

# Impact of postoperative complications on outcomes after oesophagectomy for cancer

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**Background:** To allocate healthcare resources optimally, complication-related quality initiatives should target complications that have the greatest overall impact on outcomes after surgery. The aim of this study was to identify the most clinically relevant complications after oesophagectomy for cancer in a nationwide cohort study.

**Methods:** Consecutive patients who underwent oesophagectomy for cancer between January 2011 and December 2016 were identified from the Dutch Upper Gastrointestinal Cancer Audit. The adjusted population attributable fraction (PAF) was used to estimate the impact of specific postoperative complications on the clinical outcomes postoperative mortality, reoperation, prolonged hospital stay and readmission to hospital in the study population. The PAF represents the percentage reduction in the frequency of a given outcome (such as death) that would occur in a theoretical scenario where a specific complication (for example anastomotic leakage) was able to be prevented completely in the study population.

**Results:** Some 4096 patients were analysed. Pulmonary complications and anastomotic leakage had the greatest overall impact on postoperative mortality (risk-adjusted PAF 44.1 and 30.4 per cent respectively), prolonged hospital stay (risk-adjusted PAF 31.4 and 30.9 per cent) and readmission to hospital (risk-adjusted PAF 7.3 and 14.7 per cent). Anastomotic leakage had the greatest impact on reoperation (risk-adjusted PAF 47.1 per cent). In contrast, the impact of other complications on these outcomes was relatively small.

**Conclusion:** Reducing the incidence of pulmonary complications and anastomotic leakage may have the greatest clinical impact on outcomes after oesophagectomy.

Paper accepted 21 August 2018

Published online in Wiley Online Library (www.bjs.co.uk). DOI: 10.1002/bjs.11000

## Introduction

Oesophagectomy has an important role in the treatment of oesophageal cancer, but is accompanied by a high operative risk<sup>1</sup>. Reported overall rates of complications after oesophagectomy range from 40 to 60 per cent, with pulmonary and anastomotic complications being the most common<sup>2–5</sup>. These postoperative complications have a significant effect on morbidity, duration of hospital stay, mortality and healthcare costs<sup>6–9</sup>. Although advances in surgical techniques and perioperative care have reduced the frequency of complications over the years, postoperative morbidity rates remain high<sup>10,11</sup>. Therefore, further quality improvement efforts are needed in oesophageal surgery.

To develop and prioritize quality improvement initiatives, complications that have the greatest overall impact on outcomes after oesophagectomy must be identified. Several

studies<sup>6,7,12,13</sup> have described the incidence of specific complications after oesophageal surgery, and the associations between these complications and subsequent outcomes. However, simple data on the frequency of a complication are not sufficient to establish the overall impact on a patient population.

The population attributable fraction (PAF) is a parameter that has traditionally been used in the epidemiological literature to determine the burden of a given disease (such as cancer) that is caused by a specific risk factor (for example smoking)<sup>14–16</sup>. The PAF is also an attractive measure to assess the overall impact of specific postoperative complications on a given outcome because it incorporates knowledge of the frequency of a complication and also the relative risk of a given outcome in the presence of that complication<sup>16</sup>. For example, in the context of the present

**Table 1** Demographic, clinical and treatment characteristics of 4096 patients who underwent oesophagectomy for cancer

	No. of patients*	Initial missing values‡
Age (years)†	65(9)	9
Sex ratio (M:F)	3168:928	1
BMI (kg/m <sup>2</sup> )†	26(4)	38
ASA fitness grade		24
I	710 (17.3)	
II	2490 (60.8)	
III	881 (21.5)	
IV	15 (0.4)	
Co-morbidity		
Asthma/COPD	587 (14.3)	0
Coronary artery disease§	257 (6.3)	0
History of myocardial infarction	260 (6.3)	0
History of arrhythmia	329 (8.0)	0
Hypertension	1345 (32.8)	0
Peripheral vascular disease	157 (3.8)	0
Diabetes mellitus	619 (15.1)	0
History of stroke	122 (3.0)	0
History of thromboembolic events	168 (4.1)	0
Endocrine disorder	162 (4.0)	0
Previous abdominal or thoracic surgery	1238 (30.2)	0
Steroid use	104 (2.5)	34
Surgical approach		0
Transthoracic		
Open	636 (15.5)	
Minimally invasive	1981 (48.4)	
Hybrid	130 (3.2)	
Transhiatal		
Open	962 (23.5)	
Minimally invasive	387 (9.4)	
Conversion during surgery	104 (2.5)	0
Location of anastomosis		63
Cervical	2744 (67.0)	
Intrathoracic	1352 (33.0)	
Tumour location¶		24
Proximal oesophagus	42 (1.0)	
Middle oesophagus	496 (12.1)	
Distal oesophagus	2603 (63.5)	
Gastro-oesophageal junction	955 (23.3)	
Tumour histology		29
Adenocarcinoma	3201 (78.1)	
Squamous cell carcinoma	811 (19.8)	
Other	84 (2.1)	
cT category		175
cT1	225 (5.5)	
cT2	794 (19.4)	
cT3	2947 (71.9)	
cT4	130 (3.2)	
cN category		172
cN0	1486 (36.3)	
cN1	1729 (42.2)	
cN2	761 (18.6)	
cN3	120 (2.9)	
Neoadjuvant therapy		21
Chemoradiotherapy	3478 (84.9)	
Chemotherapy	282 (6.9)	
No therapy	336 (8.2)	

\*With percentages in parentheses unless indicated otherwise; †values are mean(s.d.). Data in this table represent the data set after imputation; ‡number of missing values for each variable before imputation. §History of angina pectoris, percutaneous transluminal coronary angioplasty and/or coronary artery bypass graft. ¶Proximal, 15–23 cm from teeth; middle, 24–32 cm from teeth; distal, 32–40 cm from teeth. COPD, chronic obstructive pulmonary disease.

study, the PAF represents the percentage reduction in the frequency of a given outcome (such as mortality) that would occur in a theoretical scenario where a specific complication (for example anastomotic leakage) could be abandoned in the study population.

Recent studies<sup>17–20</sup> have used this methodology to analyse the effect of complications after colonic and vascular surgery, and reported new insights in these fields of surgery. The surgical community has recently encouraged researchers to extend this methodology to other surgical populations, as this will facilitate the development of more targeted and effective surgical quality improvement programmes<sup>17,18</sup>. Accordingly, the aim of the present study was to use the PAF to identify the most clinically relevant complications after oesophagectomy for cancer.

## Methods

Patient data were obtained from the Dutch Upper Gastrointestinal Cancer Audit (DUCA). The DUCA, founded in 2011, is a nationwide registration of all patients undergoing surgery with curative intent for oesophageal or gastric cancer in the Netherlands<sup>21,22</sup>. The DUCA collects preoperative, intraoperative and postoperative data to provide surgical teams with periodic feedback on process and outcome measures. It is thought that the DUCA may improve the quality of cancer care by stimulating quality improvements. Participation is mandatory for all Dutch hospitals performing oesophagectomies and gastrectomies. Data are registered in the online registry programme during the hospital stay until 30 days after initial discharge. Detailed descriptions of definitions are provided to ensure uniform data registration. An independent monitoring team audits the data to evaluate completeness and concordance. The present study was approved by the scientific committee of the DUCA and according to the Central Committee on Research involving Human Subjects; this type of study does not require approval from an ethics committee in the Netherlands.

## Study population and treatment

Consecutive patients who underwent elective resection for primary oesophageal cancer (cT1N+ or cT2–4a Nany) between January 2011 and December 2016 were identified from the DUCA. Surgical treatment consisted of an open (both abdomen and chest), hybrid (abdomen minimally invasive and open chest) or totally minimally invasive transthoracic or transhiatal oesophagectomy followed by gastric tube reconstruction with a cervical or intrathoracic anastomosis. Patients received neoadjuvant treatment according to national guidelines.

**Table 2** Postoperative complications and clinical outcomes after oesophagectomy in 4096 patients

	No. of patients	Initial missing values†
Postoperative complications		
Pulmonary‡	1257 (30.7)	0
Anastomotic leakage§	807 (19.7)	0
Cardiac¶	555 (13.5)	0
Chyle leakage	313 (7.6)	0
Acute delirium	232 (5.7)	0
Recurrent nerve paresis#	201 (4.9)	0
Wound infection	180 (4.4)	0
Thromboembolic**	94 (2.3)	0
Postoperative bleeding	46 (1.1)	0
Clinical outcomes		
Postoperative mortality††	142 (3.5)	0
Duration of hospital stay (days)*	12 (9–20)	46
Prolonged hospital stay‡‡	1057 (25.8)	46
Reoperation§§	576 (14.1)	0
Readmission to hospital¶¶	546 (13.3)	0

Values in parentheses are percentages unless indicated otherwise; \*values are median (i.q.r.). Data in this table represent the data set after imputation; †number of missing values for each variable before imputation. ‡Pneumonia, pleural effusion, respiratory failure, pneumothorax and/or acute respiratory distress syndrome. §Any clinically or radiologically proven anastomotic leakage. ¶Supraventricular and ventricular arrhythmia, myocardial infarction and/or heart failure. #Any vocal cord dysfunction after resection. \*\*Pulmonary embolism and/or deep venous thrombosis. ††Death during initial hospital admission or within 30 days after surgery. ‡‡Duration of hospital stay at least 75th percentile (for each surgical approach). §§Postoperative surgical procedure under general anaesthesia. ¶¶Readmission to hospital within 30 days after initial discharge.

### Patient- and treatment-related characteristics, complications and study outcomes

Patient and treatment-related characteristics included: age, sex, BMI, ASA fitness grade, co-morbidity, previous abdominal or thoracic surgery, steroid use, surgical approach, conversion during surgery, location of anastomosis, tumour location, histology of the tumour, cTNM stage and type of neoadjuvant therapy.

The most common postoperative complications that occurred during hospital admission or readmission (within 30 days) were retrieved from the DUCA. Selected complications included: pulmonary complications (clinically proven pneumonia, pleural effusion leading to drainage, pleural empyema and/or acute respiratory distress syndrome), clinically or radiologically proven anastomotic leakage, cardiac complications (supraventricular and ventricular arrhythmia, myocardial infarction and/or heart failure), chyle leakage, acute delirium, recurrent nerve paresis, wound infection, thromboembolic events (pulmonary embolism and/or deep venous thrombosis) and postoperative bleeding.

The study outcomes included: postoperative death during the initial hospital admission or within 30 days after surgery; reoperation, defined as a postoperative surgical procedure under general anaesthesia; prolonged hospital stay; and readmission to hospital within 30 days after initial discharge. Prolonged hospital stay was defined as a length of hospital stay above or equal to the 75th percentile for each surgical approach (at least 24 days for transthoracic open, 21 days for transthoracic minimally invasive, 23 days for transthoracic hybrid, 15 days for transhiatal open, and 20 days for transhiatal minimally invasive) in order to account for differences between surgical procedures.

### Statistical analysis

Patient- and treatment-related characteristics are described as counts with percentages, mean(s.d.) or median (i.q.r.). Missing data were considered to be missing at random and handled using imputation with the iterative Markov chain Monte Carlo method (5 iterations)<sup>23</sup>. Statistical analysis was undertaken using SPSS® version 24.0 (IBM, Armonk, New York, USA) and R language environment (version 3.3.1, geeglm, sandwich, mice and AF packages; <http://www.R-project.org>).  $P < 0.050$  was considered statistically significant.

The frequency of each of the complications and of the four outcome measures was calculated. Before analysis, a directed acyclic graph was created to visualize the potential causal pathways from postoperative complications to the study outcomes, and to identify potential sources of confounding ([www.dagitty.net/mEpwOF4](http://www.dagitty.net/mEpwOF4))<sup>24</sup>. The pathways displayed in the graph were based on associations identified in previous literature<sup>25–29</sup> or, if the former were lacking, on plausible assumptions<sup>30</sup>. The DAGitty web-based software interface (version 2.3) was used to select a sufficient set of variables for adjustment to minimize bias<sup>31</sup>. The selected confounders included: age (continuous), sex (binary), BMI (continuous), ASA fitness grade (I, II, III and IV), each of the co-morbidities listed in *Table 1* (binary), previous abdominal or thoracic surgery (binary), steroid use (binary), conversion during surgery (binary), location of anastomosis (binary), surgical approach (open transthoracic, minimally invasive transthoracic, hybrid, open transhiatal, minimally invasive transhiatal) and neoadjuvant therapy (none, neoadjuvant chemoradiotherapy, chemotherapy). The adjusted relative risk (aRR) (with 95 per cent confidence interval) for each complication–outcome pair was calculated using multivariable Poisson regression models with log link and robust error variance, while conditioning for the selected confounders.

**Table 3** Risk-adjusted associations and population attributable fractions between postoperative mortality and complications after oesophagectomy for cancer

Postoperative complication	Proportion who died*	Risk-adjusted association‡		Risk-adjusted PAF§	
		Adjusted relative risk†	P	PAF (%)†	P
Pulmonary	96 of 1257 (7.6)	3.98 (2.79, 5.77)	< 0.001	44.1 (30.9, 57.2)	< 0.001
Anastomotic leakage	71 of 807 (8.8)	3.64 (2.59, 5.10)	< 0.001	30.4 (19.2, 41.7)	< 0.001
Cardiac	42 of 555 (7.6)	2.09 (1.43, 3.01)	< 0.001	8.6 (−0.7, 17.9)	0.070
Chyle leakage	17 of 313 (5.4)	1.36 (0.78, 2.24)	0.229	–	–
Acute delirium	14 of 232 (6.0)	1.33 (0.73, 2.26)	0.300	–	–
Recurrent nerve paresis	3 of 201 (1.5)	0.37 (0.12, 1.16)	0.087	–	–
Wound infection	5 of 180 (2.8)	0.78 (0.28, 1.72)	0.571	–	–
Thromboembolic	11 of 94 (12)	3.24 (1.63, 5.81)	< 0.001	3.7 (−0.4, 8.0)	0.077
Postoperative bleeding	7 of 46 (15)	3.37 (1.37, 7.00)	0.006	2.8 (0.7, 4.8)	0.008

Values in parentheses are \*percentages and †95 per cent confidence intervals. PAF, population attributable fraction. ‡Multivariable Poisson regression; §logistic regression-based estimates of confounder-adjusted attributable fractions.

**Table 4** Risk-adjusted associations and population attributable fractions between prolonged hospital stay and complications after oesophagectomy for cancer

Postoperative complication	Proportion with prolonged stay*	Risk-adjusted association‡		Risk-adjusted PAF§	
		Adjusted relative risk†	P	PAF (%)†	P
Pulmonary	642 of 1257 (51.1)	3.29 (2.90, 3.75)	< 0.001	31.4 (28.2, 34.6)	< 0.001
Anastomotic leakage	527 of 807 (65.3)	3.92 (3.46, 4.43)	< 0.001	30.9 (27.1, 34.8)	< 0.001
Cardiac	248 of 555 (44.7)	1.78 (1.54, 2.06)	< 0.001	4.0 (1.9, 5.9)	< 0.001
Chyle leakage	136 of 313 (43.5)	1.79 (1.48, 2.15)	< 0.001	5.2 (3.6, 6.8)	< 0.001
Acute delirium	127 of 232 (54.7)	2.11 (1.65, 2.42)	< 0.001	2.3 (0.9, 3.7)	< 0.001
Recurrent nerve paresis	69 of 201 (34.3)	1.28 (1.06, 1.57)	0.013	0.4 (−0.7, 1.5)	0.496
Wound infection	78 of 180 (43.3)	1.63 (1.28, 2.05)	< 0.001	1.7 (0.6, 2.7)	0.002
Thromboembolic	59 of 94 (63)	2.39 (1.82, 3.90)	< 0.001	1.6 (0.9, 2.4)	< 0.001
Postoperative bleeding	32 of 46 (70)	2.47 (1.69, 3.47)	< 0.001	1.2 (0.5, 1.8)	< 0.001

Values in parentheses are \*percentages and †95 per cent confidence intervals. PAF, population attributable fraction. ‡Multivariable Poisson regression; §logistic regression-based estimates of confounder-adjusted attributable fractions.

Accordingly, for each complication–outcome pair with a significant association in the previous analyses, the risk-adjusted PAF was calculated while adjusting for the previously mentioned confounders and for the presence of other complications. The PAF calculations were performed with the AF package in R software which allows confounder-adjusted estimation of PAFs for cohort studies<sup>32</sup>.

The risk-adjusted PAF was used to assess the overall impact of each postoperative complication on each of the study outcomes in the study population. In this study, the risk-adjusted PAF represents the percentage reduction in the frequency of a given outcome (postoperative mortality, prolonged hospital stay, reoperation and readmission to hospital) that would occur in a theoretical scenario where a specific complication could be prevented completely in the present study population.

## Results

A total of 4096 patients with oesophageal cancer who underwent transthoracic or transhiatal oesophagectomy with gastric tube reconstruction were eligible for analysis. Among these patients, 3168 were men (77.3 per cent) and the mean(s.d.) age was 65(9) years. Patient and treatment characteristics are shown in *Table 1*.

## Complications and study outcomes

Postoperative complications and outcome data are shown in *Table 2*. The most common postoperative complications were pulmonary complications, which occurred in 1257 of 4096 patients (30.7 per cent), anastomotic leakage in 807 (19.7 per cent) and cardiac complications in 555 (13.5 per cent). There were 142 postoperative deaths (3.5 per cent),

## Complications after oesophagectomy

**Table 5** Risk-adjusted associations and population attributable fractions between reoperation and complications after oesophagectomy for cancer

Postoperative complication	Proportion who had reoperation*	Risk-adjusted association‡		Risk-adjusted PAF§	
		Adjusted relative risk†	P	PAF (%)†	P
Pulmonary	314 of 1257 (25.0)	2.45 (2.07, 2.90)	< 0.001	17.7 (11.8, 23.6)	< 0.001
Anastomotic leakage	350 of 807 (43.4)	6.11 (5.15, 7.25)	< 0.001	47.1 (42.2, 51.9)	< 0.001
Cardiac	128 of 555 (23.1)	1.66 (1.35, 2.02)	< 0.001	3.1 (– 0.1, 6.3)	0.054
Chyle leakage	82 of 313 (26.2)	1.78 (1.39, 2.26)	< 0.001	5.7 (3.2, 8.2)	< 0.001
Acute delirium	62 of 232 (26.7)	1.86 (1.41, 2.41)	< 0.001	1.7 (– 0.4, 3.9)	0.114
Recurrent nerve paresis	35 of 201 (17.4)	1.18 (0.82, 1.64)	0.299	–	–
Wound infection	48 of 180 (26.7)	2.02 (1.48, 2.69)	< 0.001	2.8 (0.9, 4.6)	0.003
Thromboembolic	28 of 94 (30)	2.03 (1.35, 2.92)	< 0.001	0.9 (– 0.6, 2.4)	0.260
Postoperative bleeding	37 of 46 (80)	5.79 (4.03, 8.07)	< 0.001	4.6 (2.9, 6.2)	< 0.001

Values in parentheses are \*percentages and †95 per cent confidence intervals. PAF, population attributable fraction. ‡Multivariable Poisson regression; §logistic regression-based estimates of confounder-adjusted attributable fractions.

**Table 6** Risk-adjusted associations and population attributable fractions between readmission to hospital and complications after oesophagectomy for cancer

Postoperative complication	Proportion readmitted*	Risk-adjusted association‡		Risk-adjusted PAF§	
		Adjusted relative risk†	P	PAF (%)†	P
Pulmonary	211 of 1257 (16.8)	1.40 (1.17, 1.67)	< 0.001	7.3 (1.2, 13.4)	0.017
Anastomotic leakage	179 of 807 (22.2)	1.93 (1.61, 2.32)	< 0.001	14.7 (9.9, 19.5)	< 0.001
Cardiac	89 of 555 (16.0)	1.21 (0.96, 1.52)	0.069	–	–
Chyle leakage	56 of 313 (17.9)	1.29 (0.99, 1.69)	0.051	–	–
Acute delirium	33 of 232 (14.2)	1.04 (0.71, 1.46)	0.812	–	–
Recurrent nerve paresis	25 of 201 (12.4)	0.94 (0.61, 1.38)	0.760	–	–
Wound infection	39 of 180 (21.7)	1.79 (1.27, 2.46)	< 0.001	2.8 (0.7, 4.8)	0.009
Thromboembolic	17 of 94 (18)	1.41 (0.84, 2.22)	0.123	–	–
Postoperative bleeding	10 of 46 (22)	1.69 (0.98, 2.90)	0.058	–	–

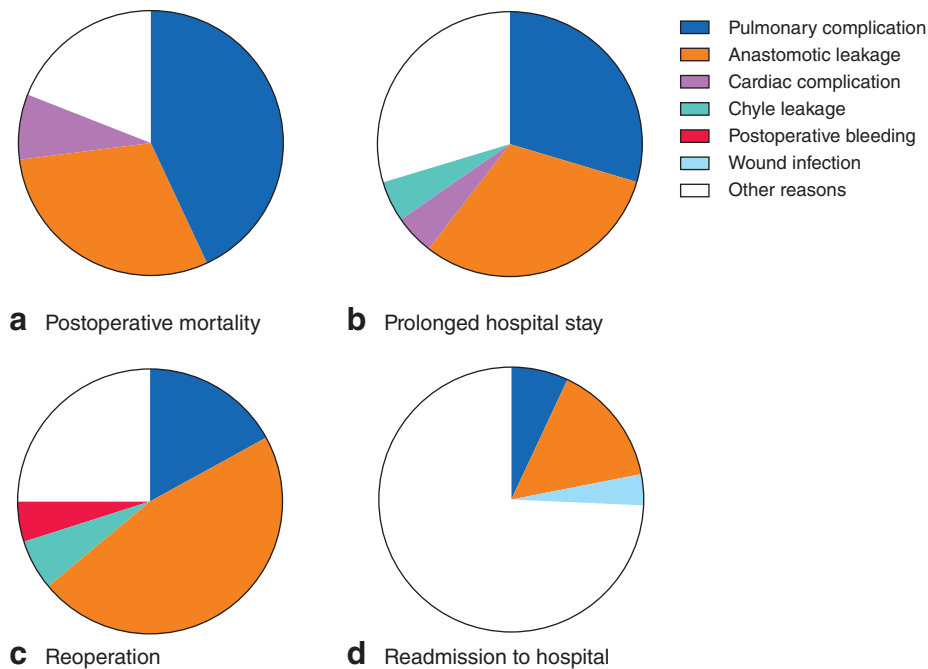
Values in parentheses are \*percentages and †95 per cent confidence intervals. PAF, population attributable fraction. ‡Multivariable Poisson regression; §logistic regression-based estimates of confounder-adjusted attributable fractions.

1057 patients (25.8 per cent) had a prolonged hospital stay, reoperation was necessary in 576 (14.1 per cent) and 546 patients (13.3 per cent) were readmitted to hospital. The median duration of hospital stay was 12 (i.q.r. 9–20) days.

Risk-adjusted associations between postoperative complications and outcomes are shown in *Tables 3–6*. Pulmonary complications (aRR 3.98, 95 per cent c.i. 2.79 to 5.77) and anastomotic leakage (aRR 3.64, 2.59 to 5.10) were associated with the greatest relative risk of postoperative mortality. All postoperative complications were significantly associated with prolonged hospital stay; pulmonary complications (aRR 3.29, 2.90 to 3.75) and anastomotic leakage (aRR 3.92, 3.46 to 4.43) showed the strongest association. Apart from recurrent nerve paresis, all of the postoperative complications were significantly associated with reoperation. Anastomotic leakage (aRR 6.11, 5.15 to 7.25) and postoperative bleeding (aRR 5.79, 4.03 to 8.07) were associated with the greatest relative risk of reoperation. Anastomotic leakage (aRR 1.93, 1.61 to 2.32) and wound infection (1.79, 1.27 to 2.46) were associated with the greatest relative risk of hospital readmission.

The risk-adjusted PAF for each complication–outcome pair is shown in *Tables 3–6*, and summarized in *Fig. 1*. Based on the risk-adjusted PAFs, pulmonary complications and anastomotic leakage had the greatest overall impact on postoperative mortality. Complete elimination of these complications in the present study population would result in an anticipated reduction of 44.1 (95 per cent c.i. 30.9 to 57.2) and 30.4 (19.2 to 41.7) per cent respectively in postoperative mortality. Anastomotic leakage had a high overall impact on reoperation (PAF 47.1 (42.2 to 51.9) per cent), prolonged hospital stay (PAF 30.9 (27.1 to 34.8) per cent) and readmission to hospital (PAF 14.7 (9.9 to 19.5) per cent). Pulmonary complications also had a large impact on reoperation (PAF 17.7 (11.8 to 23.6) per cent), prolonged hospital stay (PAF 31.4 (28.2 to 34.6) per cent) and readmission (PAF 7.3 (1.2 to 13.4) per cent). In contrast, the impact of the other postoperative complications on the selected study outcomes was relatively small.





**Fig. 1** Risk-adjusted population attributable fractions for the complications contributing most to each outcome: **a** postoperative mortality, **b** prolonged hospital stay, **c** reoperation and **d** readmission to hospital

## Discussion

In this nationwide cohort study, the most clinically relevant complications after oesophagectomy in patients with newly diagnosed oesophageal cancer were identified by using the PAF as measure of overall impact. Pulmonary complications and anastomotic leakage had the greatest overall impact on postoperative mortality, prolonged hospital stay, reoperations and readmissions to hospital.

In this study, the PAF was used to quantify the proportion of an outcome in the total population that can be attributed to a specific postoperative complication<sup>14–16</sup>. The advantage of using the PAF is that it combines both the frequency of a complication and the relative risk of a given outcome in the presence of that complication. For example, a particularly severe complication may have a small impact at population level if it occurs rarely, and vice versa. Accordingly, assessing the impact of postoperative complications by using the PAF may guide policymakers in prioritizing initiatives that can reduce the clinical and economic burden of specific complications. A recent study<sup>17</sup> used this methodology to quantify the impact of specific postoperative complications on outcomes after elective colonic surgery. The authors concluded that their findings provided strong evidence that existing quality improvement programmes were not targeting the complications that are the most relevant in colorectal surgery. This underlines the

importance of gaining insight into nationwide outcomes after (oesophageal) surgery by using the PAF, not only to highlight the negative impact of postoperative complications but also to identify opportunities for improvement.

Although anastomotic leakage had a lower incidence than pulmonary complications, it had the largest clinical impact on two of the four outcomes in the present study. If anastomotic leakage could be eliminated completely, the incidence of prolonged hospital stay, reoperation and readmission to hospital would decrease by 31, 47 and 15 per cent respectively. Pulmonary complications also had a large impact on these outcomes, and had the largest contribution to postoperative mortality (risk-adjusted PAF 44.1 per cent). Interestingly, in the relative risk analysis, postoperative bleeding and thromboembolic complications were both highly associated with postoperative mortality, reoperation and prolonged hospital stay. However, the PAF indicated that their impact on the total population was relatively small. Thus, even if it were possible to reduce the incidence of postoperative bleeding and thromboembolic complications, the estimated effect of these efforts on clinical outcomes in the present population would be limited. In general, the study findings suggest that postoperative pulmonary complications and anastomotic leakage should receive priority as

targets of complication-related quality improvement initiatives in patients undergoing oesophageal resection for cancer. However, in the event that new initiatives are considered, it is necessary to determine which outcomes deserve the greatest attention because the impact of a specific postoperative complication depends on the outcome under investigation.

The relevance of pulmonary complications and anastomotic leakage after oesophagectomy for cancer has been acknowledged in previous studies<sup>2–5,8,9</sup>. Several strategies have been shown to protect against pulmonary complications and anastomotic leakage<sup>33,34</sup>. For anastomotic leakage, this includes use of precise suturing techniques with prevention of tension and avoidance of reduction in perfusion of the conduit, reinforcement of the anastomosis with omentoplasty, and delaying oral intake after oesophagectomy<sup>35–37</sup>. Pulmonary complications can be prevented by stopping smoking before surgery, perioperative pulmonary rehabilitation, minimally invasive surgery and effective pain management<sup>34,35,38,39</sup>. Furthermore, it has been shown that complication rates after oesophagectomy are lower in high-volume centres and that the use of enhanced recovery after surgery protocols can reduce duration of hospital stay<sup>22,36–38,40</sup>.

Despite previous efforts to reduce anastomotic leakage and pulmonary complications, the proven impact of these complications justifies further initiatives to reduce their incidence and severity. Although the extent to which complications can be prevented is unknown, even a small reduction could potentially result in large cost savings to a hospital<sup>9</sup>. This effect on its own could provide the business case for such initiatives. Furthermore, monitoring and (publicly) reporting of outcomes after oesophagectomy in audits may provide healthcare providers with a very direct and tangible incentive to further explore initiatives for preventing such complications<sup>41</sup>. In a market-based healthcare system, hospitals that provide optimal quality of care will increase patient satisfaction and desirability to healthcare payers (such as insurance companies), resulting in enhanced referrals. On the contrary, providing low-quality care will lead to poor patient outcomes, patient dissatisfaction and loss of future patient referrals<sup>42</sup>.

In this context, it has been recognized that the anastomotic leakage rate in the present cohort remains high compared with rates in other international cohort studies<sup>43,44</sup>. Some centres in the Netherlands have moved from a cervical to an intrathoracic anastomosis<sup>45</sup>. However, the introduction of an intrathoracic anastomosis is initially associated with a considerable learning curve<sup>46</sup>, so the leak rate may decrease only after several more years. A

randomized study<sup>47</sup> comparing cervical with intrathoracic anastomosis is currently recruiting patients (ICAN trial).

Methodological strengths of this study include its population-based nationwide design, the complete and validated prospective data collection, and large sample size<sup>21</sup>. To correct for potential confounders, adjustments were made for selected patient and clinical characteristics. Furthermore, some patients in this cohort had more than one type of complication, so all nine complications were included in the adjusted PAF analysis. Possible limitations apply to this study. First, it was not possible to specify all pulmonary and cardiac complications because the DUCA did not discriminate between pneumonia, pleural effusion and pleural empyema, or atrial fibrillation and myocardial infarction. According to the literature, it is most likely that pneumonia represents the majority of the pulmonary complications and atrial fibrillation the majority of cardiac complications<sup>6,33,38</sup>. Second, it was not always clear whether a postoperative complication (such as pulmonary complications) led to a given outcome (for example prolonged hospital stay) or, conversely, the complication occurred as a result of the outcome. Third, there is a possibility that the associations between postoperative complications and subsequent outcomes were influenced by unknown confounding variables. Finally, the perioperative care and management of postoperative complications changed over time, which may also have influenced these associations.

## Acknowledgements

L.G. and J.M. contributed equally to this work. The authors thank all surgeons, registrars, physician assistants and administrative nurses for data registration in the DUCA database, as well as the DUCA group for scientific input. This paper reports the results of a preregistered study with complete analysis plans (<https://www.dica.nl/duca/onderzoek>). The authors certify that the results of all preregistered analyses are reported. Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the DUCA at [onderzoek@dica.nl](mailto:onderzoek@dica.nl).

*Disclosure:* The authors declare no conflict of interest.

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