



# Incidence and treatment of anastomotic leakage after esophagectomy in German acute care hospitals: a retrospective cohort study

Marie-Christin Weber, MD<sup>a</sup>, Nicolas Jorek, MD<sup>a</sup>, Philipp-Alexander Neumann, MD<sup>a</sup>, Jeannine Bachmann, MD<sup>a</sup>, Rebekka Dimpel, MD<sup>a</sup>, Marc Martignoni, MD<sup>a</sup>, Marcus Feith, MD<sup>a</sup>, Helmut Friess, MD<sup>a</sup>, Alexander Novotny, MD<sup>a</sup>, Maximilian Berlet, MD<sup>a</sup>, Daniel Reim, MD<sup>a,\*</sup>

**Background:** Anastomotic leakage (AL) is a major concern following esophagectomy due to the associated morbidity and mortality. The impact of hospital volume on postoperative outcomes after esophagectomy has previously been reported. The aim of this study was to analyze the current trends in postoperative anastomotic leakage and associated failure-to-rescue after esophagectomy in relation to hospital volume in German acute care hospitals using real-world data from the German Diagnosis-Related Groups (G-DRG) database.

**Materials and methods:** A retrospective secondary data analysis of the G-DRG database was performed for all in-hospital cases of patients undergoing esophagectomy from 2013 to 2021. AL and in-house mortality rates were assessed in relation to hospital case volume and endoscopic treatment modalities.

**Results:** The study included 32 335 cases. The mean reported AL rate was 17.1% with a mean failure-to-rescue rate of 18.9%. AL rates did not differ between hospitals with an annual case-volume  $\leq 25$  procedures/year vs.  $>25$  procedures/year (16.8% vs. 17.6%, OR 1.06,  $P = 0.07$ ). However, in high-volume centers ( $> 25$  procedures/year), in-hospital mortality for cases with AL (failure-to-rescue) was lower compared to medium-volume (10-25 cases/year) and low-volume (1-9 cases/year) centers (14.2% vs. 21.5% vs. 25.1%). The use of endoscopic vacuum therapy (EVT) increased over time, reaching 58.1% of AL cases in 2021 compared to 14.2% in 2013, while the use of self-expanding metal stents (SEMS) decreased from 37.0% in 2013 to 9.3% in 2021.

**Conclusions:** AL rates after esophagectomy remain high. In-house mortality is significantly lower in high-volume hospitals highlighting the importance to consider improvements in centralization of procedures. Further efforts are needed to reduce AL rates and improve outcomes after esophagectomy.

**Keywords:** anastomotic healing, anastomotic leakage, esophagectomy, EVT, failure-to-rescue, gastrectomy, hospital volume, SEMS

## Introduction

Anastomotic leakage (AL) is one of the most common but also most detrimental surgical complications following esophagectomy for esophageal cancer. In addition to reducing the risk of postoperative respiratory and cardiac complications, the promotion of

intact anastomotic healing and successful management of AL significantly determine postoperative outcomes<sup>[1,2]</sup>.

Reported AL rates in larger cohort studies and meta-analyses range from 6.3% to 19%<sup>[3-8]</sup>. AL is most commonly treated endoscopically with self-expanding metal stents (SEMS) or endoscopic vacuum therapy (EVT). EVT is increasingly being used, but recent meta-analyses show inconclusive results on whether its use is associated with reduced postoperative mortality<sup>[9,10]</sup>. Hence, prospective data from randomized controlled trials are still lacking.

Since the early 2000s, an inverse relationship between center-volume and postoperative mortality rates for esophagectomies has been apparent, with lower mortality rates in high-volume centers compared to low-volume centers<sup>[11-13]</sup>. More recent publications have repetitively shown similar results<sup>[14-16]</sup>. Using German population-based hospital reimbursement data, Nimptsch *et al* demonstrated that reduced postoperative mortality in high-volume centers is not related to an overall reduction in postoperative complications, but rather to the overall management of cases with postoperative complications<sup>[17]</sup>. As such, the Federal Joint Committee (Gemeinsamer Bundesausschuss, GBA), the highest decision-making joint self-government institution of German physicians, hospitals, and insurance funds, increased the minimum center volumes for complex esophageal surgeries/esophagectomies from  $>10$  to  $>25$  cases per year in 2023. However,

<sup>a</sup>Department of Surgery, Technical University of Munich, TUM School of Medicine and Health, TUM University Hospital, Klinikum rechts der Isar, Munich, Germany

Marie-Christin Weber and Nicolas Jorek contributed equally to this study. Maximilian Berlet and Daniel Reim contributed equally as co-senior authors.

\*Corresponding author. Address: Department of Surgery, Technical University of Munich, TUM University Hospital, Ismaninger Str. 22, 81675 Munich, Germany. Tel.: +49 89 4140 5019. E-mail: daniel.reim@tum.de (Daniel Reim).

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution-ShareAlike License 4.0, which allows others to remix, tweak, and build upon the work, even for commercial purposes, as long as the author is credited and the new creations are licensed under the identical terms.

International Journal of Surgery (2025) 111:2953–2961

Received 1 August 2024; Accepted 9 January 2025

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, [www.ijso.com/international-journal-of-surgery](http://www.ijso.com/international-journal-of-surgery).

Published online 29 January 2025

<http://dx.doi.org/10.1097/JS9.0000000000002274>

centralization of complex surgical procedures is not always easy to implement, especially with regard to patient interests (easier access to local hospitals, etc.) and missing infrastructure of high-volume centers to manage increasing case volumes. In consideration of the current change in surgical techniques in esophageal resections with a shift from open surgery to laparoscopic and robotic-assisted procedures, there is a knowledge gap regarding the development of AL rates, associated mortality/failure-to-rescue, and their correlation with hospital volume. In particular, nationwide real-world data that not only cover cases operated on in large centers and university hospitals are currently not available for European countries and Germany specifically. Closing this knowledge gap may be of great importance in order to evaluate the effects of previous attempts to centralize esophageal surgery in Germany and to draw possible consequences for the further enforcement of centralization of complex esophageal surgeries.

To gain more detailed information on this complex relationship between hospital volume, AL, and postoperative in-house mortality/failure-to-rescue, we performed a nationwide population-based study on AL after esophagectomy based on the German hospital reimbursement database (German Diagnosis-Related Groups (G-DRG) database). The focus of this study was also on current trends in endoscopic management of AL after esophagectomy and the assessment of the impact of SEMs and EVT.

## Methods

### Data access

Commonly accepted methods of secondary data analysis to approach the epidemiologic analysis of postoperative complications using data from the G-DRG database have been described in detail previously<sup>[18–21]</sup>. To summarize, the German Diagnosis-Related Groups (G-DRG) statistics provide a complete overview of hospital reimbursement data for all inpatient cases of every German acute care hospital. Data can be retrieved by remote-controlled data access through the Federal Statistical Office (DESTATIS). The G-DRG database contains non-longitudinal data on individual treatment cases from all acute care hospitals in Germany. The database contains case information including ICD (International Classification of Diseases)- and OPS (Operation and Procedure Classification System)-codes, data on the mode of discharge including in-house mortality, length of hospital stay, hospital reimbursement volume, and other hospital-related data per individual case.

The source code for the G-DRG database query was generated using the SAS programming language (SAS Base version 9.4), in accordance with the specifications as required by DESTATIS. Data were obtained for each year queried via remote-controlled data processing and delivered in aggregated form<sup>[22]</sup>. Study design, data analysis, and reporting were performed according to the recommendations of the Good Practice of Secondary Data Analysis (GPS), the German Reporting Standard for Secondary Data Analyses (STROSA) guidelines, and the STROCSS guidelines<sup>[23–25]</sup>. No ethics committee statement is required for the secondary data analysis used in this study. To ensure data protection, DESTATIS obscures case numbers  $\leq 2$ , making them inaccessible to the authors.

### Patient criteria

All inpatient cases undergoing complex esophageal surgery with reconstruction (esophagectomy and esophagogastrectomy) between 2013 and 2021 in German acute care hospitals defined by the OPS-codes 5-424, 5-426, 5-427.0, 5-427.1, 5-438.0, and 5-438.1 (according to the definition by the Federal Joint Committee, GBA) were included for secondary data analysis. A detailed description of the OPS codes is provided in the Supplemental Online Material (Table S1, <http://links.lww.com/JS9/D811>).

Robotic-assisted procedures were defined by the additional OPS code 5-987.

Primary outcomes were AL (K91.83) and in-house mortality rates in relation to the hospital volume and the use of endoscopic procedures. Hospital volume was defined by the number of cases of complex esophageal surgery with reconstruction per year, as defined above. Three categories were defined:  $\leq 9$  cases/year (low-volume centers), 10–25 cases/year (medium-volume centers), and  $>25$  cases/year (high-volume centers) according to the old ( $>10$  cases/year) and the new ( $>25$  cases/year) minimum volume standard defined by the German Federal Joint Committee. The use of endoscopic vacuum therapy (EVT) and endoscopic stenting (self-expandable metal stents, SEMs) as a secondary outcome was defined by the OPS-codes 5-916.a and 5-429.j.

Secondary outcomes were the case mix reimbursement volume (mean hospital reimbursement sum per case) and the length of hospital stay. The Charlson Comorbidity Index (CCI) was used for the assessment of general comorbidity<sup>[26]</sup>. Additionally, secondary diagnoses, diabetes (E11.-), obesity (E66.-), cachexia (R64), hypertension (I10.-), chronic kidney disease (N18.-), chronic heart disease (I25.-), COPD/Emphysema (J43.-; J44.-), and asthma (J45) were assessed individually for their relation to AL rates (Table S1, <http://links.lww.com/JS9/D811>).

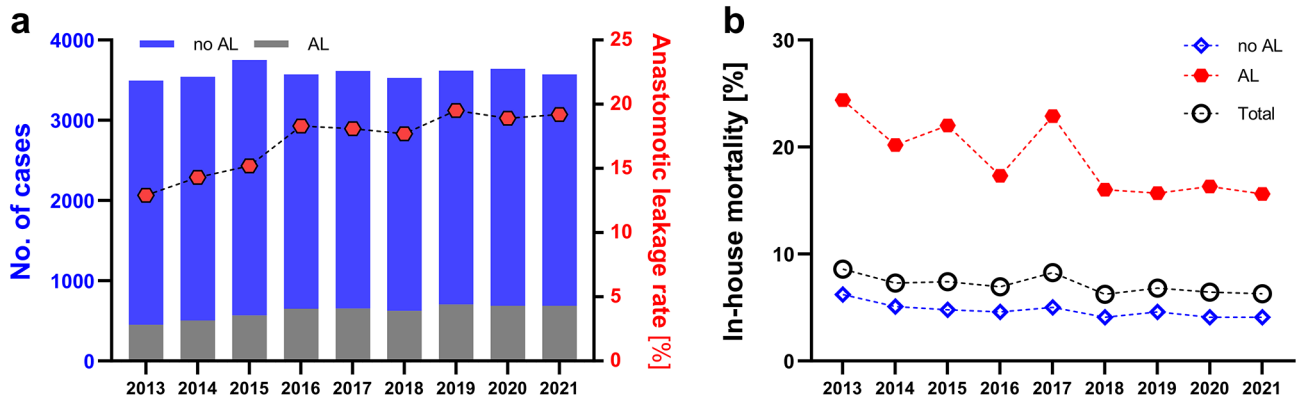
### Statistical analysis

Data visualization and statistical analysis were performed using GraphPad Prism (Version 10.1.0, GraphPad Software, CA, USA). Data were analyzed for each year, as only yearly statistics can be retrieved from the G-DRG database. AL and in-hospital mortality rates are presented as relative frequencies for each subgroup of patient cases per year as depicted in the graphs. Statistical tests were applied as described in the table and figure legends. A  $P$ -value  $<0.05$  was considered as statistically significant.

## Results

### General anastomotic leakage rates

A total number of 32 335 cases with esophagectomy were identified by the data query and included in the study. Case numbers for esophagectomy were stable over the study period from 2013 to 2021 with a mean of 3593 cases per year (3496 in 2013 and 3572 in 2021) (Fig. 1a, Table 1). The mean reported AL rate was  $17.1\% \pm 2.4\%$  (Table 1). From 2013 to 2016, reported AL rates were increasing as the ICD code K91.83 for AL was only introduced in the G-DRG database in 2013. From 2016 to 2021, reported AL rates per year ranged from 18.3% to 19.5% with



**Figure 1.** Case numbers, anastomotic leakage, and in-house mortality rates after esophagectomy. (a) Number of cases without (blue) and with anastomotic leakage (AL) per year (left y-axis) and mean AL rates per year (red, right y-axis). (b) In-house mortality rates per year for cases without AL (blue), with AL (red), and the total number of cases per year (black).

a mean AL rate of 18.6% (Fig. 1a, Table 1). In-house mortality rates were more than three-fold higher in cases with AL than in cases without AL with a mean in-house mortality rate of 4.7% in cases without AL and 18.9% in cases with AL (Fig. 1b). The mean in-house mortality rate for all cases analyzed in this study was 7.1%. The overall in-house mortality rates decreased from 8.6% in 2013 to 6.3% in 2021.

We analyzed relevant secondary diagnoses in relation to AL and in-house mortality rates. Diabetes (OR 1.17,  $P = 0.0008$ ), obesity (OR 1.34,  $P < 0.0001$ ), hypertension (OR 1.16,  $P < 0.0001$ ), chronic kidney disease (OR 1.35,  $P < 0.0001$ ), and chronic heart disease (OR 1.21,  $P = 0.0005$ ) as secondary diagnoses showed statistically significant association with AL. Meanwhile, diabetes (OR 1.38,  $P < 0.0001$ ), cachexia (OR 1.47,  $P < 0.001$ ), chronic kidney disease (OR 2.72,  $P < 0.0001$ ), chronic heart disease (OR 1.94,  $P < 0.0001$ ), and COPD/emphysema (OR 1.79,  $P < 0.0001$ ) as secondary diagnoses showed a statistically significant association with in-house mortality (Table S3, <http://links.lww.com/JS9/D811>).

Unfortunately, the use of laparoscopic surgical techniques during esophagectomy is not represented in the G-DRG system and is thus not available for analysis in this study. However, the use of robotic assistance systems during surgery is represented by the OPS-code 5-987.0. The number of esophagectomies performed with a robotic assistance system was 3 (0.1%) in 2013 and 741 (20.7%) in 2021 (Fig. S1a, <http://links.lww.com/JS9/D811>). AL rates for esophagectomies performed with a robotic assistance system were available from 2014. However, reported AL rates were substantially higher in robotic procedures than in those without robotic assistance from 2014 to 2016 (29.6–32.0% vs. 14.2–18%) (Fig. S1a, <http://links.lww.com/JS9/D811>, Table S3, <http://links.lww.com/JS9/D811>). AL rates for robotic esophagectomy decreased in 2015 but were still higher than for non-robotic esophagectomy until the end of the study period in 2021 (22.9% vs. 18.3%) (Fig. S1b, <http://links.lww.com/JS9/D811>).

#### Anastomotic leakage and mortality rates in relation to hospital case volume

The mean AL rates were similar in all three categories of hospital case volume with a mean AL rate of 16.9% in low-volume

centers ( $\leq 9$  cases/year), 16.8% in medium-volume centers (10–25 cases/year), and 17.6% in high-volume centers ( $> 25$  cases/year) (Fig. 2a, Table 1). However, when looking at the related in-house mortality rates, mortality was considerably lower in high-volume centers for both cases with and without AL (Fig. 2b). The mean in-house mortality rates for cases with AL were 25.1% in low-volume, 21.5% in medium-volume, and 14.2% in high-volume centers. Even in cases without AL, in-house mortality was lower in high-volume centers with the mean in-house mortality rates for cases without AL of 7.0% in low-volume, 5.1% in medium-volume, and 3.5% in high-volume centers. When comparing AL and in-house mortality rates between hospitals with an annual case volume  $\leq 25$  cases/year and  $> 25$  cases/year, the AL rate was not statistically significantly different (16.8% vs. 17.6%, OR 1.06,  $P = 0.07$ ), whereas mortality rates were significantly lower in hospitals  $> 25$  cases/year (8.5% vs. 5.3%, OR 0.60,  $P < 0.0001$ ) (Table 2). Even though a minimal center volume of 10 cases per year was introduced in Germany by the GBA in 2006, a high percentage of cases were still operated on in low-volume centers (26.3% in 2013, 14.8% in 2021, Fig. 2c). The CCI as a measure for general comorbidity was higher in low-volume centers than in high-volume centers with a mean CCI of  $3.8 \pm 0.22$  in low,  $3.7 \pm 0.11$  in medium, and  $3.6 \pm 0.11$  in high-volume centers for cases with AL (Fig. 2d).

#### Endoscopic management

Regarding endoscopic management of AL, cases with AL and EVT, SEMS, a combination of EVT and SEMS, and no coded endoscopic treatment were analyzed. A considerable increase in the use of EVT was seen, and 14.2% of AL cases were treated with EVT in 2013 and 58.1% in 2021. Accordingly, case numbers with SEMS treatment for AL decreased from 37.9% in 2013 to 9.3% in 2021. Cases in which both procedures were performed increased from 7.1% in 2013 to 17.8% in 2021. Cases in which none of these procedures were documented decreased from 41.7% in 2013 to 14.8% in 2021 (Fig. 3a). Mortality rates in cases with EVT showed a steady decrease during the study period with a mortality rate of 25.0% in 2013 and 12.3% in 2021 (Fig. 3b). Trends toward lower mortality rates for the other treatment modalities were not obvious.

**Table 1**  
**Overview of anastomotic leakage (AL) rates per year regarding center volume**

| Year             | Total number of surgeries | Center volume |                  |                |
|------------------|---------------------------|---------------|------------------|----------------|
|                  |                           | ≤9 cases/year | 10–25 cases/year | >25 cases/year |
| 2013–2021        |                           |               |                  |                |
| <i>n</i> (total) | 32 335                    | 6265          | 13 094           | 12 976         |
| <i>n</i> (AL)    | 5540                      | 1057          | 2198             | 2285           |
| AL rate          | 17.1%                     | 16.9%         | 16.8%            | 17.6%          |
| 2013             |                           |               |                  |                |
| <i>n</i> (total) | 3496                      | 955           | 1448             | 1093           |
| <i>n</i> (AL)    | 451                       | 115           | 189              | 147            |
| AL rate          | 12.9%                     | 12.0%         | 13.1%            | 13.4%          |
| 2014             |                           |               |                  |                |
| <i>n</i> (total) | 3543                      | 923           | 1301             | 1319           |
| <i>n</i> (AL)    | 506                       | 127           | 192              | 187            |
| AL rate          | 14.3%                     | 13.8%         | 14.8%            | 14.2%          |
| 2015             |                           |               |                  |                |
| <i>n</i> (total) | 3752                      | 832           | 1581             | 1339           |
| <i>n</i> (AL)    | 569                       | 139           | 229              | 201            |
| AL rate          | 15.2%                     | 16.7%         | 14.5%            | 15.0%          |
| 2016             |                           |               |                  |                |
| <i>n</i> (total) | 3573                      | 695           | 1524             | 1354           |
| <i>n</i> (AL)    | 653                       | 122           | 290              | 241            |
| AL rate          | 18.3%                     | 17.6%         | 19.0%            | 17.8%          |
| 2017             |                           |               |                  |                |
| <i>n</i> (total) | 3614                      | 662           | 1489             | 1463           |
| <i>n</i> (AL)    | 654                       | 127           | 270              | 257            |
| AL rate          | 18.1%                     | 19.2%         | 18.1%            | 17.6%          |
| 2018             |                           |               |                  |                |
| <i>n</i> (total) | 3527                      | 578           | 1423             | 1526           |
| <i>n</i> (AL)    | 626                       | 111           | 248              | 267            |
| AL rate          | 17.7%                     | 19.2%         | 17.4%            | 17.5%          |
| 2019             |                           |               |                  |                |
| <i>n</i> (total) | 3617                      | 578           | 1469             | 1570           |
| <i>n</i> (AL)    | 705                       | 113           | 265              | 327            |
| AL rate          | 19.5%                     | 19.6%         | 18.0%            | 20.8%          |
| 2020             |                           |               |                  |                |
| <i>n</i> (total) | 3641                      | 512           | 1461             | 1668           |
| <i>n</i> (AL)    | 689                       | 102           | 261              | 326            |
| AL rate          | 18.9%                     | 19.9%         | 17.9%            | 17.9%          |
| 2021             |                           |               |                  |                |
| <i>n</i> (total) | 3572                      | 530           | 1398             | 1644           |
| <i>n</i> (AL)    | 687                       | 101           | 254              | 332            |
| AL rate          | 19.2%                     | 19.1%         | 18.2%            | 20.2%          |

The use of EVT increased over time for the entire study population, with the highest rates of use in high-volume centers and the lowest rates in low-volume centers (Fig. 3c). Mortality in cases treated with EVT differed according to the center volume. While mortality rates were stable in high-volume centers (16.0% in 2013, 14.3% in 2020), mortality decreased from 29.6% in 2013 to 18.0% in 2020 in medium-volume centers for cases with EVT (Fig. 3c).

Inversely to the use of EVT, application rates of SEMS were highest in low-volume centers and lowest in high-volume centers (Fig. 3d). In-house mortality rates for cases with AL and the application of SEMS were lowest in high-volume centers (Fig. 3d).

As described above, the number of cases in which the use of neither EVT nor SEMS was documented decreased over the

study period, with no obvious difference between centre volumes (Fig. 3e).

The combination or consecutive application of EVT and SEMS was most commonly applied in medium- and high-volume centers, while mortality again was lowest in high-volume centers (Fig. 3f).

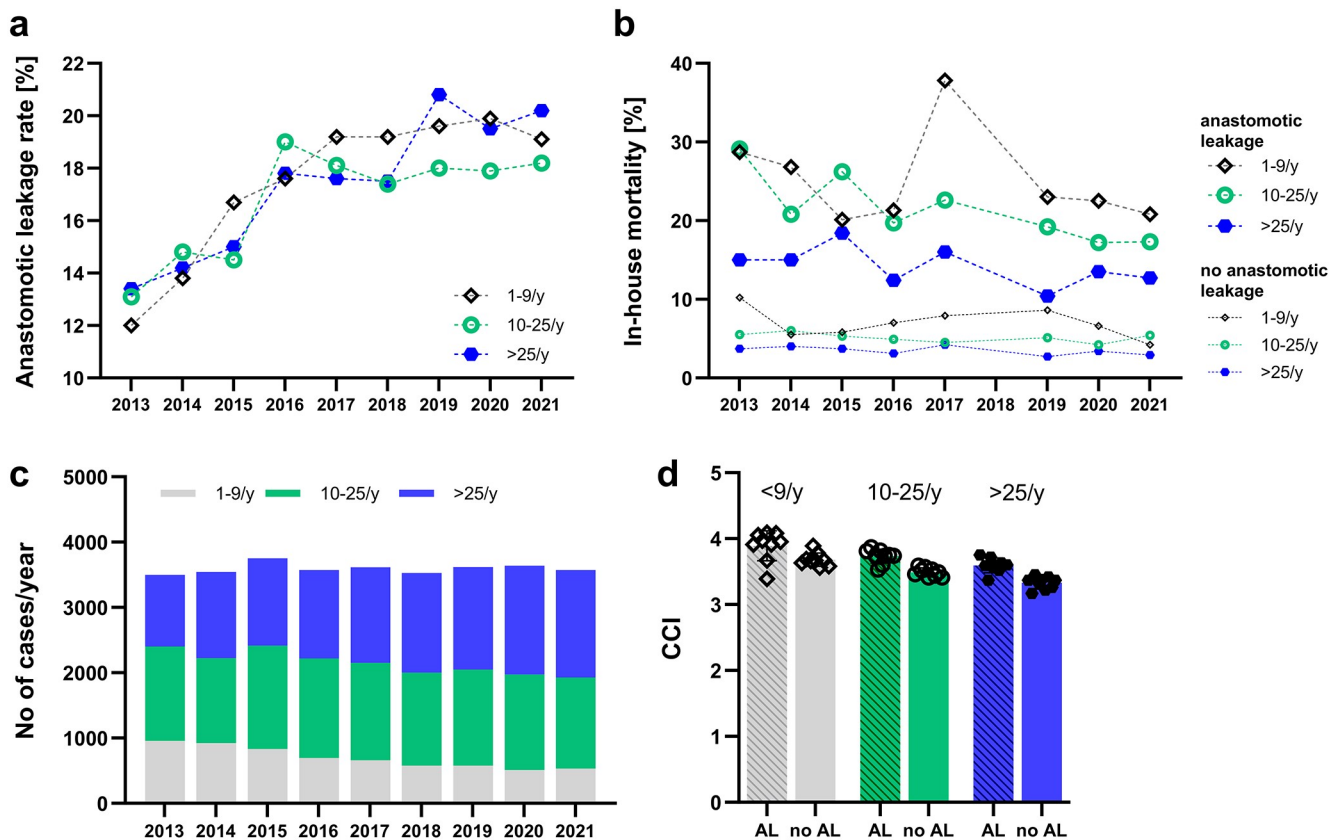
#### Hospital length of stay and socioeconomic costs

As expected, the hospital length of stay was generally longer in cases with AL compared to cases without AL. In cases without AL, a trend toward shorter hospital stays was seen for all center sizes (mean length of hospital stay: low-volume centers: 25.9 days in 2013, 26.5 days in 2016, 22.9 days in 2021; medium-volume centers: 27.5 days in 2013, 24.4 days and 22.0 days in 2021; high-volume centers: 25.5 days in 2013, 23.5 days in 2016, and 19.8 days in 2021; Fig. S2a, <http://links.lww.com/JS9/D811>). For patients with AL, only in high-volume centers, a discernible decrease in the length of hospital stay was observed with a mean length of hospital stay of 51.1 days in 2013 and 43.6 days in 2021 (Fig. S2a, <http://links.lww.com/JS9/D811>). The mean hospital reimbursement from 2013 to 2021 was €55 738 per case for cases with AL, while the mean hospital reimbursement for cases without AL was €26 267 per case (Fig. S2b, <http://links.lww.com/JS9/D811>).

We calculated the hypothetical savings if no AL would occur after esophagectomy (Table S4, <http://links.lww.com/JS9/D811>). By preventing AL, the hypothetical annual savings would have been between 10 956 860 and 25 081 476 Euro (mean 18 116 720 Euro) (Table S4, <http://links.lww.com/JS9/D811>).

#### Discussion

We present here the first secondary data analysis of nationwide hospital reimbursement data for esophagectomy in Germany with regard to AL. We focused on in-hospital mortality associated with AL and recent developments in endoscopic treatment of AL related to annual hospital case volume. The unique feature of this study is that there is no selection bias, as all hospital cases in Germany were included, not only cases from certified centers or academic hospitals. Briefly summarized, the data show that AL rates are not dependent on hospital volume for esophagectomy when comparing hospitals with an annual volume of ≤ 25 cases to hospitals with >25 cases per year (OR 1.06, 95% CI 0.99–1.12,  $P = 0.07$ ); however, in-hospital mortality is significantly lower in high-volume centers with >25 cases per year (OR 0.60, 95% CI 0.54–0.66,  $P < 0.0001$ ; Table 2). However, it is noted that reported AL rates are still disproportionately high in the study population with a mean reported AL of 19.2% in 2021. Still, overall mortality rates decreased during the study period (8.6% in 2013 to 6.3% in 2021); however, in cases with AL, the mean in-house mortality was about three times higher than in cases without AL (18.9% vs. 4.7%). The association of yearly hospital case volume and in-house mortality rates has been reported previously by Nimptsch and colleagues<sup>[17]</sup> who also used a secondary data analysis of the G-DRG database. Based on their results, the minimum required yearly volume of complex esophageal surgeries has been increased by the GBA from 10 to 26 recently. However, in their analysis, they were only able to evaluate AL as a specific postoperative complication indirectly by analyzing the number of endoscopic interventions



**Figure 2.** Anastomotic leakage and in-house mortality in relation to hospital case volume. (a) Anastomotic leakage (AL) rates per year for low volume centers ( $\leq 9$  cases/year, black rhombus), medium volume centers (10–25 cases/year, green circle), and high-volume centers ( $> 25$  cases/year, blue hexagon). (b) In-house mortality rates for low-, medium-, and high-volume centers and for cases with AL (large symbols) and without AL (small symbols). Data for 2018 not available. (c) Total number of cases per year treated in low-, medium-, and high-volume centers. (d) Charlson Comorbidity Index (CCI). Bars show the mean CCI for low-, medium-, and high-volume centers, and cases with and without anastomotic leakage. Dots are the mean CCI for each year 2013–2021.

as the ICD code for anastomotic leakage was only introduced to the German DRG system in 2013, highlighting the added value of our study to the topic.

Failure to rescue, defined as the mortality of patients with major postoperative complications such as AL, has emerged as an indicator of the quality of postoperative care. It is increasingly used to describe relationships between hospital volume and postoperative outcomes<sup>[27]</sup>. The mean in-house mortality rate for cases with AL (failure-to-rescue rate) in the present study was 18.9% with an inverse correlation regarding hospital volume. Abdelsattar *et al* reported a similar failure-to-rescue rate of 18.5% based on a major complication rate after esophagectomy of 26.6% from a retrospective analysis of 26 820 patients from the American Agency for Healthcare Research and Quality Nationwide Readmission Database; however, they did not report on specific failure-to-rescue rates with regard to AL<sup>[28]</sup>. Harris *et al* also reported a failure-to-rescue rate after esophagectomy of 11% in esophagectomy-targeted vs. 17% in standard hospitals based on the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) esophagectomy-targeted registry demonstrating a lower failure-to-rescue rate in hospitals participating in the NSQIP esophagectomy-targeted registry<sup>[29]</sup>. In a multicenter, retrospective cohort study including 1509 patients led by the TENTACLE–

Esophagus study group, the failure-to-rescue rate after AL was 11.7%, with a lower failure-to-rescue rate in middle- and high-volume centers<sup>[30]</sup>. Endoscopic treatment is the preferred therapeutic modality to treat cases with AL when revision surgery can be avoided and when aiming to preserve the anastomosis. Since 2012, EVT has been increasingly applied for the management of AL after esophagectomy in Germany and has even been applied as a preventative method to reduce the risk of AL in high-risk patients<sup>[31,32]</sup>. In our data analysis, we found that the use of EVT increased from 14.2% of cases with AL in 2013 to 58.1% of cases in 2021. Correspondingly, the percentage of cases with AL treated with SEMS or with neither EVT nor SEMS decreased (Fig. 3A). One could speculate that the addition of EVT to the potential rescue options and its increasing use for cases with AL may be associated with a decrease in all-cause and AL-related in-hospital mortality, but causal conclusions cannot be drawn from the present data. Due to the retrospective nature of the dataset analyzed in the study and the missing information on a variety of other possible causes of decreased mortality, such as strategies to detect AL, use of conservative treatment options (antibiotics, parenteral nutrition, etc.), and severity of leakage, reliable conclusions about a true causal relationship between the use of EVT and decreased mortality cannot be made based on the DRG statistics data.

**Table 2**  
**Risk of anastomotic leakage and in-house mortality in relation to center volume**

| Year             | Center volume (cases/ year) | Anastomotic leakage |        |      |           |                | In-house mortality (all cases, with + without anastomotic leakage) |        |      |           |                   |
|------------------|-----------------------------|---------------------|--------|------|-----------|----------------|--|--------|------|-----------|-------------------|
|                  |                             | YES [n, (%)]        | NO [n] | OR   | 95% CI    | P <sup>a</sup> | YES [n] [n, (%)]   | NO [n] | OR   | 95% CI    | P <sup>a</sup>    |
| <b>2013-2021</b> | <b>&gt;25</b>               | 2285 (17.6)         | 10 691 | 1.06 | 0.99–1.12 | 0.07           | 603 (5.3)  | 10 847 | 0.60 | 0.54–0.66 | <b>&lt;0.0001</b> |
|                  | <b>≤25</b>                  | 3255 (16.8)         | 16 104 |      |           |                | 1484 (8.5)   | 15 874 |      |           |                   |
| 2013             | <b>&gt;25</b>               | 147 (13.4)          | 946    | 1.07 | 0.86–1.33 | 0.55           | 57 (5.2)   | 1036   | 0.49 | 0.36–0.66 | <b>&lt;0.0001</b> |
|                  | <b>≤25</b>                  | 304 (12.7)          | 2099   |      |           |                | 243 (10.1)   | 2160   |      |           |                   |
| 2014             | <b>&gt;25</b>               | 187 (14.2)          | 1132   | 0.99 | 0.81–1.20 | 0.93           | 73 (5.5)   | 1246   | 0.65 | 0.48–0.86 | <b>0.003</b>      |
|                  | <b>≤25</b>                  | 319 (14.3)          | 1905   |      |           |                | 185 (8.3)  | 2039   |      |           |                   |
| 2015             | <b>&gt;25</b>               | 201 (15.0)          | 1138   | 0.98 | 0.81–1.19 | 0.88           | 79 (5.9)   | 1260   | 0.70 | 0.53–0.92 | <b>0.01</b>       |
|                  | <b>≤25</b>                  | 368 (15.3)          | 2045   |      |           |                | 199 (8.2)  | 2214   |      |           |                   |
| 2016             | <b>&gt;25</b>               | 241 (17.8)          | 1113   | 0.95 | 0.79–1.14 | 0.6            | 65 (4.8)   | 1289   | 0.56 | 0.41–0.76 | <b>0.0001</b>     |
|                  | <b>≤25</b>                  | 412 (18.6)          | 1807   |      |           |                | 183 (8.2)  | 2036   |      |           |                   |
| 2017             | <b>&gt;25</b>               | 257 (17.6)          | 1206   | 0.94 | 0.79–1.12 | 0.52           | 92 (6.3)   | 1371   | 0.63 | 0.49–0.82 | <b>0.0005</b>     |
|                  | <b>≤25</b>                  | 397 (18.5)          | 1754   |      |           |                | 206 (9.6)  | 1945   |      |           |                   |
| 2018             | <b>&gt;25</b>               | 267 (17.5)          | 1259   | 0.97 | 0.81–1.16 | 0.77           | n/a  | n/a    | n/a  | n/a       | n/a               |
|                  | <b>≤25</b>                  | 359 (17.9)          | 1642   |      |           |                | n/a  | n/a    |      |           |                   |
| 2019             | <b>&gt;25</b>               | 327 (20.8)          | 1243   | 1.16 | 0.98–1.38 | 0.08           | 68 (4.3)   | 1502   | 0.48 | 0.35–0.64 | <b>&lt;0.0001</b> |
|                  | <b>≤25</b>                  | 378 (18.5)          | 1669   |      |           |                | 178 (8.7)  | 1869   |      |           |                   |
| 2020             | <b>&gt;25</b>               | 326 (19.5)          | 1342   | 1.08 | 0.91–1.28 | 0.4            | 89 (5.3)   | 1579   | 0.71 | 0.54–0.94 | <b>0.02</b>       |
|                  | <b>≤25</b>                  | 363 (18.4)          | 1610   |      |           |                | 145 (7.3)  | 1828   |      |           |                   |
| 2021             | <b>&gt;25</b>               | 332 (20.2)          | 1312   | 1.12 | 0.95–1.33 | 0.19           | 80 (4.9)   | 1564   | 0.63 | 0.47–0.84 | <b>0.001</b>      |
|                  | <b>≤25</b>                  | 355 (18.4)          | 1573   |      |           |                | 145 (7.5)  | 1783   |      |           |                   |

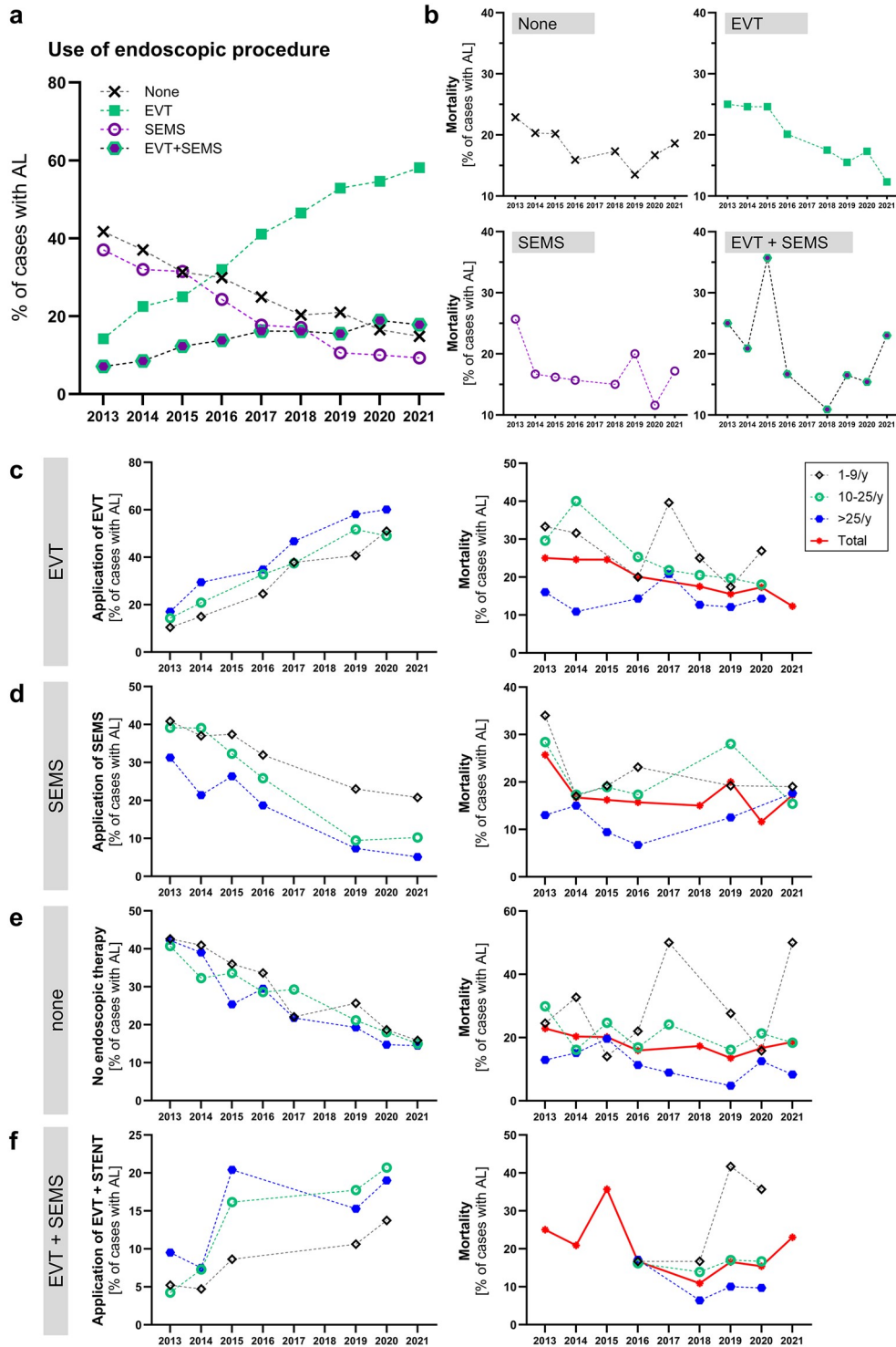
<sup>a</sup>Chi-square test, significant values are highlighted by bold text.

Two meta-analyses have analyzed several retrospective studies comparing EVT and SEMS with regard to the treatment success for AL after esophagectomy<sup>[9,10]</sup>. Only the first showed an advantage of EVT over SEMS regarding mortality rates. Regarding these data, it would be highly speculative (as mentioned in the original manuscript) to draw causal conclusions about the association between the use of EVT and an overall reduction of in-hospital mortality from the data presented in the present study. This only underlines the need to conduct high-quality prospective, multi-center randomized controlled trials on the effect of endoscopic rescue procedures and failure to rescue after esophagectomy. Interestingly, however, the increased application of EVT did not lead to an increase in the length of hospital stay, which actually decreased during the study period Supplemental Online Material (Figure S2a, <http://links.lww.com/JS9/D811>). For robot-assisted esophagectomies, AL rates were significantly higher from 2014 to 2016 and then decreased in 2017 to levels similar to those for non-robot-assisted esophagectomies (Table S3, <http://links.lww.com/JS9/D811>, Figure S1, <http://links.lww.com/JS9/D811>). However, at the end of the study period in 2021, AL rates were still higher for robotic-assisted esophagectomies (22.9% vs. 18.3%; Table S3, <http://links.lww.com/JS9/D811>). The high AL rates during the introduction of robotic surgery can most likely be attributed to the learning curve of the new surgical procedure, but the robotic approach did not lead to an overall decrease in AL rates. To our knowledge, real-world data comparing AL rates from robotic-assisted vs. conventional (open, minimally-invasive) esophagectomies have not been reported yet. Meta-analysis comparing robotic-assisted with minimally-invasive approaches did not show differences in AL rates<sup>[33,34]</sup>. This highlights the importance of reporting real-world data using nationwide statistical data. In addition, the data suggest that there may be value in considering national quality control

measures, particularly when introducing novel surgical techniques such as robotic surgery for procedures with inherent complexity, such as esophageal surgery. This could help ensure that optimal patient care is consistently provided.

### Limitations

Despite the advantage of excluding selection bias for reported cases, there are several limitations to the study, as discussed in the following. Although this data analysis includes all inpatient cases treated in a German acute care hospital and thus represents a large study population, it has some limitations, as previously reported<sup>[35]</sup>. A major disadvantage of the type of data analyzed is that the analysis is based on hospital reimbursement data and not on individual longitudinal analysis of individual patient cases. As such, individual patient outcomes such as successful treatment of AL and cancer-specific data cannot be analyzed. In addition, information on the general condition of the patients or the severity of the infection after the leakage, the timing of the rescue treatment and the sequential strategy for the rescue cannot be derived from the data set. As previously reported, this type of data analysis has an inherent risk for under- or overreporting of certain ICD codes and different coding practices in individual hospitals. However, the risk of over- and underreporting is reduced through external validation through the Health Insurance Medical Services (to avoid overreporting to avoid additional costs for health insurance providers) and internal validation by hospital documentation staff (to avoid underreporting to avoid financial losses for individual hospitals). As there is no specific code for revision surgery during the initial hospital stay, rates for revision surgery after esophagectomy and associated mortality could not be analyzed in this study.



**Figure 3.** Endoscopic management of anastomotic leakage. (a) Application rates for endoscopic vacuum therapy (EVT, green squares), endoscopic stenting (SEMS, purple circle), a combination or consecutive use of EVT and SEMS (hexagon), and no documented specific endoscopic treatment (diagonal cross) per year in cases with anastomotic leakage (AL). (b) In-house mortality rates for cases with AL and specific endoscopic management. (c) Application rates of EVT in cases with AL according to hospital case volume (low-volume centers  $\leq 9$  cases/year, black rhombus), medium-volume centers (10–25 cases/year, green circle), and high-volume centers ( $>25$  cases/year, blue hexagon). (d) Application rates of SEMS in cases with AL according to hospital case volume. (e) No specific endoscopic therapy coded in cases with AL according to hospital case volume. (f) Application rates of EVT and SEMS in cases with AL according to hospital case volume.

## Conclusions

To conclude, the present data reveal that AL rates remain very high with no improvement over a 9-year period. In-house mortality is slowly decreasing. Despite the known risk reduction regarding in-house mortality by centralization of complex surgeries such as esophagectomies, more than half of the patients are still treated in low- and medium-volume centers.

Despite the challenges of centralizing certain surgical procedures, it would be an effective option to reduce overall mortality after esophagectomy in Germany, and our data underscore the importance of pursuing centralization efforts led by central health care administrators in Germany and other countries with comparable health care systems.

Given the alarmingly high rates of AL, future research must focus on further improving the technical surgical aspects of anastomosis formation but also invest in understanding the biology of anastomotic healing itself to prevent postoperative pathological processes leading to AL. In addition, efforts must be made to optimize treatment strategies for severe complications such as AL to improve patient outcomes even in settings where centralization is not feasible for reasons such as availability and access to care for patients requiring esophagectomy.”

## Ethical approval

No ethics committee statement is required for the secondary data analysis based on data provided by the Federal Statistical Office Germany (DESTATIS) used in this study. To ensure data protection, DESTATIS obscures case numbers  $\leq 2$ , making them inaccessible to the authors.

## Consent

Not applicable.

## Sources of funding

All the authors declare to have received no financial support or sponsorship for this study.

## Author contributions

Conceptualization: M.C.W., N.J., A.N., M.B., D.R.; Data curation: M.C.W., N.J., M.B., D.R.; Formal Analysis: M.C.W., N.J., M.B.; Methodology: M.C.W., M.B.; Software: M.C.W., M.B.; Supervision: P.A.N., J.B., R.D., M.M., MF, H.F., A.N., D.R.; Validation: P.A.N., A.N., D.R.; Visualization: M.C.W.; Writing – original draft: M.C.W., N.J., M.B.; Writing – review & editing: A.N., J.B., R.D., M.M., MF, H.F., A.N., D.R.

## Conflicts of interest disclosure

All the authors declare to have no conflicts of interest relevant to this study.

## Research registration unique identifying number (UIN)

Not applicable.

## Guarantor

Marie-Christin Weber, Maximilian Berlet, and Daniel Reim.

## Provenance and peer review

The paper was not invited.

## Data sharing statement

The SAS code that was used to request data from the German Federal Statistical Office (DESTATIS) can be requested through the corresponding author.

## Acknowledgements

No third-party funding was required for this study.

## Assistance with the study

None.

## Presentation

Preliminary data was presented at “Deutscher Chirurgie Kongress” (DCK) 2024, Leipzig.

## References

- [1] Low DE, Kuppusamy MK, Alderson D, *et al.* Benchmarking complications associated with esophagectomy. *Ann Surg* 2019;269:291–98.
- [2] Bachmann J, Feith M, Schlag C, *et al.* Anastomotic leakage following resection of the esophagus-introduction of an endoscopic grading system. *World J Surg Oncol* 2022;20:104.
- [3] Kamarajah SK, 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:doz089.
- [4] Kassis ES, Kosinski AS, Ross P Jr, *et al.* Predictors of anastomotic leak after esophagectomy: an analysis of the society of thoracic surgeons general thoracic database. *Ann Thorac Surg* 2013;96:1919–26.
- [5] Fischer C, Lingsma H, Klazinga N, *et al.* Volume-outcome revisited: the effect of hospital and surgeon volumes on multiple outcome measures in oesophago-gastric cancer surgery. *PLoS One* 2017;12:e0183955.
- [6] Ohkura Y, Miyata H, Konno H, *et al.* Development of a model predicting the risk of eight major postoperative complications after esophagectomy based on 10 826 cases in the Japan National Clinical Database. *J Surg Oncol* 2020;121:313–21.
- [7] Busweiler LA, Henneman D, Dikken JL, *et al.* Failure-to-rescue in patients undergoing surgery for esophageal or gastric cancer. *Eur J Surg Oncol* 2017;43:1962–69.
- [8] Markar S, Gronnier C, Duhamel A, *et al.* The impact of severe anastomotic leak on long-term survival and cancer recurrence after surgical resection for esophageal malignancy. *Ann Surg* 2015;262:972–80.
- [9] Tavares G, Tustumi F, Tristão LS, *et al.* Endoscopic vacuum therapy for anastomotic leak in esophagectomy and total gastrectomy: a systematic review and meta-analysis. *Dis Esophagus* 2021;34:doaa132.
- [10] Scognamiglio P, Reeh M, Melling N, *et al.* Management of intra-thoracic anastomotic leakages after esophagectomy: updated systematic review and meta-analysis of endoscopic vacuum therapy versus stenting. *BMC Surg* 2022;22:309.

- [11] Kuo EY, Chang Y, Wright CD. Impact of hospital volume on clinical and economic outcomes for esophagectomy. *Ann Thorac Surg* 2001;72:1118–24.
- [12] van Lanschot JJ, Hulscher JB, Buskens CJ, *et al.* Hospital volume and hospital mortality for esophagectomy. *Cancer* 2001;91:1574–78.
- [13] Casson AG, van Lanschot JJ. Improving outcomes after esophagectomy: the impact of operative volume. *J Surg Oncol* 2005;92:262–66.
- [14] Giwa F, Salami A, Abioye AI. Hospital esophagectomy volume and postoperative length of stay: a systematic review and meta-analysis. *Am J Surg* 2018;215:155–62.
- [15] Gandjian M, Williamson C, Sanaiha Y, *et al.* continued relevance of minimum volume standards for elective esophagectomy: a national perspective. *Ann Thorac Surg* 2022;114:426–33.
- [16] Meng R, Bright T, Woodman RJ, *et al.* Hospital volume versus outcome following oesophagectomy for cancer in Australia and New Zealand. *ANZ J Surg* 2019;89:683–88.
- [17] Nimptsch U, Haist T, Krautz C, *et al.* Hospital volume, in-hospital mortality, and failure to rescue in esophageal surgery. *Dtsch Arztebl Int* 2018;115:793–800.
- [18] Peschke D, Nimptsch U, Mansky T. Achieving minimum caseload requirements – an analysis of hospital discharge data from 2005-2011. *Dtsch Arztebl Int* 2014;111:556–63.
- [19] Nimptsch U, Mansky T. Hospital volume and mortality for 25 types of inpatient treatment in German hospitals: observational study using complete national data from 2009 to 2014. *BMJ Open* 2017;7:e016184.
- [20] Nimptsch U, Mansky T. Deaths following cholecystectomy and herniotomy: an analysis of nationwide German Hospital Discharge Data From 2009 to 2013. *Dtsch Arztebl Int* 2015;112:535–43.
- [21] Weber MC, Berlet M, Stoess C, *et al.* A nationwide population-based study on the clinical and economic burden of anastomotic leakage in colorectal surgery. *Langenbecks Arch Surg* 2023;408:55.
- [22] Research data centres of the Federal Statistical Office and the statistical offices of the Federal States. *Diagnosis-Related Group Statistics (DRG Statistics) 2013–2018*, own calculations. doi:10.21242/23141.2021.00.00.1.1.0.
- [23] Swart E, Bitzer EM, Gothe H, *et al.* A consensus german reporting standard for secondary data analyses, Version 2 (STROSA-STandardisierte BerichtsROutine für SekundärdatenAnalysen)]. *Gesundheitswesen (Bundesverband der Ärzte Des Öffentlichen Gesundheitsdienstes (Germany))* 2016;78:e161.
- [24] Swart E, Gothe H, Geyer S, *et al.* [Good Practice of Secondary Data Analysis (GPS): guidelines and recommendations]. *Gesundheitswesen (Bundesverband der Ärzte Des Öffentlichen Gesundheitsdienstes (Germany))* 2015;77:120–26.
- [25] Mathew G, Agha R, Albrecht J, *et al.* STROCCS 2021: strengthening the reporting of cohort, cross-sectional and case-control studies in surgery. *Int J Surg (Lond, England)* 2021;96:106165.
- [26] Charlson ME, Pompei P, Ales KL, *et al.* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
- [27] Rosero EB, Romito BT, Joshi GP. Failure to rescue: a quality indicator for postoperative care. *Best Pract Res Clin Anaesthesiol* 2021;35:575–89.
- [28] Abdelsattar ZM, Habermann E, Borah BJ, *et al.* Understanding failure to rescue after esophagectomy in the United States. *Ann Thorac Surg* 2020;109:865–71.
- [29] Harris LB, Vyas V, Marino K, *et al.* Mortality and failure-to-rescue after esophagectomy in the procedure-targeted National Surgical Quality Improvement Program registry. *World J Surg* 2024;48:2235–42.
- [30] Ubels S, Matthée E, Verstegen M, *et al.* Practice variation in anastomotic leak after esophagectomy: unravelling differences in failure to rescue. *Eur J Surg Oncolgy* 2023;49:974–82.
- [31] Neumann PA, Mennigen R, Palmes D, *et al.* Pre-emptive endoscopic vacuum therapy for treatment of anastomotic ischemia after esophageal resections. *Endoscopy* 2017;49:498–503.
- [32] Schorsch T, Müller C, Loske G. Endoscopic vacuum therapy of anastomotic leakage and iatrogenic perforation in the esophagus. *Surgical Endoscopy* 2013;27:2040–45.
- [33] Zhang Y, Dong D, Cao Y, *et al.* Robotic Versus Conventional Minimally Invasive Esophagectomy for Esophageal Cancer: a Meta-analysis. *Annals of Surgery* 2023;278:39–50.
- [34] Mederos MA, de Virgilio MJ, Shenoy R, *et al.* Comparison of clinical outcomes of robot-assisted, video-assisted, and open esophagectomy for esophageal cancer: A systematic review and meta-analysis. *JAMA Network Open* 2021;4:e2129228–e.
- [35] Nimptsch U, Spoden M, Mansky T. [Definition of variables in hospital discharge data: Pitfalls and proposed solutions]. *Gesundheitswesen (Bundesverband der Ärzte Des Öffentlichen Gesundheitsdienstes (Germany))* 2020;82:S29–s40.