

**Original Article** 

# Improved anastomotic leakage rates after the "flap and wrap" reconstruction in Ivor Lewis esophagectomy for cancer

Annelijn E. Slaman, D Wietse J. Eshuis, Mark I. van Berge Henegouwen, Suzanne S. Gisbertz

Department of Surgery, Amsterdam UMC location AMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, The Netherlands

SUMMARY. Anastomotic leakage after esophagectomy has serious consequences. In Ivor Lewis esophagectomy, a shorter and possibly better vascularized gastric conduit is created than in McKeown esophagectomy. Intrathoracic anastomoses can additionally be wrapped in omentum and concealed behind the pleura ("flap and wrap" reconstruction). Aims of this observational study were to assess the anastomotic leakage incidence after transhiatal esophagectomy (THE), McKeown esophagectomy (McKeown), Ivor Lewis esophagectomy (IL) without "flap and wrap" reconstruction, and IL with "flap and wrap" reconstruction. Consecutive patients undergoing esophagectomy at a tertiary referral center between January 2013 and April 2019 were included. Primary outcome was the anastomotic leakage rate. Secondary outcomes were postoperative outcomes, mortality, and 3-year overall survival. A total of 463 patients were included. The anastomotic leakage incidence after THE (n = 37), McKeown (n = 97), IL without "flap and wrap" reconstruction (n = 39), and IL with "flap and wrap" reconstruction (n = 290) were 24.3, 32.0, 28.2, and 7.2% (P < 0.001). THE and IL with "flap and wrap" reconstruction required fewer reoperations for anastomotic leakage (0 and 1.4%) than McKeown and IL without "flap and wrap" reconstruction (6.2 and 17.9%, P < 0.001). Fewer anastomotic leakages are observed after Ivor Lewis esophagectomy with "flap and wrap" reconstruction compared to transhiatal, McKeown and Ivor Lewis esophagectomy without "flap and wrap" reconstruction. The "flap and wrap" reconstruction seems a promising technique to further reduce anastomotic leakages and its severity in esophageal cancer patients who have an indication for Ivor Lewis esophagectomy.

KEY WORDS: esophagectomy, anastomotic leakage, minimally invasive, esophagectomy, esophagogastric anastomosis, esophageal cancer, surgery, cancer esophagus, survival, complications, digestive surgery.

# INTRODUCTION

Over the years, morbidity after esophagectomy has decreased, but population-based studies still report high anastomotic leakage rates (15–34%).<sup>1,2</sup> Anastomotic leakage is difficult to manage and has several negative consequences. On patient-level, it results in a prolonged hospital stay, higher mortality risk, impaired quality of life, and worse long-term survival.<sup>3,4</sup> On institutional and national level, it is associated with higher workload for healthcare workers and increased costs.<sup>5</sup> Despite the risk of leakage and other complications, esophagectomy remains the most important component in the curative treatment for esophageal cancer, with superior survival as compared to chemo(radio)therapy alone.<sup>6</sup> Hence, prevention of anastomotic leakage is paramount in

light of increasing numbers of esophageal carcinoma worldwide.<sup>7</sup> Attempting to reduce the leakage incidence, esophagectomy techniques and perioperative care underwent various modifications over time. Recent trials have demonstrated the association of anastomotic leakage with the anastomosis location in transthoracic esophagectomy. Additionally, protective effects of omentoplasty on intrathoracic anastomoses have been suggested by other reports.<sup>2,3,8,9</sup>

The objectives of this study are to assess the anastomotic leakage incidence after different esophagectomy and reconstruction techniques at a tertiary referral hospital in the Netherlands, and to investigate whether Ivor Lewis anastomosis benefits from omentoplasty and pleural flap concealment ("flap and wrap" reconstruction) as compared to intrathoracic anastomoses without "flap and wrap" reconstruction.

Address correspondence to: Dr S.S. Gisbertz, Department of Surgery, Amsterdam UMC location AMC, University of Amsterdam, Cancer Center Amsterdam, Meibergdreef 9, Amsterdam, AZ 1105, the Netherlands. Email: s.s.gisbertz@amc.uva.nl

© The Author(s) 2022. Published by Oxford University Press on behalf of International Society for Diseases of the Esophagus. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (http:// creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

## METHODS

This observational study included consecutive patients undergoing curative-intended esophagectomy at a tertiary university hospital in the Netherlands between February 2013 and April 2019. Patients with histologically proven cT1-4aN0-3M0 carcinomas of the mid-to-distal esophagus, gastroesophageal junction, and cardia who were scheduled for open or minimally invasive (MI) esophagectomy were selected from a prospective database. Palliative and/or emergency esophagectomy and colonic reconstructions were excluded.

#### Staging and oncologic treatment

Cancer staging according to the American Joint Committee on Cancer classification (8th edition) was performed by endoscopy with biopsies, endoscopic ultrasound, neck ultrasound, computed tomography (CT), and positron emission tomography/computed tomography.<sup>10</sup> Neoadjuvant or perioperative chemo(radio)therapy was administered as per Dutch guideline for esophageal cancer.<sup>11</sup> During followup, patients visited the outpatient clinic in 14 days, 6 weeks, and every 3 months in the first postoperative year. Subsequently, patients were seen every 6 months until the 4th year and once more after 5 years. Endoscopy and radiography were only performed on indication.

#### **Perioperative treatment**

Patients" physical preoperative condition were optimized by dieticians and physiotherapists. Routine Creactive protein (CRP) serum levels were measured on postoperative day (POD) 3, 5, and 7. To detect possible anastomotic leakages, CT was performed if CRP was >150 mg/L. Patients were only admitted to the ICU if it was required by severe comorbidities or complications. If no complications occurred, patients were discharged at POD 7 according to the Enhanced Recovery after Surgery program.<sup>12</sup>

A total of three surgeons performed 80-100 esophagectomies per year at this center. Surgeons had already gained experience with MI and open transhiatal (THE) and McKeown esophagectomy prior to the inclusion period. Ivor Lewis esophagectomy was introduced in February 2013 and modified in January 2014 by wrapping the anastomosis in omentum and concealing it behind a pleural flap ("flap and wrap" reconstruction). Following its introduction, MI Ivor Lewis esophagectomy became the standard technique for distal esophageal, junction, and cardia carcinomas. MI McKeown esophagectomy was the standard procedure for patients with proximal-tomid esophageal tumors, positive lymph nodes in the superior mediastinum and if radiation fields extended above the carina. Both procedures consisted

of an extended two-field lymphadenectomy, including the aortopulmonary and lower paratracheal region (on both sides). THE was usually performed in patients who were considered not to be fit enough for TTE (i.e. due to comorbidities). Extended one-field lymphadenectomy toward the lower mediastinum up to the level of the pulmonary vein was performed here. If MI surgery did not seem feasible beforehand (i.e. due to bulky tumors), open esophagectomy was scheduled. Procedures were performed as previously described.<sup>13</sup> The right gastroepiploic artery and first part of the right gastric arteries and veins were preserved to supply blood to the gastric conduit. A 60-mm linear stapler was used for the conduit (approximately 3-4 cm wide). Hand-sewn cervical anastomoses were created end-to-side or end-to-end with single-layered PDS 3.0. After securing the anvil with a purse-string suture, intrathoracic anastomoses were created end-to-side with a double stapling technique using 25/29-mm circular stapler (depending on the esophageal stump diameter). During the "flap and wrap" reconstruction the anastomosis was additionally wrapped in omentum followed by a single suture fixating and lifting the tip of the gastric conduit behind a pleural flap, which was created superior to the transected arch of the azygos vein. Hereby, the conduit was concealed with greater omentum, completely covered by the pleural flap and tensile forces on the circular anastomosis were reduced.

## **Data collection**

Cases were collected by checking the operation schedule of the following week. Surgeons were asked to report perioperative information directly after surgery (Appendix A). Postoperative outcomes were discussed with the surgeons on a weekly basis. Latest follow-up was collected on 12 April 2022.

The primary outcome was the incidence of anastomotic leakage (AL), defined as "full thickness gastrointestinal defect involving esophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification" (Esophagectomy Complications Consensus Group).<sup>14</sup> Secondary outcomes were: AL type,<sup>14</sup> morbidity, Comprehensive Complication Index (CCI),<sup>15</sup> reoperations, ICU admissions, mortality, and 3-year overall survival (OS) (Appendix B).

## Statistics

Patient groups were classified as follows: (1) THE, (2) McKeown esophagectomy (McKeown), (3) Ivor Lewis esophagectomy (IL) without "flap and wrap" reconstruction, and (4) IL with "flap and wrap" reconstruction. Chi-square/Fisher's exact tests (categorical variables) and Mann–Whitney U/Kruskal– Wallis tests (continuous variables) were used for the analyses. To assess the predictive value of the "flap

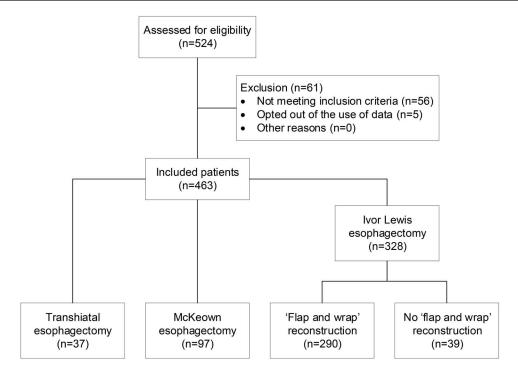


Fig. 1 Flow chart.

and wrap" reconstruction on anastomotic leakages, dichotomized variables with P < 0.20 in the univariate analyses were entered in a multivariate logistic regression analysis. A proficiency-gain curve of Ivor Lewis esophagectomy was plotted for all surgeons together using the patients' individual anastomotic leakage incidence calculated by a centered-moving average (width: 51 cases). Visual inspection was used to assess plateau level in the curve. Kaplan– Meier curves were plotted. P < 0.050 was considered as significant using SPSS Statistics 26.0.0.1 (2019, Armonk, NY: IBM Corp.) was for all analyses.

## RESULTS

Baseline characteristics of 463 patients differed significantly between THE (n = 37), McKeown (n = 97), IL without "flap and wrap" (n = 39) and IL with "flap and wrap" reconstruction (n = 290; Fig. 1). Characteristics of IL without "flap and wrap" reconstruction and IL with "flap and wrap" reconstruction were comparable. Mean age was 64 years (95% CI 63–65) and body mass index was 25.9 kg/m<sup>2</sup> (95% CI 63–65) and body mass index was 25.9 kg/m<sup>2</sup> (95% CI 25.5–26.3; Table 1). Patients after THE were generally older (69 years, 95% CI 66–71) than patients of other procedures (P = 0.003). Median follow-up for surviving patients was 61.7 months (IQR 50.4–69.4).

## Anastomotic leakage

The anastomotic leakage incidence after Ivor Lewis esophagectomy was 9.7%. Incidences after THE,

McKeown, IL without "flap and wrap" and IL with "flap and wrap" reconstruction were resp. 24.3, 32.0, 28.2, and 7.2% (P < 0.001; Table 2). Most leakages were treated with interventional therapy (Table 3). No reoperations were performed for anastomotic leakages after THE, followed by 1.4% after IL with "flap and wrap" reconstruction, 6.2% after McKeown, and 17.9% after IL without "flap and wrap" reconstruction (P < 0.001). Following Ivor Lewis esophagectomy, leakage severity was lower if "flap and wrap" reconstruction was applied. This reconstruction was an independent predictor for fewer anastomotic leakages (OR 0.170 95% CI 0.096-0.301, P < 0.001; Appendix D). Plateau level in the proficiency-gain curve (including "flap and wrap" reconstruction) was reached after 63 cases (Fig. 2).

## Secondary outcomes

IL with "flap and wrap" reconstruction resulted in fewest pulmonary complications (51.3%, P < 0.001) and shortest ICU stay (0 days, P < 0.001; Table 2). Highest 90-day mortality was found after McKeown (8.2%) versus 0.0, 5.1, and 0.7% after THE, IL without "flap and wrap," and IL with "flap and wrap" reconstruction (P < 0.001). Lymph node yield was highest after McKeown and IL with "flap and wrap" reconstruction (P < 0.001). Three-year OS after THE, McKeown, IL without, and IL with "flap and wrap reconstruction was 45.9, 44.3, 64.1, and 61.1% (P = 0.009; Fig. 3).

#### Table 1 Baseline characteristics

	THE	McKeown	IL without "flap		Total	
	<i>n</i> = 37	<i>n</i> = 97	and wrap" n = 39	and wrap" n = 290	<i>n</i> = 463	P value
Age (years)	69 (66–71)	64 (63–66)	63 (60–65)	64 (63–65)	64 (63–65)	*0.003
Sex (males)	25 (67.6)	65 (67.0)	31 (79.5)	241 (83.1)	362 (78.2)	*0.003
BMI (kg/m <sup>2</sup> ) Comorbidity	26.7 (25.1–28.2)	24.7 (23.8–25.5)	26.4 (25.1–27.5)	26.1 (25.6–26.6)	25.9 (25.5–26.3)	*0.016
Cardiovascular	14 (37.8)	34 (35.1)	19 (48.7)	125 (43.1)	192 (41.5)	0.218
Diabetes mellitus	6 (16.2)	11 (11.3)	5 (12.8)	32 (11.0)	54 (11.7)	0.822
COPD	4 (10.8)	4 (4.1)	0	15 (5.2)	23 (5.0)	0.180
Previous upper GI surgery ASA	0	1 (1.0)	2 (5.1)	10 (3.4)	13 (2.8)	0.334 0.247
1	8 (21.6)	31 (32.0)	14 (35.9)	90 (31.0)	143 (30.9)	
2	18 (48.6)	55 (56.7)	17 (43.6)	145 (50.0)	235 (50.8)	
3	11 (29.7)	11 (11.3)	8 (20.5)	55 (19.0)	85 (18.4)	
Histology						*0.001
Adenocarcinoma	34 (91.9)	48 (49.5)	37 (94.9)	252 (86.9)	370 (79.9)	
SCC	3 (8.1)	45 (46.4)	2 (5.1)	35 (12.1)	85 (18.4)	
Other	0	4 (4.1)	0	3 (1.0)	7 (1.5)	
Tumor site			0			* < 0.001
Mid esophagus	0	35 (36.1)	0	20 (6.9)	55 (11.9)	
Distal esophagus	22 (59.5)	60 (61.9)	35 (89.7)	207 (71.4)	324 (70.0)	
GEJ	14 (37.8)	2 (2.1)	3 (7.7)	48 (16.6)	67 (14.5)	
Cardia	1 (2.7)	0 (0)	1 (2.6)	15 (5.2)	17 (3.7)	
Tumor stage	4 (10.0)	6 (6 <b>0</b> )	2 (7 7)	<b>2</b> 2 (7 0)	26 (7.0)	0.792
T1	4 (10.8)	6 (6.2)	3 (7.7)	23 (7.9)	36 (7.8)	
T2	8 (21.6)	23 (23.7)	7 (17.9)	45 (15.5)	83 (17.9)	
T3	24 (64.9)	66 (68.0)	29 (74.4)	215 (74.1)	334 (72.1)	
T4	1 (2.7)	2 (2.1)	0	7 (2.4)	10 (2.2)	0.050
Nodal involvement	20 (54 1)	22 (22 2)	17 (42.0)	100 (24 ()	1(0)(2(7)	0.058
N0	20 (54.1)	32 (33.3)	17 (43.6)	100 (34.6)	169 (36.7)	
N1	10 (27.0)	33 (34.4)	14 (35.9)	127 (43.9)	184 (39.9)	
N2	6 (16.2)	31 (32.3)	7 (17.9)	56 (19.4)	100 (21.7)	
N3	1 (2.7)	0 (0)	1 (2.6)	6 (2.1)	8 (1.7)	*0.007
Neoadjuvant treatment	0(242)	0 (0 2)	2(7,7)	2((0,0))	47 (10.2)	0.007
None	9 (24.3)	9 (9.3)	3 (7.7) 0	26 (9.0)	47 (10.2)	
Chemotherapy	2(5.4)	1(1.0)	0	22 (7.6)	25 (5.4)	
Chemoradiotherapy	26 (70.3)	88 (89.8)	36 (92.3)	242 (83.4)	392 (84.7)	0.815
Surgery Open	1 (2.7)	1 (1.0)	1 (2.6)	9 (3.1)	12 (2.6)	0.815
Minimally invasive	1 (2.7) 36 (97.3)	95 (97.9)	36 (92.3)	9 (3.1) 272 (93.8)	12 (2.6) 439 (94.8)	
	36 (97.3) n/a	95 (97.9) 1 (1.0)				
Hybrid (thorax open) Hybrid (abdomen open)	n/a n/a	1 (1.0) 0	1 (2.6) 1 (2.6)	6 (2.1) 3 (1.0)	8 (1.7)	
Tyonu (abdomen open)	11/a	0	1 (2.0)	5 (1.0)	4 (0.9)	

ASA American Society of Anesthesiologists, COPD chronic obstructive pulmonary disease.

Continuous values are presented in means (95% confidence interval). cN-stage of two patients were missing (0.4%).

#### DISCUSSION

This prospective cohort study investigates the anastomotic leakage incidence after introduction of the Ivor Lewis esophagectomy and evaluates this incidence after recent implementation of the "flap and wrap" reconstruction in Ivor Lewis esophagectomy. Results show that Ivor Lewis esophagectomy led to a leakage rate of less than 10% at this tertiary referral center. In general, Ivor Lewis esophagectomy resulted in shorter ICU stay and improved 3-year OS compared to transhiatal and McKeown esophagectomy. The shift to the "flap and wrap" reconstruction during Ivor Lewis esophagectomy led to an anastomotic leakage incidence of 7% and lowest leakage severity. Based on patients' individual leakage incidences, plateau level in the proficiency-gained curve of Ivor Lewis esophagectomy was reached after 63 cases. The curve reflects continuous adaptation of the technique during the

implementation period. It follows an expected course that contains four phases: (1) start of the training, (2) acquiring proficiency, competence, and additional experience, (3) reaching a plateau, and (4) drop of competence (Fig. 2).<sup>16</sup> The steep gradient in the second phase corresponds to training of complex surgical procedures such as esophagectomy. The fourth phase reflects an advanced period where surgeons start to operate on more complex patients and when fellows start practicing due to confidence after previous promising results. The number of cases needed to overcome the accepted leakage rate of 8% in this study is comparable to that of other centers.<sup>17,18</sup>

In current practice, THE is only performed in a selection of patients who have severe comorbidities. It is possible that the low 90-day mortality after THE is a reflection of the less invasive character of the procedure. Researchers suggest that anastomotic leakages and morbidity are related to worse long-term

#### Table 2 Short-term outcomes

	THE	McKeown	IL without "flap and wrap"	IL with "flap and wrap"	
	<i>n</i> = 37	<i>n</i> = 97	n = 39	n = 290	P value
Operation time (min) <sup>†</sup>	307 (288–327)	420 (409–431)	449 (431–467)	417 (411–424)	* < 0.001
Intraoperative blood loss (mL) <sup>‡</sup> Blood transfusions	150 (50–250)	138 (100–200)	200 (100–300)	200 (100-300)	* < 0.001 0.095
Intraoperative Postoperative	1 (2.7) 2 (5.4)	2 (2.1) 9 (9.3)	1 (2.6) 9 (23.1)	4 (1.4) 18 (6.2)	
Conversions	0	0	2 (5.1)	7 (2.5)	0.171
R0 resections	37 (100)	94 (96.9)	39 (100)	280 (96.6)	0.447
Resected lymph nodes <sup>†</sup>	22 (19–26)	33 (30–35)	25 (22–27)	36 (34–37)	* < 0.001
Overall morbidity	25 (67.6)	60 (61.9)	27 (69.2)	157 (54.1)	0.123
Anastomotic leakage	9 (24.3)	31 (32.0)	11 (28.2)	21 (7.2)	* < 0.001
Pulmonary complications	9 (24.3)	28 (28.9)	20 (51.3)	63 (21.7)	* < 0.001
Reinterventions	7 (18.9)	34 (35.1)	14 (35.9)	67 (23.1)	*0.041
Reoperations	2 (5.4)	9 (9.3)	10 (25.6)	15 (5.2)	* < 0.001
ICU readmissions	4 (10.8)	16 (16.5)	17 (43.6)	43 (14.8)	* < 0.001
Reintubations	2 (5.4)	10 (10.3)	14 (35.9)	22 (7.6)	* < 0.001
Comprehensive Complication Index <sup>‡</sup>	8.7 (0–25)	16.6 (0–37.9)	26.2 (0–50.1)	8.7 (0–26.2)	*0.010
Length of stay (days) <sup>‡</sup>					
ICU	1 (0–1)	1 (0–3)	1 (0-7)	0 (0–1)	* < 0.001
Hospital	10 (8–17)	11 (8–17)	12 (9–34)	10 (8–15)	*0.039
Mortality					
In-hospital	0	4 (4.1)	1 (2.6)	1 (0.3)	*0.028
30-days	0	4 (4.1)	1 (2.6)	2 (0.7)	0.085
90-days	0	8 (8.2)	2 (5.1)	2 (0.7)	* < 0.001

Values are presented in means<sup>†</sup> (95% confidence interval) or in medians<sup>‡</sup> (interquartile range). Blood loss of seven patients (1.5%) were missing.

Table 3 Outcome values related to anastomotic leakage

	THE n = 37	McKeown $n = 97$	IL without "flap and wrap" n = 39	IL with "flap and wrap" n = 290	<i>P</i> value
Type (ECCG)					* < 0.001
Î	1 (2.7)	3 (3.1)	0 (0)	1 (0.3)	
II	8 (21.6)	22 (22.7)	4 (10.3)	16 (5.5)	
III	0 (0)	6 (6.2)	7 (17.9)	4 (1.4)	
ICU admissions caused by AL	0 (0)	1 (1.0)	10 (25.6)	14 (4.8)	* < 0.001
Readmissions caused by AL	0 (0)	7 (7.2)	0 (0)	4 (1.4)	*0.005
Deaths caused by AL	0 (0)	2(2.1)	0 (0)	1 (0.3)	0.270

survival.<sup>4</sup> Higher 90-day mortality and cN-stages probably explain the steep Kaplan–Meier curve in the first 12 months and worse survival after McKeown esophagectomy. Although the survival curve of Ivor Lewis with "flap and wrap" reconstruction suggests non-inferiority, outcomes should be interpreted with caution due to small numbers in other groups.

The anastomotic leakage rate after Ivor Lewis esophagectomy lies within that of previous studies (5–21%).<sup>2,19–22</sup> Few studies compare leakage rates between Ivor Lewis, McKeown, *and* transhiatal esophagectomy as primary outcome parameter. One Dutch multicenter study investigated short-term outcomes of patients with anastomotic leakage after transhiatal, McKeown, and Ivor Lewis esophagectomy.<sup>23</sup> It reported the lowest leakage incidence after

Ivor Lewis esophagectomy (17%). This was higher than the current incidence after IL with "flap and wrap" reconstruction, but lower than after IL without "flap and wrap" reconstruction. Mortality, reinterventions, and reoperations after anastomotic leakage in that study were disadvantageous for Ivor Lewis esophagectomy, which is also in contrast to results of IL with "flap and wrap" reconstruction. A recent randomized controlled trial compared anastomotic leakages with ECCG type II/III between intrathoracic and cervical anastomoses, all with omentoplasty.<sup>2</sup> A rate of 12% after Ivor Lewis esophagectomy was observed, which is slightly higher than after Ivor Lewis esophagectomy in this study (9.4%). They hypothesized that the incidence may have been negatively influenced by participating centers that were still experiencing learning-associated morbidity.

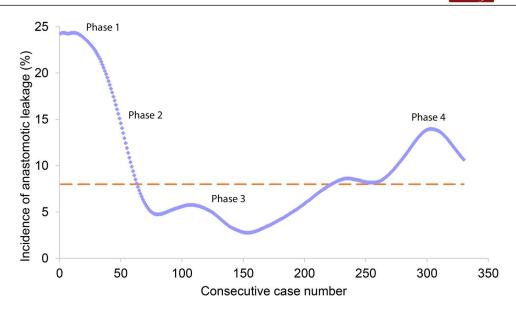
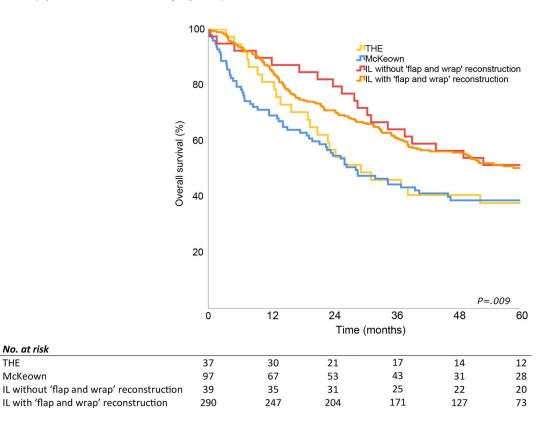
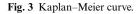


Fig. 2 Proficiency-gain curve of Ivor Lewis esophagectomy.





It is difficult to compare outcomes of the "flap and wrap" reconstruction to the literature. Research studies that investigated omentoplasty after TTE have shown that anastomotic leakage rates vary between 3 and 16%, which seems comparable to that of the "flap and wrap" reconstruction.<sup>8,9</sup> The studies have shown that omentoplasty leads to lower leakage rates, but were often performed with small patient numbers, in the era prior to neoadjuvant chemoradiotherapy and minimally invasive surgery, or included different esophagectomy procedures. Despite of this lack of homogeneity, omentoplasty was found to be a significant negative predictor of anastomotic leakages by two systematic reviews.<sup>3,24</sup>

The benefit of the "flap and wrap" reconstruction concerning anastomotic leakage and its severity compared to other procedures can be explained by several hypotheses. First, the gastric conduit in Ivor



Lewis is shorter than in transhiatal and McKeown esophagectomy, resulting in better perfusion at the site of the anastomosis. Second, vertical traction on the anastomosis can be avoided by stitching the gastric conduit to the pleural flap. Third, covering the anastomosis behind the pleural flap and wrapping greater omentum around it serve as mechanical protection mechanisms against negative intrathoracic pressure, and create barriers for infections to spread throughout the thoracic cavity. Additionally, angiogenic and growth factors produced by the omentum may lead to revascularization, especially in infected areas. This may lead to faster leakage healing.<sup>25</sup> Furthermore, omentum has shown immunologic areas, which can react fast with immune cells in response to infection.<sup>25</sup> Consequently, leakages could follow a less severe course, leading to less invasive treatment possibilities, e.g. intraluminal vacuum therapy or endoscopic stenting instead of surgery.

A strength of the present study is that it shows change of a surgical technique using prospective data with information about anastomotic leakages during the implementation of Ivor Lewis esophagectomy followed by modification of its reconstruction. The study is a reflection of the daily esophageal cancer treatment in a tertiary referral center, where 80-100 esophagectomies/year are performed. In practice, patients with treatable esophageal cancer are usually selected for TTE if they are physical fit, while McKeown esophagectomy is reserved for tumors and/or radiation fields extending above the carina. The study shows that assessment of the proficiency-gain curve is important when interpreting results of a new technique. Furthermore, discussing postoperative data of each patient with surgeons before entering the database and the use of ECCG definitions secure accurate data collection and generalizability of the study. A more precise analysis of complication severity was pursued using CCI instead of the Clavien–Dindo classification.<sup>15,26</sup>

As a limitation, plateau level of the proficiencygain curve was reached after consecutive Ivor Lewis esophagectomy number 63, thus patients without "flap and wrap" reconstruction have experienced more learning-associated morbidity than patients with "flap and wrap" reconstruction. However, even with learning-associated morbidity, Ivor Lewis esophagectomy with "flap and wrap" reconstruction seems feasible in terms of anastomotic leakage, short-term outcomes, and 3-year OS. Due to the study design-representing results of daily practice ("natural occurring sample"), selection bias is likely to have influenced outcomes by selection of different patients for Ivor Lewis esophagectomy than other procedures. However, the objective of this study was not to show superiority of either technique, as there will always indication for a specific technique due to patient and tumor characteristics. The aim was to describe the outcomes when patients are selected for a procedure in daily practice.

## CONCLUSIONS

This observational study showed that the incidence and severity of anastomotic leakages differed between patients after transhiatal, McKeown, and Ivor Lewis esophagectomy, with lowest incidences for the "flap and wrap" reconstruction in Ivor Lewis esophagectomy. Therefore, Ivor Lewis esophagectomy with "flap and wrap" reconstruction is the preferred curative procedure in patients with distal esophageal or gastroesophageal junction cancer who are fit enough for TTE. However, since THE and McKeown esophagectomy will always remain essential procedures for selected patients, upper gastrointestinal surgeons must pursue to gain proficiency in these procedures. Due to the high leakage rate after McKeown esophagectomy, surgeons of this center have adapted the anastomotic technique in 2020. Based on the technique that is performed in some Japanese centers, surgeons now use a double-layered suturing (mucosa-to-mucosa with PDS 5.0 and gastric conduit serosa to esophageal muscle layers with interrupted Vicryl 4.0). Awaiting the results of this change at the current center, this technique could result in fewer anastomotic leakages.

#### SUPPLEMENTARY DATA

Supplementary data mentioned in the text are available to subscribers in DOTESO online.

#### ACKNOWLEDGEMENTS

This article was not financed by any funds or grants. Prof. van Berge Henegouwen reports grants from Olympus and Stryker, and consulting fees from Medtronic, Mylan Alesi Surgical, BBraun, and Johnson & Johnson.

Conflict of interest: None.

#### References

- van Hagen P, Hulshof M C C M, van Lanschot J J B et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med 2012; 366(22): 2074–84. https://doi.org/10.1056/nejmoa1112088.
- Van Workum F, Verstegen M H P, Klarenbeek B R et al. Intrathoracic vs cervical anastomosis after totally or hybrid minimally invasive Esophagectomy for esophageal cancer: a randomized clinical trial. JAMA Surg 2021; 156(7): 601–10. https://doi.org/10.1001/jamasurg.2021.1555.
- 3. Kamarajah S K, Lin A, Tharmaraja T *et al.* Risk factors and outcomes associated with anastomotic leaks following esophagectomy: a systematic review and meta-analysis. Dis Esophagus 2020; 33(3): 1–14. https://doi.org/10.1093/dote/doz089.

- 4. Van Der Werf L R, Wijnhoven B P L, Fransen L F C et al. A National Cohort Study evaluating the association between short-term outcomes and long-term survival after esophageal and gastric Cancer surgery. Ann Surg 2019; 270(5): 868–76. https://doi.org/10.1097/SLA.00000000003520.
- Agzarian J, Visscher S L, Knight A W et al. The cost burden of clinically significant esophageal anastomotic leaks—a steep price to pay. J Thorac Cardiovasc Surg 2019; 157(5): 2086–92. https://doi.org/10.1016/j.jtcvs.2018.10.137.
- 6. Wang B Y, Wu S C, Chen H C *et al.* Survival after neoadjuvant chemoradiotherapy and oesophagectomy versus definitive chemoradiotherapy for patients with oesophageal squamous cell carcinoma. Br J Surg 2019; 106(3): 255–62. https://doi.org/10.1002/bjs.11004.
- Kastelein F, Van Olphen S H, Steyerberg E W et al. Impact of surveillance for Barrett's oesophagus on tumour stage and survival of patients with neoplastic progression. Gut 2016; 65(4): 548–54. https://doi.org/10.1136/gutjnl-2014-308802.
- Lu M, Luketich J D, Levy R M et al. Anastomotic complications after esophagectomy: influence of omentoplasty in propensity-weighted cohorts. J Thorac Cardiovasc Surg 2020; 159(5): 2096–105. https://doi.org/10.1016/j.jtcvs.2019.09.157.
- 9. Tuo G, Jin G, Pang Y *et al.* Omentoplasty decreases leak rate after esophagectomy: a metaanalysis. J Gastrointest Surg 2020; 24(6): 1237–43. https://doi.org/10.1007/s11605-019-04284-z.
- Rice T W, Patil D T, Blackstone E H. 8th edition AJCC/UICC staging of cancers of the esophagus and esophagogastric junction: application to clinical practice. Ann Cardiothorac Surg 2017; 6(2): 119–30. https://doi.org/10.21037/acs.2017.03.14.
- Vereniging van Maag-darm-leverartsen. Dutch guideline for esophageal cancer, version 3.1. Federatie Medisch Specialisten. https://richtlijnendatabase.nl/richtlijn/oesofaguscarcinoom/ oesofaguscarcinoom\_-\_startpagina.html (Published 2015. 21 September 2021, Date accessed).
- 12. Blom R L G M, Van Heijl M, Bemelman W A *et al.* Initial experiences of an enhanced recovery protocol in esophageal surgery. World J Surg 2013; 37(10): 2372–8. https://doi.org/10.1007/s00268-013-2135-1.
- Anderegg M C J J, Gisbertz S S, van Berge Henegouwen M I. Minimally invasive surgery for oesophageal cancer. Best Pract Res Clin Gastroenterol 2014; 28(1): 41–52. https://doi.org/10.1016/j.bpg.2013.11.002.
- Low D E, Alderson D, Cecconello I et al. International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG). Ann Surg 2015; 262(2): 286–94. https://doi.org/10.1097/SLA.000000000001098.
- Slankamenac K, Graf R, Barkun J, Puhan M A, Clavien P A. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. Ann Surg 2013; 258(1): 1–7. https://doi.org/10.1097/SLA.0b013e318296c732.

- Hopper A N, Jamison M H, Lewis W G. Learning curves in surgical practice. Postgrad Med J 2007; 83(986): 777–9. https://doi.org/10.1136/pgmj.2007.057190.
- Claassen L, van Workum F, Rosman C. Learning curve and postoperative outcomes of minimally invasive esophagectomy. J Thorac Dis 2019; 11(Suppl 5): S777–85. https://doi. org/10.21037/jtd.2018.12.54.
- Van Workum F, Stenstra M H B C, Berkelmans G H K et al. Learning curve and associated morbidity of minimally invasive esophagectomy: a retrospective multicenter study. Ann Surg 2019; 269(1): 88–94. https://doi.org/ 10.1097/SLA.00000000002469.
- Straatman J, Van Der Wielen N, Cuesta M A et al. Minimally invasive versus open esophageal resection. Ann Surg 2017; 266(2): 232–6. https://doi.org/ 10.1097/SLA.00000000002171.
- Sabra M J, Alwatari Y A, Wolfe L G et al. Ivor Lewis vs Mckeown esophagectomy: analysis of operative outcomes from the ACS NSQIP database. Gen Thorac Cardiovasc Surg 2020; 68(4): 370–9. https://doi.org/10.1007/s11748-020-01290-w.
- Schröder W, Raptis D A, Schmidt H M et al. Anastomotic techniques and associated morbidity in total minimally invasive transthoracic esophagectomy: results from the Eso benchmark database. Ann Surg 2019; 270(5): 820–6. https://doi.org/10.1097/SLA.00000000003538.
- 22. van Workum F, Berkelmans G H, Klarenbeek B R, Nieuwenhuijzen G A P, Luyer M D P, Rosman C. McKeown or Ivor Lewis totally minimally invasive esophagectomy for cancer of the esophagus and gastroesophageal junction: systematic review and meta-analysis. J Thorac Dis 2017; 9: S826–33. https://doi.org/10.21037/jtd.2017.03.173.
- 23. Verstegen M H P, Slaman A E, Klarenbeek B R et al. Outcomes of patients with anastomotic leakage after transhiatal, McKeown or Ivor Lewis esophagectomy: a nationwide cohort study. World J Surg 2021; 45: 3341–9. https://doi.org/10.1007/s00268-021-06250-w.
- 24. Grigor E J M, Kaaki S, Fergusson D A, Maziak D E, Seely A J E. Interventions to prevent anastomotic leak after esophageal surgery : a systematic review and meta - analysis. BMC Surg 2021; 21: 42. https://doi.org/10.1186/s12893-020-01026-w.
- 25. Wang A W, Prieto J M, Cauvi D M, Bickler S W, De Maio A. The greater omentum a vibrant and enigmatic immunologic organ involved in injury and infection resolution. Shock 2020; 53(4): 384–90. https://doi.org/10.1097/SHK.00000000001428.
- 26. Slaman A E, Lagarde S M, Gisbertz S S, Van Berge Henegouwen M I. A quantified scoring system for postoperative complication severity compared to the Clavien-Dindo classification. Dig Surg 2015; 32(5): 361–6. https://doi.org/10.1159/000433608.