PART III

Surgical quality assurance

CHAPTER 16

Differences in outcomes of esophageal and gastric cancer surgery across Europe

Johan L. Dikken[a,b], Johanna W. van Sandick[c], William H. Allum[d], Jan Johansson[e], Lone S. Jensen[f], Hein Putter[g], Victoria H. Coupland[h], Michel W.J.M. Wouters[a,c], Valery E.P.P. Lemmens[i], Cornelis J.H. van de Velde[a]

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Departments of Surgery[a] and Medical Statistics[g], Leiden University Medical Center, Leiden, the Netherlands
Departments of Radiotherapy[b] and Surgery[c], the Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands
Department of Surgery[d], The Royal Marsden NHS Foundation Trust, London, United Kindom
Department of Surgery[e], Lund University Hospital, Lund, Sweden
Department of Surgery[f], Aarhus University Hospital, Aarhus, Denmark
King's College London, Thames Cancer Registry[h], London, United Kingdom
Comprehensive Cancer Centre South[i], Eindhoven, the Netherlands

ABSTRACT

BACKGROUND

In several European countries, centralization of esophagogastric cancer surgery has been realized and clinical audits have been initiated. Aims of the present study were to evaluate differences in resection rates, outcomes, and annual hospital volumes between these countries, and to analyze the relation between annual hospital volume and outcomes.

PATIENTS AND METHODS

National data were obtained from cancer registries or clinical audits in the Netherlands, Sweden, Denmark, and England. Differences in outcomes were analyzed between countries and between hospital volume categories, adjusting for available case-mix factors.

RESULTS

Between 2004 and 2009, 10,854 esophagectomies and 9,010 gastrectomies were registered. Resection rates in England were 18.2% and 21.6% for esophageal and gastric cancer, compared with 28.5-29.9% and 41.4-41.9% in the Netherlands and Denmark ($P < 0.001$). Adjusted 30-day mortality after esophagectomy was lowest in Sweden (1.9%). After gastrectomy, adjusted 30-day mortality was significantly higher in the Netherlands (6.9%) compared with Sweden (3.5%) and Denmark (4.3%) ($P < 0.05$). Increasing hospital volume was associated with lower 30-day mortality after esophagectomy (odds ratio 0.55 for ≥41/year versus 1-10/year, 95%CI 0.42-0.72) and gastrectomy (odds ratio 0.64 for ≥21/year versus 1-10/year, 95%CI 0.41-0.99)

CONCLUSIONS

The present results demonstrate a lower 30-day mortality in hospitals performing higher numbers of esophagogastric cancer resections. However, differences in outcomes between several European countries could not be explained by existing differences in hospital volumes. To understand these differences in outcomes and resection rates, and to provide more reliable case-mix adjustments, a uniform European Upper GI Cancer Audit recording standardized data is warranted.

INTRODUCTION

Quality assurance is increasingly acknowledged as a crucial factor for improvement of care for patients with esophageal and gastric cancer. In Europe, the average five-year survival rate is 11% for esophageal cancer, and 25% for gastric cancer, but variation between and within countries is considerable.[1] The reasons for these inter and intra country variations are difficult to assess. In some countries there are nationally sponsored cancer registries whereas others have established clinical audits. Furthermore the data recorded is variable and there are differences in data interpretation. Thus comparison of outcomes can be limited. One of the key elements to any comparison is the completeness of the recorded data in order to eliminate any bias as this would adversely affect any resultant change in service configuration and therefore outcome.

In the Netherlands, Sweden, Denmark, and England programs and processes have been established which are designed to achieve as comprehensive data collection as possible with the aim of quality assuring treatment of esophageal and gastric cancer.

The purposes of the current study are to evaluate differences in annual hospital volumes, resection rates and treatment outcomes in these four countries and to determine where improvements can be made to allow better inter country comparisons.

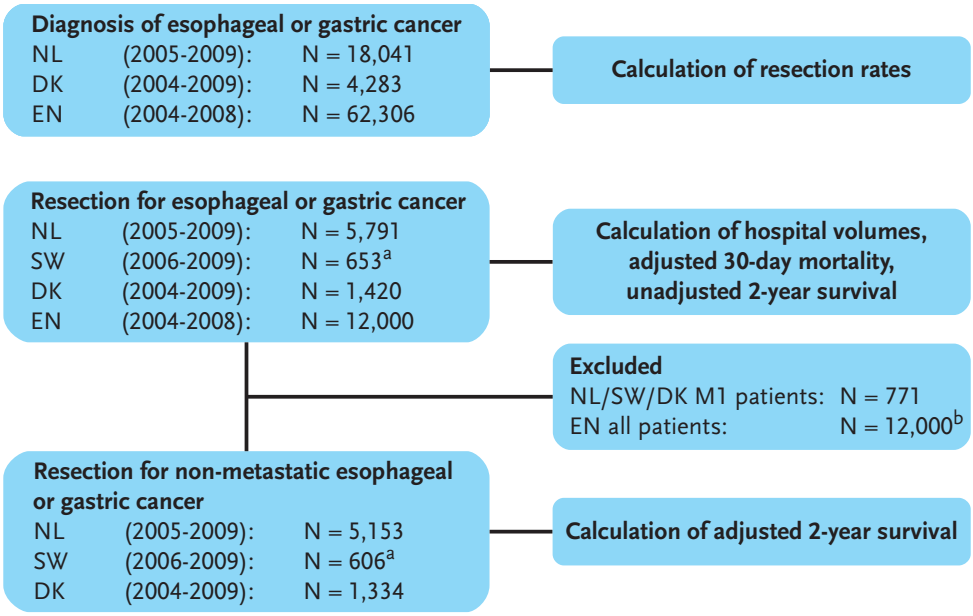
PATIENTS AND METHODS

National data were obtained from cancer registries in the Netherlands and England, and from clinical audits in Sweden and Denmark (Table 1). The Cancer Registries from the Netherlands and England, and the audit from Denmark, provide national coverage of all patients with a diagnosis of esophagogastric cancer. In the Swedish audit, only patients who underwent surgery were included, and therefore no resection rates could be calculated for Sweden. Furthermore, in several Swedish regions, not all patients who underwent surgical resection were registered. To reduce the chance of selection bias, only Swedish regions with a case ascertainment above 90% were included. These were Uppsala-Örebro (2006-2009), Norra (2006-2009), Sydöstra (2007-2009), and Stockholm-Gotland (2008-2009).

Detailed data from patients included in the UK National Esophago-Gastric Cancer Audit (NOGCA) have not been included as the case ascertainment at 71% is lower than the population based English Cancer Registry data, which partly reflects the voluntary nature of the NOGCA.[2]

Resection rates were calculated in the cohort of patients with a diagnosis of esophageal or gastric cancer between 2004 and 2009 (not all countries had data in each year, (Figure 1). Postoperative mortality, survival, and annual hospital volumes were calculated in the cohort of patients who underwent surgical resection between 2004 and 2009.

Figure 1. Study profile



NL: Netherlands, SW: Sweden, DK: Denmark, EN: England

DATA AVAILABILITY

Demographic data were available in all datasets, but comorbidity data were not uniformly registered and could therefore not be used for case-mix adjustments. Tumor location and histology based on the International Classification of Diseases for Oncology (ICD-O) were available in all datasets.[3] Tumor location was defined as esophagus (ICD-O C15.0-16.0), or stomach (ICD-O C16.1-16.9). Staging was performed according to the 6th edition of the International Union Against Cancer (UICC) TNM classification.[4] Information on TNM stage group was not available for the English data as stage was not routinely recorded during the study period by the English registries.

CALCULATION OF ANNUAL HOSPITAL VOLUMES

The hospital (in England: trusts, some of which manage several hospitals) where the operation was performed was available in all datasets. Annual hospital volume was defined separately for esophagectomy and gastrectomy as the number of resections per hospital in each calendar year. Volume categories were defined according to the distribution of resection numbers among hospitals (Figure 2).

STATISTICAL ANALYSES

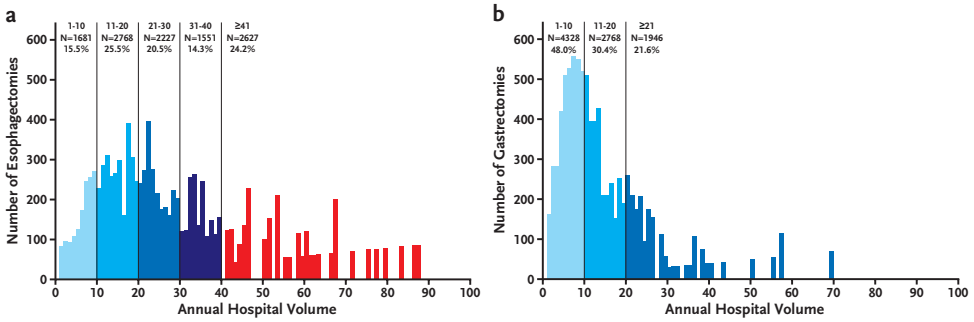
Data regarding esophagectomies and gastrectomies were analyzed separately. Differences in patient characteristics, resection rates, and annual hospital volumes between countries were analyzed with the Chi-square test.

Table 1. Characteristics of participating countries and available datasets

Country	Netherlands	Sweden	Denmark	England
inhabitants (x10^6)	16.7	9.4	5.5	52
incidence esophageal cancer (m/f)[a]	8.0 / 2.5	3.9 / 0.9	6.1 / 1.7	9.2 / 3.4
incidence gastric cancer (m/f)[a]	9.7 / 4.2	6.2 / 2.9	7.1 / 3.5	8.9 / 3.7
Centralization of surgery				
centralization of esophagectomy	2006: 10/year[b]	no	2003: 5 centres 2008: 4 centres	2001: 40/year[b]
centralization of gastrectomy	no	no	2003: 5 centres 2008: 4 centres	2001: 60/year[b]
Registry				
registry used	Netherlands Cancer Registry	National Quality Registry of Esophageal and Gastric Cancer	National Database of Esophagogastric Cancer; National Pathology Registry; National Registry of Patients; Danish Civil Registration System	English Cancer Registries
registry type	cancer registry	clinical audit	clinical audit	cancer registry
registry active since	1989	2006	2003	multiple years
data collection	trained registrars	trained doctors and nurses	surgeons treating the patients	multiple sources
years of diagnosis in dataset	2005-2009	2006-2009	2004-2009	2004-2008
follow-up until	January 2010	April 2011	January 2011	December 2009
case ascertainment	nationwide	partial[c]	nationwide	nationwide
Data availability				
patient age and sex	+	+	+	+
comorbidity (Charlson/ASA)	-/-	-/+	+/+	-
tumor location (E/EGJ/S)	+	+	+	+
tumor histology (AC/SCC/other)	+	+	+	+
TNM stage group	+	+	+	-
number of lymph nodes evaluated	+	+	+	-
surgery type	+	+	+	+
surgery hospital	+	+	+	+
(neo-)adjuvant therapy	+	+	-	-
30-day postoperative mortality	+	+	+	+
in-hospital mortality	-	-	+	-
2-year survival from surgery	+	+	+	+

[a]incidence per 100,000 world standard ratio, Karim-Kos et al.[39]
[b]minimal annual hospital volume
[c]in certain regions in Sweden, case ascertainment was incomplete. Therefore, regions with a case ascertainment below 90% were excluded
E: esophagus, EGJ: esophagogastric junction, S: stomach, AC: adenocarcinoma, SCC: squamous cell carcinoma,
+ yes, - no, ± sometimes

Figure 2. Distribution of (a) esophagectomy (N = 10,854), (b) gastrectomy (N = 9,010) over different hospital volume categories



Postoperative mortality was defined as death from any cause within 30 days after surgery. In-hospital mortality data was not available from all the four data sources. Differences in 30-day mortality between countries were analyzed with generalized estimating equations, adjusting for available case-mix factors (sex, age, morphology) and clustering of patients within hospitals using a random hospital effect model.[5] Two-year overall survival after surgery was chosen as the long term outcome because of the relatively short follow-up period due to the recent nature of the data, and was calculated from the day of surgery until death from any cause (event) or alive at last follow-up (censored). Detail of cause of death was not available. Unadjusted two-year overall survival for each country was calculated with Kaplan Meier analysis. Adjusted differences in two-year overall survival between countries were analyzed with Cox regression, adjusting for case-mix factors as categorical covariates (sex, age, morphology, stage group) and clustering of patients within hospitals. English patients were excluded from the adjusted two-year survival analyses as stage data were not available.

Differences in outcomes between hospital volume categories were evaluated in the same way as differences in outcomes between countries, including the adjustment for clustering of patients within hospitals. An interaction analysis was performed between country and annual hospital volume. Annual hospital volume was analyzed as a categorical variable and also as a linear variable. Statistical analyses were performed with SPSS (version 17.0.2) and R (version 2.12.2).

RESULTS

RESECTION RATES

Between January 2004 and December 2009, 84,630 patients with a diagnosis of esophageal or gastric cancer were registered in the Netherlands, Denmark, or England (Figure 1). Resection rates were similar in the Netherlands and Denmark, approximately 29% for esophageal cancer, and 41% for gastric cancer. Resection rates in England were significantly lower: 18% for esophageal cancer and 22% for gastric cancer (both $P < 0.001$).

PATIENT CHARACTERISTICS OF RESECTED PATIENTS

Between 2004 and 2009 19,864 patients underwent esophagectomy or gastrectomy for cancer (Table 2). Median age was 64 years for all patients who underwent esophagectomy and 71 for all patients who underwent gastrectomy. The percentage of patients undergoing resection with an age above 75 years was lowest in Denmark: 7.1% (63/892) for esophagectomy, and 22.7% (120/528) for gastrectomy, compared with 9.9-10.8% for esophagectomy and 32.4-38.4% for gastrectomy in the other countries. The highest proportion of stage I patients (esophagectomy: 15.8%, [446/2819] and gastrectomy 34.2%, [1015/2972]) and the highest proportion of stage IV patients (oesophagectomy: 12.0% [339/2819] and gastrectomy 17.1% [508/2972]) were recorded in the Netherlands.

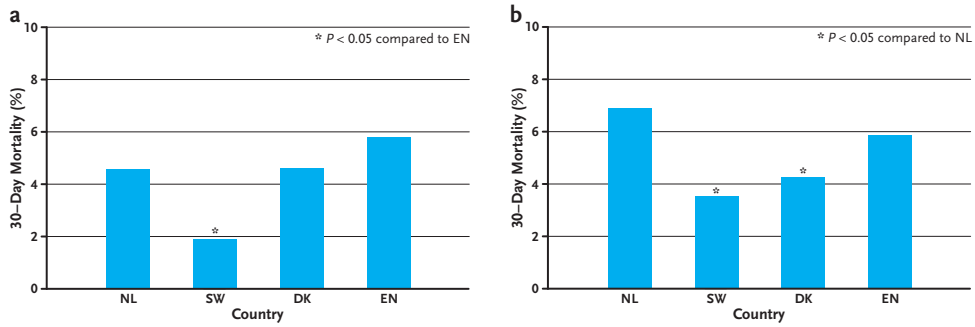
Table 2. Patient characteristics for patients who underwent esophagectomy (N = 10,854) or gastrectomy (N = 9010) for cancer

Country	Netherlands		Sweden		Denmark		England		
	N	%	N	%	N	%	N	%	*P*
Esophagectomy	2819	*100.0*	231	*100.0*	892	*100.0*	6912	*100.0*	
Sex									
male	2179	*77.3*	185	*80.1*	699	*78.4*	5295	*76.6*	0.4
female	640	*22.7*	46	*19.9*	193	*21.6*	1617	*23.4*	
Age									
<60	973	*33.5*	73	*31.6*	299	*33.5*	2171	*31.4*	0.003
60-75	1567	*55.6*	133	*57.6*	530	*59.4*	4001	*57.9*	
>75	279	*9.9*	25	*10.8*	63	*7.1*	740	*10.7*	
mean age	63		64		63		64		
median age	63		64		63		64		
Histology									
adenocarcinoma	2141	*76.0*	162	*70.1*	637	*71.4*	5483	*79.3*	<0.001
SCC	615	*21.8*	42	*18.2*	201	*22.5*	1190	*17.2*	
other carcinoma	63	*2.2*	27	*11.7*	54	*6.1*	239	*3.5*	
TNM stage group									
0	10	*0.4*	15	*6.5*	20	*2.2*			<0.001[b]
I	446	*15.8*	18	*7.8*	67	*7.5*			
II	977	*34.7*	101	*43.7*	381	*42.7*			
III	912	*32.4*	71	*30.7*	334	*37.4*			
IV[a]	339	*12.0*	12	*5.2*	37	*4.1*			
unknown	135	*4.8*	14	*6.1*	53	*5.9*	6912	*100.0*	
mean stage[c]	2.43		2.38		2.42				
median stage[c]	II		II		II				

Country	Netherlands		Sweden		Denmark		England		
	N	%	N	%	N	%	N	%	*P*
Gastrectomy	2972	*100.0*	422	*100.0*	528	*100.0*	5088	*100.0*	
Sex									
male	1838	*61.8*	241	*57.1*	305	*57.8*	3304	*64.9*	<0.001
female	1134	*38.2*	181	*42.9*	223	*42.2*	1784	*35.1*	
Age									
<60	599	20.2	67	15.9	141	26.7	820	16.1	<0.001
60-75	1409	47.4	193	45.7	267	50.6	2585	50.8	
>75	964	32.4	162	38.4	120	22.7	1683	33.1	
mean age	69		71		66		70		
median age	71		72		67		72		
Histology									
adenocarcinoma	2929	98.6	396	93.8	502	95.1	4879	95.9	<0.001
other carcinoma	43	1.4	26	6.2	26	4.9	209	4.1	
TNM stage group									
0	15	0.5	13	3.1	6	1.1			<0.001[b]
I	1015	34.2	110	26.1	83	15.7			
II	695	23.4	105	24.9	109	20.6			
III	666	22.4	111	26.3	159	30.1			
IV[a]	508	17.1	54	12.8	40	7.6			
unknown	73	2.5	29	6.9	131	24.8	5088	100.0	
mean stage[c]	2.23		2.29		2.4				
median stage[c]	II		II		III				

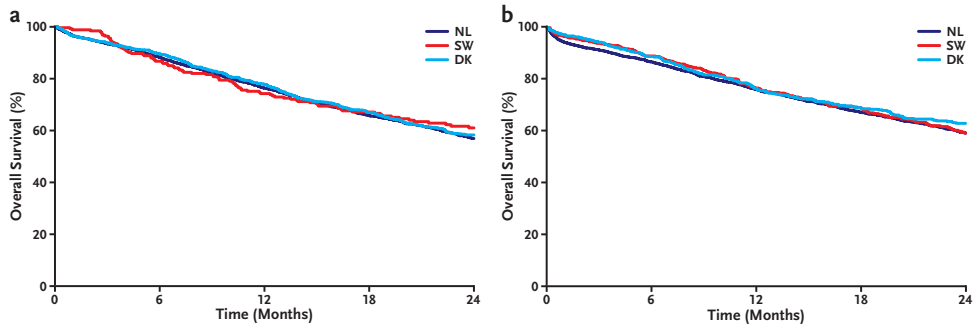
[a] Majority of this group: in the 6th edition TNM classification for gastric cancer, T4N+M0 and T1-3N3 cancers were assigned stage IV. A smaller part of this group are palliative resections for gastric cancers.
[b]Chi square test: England excluded
[c]Calculated by excluding unknown stage and considering stage group as continuous variable
SCC: squamous cell carcinoma

Figure 3. Postoperative 30-day mortality after (a) esophagectomy and (b) gastrectomy, adjusted for sex, age, and histology



NL: Netherlands, SW: Sweden, DK: Denmark, EN: England

Figure 4. Two-year survival after (a) esophagectomy and (b) gastrectomy, adjusted for sex, age, histology, and stage group



NL: Netherlands, SW: Sweden, DK: Denmark

DIFFERENCES IN OUTCOMES BETWEEN COUNTRIES

Median follow-up for all patients was 37 months. In all countries, postoperative 30-day mortality was lower after esophagectomy (4.6%) than after gastrectomy (6.7%), but variation between countries was considerable. Adjusted 30-day mortality after esophagectomy was lowest in Sweden (1.9%), and highest in England (5.8%), (P = 0.028) (Figure 3a, Table 3). Differences between other countries were not significant. After gastrectomy, adjusted 30-day mortality in the Netherlands (6.9%) was significantly higher when compared to Sweden (3.5%, P = 0.017), and Denmark (4.3%, P = 0.029), (Figure 3b). Unadjusted 2-year overall survival estimates were not significantly different between countries, except for 2-year survival after gastrectomies between the Netherlands and England (51.9% versus 56.3%, $P < 0.001$) (Table 3). Adjusted two-year survival rates were not significantly different between the Netherlands, Sweden, and Denmark, in either resection group (Figure 4, Table 3).

Table 3. Differences in postoperative 30-day mortality and two-year survival between countries

	Esophagectomy				Gastrectomy			
	30-day mortality (NL, SW, DK, EN)		two-year survival (NL, SW, DK)		30-day mortality (NL, SW, DK, EN)		two-year survival (NL, SW, DK)	
Absolute adjusted	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Country								
Netherlands	4.6	3.3-5.9	56.8	54.5-59.3	6.9	5.1-8.8	59.0	56.8-61.3
Sweden	1.9	0.0-3.8	61.0	54.6-68.0	3.5	1.5-5.6	59.0	54.2-64.3
Denmark	4.6	2.4-6.8	58.2	54.8-61.9	4.3	2.4-6.2	62.8	58.5-67.5
England	5.8	4.7-6.9			5.9	4.3-7.4		
Absolute unadjusted			%	95% CI			%	95% CI
Country								
Netherlands			52.4	50.2-54.6			51.9	49.9-53.9
Sweden			56.7	50.0-63.4			51.7	46.8-56.6
Denmark			53.3	50.0-56.6			53.7	49.4-58.0
England			54.4	53.2-55.6			56.3	54.9-57.7
Adjusted Odds Ratio's	OR	95% CI	HR	95% CI	OR	95% CI	HR	95% CI
Country								
Netherlands (ref.)	1.00		1.00		1.00		1.00	
Sweden	0.40	0.14-1.16	0.93	0.75-1.15	**0.50**	**0.28-0.88**	0.97	0.85-1.11
Denmark	1.00	0.60-1.69	0.96	0.80-1.15	**0.60**	**0.38-0.95**	0.89	0.80-1.00
England	1.28	0.96-1.72			0.84	0.65-1.07		
Sex								
male (ref.)	1.00		1.00		1.00		1.00	
female	**0.75**	**0.61-0.93**	**0.78**	**0.69-0.89**	0.81	0.68-0.96	0.93	0.83-1.03
Age								
<60 (ref.)	1.00		1.00		1.00		1.00	
60-75	**1.80**	**1.44-2.25**	**1.40**	**1.27-1.55**	**2.58**	**1.79-3.73**	**1.29**	**1.08-1.54**
>75	**3.88**	**2.96-5.05**	**1.89**	**1.60-2.24**	**5.98**	**1.09-8.75**	**1.94**	**1.65-2.29**
Histology								
adenocarcinoma (ref.)	1.00		1.00		1.00		1.00	
SCC	**1.44**	**1.16-1.79**	**1.27**	**1.14-1.41**				
other carcinoma	1.33	0.84-2.11	**1.46**	**1.02-2.09**	**1.57**	**1.01-2.45**	0.97	0.66-1.43
TNM stage group								
I (ref.)			1.00				1.00	
II			**1.95**	**1.46-2.60**			**2.10**	**1.81-2.42**
III			**3.68**	**2.73-4.95**			**3.81**	**3.29-4.41**
IV			**8.21**	**4.42-15.3**			**6.40**	**5.37-7.62**
unknown			1.73	0.99-3.02			**2.06**	**1.60-2.64**
0			0.58	0.29-1.15			0.52	0.20-1.37

NL: Netherlands, SW: Sweden, DK: Denmark, EN: England, 95%CI: 95% confidence interval, OR: odds ratio, HR: hazard ratio, ref.: reference category, SCC: squamous cell carcinoma, **Bold:** significant ($P < 0.05$)

DIFFERENCES IN OUTCOMES IN RELATION TO HOSPITAL VOLUME

Overall, annual hospital volumes for esophagectomies were higher than for gastrectomies (Figure 2). Variation between countries is shown in Figure 5. In Denmark, 65.6% of esophagectomies were performed in hospitals with an annual volume above 30 per year, while a similar proportion (63.6%) was performed in Sweden in hospitals with an annual volume of less than 11 per year. Fifty nine per cent of all gastrectomies for cancer were performed in Denmark in hospitals with an annual volume above 20 per year, whereas over 75% of gastric resections were performed in the Netherlands and in Sweden in

hospitals with an annual volume of less than 11 per year, and 68.9% of gastrectomies in England were performed in annual hospital volumes of less than 21 per year.

Increasing hospital volume was significantly associated with lower postoperative mortality, both after esophagectomy and gastrectomy (Figure 6, Table 4). Adjusted 30-day mortality after esophagectomy in hospitals with an annual volume of at least 41 per year was lower than in hospitals with an annual volume of less than 11 per year (4.3% versus 7.2%; $P < 0.001$). Adjusted 30-day mortality after gastrectomy in hospitals with an annual volume of at least 21 per year was also lower at 4.4% than in hospitals with an annual volume of less than 11 per year (6.7%, $P = 0.047$). Testing for interaction between country and hospital volume category revealed a significant interaction regarding postoperative 30-day mortality after esophagectomy, which was the result of a stronger volume-outcome relation in Denmark than in the other countries (not shown). No such interaction was found for gastrectomy.

High hospital volume was also significantly associated with better two-year survival after esophagectomy, with a hazard ratio of 0.79 (95%CI 0.66-0.96) for the highest volume group (≥41 per year) compared with the lowest volume group (1-10 per year). There was no statistically significant association between hospital volume and two-year survival after gastrectomy (Table 4, Figure 7). No interaction was found between country and hospital volume category regarding two-year survival.

DISCUSSION

This study has shown variations in annual hospital volumes for esophagectomy and gastrectomy with highest volumes in Denmark. Resection rates were similar in the Netherlands and Denmark but considerably lower in England. Postoperative 30-day mortality was lowest in Sweden, both after esophagectomy and gastrectomy, and 30-day mortality after gastrectomy in the Netherlands was significantly higher compared with Sweden and Denmark. Higher numbers of stage I and stage IV esophageal and gastric cancers were resected in the Netherlands than in the other countries. Increasing hospital volume was associated with lower postoperative mortality after both esophagectomy and gastrectomy. Two year adjusted survival after surgery was similar in each country, with longer overall survival after esophagectomy.

SOURCES OF DATA

Studies on outcomes after cancer surgery are commonly based on data from clinical trials or on patient series from specialized surgical centers. Due to selection of patients, such series do not reflect the general practice and cannot be used to compare outcomes between countries. Population-based studies, as performed by EUROCARE, provide insight in differences in mortality and survival patterns between countries.[1] In the EUROCARE framework, however, for some countries only part of the national cancer registries is covered, and no data from recent years are available. Furthermore, it is

intended for incidence and survival trend analyses, and not to monitor clinical practice or to provide feedback to individual health care providers. Nationwide clinical audits, as currently performed in the UK, Sweden, Denmark, and the Netherlands, provide detailed information on patient, tumor, treatment, and hospital characteristics, and data are quickly available for comparative analyses. However, a disadvantage of clinical audits is that data are reported by the health care provider and are therefore not always complete. In contrast, cancer registries mostly include all available patients, but the captured information is less detailed. For example, patient comorbidity was missing in the Dutch and English dataset, and tumor stage in the English dataset. The lack of this information may bias the outcome data and may even partly explain some of the differences.

RESECTION RATES

In the current study, resection rates for both esophageal and gastric cancer were lower in England than in the Netherlands and Denmark (and not available in Sweden). The UK NOGCA has confirmed a steady reduction in resection rates over the past decade describing rates of curative resection for esophageal junctional and gastric cancer respectively of 33% and 31% in 1998 decreasing to 24% and 23% in 2005,[6] which has been attributed to improved preoperative staging and multidisciplinary management, thereby better selecting patients for surgery.[7] Comparison of resection rates is also confounded by differences in clinical practice, but with the current datasets no conclusions can be drawn on which country has the optimal resection rate. This should be addressed in future studies with adequate information on preoperative staging.

DIFFERENCES IN CENTRALIZATION OF SURGERY

A Dutch study published in 2001 showed lower postoperative mortality after esophagectomies in high volume hospitals, and as of 2006 esophagectomies in the Netherlands were centralized with a minimum annual volume of 10/year.[8] As of 2011, this was increased to 20/year. Over the study period, there was no minimum volume standard for gastrectomy, but gastrectomies will be centralized as of 2012. In addition in 2011, a national esophagogastric cancer audit has started.[9] This may answer why the resection rate in stage IV disease is higher than elsewhere as it may reflect clinical practice in peripheral hospitals where preoperative assessment is less robust.

In Sweden, a national esophagogastric cancer audit was initiated in 2006. Both esophagectomies and gastrectomies were performed in low volumes, but very recently, also Sweden has started centralization of upper GI surgery. In Denmark, a nationwide esophagogastric cancer registry has been initiated, and upper GI surgery was restricted to five centers in 2003, and further to four centers in 2008.[10] This was accompanied by a strongly reduced postoperative mortality after gastrectomy and an increase in the number of evaluated lymph nodes, which is often used as a quality indicator in gastric cancer surgery.[11] In the current study, hospital volumes in Denmark were higher than

Table 4. Multivariate analysis on the effect of annual hospital volume on 30-day mortality and two-year survival

	Esophagectomy				Gastrectomy			
	30-day mortality (NL, SW, DK, EN)		two-year survival (NL, SW, DK)		30-day mortality (NL, SW, DK, EN)		two-year survival (NL, SW, DK)	
	OR	95% CI	HR	95% CI	OR	95% CI	HR	95% CI
Annual hospital volume								
1-10 (ref.)	1.00		1.00		1.00		1.00	
11-20	0.82	0.61-1.11	0.92	0.78-1.08	0.84	0.67-1.05	1.04	0.93-1.15
21-30[a] / ≥21[b]	**0.68**	**0.50-0.93**	0.84	0.63-1.11	**0.64**	**0.41-0.99**	1.01	0.84-1.22
31-40	**0.58**	**0.39-0.85**	**0.77**	**0.63-0.94**				
≥41	**0.55**	**0.42-0.72**	**0.79**	**0.66-0.96**				
P-value for trend	<0.001		0.004		0.03		0.56	
Sex								
male (ref.)	1.00		1.00		1.00		1.00	
female	**0.77**	**0.62-0.95**	**0.78**	**0.69-0.90**	**0.80**	**0.67-0.95**	0.92	0.83-1.02
Age								
<60 (ref.)	1.00		1.00		1.00		1.00	
60-75	**1.82**	**1.45-2.28**	**1.40**	**1.27-1.55**	**2.58**	**1.78-3.72**	**1.30**	**1.09-1.55**
>75	**3.99**	**3.06-5.21**	**1.87**	**1.58-2.23**	**5.88**	**4.04-8.58**	**1.96**	**1.67-2.30**
Histology								
adenocarcinoma (ref.)	1.00		1.00		1.00		1.00	
SCC	**1.44**	**1.15-1.79**	**1.29**	**1.15-1.44**				
other carcinoma	1.28	0.81-2.04	**1.45**	**1.03-2.05**	1.50	0.96-2.33	0.97	0.65-1.43
TNM stage group								
I (ref.)			1.00				1.00	
II			**1.96**	**1.46-2.62**			**2.08**	**1.80-2.40**
III			**3.71**	**2.74-5.04**			**3.75**	**3.24-4.35**
IV			**8.13**	**4.39-15.1**			**6.38**	**5.34-7.62**
unknown			**1.77**	**1.01-3.11**			**1.94**	**1.51-2.48**
0			0.57	0.29-1.14			0.52	0.20-1.35

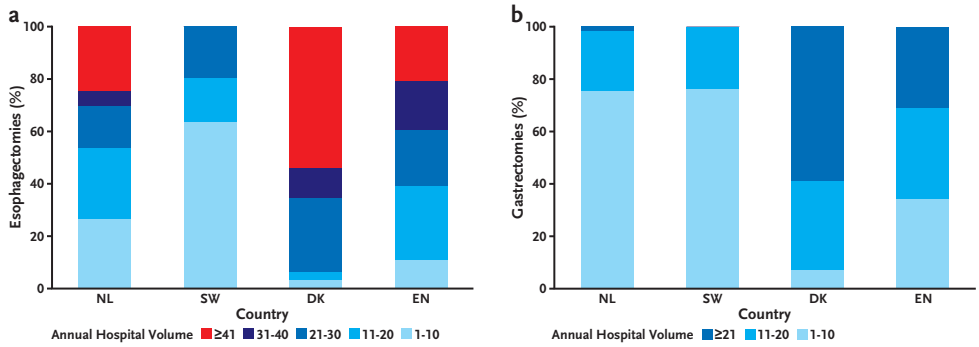
[a]esophagectomy, [b]gastrectomy
NL: Netherlands, SW: Sweden, DK: Denmark, EN: England, OR: odds ratio, HR: hazard ratio, ref.: reference category, SCC: squamous cell carcinoma, **Bold:** significant ($P < 0.05$)

in any other country, with the majority of esophagectomies being performed in hospital volumes of over 40/year. In the UK, a National Health Services (NHS) Cancer Plan became effective in 2001.[12] In this plan, recommendations were made to centralize esophagogastric cancer surgery, to establish specialist treatment teams, and to audit all steps in esophagogastric cancer care.[13] Over the last 10 years, centralization of esophagogastric cancer surgery has occurred. In 2008 and 2009, 82% of esophageal and gastric cancer resections were done in 41 designated centers with 63% of esophagectomies and 65% of gastrectomies being performed in high-volume centers (at least 50 resections per year).[14] Centralization of surgery is not unique to Europe. A recent US study describes centralization of several surgical procedures including esophagectomy for cancer, resulting in a decrease in postoperative mortality over the past decade.[15]

DIFFERENCES IN OUTCOMES BETWEEN COUNTRIES

Due to its population-based nature, the present study provides an accurate comparison of postoperative mortality and long-term survival after esophagectomy and gastrectomy

Figure 5. Annual hospital volumes for (a) esophagectomy and (b) gastrectomy



NL: Netherlands, SW: Sweden, DK: Denmark, EN: England

Figure 6. Postoperative 30-day mortality after (a) esophagectomy and (b) gastrectomy, adjusted for sex, age, and histology, by annual hospital volume category

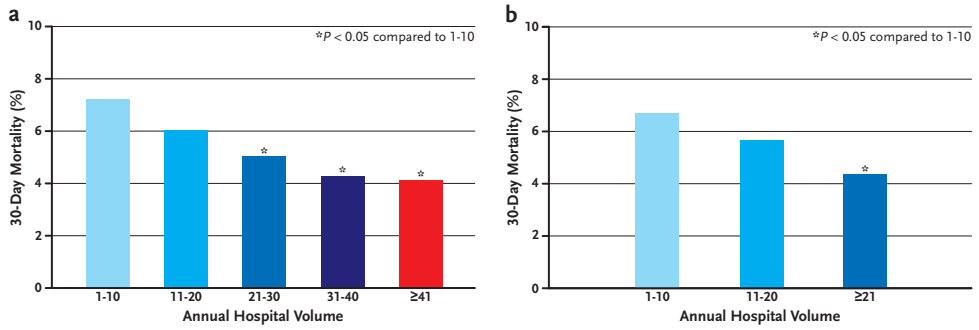
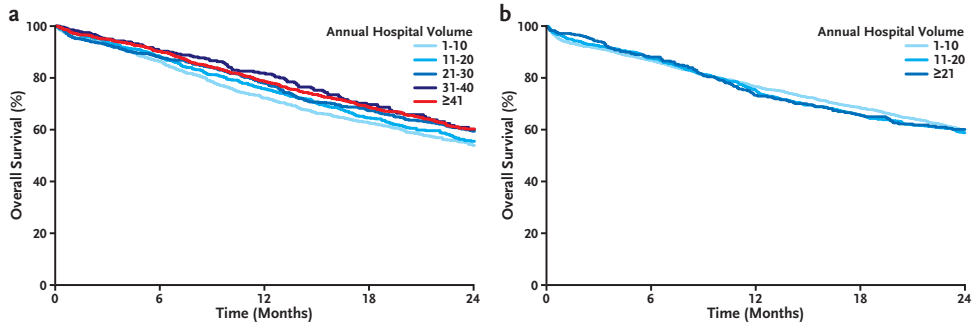


Figure 7. Two-year survival after (a) esophagectomy and (b) gastrectomy, adjusted for sex, age, histology, and stage group, by annual hospital volume category.



between several countries in Europe. However, the variability in the recorded data and missing information on patient comorbidities, multimodality therapy, and cause-specific survival do not justify explaining the differences between countries simply on annual hospital volumes. Sweden has superior postoperative mortality rates when compared to

the other participating countries, even after adjustment for case-mix, without performing surgery in high annual volumes. It is known that Sweden in general has a high quality health care with nationwide quality assurance programs, which might have contributed to the current results.[16] A second, hypothetical explanation might be differences in selecting patients for surgery between Sweden and the other countries. Furthermore the inclusion of only regions in Sweden with high case ascertainment may have excluded patients who did less well and hence bias the findings. Completeness of the data requires dedication of the surgical team to report all cases, which might be correlated to a high standard of care in these regions. On the contrary, postoperative mortality after gastrectomies in the Netherlands is high. This might be explained by the absence of a quality assurance program during the studied period for gastric cancer surgery in the Netherlands. A centralization program for gastrectomies has been initiated as of 2012. It should be noted that differences in unadjusted two-year survival rates between countries should be interpreted with care, as tumor stage distributions in the group of patients who underwent surgical resection might differ between countries.

DIFFERENCES IN OUTCOMES IN RELATION TO HOSPITAL VOLUME

The relationship between annual hospital volume and postoperative mortality after esophagectomy and gastrectomy has been investigated extensively.[15,17] In the majority of studies on esophagectomy, a benefit for high volume surgery was found.[18] Results from studies on hospital volumes for gastrectomies are less uniform. In a significant number of studies, no effect of hospital volume on postoperative mortality was found.[19-22] However, patient numbers in these studies were relatively small (below 5,000) when compared to studies in which a benefit for high volume gastrectomies was found (up to 56,000).[23-26] The available evidence on hospital volume in relation to long term survival is more limited: two out of four available studies for esophagectomy were positive,[27-30] and five out of seven available studies on gastrectomy were positive.[26,31-35] In the current study, a significant relation between annual hospital volume and postoperative mortality was found both for esophagectomy and gastrectomy. Furthermore, increasing hospital volume for esophagectomy was associated with improved long term survival. No such relation for gastrectomy was found, which might be explained by the low threshold of what was considered 'high volume surgery' (≥21/year).

It could be argued that in the current study, individual surgeon volumes should be analyzed as well as hospital volume. Quality of care and outcomes, however, are the result of collaboration between different professionals, including surgeons, anesthesiologists, ICU staff and nursing staff. All these disciplines contribute to outcomes.[36] The role of the individual surgeon is one, yet important factor.

Using hospital volume as the only basis for determining outcome quality has been criticized.[23] There can be low volume hospitals with excellent outcomes and vice versa. Outcome-based referral avoids this problem, by selecting centers of excellence based on

case-mix adjusted outcomes. It has been used to centralize esophagectomy in one part of the Netherlands, which led to a reduction in postoperative mortality from 12% to 3% over a ten-year period.[37]

CONCLUSIONS

In the current study, considerable differences between European countries were documented regarding resection rates, postoperative 30-day mortality, and annual hospital volumes in esophagogastric cancer surgery. Increasing hospital volume was associated with better outcomes, but differences in outcomes between countries could not be explained by existing differences in annual hospital volumes. Nationwide clinical audits aim to identify centers of excellence based on case-mix adjusted outcomes. On an international level, these audits can be used to understand differences in outcomes between countries. This, however, requires uniform definitions and registration of data, which is currently not the case. The current study provides a first step towards recording standard clinical data for each country to facilitate intercountry comparisons, analogous to the EURECCA initiative for colorectal cancer.[38] It is proposed to develop a European esophageal and Gastric Cancer Audit to provide further insight into differences between countries with the ultimate aim of improving quality of care for esophageal and gastric cancer patients throughout Europe.

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