4)	25.5 (5.3)	25.6 (5.4)	0.259	25.6 (5.3)	25.3 (5.5)	0.982
Sex							
Male	649 (82.5%)	177 (78.3%)	472 (84.1%)	0.052	169 (80.5%)	176 (83.8%)	0.372
Female	138 (17.5%)	49 (21.7%)	89 (15.9%)		41 (19.5%)	34 (16.2%)	
ASA classification							
ASA 1	122 (15.5%)	40 (17.7%)	82 (14.6%)	0.277	39 (18.6%)	39 (18.6%)	0.876
ASA 2	492 (62.5%)	146 (64.6%)	346 (61.7%)		132 (62.9%)	130 (61.9%)	
ASA 3	169 (21.5%)	39 (17.3%)	130 (23.2%)		38 (18.1%)	40 (19.0%)	
ASA 4	4 (0.5%)	1 (0.4%)	3 (0.5%)		1 (0.5%)	1 (0.5%)	
Charlson Comorbidity Index							
0	294 (37.4)	56 (24.8%)	238 (42.4%)	<b>&lt;0.001</b>	56 (26.7%)	56 (26.7%)	0.711
1	164 (20.8)	44 (19.5%)	120 (21.4%)		36 (17.1%)	36 (17.1%)	
2	114 (14.5)	52 (23.0%)	62 (11.1%)		45 (21.4%)	39 (18.6%)	
3	133 (16.9)	48 (21.2%)	85 (15.2%)		47 (22.4%)	49 (23.3%)	
4	63 (8.0)	21 (9.3%)	42 (7.5%)		21 (10.0%)	24 (11.4%)	
5	16 (2.0)	5 (2.2%)	11 (2.0%)		5 (2.4%)	6 (2.9%)	
6	2 (0.3)	0 (0%)	2 (0.4%)		0 (0%)	0 (0%)	
7	1 (0.1)	0 (0%)	1 (0.2%)		0 (0%)	0 (0%)	
Tumor type							
AC	667 (84.8%)	169 (74.8%)	498 (88.8%)	<b>&lt;0.001</b>	161 (76.7%)	183 (87.1%)	<b>0.010</b>
SCC	98 (12.5%)	45 (19.9%)	53 (9.4%)		38 (18.1%)	24 (11.4%)	
Other	22 (2.8%)	12 (5.3%)	10 (1.8%)		11 (5.2%)	3 (1.4%)	
Tumor location							
Distal	655 (83.2%)	210 (92.9%)	445 (79.3%)	<b>&lt;0.001</b>	194 (92.4%)	192 (91.4%)	0.721
Junction	132 (16.8%)	16 (7.1%)	116 (20.7%)		16 (7.6%)	18 (8.6%)	
Clinical stage							
Stage I	150 (19.1%)	25 (11.1%)	125 (22.3%)	<b>&lt;0.001</b>	25 (11.9%)	26 (12.4%)	0.402
Stage II	297 (37.7%)	68 (30.1%)	229 (40.8%)		66 (31.4%)	76 (36.2%)	
Stage III	340 (43.2%)	133 (58.8%)	207 (36.9%)		119 (56.7%)	108 (51.4%)	
Neoadjuvant treatment							
No	51 (6.5%)	15 (6.6%)	36 (6.4%)	0.910	15 (7.1%)	16 (7.6%)	0.852
Yes	736 (93.5%)	211 (93.4%)	525 (93.6%)		195 (92.9%)	194 (92.4%)	

IQR indicates interquartile range; BMI, body mass index; ASA, American society of anesthesiologists; AC, adenocarcinoma, SCC, squamous cell carcinoma. Bold *p*-values indicate that differences between the groups were statistically significant.

**TABLE 2.** Comparison of Outcome Parameters Between McKeown and Ivor Lewis Esophagectomy

Variables	Before Matching			After Matching		
	McKeown (n = 226)	Ivor Lewis (n = 561)	P	McKeown (n = 210)	Ivor Lewis (n = 210)	P
Conversion abdomen	5 (2.2%)	6 (1.1%)	0.217	5 (2.4%)	1 (0.5%)	0.215
Conversion Thorax	0 (0.0%)	14 (2.5%)	<b>0.014</b>	0 (0%)	3 (1.4%)	0.248
Operating time (min)—median (IQR)	330 (72)	286.5 (138)	<b>&lt;0.001</b>	349.0 (114)	410.5 (216)	<b>&lt;0.001</b>
Anastomotic leakage grade ≥2	50 (22.1%)	70 (12.5%)	<b>0.001</b>	49 (23.3%)	26 (12.4%)	<b>0.003</b>
Anastomotic leakage	60 (26.5%)	81 (14.4%)	<b>&lt;0.001</b>	59 (28.1%)	29 (13.8%)	<b>&lt;0.001</b>
Leakage type 1	10 (4.4%)	11 (2.0%)	0.052	10 (4.8%)	3 (1.4%)	0.087
Leakage type 2	23 (10.2%)	36 (6.4%)	0.070	23 (11.0%)	13 (6.2%)	0.081
Leakage type 3	27 (11.9%)	34 (6.1%)	<b>0.005</b>	26 (12.4%)	13 (6.2%)	<b>0.029</b>
Chyle leakage	30 (13.3%)	49 (8.7%)	0.055	27 (12.9%)	19 (9.0%)	0.211
Pulmonary complications	102 (45.1%)	230 (41.0%)	0.288	98 (46.7%)	67 (31.9%)	<b>0.002</b>
Pneumonia	56 (24.8%)	156 (27.8%)	0.386	55 (26.2%)	40 (19.0%)	0.080
Cardiac complications	61 (27.0%)	117 (20.9%)	0.063	56 (26.7%)	41 (19.5%)	0.082
Atrial fibrillation	59 (26.1%)	96 (17.1%)	<b>0.004</b>	54 (25.7%)	35 (16.7%)	<b>0.023</b>
Myocardial infarction	23 (10.2%)	23 (4.1%)	<b>0.001</b>	19 (9.0%)	12 (5.7%)	0.191
Asystole	25 (11.1%)	25 (4.5%)	<b>0.001</b>	21 (10.0%)	13 (6.2%)	0.152
RLN palsy	20 (9.0%)	3 (0.5%)	<b>&lt;0.001</b>	20 (9.5%)	1 (0.5%)	<b>&lt;0.001</b>
Overall complications	141 (62.4%)	345 (61.5%)	0.816	134 (63.8%)	117 (55.7%)	0.091
Severe complications (CD≥3)	58 (25.7%)	187 (33.3%)	<b>0.036</b>	56 (26.7%)	62 (29.5%)	0.515
Reoperation	40 (17.7%)	88 (15.7%)	0.489	39 (18.6%)	23 (11.0%)	<b>0.028</b>
Reintervention	58 (25.7%)	161 (28.7%)	0.390	56 (26.7%)	56 (26.7%)	1.000
Radiologic reintervention	40 (17.7%)	74 (13.2%)	0.104	39 (18.6%)	34 (16.2%)	0.520
Endoscopic reintervention	22 (9.7%)	48 (8.6%)	0.599	23 (11.0%)	32 (15.2%)	0.193
R0 resection	217 (96.0%)	535 (95.4%)	0.688	201 (95.7%)	199 (94.8%)	0.647
Examined LN (median/IQR)	21 (16)	22 (11)	0.082	21 (15)	26 (17)	<b>&lt;0.001</b>
ICU length of stay (median/IQR)	2 (4)	1 (2)	<b>0.001</b>	2 (4)	1 (2)	<b>&lt;0.001</b>
ICU readmission	50 (22.1%)	100 (17.8%)	0.165	48 (22.9%)	34 (16.2%)	0.085
Hospital length of stay (median/IQR)	12 (14)	11 (10)	<b>&lt;0.001</b>	12 (18)	11 (9)	<b>0.046</b>
Hospital readmission	37 (16.4%)	83 (14.8%)	0.578	33 (15.7%)	37 (17.6%)	0.600
Textbook outcome	98 (43.4%)	264 (47.1%)	0.347	90 (42.9%)	106 (50.5%)	0.118
In-hospital mortality	11 (4.9%)	17 (3.0%)	0.208	11 (5.2%)	3 (1.4%)	<b>0.053</b>
30-Day mortality	5 (2.2%)	13 (2.3%)	0.929	5 (2.4%)	2 (1.0%)	0.253
90-Day mortality	16 (7.1%)	25 (4.5%)	0.134	15 (7.1%)	6 (2.9%)	<b>0.044</b>

Dichotomous variables are displayed as n (%), continuous parameters are displayed as median [interquartile range (IQR)].  
 CD indicates Clavien-Dindo grade; ICU, intensive care unit; R0 resection, radical resection; RLN, recurrent laryngeal nerve.  
 Bold p-values indicate that differences between the groups were statistically significant.

**Other Outcome Parameters**

After matching, median operative time was 349 minutes for McKeown TMIE compared to 410 minutes for Ivor Lewis TMIE ( $P < 0.001$ ). The reoperation rate was 18.6% in the McKeown TMIE group and 11.0% in the Ivor Lewis TMIE group ( $P = 0.028$ ). Median ICU length of stay was 2 days after McKeown TMIE compared to 1 day after Ivor Lewis TMIE ( $P < 0.001$ ) and median hospital length of stay was 12 days in the McKeown TMIE group and 11 days in the Ivor Lewis TMIE group ( $P = 0.046$ ). The 30-day, 90-day, and in hospital mortality rates were 2.4%, 7.1%, and 5.2%, respectively after McKeown TMIE compared to 1.0%, 2.9%, and 1.4%, respectively after Ivor Lewis TMIE ( $P = 0.253$ ,  $P = 0.044$ , and  $P = 0.053$ , respectively). The median number of examined lymph nodes was 21 after McKeown TMIE and 26 after Ivor Lewis TMIE ( $P < 0.001$ ). The overall R0 resection rate was 96.1% with no significant difference between the groups. All other secondary outcome parameters were not significantly different between the groups (Table 2).

**DISCUSSION**

In this study, Ivor Lewis TMIE was associated with a significantly lower incidence of anastomotic leakage requiring reintervention or reoperation compared to McKeown TMIE. The widespread belief that anastomotic leakage after cervical anastomosis is less

severe and can be solved with drainage through the cervical wound only, is therefore not in line with the findings of the present study. In addition, Ivor Lewis TMIE was significantly associated with a lower incidence of pulmonary complications, recurrent laryngeal nerve palsy, atrial fibrillation, reoperations, 90-day mortality, and shorter ICU and hospital length of stay compared to McKeown TMIE.

The strength of this study is that it is the first study that performed a multicenter, propensity score–matched analysis comparing Ivor Lewis TMIE with McKeown TMIE in a substantial number of patients. Because only patients with tumors in the distal esophagus and gastroesophageal junction were included, the study population is more homogeneous because both Ivor Lewis TMIE and McKeown TMIE are both feasible and oncologically safe in these patients. This resulted in a lower risk of selection bias than other studies that have been published on this subject.<sup>16–20</sup> A limitation of this study is that a difference in tumor type persisted between the groups after propensity score matching. However, a post-hoc regression analysis showed that this factor did not explain the differences observed in this study. In addition, most Ivor Lewis patients were operated on in a later time period (Fig. 1). To investigate whether it was likely that the outcomes of our study could be explained by other factors that changed over time (eg, perioperative care), we performed an additional regression analysis, correcting for year of surgery for our primary outcome parameter. Although the observed difference

between the groups was smaller in this analysis, the difference in anastomotic leakage requiring reintervention or reoperation remained significantly different and it is therefore unlikely that the primary findings of our study are explained by improving general care only. Another limitation is the heterogeneous anastomotic techniques that are used in this study. The fact that no robust data are currently available on the association of the anastomotic technique (eg, hand-sewn versus stapled or different types of anastomotic configuration) with differences in outcome, led us to believe that the heterogeneous techniques probably do not contribute to the results of this study. Future research will have to clarify whether differences in anastomotic techniques are associated with differences in outcome after minimally invasive esophagectomy. Furthermore, a large proportion of the patients were included in one of the participating centers. Although the study was matched for hospital in which the operation was performed and this is unlikely to have influenced the results, it does affect the general strength of this being a multicenter analysis. Another concern is the occurrence of learning curve bias, because it has been reported that outcomes of esophagectomy improve as surgical proficiency is gained.<sup>21,22</sup> The time periods in which patients undergoing McKeown TMIE (mainly earlier period) and Ivor Lewis TMIE (mainly later period) were included, were also characterized by surgical learning curves of McKeown TMIE and Ivor Lewis TMIE. Although patients were included during both the learning curves of McKeown TMIE and Ivor Lewis TMIE, it is unfortunately not possible to assess whether learning curve effects were similar in both treatment groups. Probably, steps that had been learned during the implementation of McKeown TMIE were also applied in Ivor Lewis TMIE and this might have positively affected outcome in the Ivor Lewis TMIE group. However, large learning curve effects have also been reported for Ivor Lewis TMIE<sup>23</sup> and we therefore think it is unlikely that the findings of the present study can be solely explained by learning curve bias. In fact, the difference in anastomotic leakage incidence between McKeown TMIE and Ivor Lewis TMIE may even be larger than demonstrated in the present study. This is supported by a post-hoc analysis showing that the incidence of anastomotic leakage in the Ivor Lewis TMIE group decreased from 12.7% in the first 50% of patients to 7.4% in the second 50% of patients. In contrast, no learning curve effect was found regarding anastomotic leakage in the TMIE McKeown group.

Median ICU length of stay and hospital length of stay were significantly shorter after Ivor Lewis TMIE compared to McKeown TMIE, which might be explained by the lower incidence of complications after Ivor Lewis TMIE. Postoperative mortality was also lower in the Ivor Lewis TMIE group and this was primarily caused by the relatively high incidence of in-hospital mortality in the McKeown TMIE group. Oncologically, R0 resection rate was high in both groups, but Ivor Lewis TMIE was associated with a higher number of retrieved lymph nodes. During this study period, the surgical extent and technique of the lymph node dissection was equal in both groups and therefore, this finding may reflect a learning curve of performing minimally invasive lymph node dissection or of the retrieval of lymph nodes in the resected specimen by the pathologist.

Five other studies have previously compared McKeown TMIE with Ivor Lewis TMIE.<sup>16–20</sup> A recent meta-analysis of these studies showed no significant difference in anastomotic leakage, but did find that Ivor Lewis TMIE was associated with a shorter hospital length of stay and less blood loss.<sup>8</sup> The studies in this meta-analysis were heterogenic regarding the methodology and definitions used which might explain why outcome differs from the present study. The fact that findings in the present study are, however, different from findings in previously published literature underlines that there is

still uncertainty whether McKeown TMIE or Ivor Lewis TMIE should be the preferred surgical procedure for patients with resectable esophageal cancer. Another important consideration is that there is no high-quality data on whether an intrathoracic anastomotic leakage is of equal severity as a cervical anastomotic leakage in terms of morbidity. It is therefore uncertain whether differences in anastomotic leakage should be solely assessed based on incidences of anastomotic leakage in comparative studies. Finally, data on long-term outcome parameters, survival, quality of life, and cost-effectiveness, are lacking and these data are needed to fully justify a preferred TMIE technique. The randomized controlled ICAN trial, comparing McKeown TMIE with Ivor Lewis TMIE regarding anastomotic leakage, functional outcome, and quality of life, is currently being conducted in the Netherlands.<sup>24</sup> The outcomes of this trial may further elucidate whether McKeown TMIE or Ivor Lewis TMIE should be preferred for patients with esophageal cancer.

## CONCLUSIONS

Ivor Lewis TMIE was associated with lower postoperative morbidity and mortality than McKeown TMIE for patients in whom both procedures are oncologically feasible. Results of a randomized controlled trial are warranted for level I evidence on whether McKeown TMIE or Ivor Lewis TMIE should be preferred for patients with esophageal cancer.

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