Aortic Calcification Increases the Risk of Anastomotic Leakage After Ivor-Lewis Esophagectomy

Lucas Goense, MD, Peter S. N. van Rossum, MD, Teus J. Weijs, MD, Marc J. van Det, MD, Grard A. Nieuwenhuijzen, MD, PhD, Misha D. Luyer, MD, PhD, Maarten S. van Leeuwen, MD, PhD, Richard van Hillegersberg, MD, PhD, Jelle P. Ruurda, MD, PhD, and Ewout A. Kouwenhoven, MD, PhD

Departments of Surgery and Radiotherapy, University Medical Center Utrecht, Utrecht; Department of Surgery, Catharina Hospital Eindhoven, Eindhoven; Department of Surgery, Ziekenhuisgroep Twente, Almelo; and Department of Radiology, University Medical Center Utrecht, Utrecht, The Netherlands

Background. **Anastomotic leakage is associated with increased morbidity and mortality after esophagectomy. Calcification of the arteries supplying the gastric tube has been identified as a risk factor for leakage of the cervical anastomosis, but its potential contribution to the risk of intrathoracic anastomotic leakage has not been elucidated. This study evaluated the relationship between calcification and the occurrence of leakage of the intrathoracic anastomosis after Ivor-Lewis esophagectomy.**

Methods. **Consecutive patients who underwent minimally invasive esophagectomy for cancer at 2 institutions were analyzed. Diagnostic computed tomography images were used to detect calcification of the arteries supplying the gastric tube (eg, aorta, celiac axis). Multivariable logistic regression analysis was used to determine the relationship between vascular calcification and anastomotic leakage.**

Results. **Of 167 included patients, anastomotic leakage occurred in 40 (24%). In univariable analysis, leakage was most frequently observed in patients with calcification of the aorta (major calcification: 37% leakage [16 of 43]; minor calcification: 32% [18 of 56]; no calcification: 9% [6 of 70], $p < 0.001$). Calcification of other studied arteries was not significantly associated with leakage. A significant association with leakage remained for minor (odds ratio, 5.4; 95% confidence interval, 1.7 to 16.5) and major (odds ratio, 7.0; 95% confidence interval, 1.9 to 26.4) aortic calcifications in multivariable analysis.**

Conclusions. **Atherosclerotic calcification of the aorta is an independent risk factor for leakage of the intrathoracic anastomosis after Ivor-Lewis esophagectomy for cancer. The calcification scoring system may aid in patient selection and lead to earlier diagnosis of this potentially fatal complication.**

(Ann Thorac Surg 2016;102:247–52)

Surgical resection of the esophagus combined with neoadjuvant chemoradiation or perioperative chemotherapy is the cornerstone of treatment with curative intent for patients with resectable nonmetastatic esophageal cancer [1–3]. Anastomotic leakage is a frequently encountered complication after esophagectomy that is associated with increased postoperative morbidity, length of hospital stay, and mortality [4–7]. Furthermore, anastomotic leakage has been shown to negatively affect long-term cancer specific-survival after esophagectomy [8]. Despite advances in surgical treatment and improvement in perioperative care, incidence rates of up to 24% to 30% have been reported for anastomotic leakage after esophagectomy [3, 9].

Identifying risk factors for anastomotic leakage after esophagectomy could aid in early recognition and subsequently limit the effect of this complication. Accurately predicting anastomotic leakage based only on standard patient or treatment-related characteristics is currently difficult. Tissue ischemia and compromised perfusion of the gastric tube are considered the main causes of insufficient anastomotic healing [4, 10].

As an important contributor to tissue ischemia, atherosclerosis is associated with a detrimental effect on anastomotic healing [11]. In a recently published study, atherosclerotic calcification of the arteries supplying the gastric tube, as determined by routine diagnostic computed tomography (CT) scans, was identified as independent risk factor for anastomotic leakage of the cervical anastomosis after esophagectomy [12].

The potential contribution of atherosclerotic calcification to the risk of anastomotic leakage after esophagectomy with an intrathoracic anastomosis has not been elucidated. The shorter length of the gastric tube in case of an intrathoracic anastomosis may cause relatively less ischemia compared with a cervical anastomosis [5]. Accordingly, the aim of this study was to evaluate the

Accepted for publication Jan 28, 2016.

Address correspondence to Dr Kouwenhoven, Department of Surgery, Ziekenhuisgroep Twente, Almelo, Zilvermeeuw 1, PO Box 7600, 7600 SZ Almelo, The Netherlands; email: e.kouwenhoven@zgt.nl.

Published by Elsevier

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2016.01.093

relationship between atherosclerotic calcification of the arteries supplying the gastric tube (as determined by scoring calcifications on CT) and the occurrence of leakage of the intrathoracic anastomosis after Ivor-Lewis esophagectomy for cancer.

Material and Methods

The Institutional Review Board approved this retrospective study and waived the requirement to obtain informed consent.

Study Population

All consecutive patients who underwent an elective, minimally invasive Ivor-Lewis esophagectomy for cancer in the Catharina Hospital, Eindhoven, and the Ziekenhuisgroep Twente, Almelo, between April 2012 and March 2015 were selected from prospectively collected institutional databases. Within these databases, patients with an available preoperative thoracoabdominal contrast-enhanced CT scan were included.

All patients underwent a total minimally invasive esophagectomy with gastric tube reconstruction using an intracorporal anastomosis. The intrathoracic anastomosis was created using a side-to-side linear stapling technique or end-to-side hand-sewn technique at the level of the carina. The study excluded patients who underwent preoperative vascular conditioning (eg, stenting of the celiac artery) or a reconstruction other than a gastric tube. Patient and treatment-related characteristics from the remaining eligible patients were extracted from the prospectively acquired databases. Variables of interest included gender, age, body mass index, American Society of Anesthesiologists Physical Status Classification, chronic obstructive pulmonary disease, coronary artery disease, and other cardiac comorbidities, hypertension, peripheral vascular disease, diabetes mellitus, smoking status at diagnosis, neoadjuvant treatment, and anastomotic technique.

Image Acquisition and Evaluation

Thoracoabdominal CT images were acquired using commercially available 16- or 64-section CT scanners at our own or referring centers. All contrast-enhanced routine CT protocols were considered suitable if the field of view at least included the total thoracic aorta, celiac axis, right postceliac arteries (ie, common hepatic, gastroduodenal, and right gastroepiploic arteries) and left postceliac arteries (splenic and left gastroepiploic arteries). Images were acquired with a slice thickness of 2 mm (5% of patients), 2.5 mm (12% of patients), 3.0 mm (47% of patients), or 5 mm (36.0% of patients). When more than 1 CT scan was available, the first diagnostic scan conducted during the diagnostic workup was used. An iodinated contrast bolus was administered intravenously in all patients. The CT images were acquired during the arterial phase or the portal venous phase.

The CT images were retrospectively reviewed and scored for location and amount of calcification by 1 reader (L.G.). The reader was trained to use a previously described simple vascular scoring system for calcifications of the arteries of the gastric tube [12] by the authors who proposed the system using a training set of 25 randomly selected patients who were not part of the study sample. This scoring system has been shown to yield good to excellent interobserver and intraobserver reproducibility [12]. The reader was blinded to patient and treatment-related characteristics and surgical outcome.

Calcification of the thoracic aorta was scored on transverse CT images from the origin of the left subclavian artery down to the origin of the celiac axis (score 0 to 2). An aortic calcification score of 1 was assigned in case of 9 or fewer calcified foci and 3 or fewer calcified foci extending over 3 or more contiguous axial images. A score of 2 was assigned in case more than 9 calcified foci or more than 3 calcified foci extending over 3 or more contiguous axial images were observed.

Calcification of the celiac axis was also scored (score 0 to 2). A score of 1 was assigned when calcifications extended over fewer than 3 contiguous axial images or a single calcified focus was 10 mm or smaller (long axis). In case of larger calcifications or involvement of both the proximal (aortoceliac) and distal (hepatosplenic bifurcation) parts of the celiac axis, a score of 2 was assigned. Scores of 0, 1, and 2 were considered as absence, minor, or major presence of calcification, respectively. The right and left postceliac arteries were scored according to the absence or presence of calcification (score 0 to 1). The threshold of 3 or more contiguous axial images was initially proposed for CT scans with 5-mm slices. The grading system was adjusted accordingly for thinner slices. Examples of image characteristics are presented in Figure 1.

Statistical Analysis

The primary outcome measure of this study was anastomotic leakage defined as clinical signs of leakage from a thoracic drain, radiologic signs of leakage, including contrast leakage or fluid and air levels surrounding the anastomosis, or signs of anastomotic dehiscence during endoscopy or reoperation. In case anastomotic leakage was clinically suspected, a CT scan or endoscopy was performed; no routine diagnostic tests were performed [13].

The association of patient and treatment-related characteristics and calcification scores with anastomotic leakage was studied univariably. Categoric variables were compared using the χ^2 test or the Fisher exact test in case of small cell count. The Student t test and Mann-Whitney U test were used to compare groups with and without anastomotic leakage for parametric and nonparametric continuous variables, respectively. Subsequently, variables with a p of 0.25 or less in univariable analysis were entered in a multivariable logistic regression model to evaluate whether these factors were independently associated with the occurrence of anastomotic leakage. Odds ratios with 95% confidence intervals were calculated. Statistical analysis was performed using SPSS 20.0 software (IBM Corp, Armonk, NY). A p value of less than 0.05 was considered statistically significant.

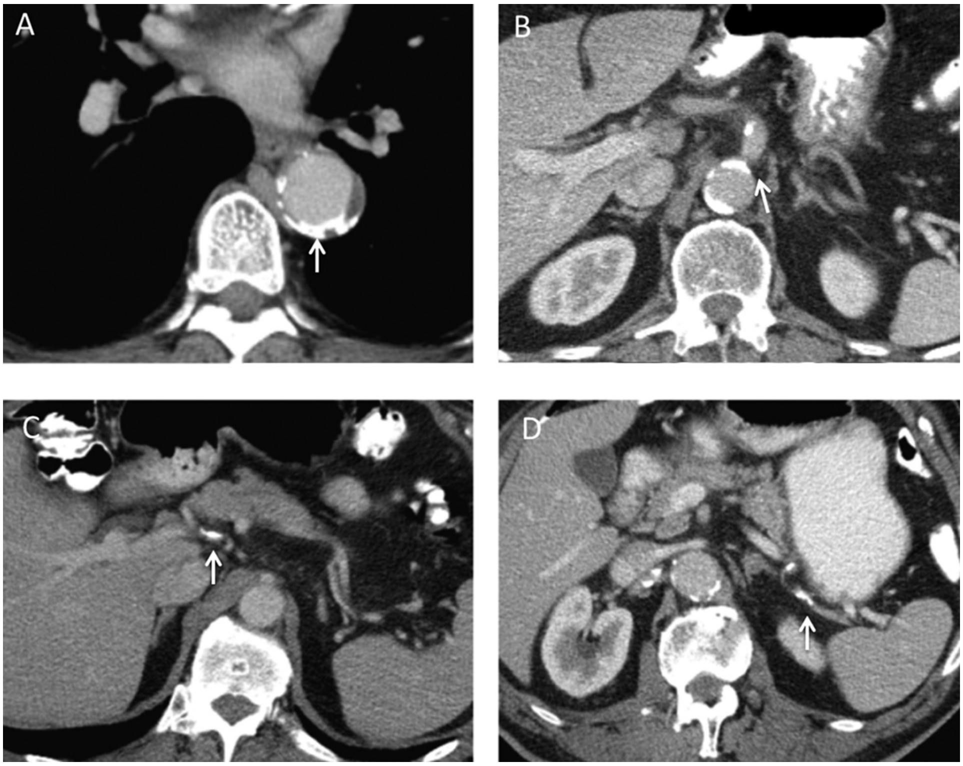

Fig 1. Examples of calcification on preoperative computed tomography images in patients with esophageal cancer. (A) Image shows the descending aorta with plaques and calcified foci (arrow). A calcification score of 2 was assigned. (B) Image shows calcification of the celiac axis (arrow). A calcification score of 2 was assigned. (C) Image shows calcification of the common hepatic artery (arrow), yielding a right postceliac artery calcification score of 1. (D) Image shows calcified foci in the splenic artery (arrow), yielding a left postceliac artery score of 1.

Results

In the study period, 170 patients underwent a total minimally invasive esophagectomy with gastric tube reconstruction and intrathoracic anastomosis (Ivor-Lewis). Of these patients, 3 were excluded because gastric tube formation could not be performed during the operation (n = 1) or preoperative vascular conditioning was performed (n = 2). Anastomotic leakage occurred in 40 of the remaining 167 patients (24%) at a median of 5 days (range, 1 to 14 days) after esophagectomy. Of these, 10 patients (25%) showed some signs of tissue ischemia or necrosis of the gastric conduit during postoperative endoscopy. Treatment of anastomotic leakage consisted of antibiotics and nil-by-mouth in 4 of 40 patients (10%), endoscopic reintervention (stent placement or mediastinal drainage) in 18 (45%), and surgical reintervention in 18 (45%).

Baseline patient and treatment-related characteristics are presented in Table 1. None of these characteristics were significantly associated with the occurrence of anastomotic leakage in univariable analysis. However, patients with anastomotic leakage were slightly older than patients without anastomotic leakage (mean: 66.5 vs 63.5 years, respectively; $p = 0.053$).

The overall prevalence of calcification of the studied arteries, including the thoracic aorta, celiac axis, and left postceliac arteries, was high (ie, 59%, 43%, and 25%, respectively). In contrast, calcification of the right postceliac arteries was found in only 5 of 167 patients (3%). A comparison of calcification per trajectory for patients with vs without anastomotic leakage is reported in Table 2. In univariable analysis, the presence of aortic calcification was significantly associated with a higher risk of anastomotic leakage (32% leakage [18 of 56] and 37% leakage [16 of 43] in groups with minor and major calcification, respectively, vs 9% leakage [6 of 70] in the group without calcification; $p < 0.001$). Calcification of the celiac axis was not significantly associated with anastomotic leakage (18% leakage [7 of 39] and 33% leakage [11 of 33] in groups with minor and major calcification, respectively, vs 23% leakage [22 of 95] in the group without calcification; $p = 0.496$). Although the risk of anastomotic leakage in patients with calcification of the right and left postceliac arteries appeared higher than in patients without these calcifications, the risk differences were not statistically significant (40% leakage [2 of 5] vs 24% leakage [38 of 162], $p = 0.393$, and 32% leakage [13 of 41] vs 21% [27 of 126], $p = 0.180$, respectively).

Age and presence of coronary artery disease along with the calcification scores of the aorta and left postceliac arteries were selected for multivariable logistic regression analysis (Table 3). Minor (score 1) and major (score 2) aortic calcification remained significantly and independently associated with an increased risk of anastomotic leakage, with adjusted odds ratios of 5.35 (95% confidence interval, 1.73 to 16.55) and 7.01 (95% confidence interval, 1.96 to 26.44), respectively. Age, presence of cardiac comorbidity, and calcification of the left postceliac arteries were not independently associated with anastomotic leakage in multivariable analysis.

Table 1. Patient and Treatment-Related Characteristics in Relation to Anastomotic Leakage

Characteristic[a]	Anastomotic Leakage No (n = 127)	Anastomotic Leakage Yes (n = 40)	p Value
Male gender	105 (82.7)	34 (85.0)	0.732
Age, y	63.5 ± 8.8	66.5 ± 9.2	0.053
Body mass index, kg/m^2	26.3 ± 4.4	26.8 ± 5.9	0.893
ASA score			0.548
1	9 (7.1)	4 (10.0)	
2	86 (67.7)	29 (72.5)	
3	32 (25.2)	7 (17.5)	
COPD	20 (15.7)	7 (17.5)	0.793
Coronary artery disease[b]	14 (11.0)	8 (20.0)	0.143
Other cardiac comorbidity[c]	12 (9.4)	4 (10.0)	0.564
Hypertension[d]	40 (31.5)	13 (32.5)	0.443
Peripheral vascular disease[e]	9 (7.1)	2 (2.0)	0.643
Diabetes mellitus	22 (17.3)	6 (15.0)	0.732
Renal insufficiency[f]	7 (5.5)	2 (5.0)	1
Smoker at diagnosis	24 (18.9)	8 (20.0)	0.52
Neoadjuvant therapy			0.776
No therapy	10 (7.9)	4 (10.0)	
Chemotherapy	110 (86.6)	35 (87.5)	
Chemoradiotherapy	7 (5.5)	1 (2.5)	
Anastomotic technique			0.94
Side-to-side stapling	96 (75.6)	30 (75.0)	
End-to-side hand-sewn	31 (24.4)	10 (25.0)	

[a] Categoric data are shown as number (%) and continuous data as mean ± standard deviation. [b] Requiring percutaneous coronary intervention or coronary artery bypass graft. [c] A record of historical treatment of any cardiac disorder (other than coronary artery disease) at a cardiology department. [d] Requiring pharmacologic therapy. [e] Requiring vascular reconstruction, bypass surgery, or percutaneous intervention to the extremities (excluding vein stripping) or documented aortic aneurysm with or without repair. [f] Based on a glomerular filtration rate of <60 mL/min/1.73 m^2.

ASA = American Society of Anesthesiologists; COPD = chronic obstructive pulmonary disease.

Table 2. Distribution of Calcification Scores per Trajectory and the Proportion of Patients With Anastomotic Leakage[a]

Artery	No. (%)	Anastomotic Leakage (% of row)	p Value
Thoracic aorta			<0.001
0	68 (40.7)	6 (8.8)	
1	56 (33.5)	18 (32.1)	
2	43 (25.7)	16 (37.2)	
Celiac axis			0.496
0	95 (56.9)	22 (23.2)	
1	39 (23.4)	7 (17.9)	
2	33 (19.8)	11 (33.3)	
Right postceliac arteries			0.393
0	162 (97.0)	38 (23.5)	
1	5 (3.0)	2 (40.0)	
Left postceliac arteries			0.180
0	126 (75.0)	27 (21.4)	
1	42 (25.0)	13 (31.7)	

[a] Data represent number of patients with percentages.

Comment

Accurate risk assessment of anastomotic leakage after esophagectomy could aid in the selection of patients who may benefit from preoperative preventative strategies and postoperative decision making. Unfortunately, we are currently not able to accurately predict anastomotic leakage after esophagectomy using standard patient or treatment-related characteristics. This study demonstrates that the presence and severity of calcification of the thoracic aorta, as determined on routine preoperative CT images, are independently associated with the risk of leakage of the intrathoracic anastomosis after esophagectomy for cancer. The calcification scoring method deserves attention and validation as a risk factor in future prediction models to identify patients at high risk for leakage.

This study used a previously described system for grading calcification of the arteries of the gastric tube, which has been shown to yield good to excellent interobserver and intraobserver reproducibility [12]. In turn, this calcification grading system was based on a validated visual grading system used to score vascular calcification on routine diagnostic CT images for the prediction of cardiovascular events [14, 15]. Our observed association between aortic calcification and leakage of the intrathoracic anastomosis corresponds with the results of a previous study that identified calcification of the aorta and right postceliac arteries as an independent risk factor for leakage of the cervical anastomosis after esophagectomy [12]. Similarly, another study identified calcification of the iliac arteries as a risk factor for anastomotic leakage after colorectal operations [16]. Therefore, the current study adds to the increasing body of evidence on the association between atherosclerotic calcification and leakage of gastrointestinal anastomoses.

Tissue ischemia, potentially resulting in anastomotic leakage, is thought to be moderated by compromised local perfusion and by generalized vascular disease (indicated by aortic calcification) [11, 12, 17, 18]. The left

Table 3. Results of Multivariable Logistic Regression Analysis in Assessing Risk of Developing Anastomotic Leakage

Variable	Outcome OR	Outcome 95% CI	p Value
Thoracic aorta			
Score 1 vs 0	5.35	1.73–16.55	0.004
Score 2 vs 0	7.01	1.86–26.44	0.004
Left postceliac arteries			
Score 1 vs 0	0.92	0.38–2.16	0.855
Age	0.99	0.94–1.04	0.669
Coronary artery disease	1.55	0.56–4.33	0.402

CI = confidence interval; OR = odds ratio.

and right gastric artery, the short gastric arteries, and the left gastroepiploic artery are ligated during mobilization of the stomach, causing the blood supply of the gastric tube to depend exclusively on the right gastroepiploic artery [19]. This procedure results in a compromised blood flow in the most cranial part of the gastric tube that is used to create the anastomosis.

Our finding that aortic calcification rather than calcification of the smaller vessels (ie, celiac axis and postceliac arteries) significantly increased the risk of anastomotic leakage suggests that generalized vascular disease may be more indicative for the risk of anastomotic leakage than local vascular disease of the arteries supplying the gastric tube. Vascular calcification has been associated with many typical cardiovascular risk factors that are also associated with anastomotic leakage, such as age, diabetes, peripheral vascular disease, and renal dysfunction [6]. In the current study, none of these cardiovascular comorbidities were significantly associated with anastomotic leakage. Therefore, aortic calcification may help to identify high-risk patients who have not yet been diagnosed with these typical risk factors.

Enhancement of blood flow to the gastric tube has been suggested as a possible approach to improve tissue oxygenation and anastomotic healing [20, 21]. Gastric ischemic preconditioning aims to preoperatively improve blood flow to the gastric tube by laparoscopic ligation or arterial embolization of the left gastric artery before the operation [22, 23]. Furthermore, recent experimental studies have reported novel surgical revascularization procedures that could improve blood flow at the anastomotic site, for example, by increasing the length of the arterial arcade by leaving the collaterals of the left gastroepiploic artery in situ (ligating it at the splenic hilus) [24], by transient bloodletting of the short gastric vein [25], or by microvascular additional "supercharging" anastomoses of graft vessels to recipient vessels for microvascular blood flow augmentation at the level of the gastric tube [26].

There is no strong evidence in current clinical practice to implement ischemic conditioning and surgical revascularization procedures, which may be due to the inability to adequately identify the patients who might actually benefit from this invasive intervention [27]. The aortic calcification scoring system could aid in the selection of patients who are at high risk of anastomotic leakage to further assess the potential benefit of these preventative interventions in clinical studies. This is supported by our finding that the absence of aortic calcification seems to have a relatively high negative predictive value for anastomotic leakage because the observed risk of anastomotic leakage in this group was only 9%.

Recognition of the increased risk (of up to 38%) for developing anastomotic leakage in patients with major calcification of the thoracic aorta may have important implications. When confronted with this finding preoperatively, the physical condition of the patients to tolerate a leakage requires special attention. These patients should also be monitored intensively postoperatively for indications of clinical deterioration. Furthermore, these patients may benefit from drain amylase assessment [28] and early gastric tube assessment with endoscopy in the first week after the operation, before mediastinal spread or ischemia-associated sepsis become clinically manifest.

Endoscopy after esophagectomy has proven to be an accurate method to diagnose anastomotic leakage and provide information on the condition of the gastric tube [29, 30]. Selecting patients for endoscopy by a predisposed risk for anastomotic leakage could prevent an unnecessary and invasive endoscopy for a substantial proportion of patients. Therefore, a routine comment on the thoracic aortic calcium burden in the radiology report of the diagnostic thoracoabdominal CT scan in all patients evaluated for esophageal cancer could in aid preoperative and postoperative decision making.

Postoperative anastomotic leakage was relatively common in the current series, occurring in 24% of the patients. Although this appears higher than in some other studies, our definition of anastomotic leakage is rather unrestrictive and includes any sign of clinical or radiologic evidence of leakage. As such, the leakage rate in this study appears to be comparable to the leakage rates of 22% to 30% that were reported in the recent multicenter randomized controlled CROSS (ChemoRadiotherapy for Oesophageal cancer followed by Surgery Study) trial [3].

A few limitations apply to this study. First, this study was confined to a population that underwent elective minimally invasive Ivor-Lewis esophagectomy. Outcomes might be different in populations that undergo other surgical approaches.

Second, no prospective data are yet available to prove the additional clinical benefit of the proposed calcification score in reducing morbidity.

Third, a visual grading system may not be the most accurate method to assess atherosclerotic calcifications, and there may be more distinct methods to analyze the extensiveness of vascular disease and local perfusion. However, the visual grading system used in the current study is easy to use, can be applied on routine diagnostic CT scans, and has been shown to yield good to excellent interobserver and intraobserver reproducibility [12].

In conclusion, this study demonstrated the value of assessing atherosclerotic calcification of the thoracic aorta on routine preoperative CT images to identify patients at high risk of intrathoracic anastomotic leakage after Ivor-Lewis esophagectomy. The applied calcification scoring system may aid in patient selection for interventions that optimize the condition of the anastomosis and lead to an earlier diagnosis of this potentially fatal complication.

References

1. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355:11–20.
2. Sjoquist KM, Burmeister BH, Smithers BM, et al. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: an updated meta-analysis. Lancet Oncol 2011;12:681–92.

3. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med 2012;366:2074–84.
4. Urschel JD. Esophagogastrostomy anastomotic leaks complicating esophagectomy: a review. Am J Surg 1995;169: 634–40.
5. Kassis ES, Kosinski AS, Ross P Jr, Koppes KE, Donahue JM, Daniel VC. Predictors of anastomotic leak after esophagectomy: an analysis of the society of thoracic surgeons general thoracic database. Ann Thorac Surg 2013;96:1919–26.
6. Iannettoni MD, Whyte RI, Orringer MB. Catastrophic complications of the cervical esophagogastric anastomosis. J Thorac Cardiovasc Surg 1995;110:1493–500; discussion 1500–1.
7. Alanezi K, Urschel JD. Mortality secondary to esophageal anastomotic leak. Ann Thorac Cardiovasc Surg 2004;10:71–5.
8. Lagarde SM, de Boer JD, ten Kate FJ, Busch OR, Obertop H, van Lanschot JJ. Postoperative complications after esophagectomy for adenocarcinoma of the esophagus are related to timing of death due to recurrence. Ann Surg 2008;247: 71–6.
9. Kim RH, Takabe K. Methods of esophagogastric anastomoses following esophagectomy for cancer: a systematic review. J Surg Oncol 2010;101:527–33.
10. Dewar L, Gelfand G, Finley RJ, Evans K, Inculet R, Nelems B. Factors affecting cervical anastomotic leak and stricture formation following esophagogastrectomy and gastric tube interposition. Am J Surg 1992;163:484–9.
11. Pham TH, Perry KA, Enestvedt CK, et al. Decreased conduit perfusion measured by spectroscopy is associated with anastomotic complications. Ann Thorac Surg 2011;91:380–5.
12. van Rossum PS, Haverkamp L, Verkooijen HM, van Leeuwen MS, van Hillegersberg R, Ruurda JP. Calcification of arteries supplying the gastric tube: a new risk factor for anastomotic leakage after esophageal surgery. Radiology 2015;274:124–32.
13. Boone J, Rinkes IB, van Leeuwen M, van Hillegersberg R. Diagnostic value of routine aqueous contrast swallow examination after oesophagectomy for detecting leakage of the cervical oesophagogastric anastomosis. ANZ J Surg 2008;78: 784–90.
14. Gondrie MJ, Mali WP, Jacobs PC, Oen AL, van der Graaf Y, PROVIDI Study Group. Cardiovascular disease: prediction with ancillary aortic findings on chest CT scans in routine practice. Radiology 2010;257:549–59.
15. Jacobi CA, Zieren HU, Zieren J, Muller JM. Is tissue oxygen tension during esophagectomy a predictor of esophagogastric anastomotic healing? J Surg Res 1998;74:161–4.
16. Komen N, Klitsie P, Dijk JW, et al. Calcium score: a new risk factor for colorectal anastomotic leakage. Am J Surg 2011;201: 759–65.
17. Zehetner J, DeMeester SR, Alicuben ET, et al. Intraoperative assessment of perfusion of the gastric graft and correlation with anastomotic leaks after esophagectomy. Ann Surg 2015;262:74–8.
18. Campbell C, Reames MK, Robinson M, Symanowski J, Salo JC. Conduit vascular evaluation is associated with reduction in anastomotic leak after esophagectomy. J Gastrointest Surg 2015;19:806–12.
19. Liebermann-Meffert DM, Meier R, Siewert JR. Vascular anatomy of the gastric tube used for esophageal reconstruction. Ann Thorac Surg 1992;54:1110–5.
20. Reavis KM, Chang EY, Hunter JG, Jobe BA. Utilization of the delay phenomenon improves blood flow and reduces collagen deposition in esophagogastric anastomoses. Ann Surg 2005;241:736–45; discussion 745–7.
21. Urschel JD, Antkowiak JG, Delacure MD, Takita H. Ischemic conditioning (delay phenomenon) improves esophagogastric anastomotic wound healing in the rat. J Surg Oncol 1997;66: 254–6.
22. Yetasook AK, Leung D, Howington JA, et al. Laparoscopic ischemic conditioning of the stomach prior to esophagectomy. Dis Esophagus 2013;26:479–86.
23. Diana M, Hubner M, Vuilleumier H, et al. Redistribution of gastric blood flow by embolization of gastric arteries before esophagectomy. Ann Thorac Surg 2011;91:1546–51.
24. Buunen M, Rooijens PP, Smaal HJ, et al. Vascular anatomy of the stomach related to gastric tube construction. Dis Esophagus 2008;21:272–4.
25. Kono K, Sugai H, Omata H, Fujii H. Transient bloodletting of the short gastric vein in the reconstructed gastric tube improves gastric microcirculation during esophagectomy. World J Surg 2007;31:780–4; discussion 785–6.
26. Sekido M, Yamamoto Y, Minakawa H, et al. Use of the "supercharge" technique in esophageal and pharyngeal reconstruction to augment microvascular blood flow. Surgery 2003;134:420–4.
27. Markar SR, Arya S, Karthikesalingam A, Hanna GB. Technical factors that affect anastomotic integrity following esophagectomy: systematic review and meta-analysis. Ann Surg Oncol 2013;20:4274–81.
28. Berkelmans GH, Kouwenhoven EA, Smeets BJ, et al. Diagnostic value of drain amylase for detecting intrathoracic leakage after esophagectomy. World J Gastroenterol 2015;21: 9118–25.
29. Maish MS, DeMeester SR, Choustoulakis E, et al. The safety and usefulness of endoscopy for evaluation of the graft and anastomosis early after esophagectomy and reconstruction. Surg Endosc 2005;19:1093–102.
30. Page RD, Asmat A, McShane J, Russell GN, Pennefather SH. Routine endoscopy to detect anastomotic leakage after esophagectomy. Ann Thorac Surg 2013;95:292–8.