# PART III

## Surgical quality assurance

# CHAPTER 14

## Effect of hospital volume on postoperative mortality and survival after esophageal and gastric cancer surgery in the Netherlands between 1989 and 2009

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## ABSTRACT

### BACKGROUND

High hospital volume is associated with better outcomes after esophagectomy and gastrectomy. In the Netherlands, a minimal volume standard of 10 esophagectomies per year was introduced in 2006. For gastrectomy, no minimal volume standard was set. Aims of this study were to describe changes in hospital volumes, mortality and survival, and to explore if high hospital volume is associated with better outcomes after esophagectomy and gastrectomy in the Netherlands.

### METHODS

From 1989-2009, 24,246 patients underwent esophagectomy (N = 10,025) or gastrectomy (N = 14,221) in the Netherlands. Annual hospital volumes were defined as very low (1-5), low (6-10), medium (11-20), and high (≥21). Volume-outcome analyses were performed using Cox regression, adjusting for year of diagnosis, case-mix, and the use of multimodality treatment.

### RESULTS

From 1989-2009, the percentage of patients treated in high-volume hospitals increased for esophagectomy (from 7% to 64%), but decreased for gastrectomy (from 8% to 5%). Six-month mortality (from 15% to 7%) and thee-year survival (from 41% to 52%) improved after esophagectomy, and to a lesser extent after gastrectomy (six-month mortality: 15%-10%, three-year survival: 55-58%). High hospital volume was associated with lower 6-month mortality (HR 0.48, $P < 0.001$) and longer 3-year survival (HR 0.77, $P < 0.001$) after esophagectomy, but not after gastrectomy.

### CONCLUSIONS

Esophagectomy was effectively centralized in the Netherlands, improving mortality and survival. Gastrectomies were mainly performed in low volumes, and outcomes after gastrectomy improved to a lesser extent, indicating an urgent need for improvement in quality of surgery and perioperative care for gastric cancer in the Netherlands.

## INTRODUCTION

Esophageal and gastric cancer are highly lethal malignancies.[1] Despite surgery, which is the cornerstone of curative treatment for these diseases, survival is low, and compared to other surgical procedures, postoperative mortality is high. In the Western world, five-year survival rates are below 25% for esophageal cancer,[2,3] and do not exceed 40% for gastric cancer.[2,4] Reported postoperative mortality after esophagectomy varies from 2% for specialized centers[5] to 10% for certain nationwide registries.[6] After gastrectomy, postoperative mortality varies between 3% to well above 10%.[7,8] To reduce mortality and improve survival, it has been suggested that these high-risk operations should be performed in specialized centers with adequate annual volumes. Many studies have investigated volume-outcome relations after esophagectomy and gastrectomy, but the relative importance of volume after gastrectomy in particular is disputed.[9,10]

In the Netherlands, a relation between high hospital volume and low postoperative mortality was demonstrated for esophagectomy in 2000.[11] Despite extensive discussions within the Dutch Society of Surgery, this study did not lead to significant changes in referral patterns for esophagectomies on a national level. Therefore, as of 2006 a minimum volume of 10 esophagectomies per year was enforced by the Dutch Healthcare Inspectorate, and as of 2011 the Dutch Society of Surgery recommends a minimal volume of 20 esophagectomies per year. For gastrectomy, no minimum volume standard has been established in the Netherlands.

Aims of the present study were to describe changes in annual hospital volumes, postoperative mortality, survival, and lymph node yields for esophagectomy and gastrectomy in the Netherlands between 1989 and 2009, and to explore whether there is any association between annual hospital volume for esophagectomy and gastrectomy, and postoperative mortality, survival, and lymph node yield.

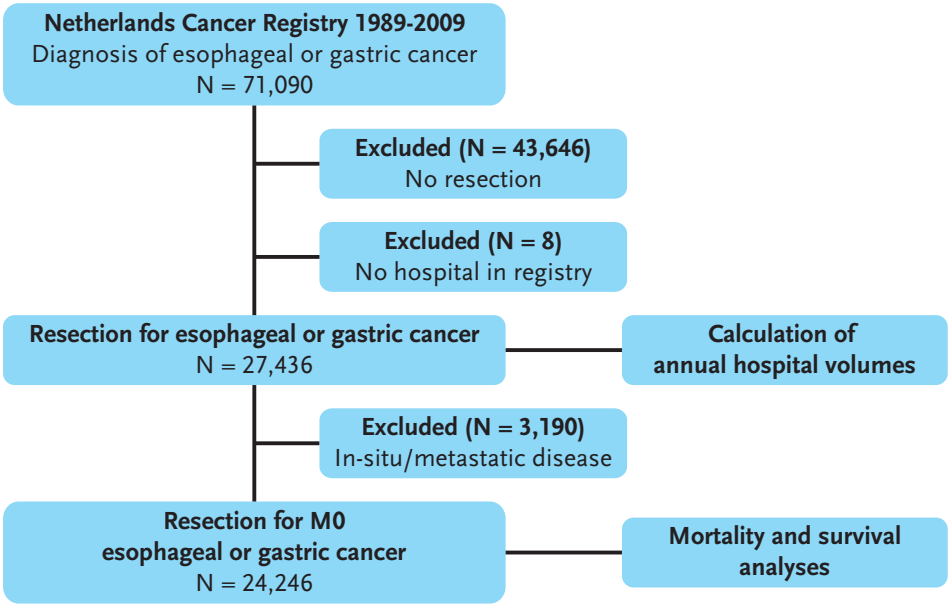
## PATIENTS AND METHODS

### NETHERLANDS CANCER REGISTRY

Data were obtained from the Netherlands Cancer Registry (NCR), which covers all hospitals in the Netherlands, a country of 16.5 million inhabitants. Information on all newly diagnosed malignancies is routinely collected by trained registrars from the hospital records 6-18 months after diagnosis. Quality and completeness of the data is high.[12]

Topography and morphology were coded according to the International Classification of Diseases for Oncology (ICD-O).[13] ICD-O morphology codes were used to classify tumors as adenocarcinoma (8140-8145, 8190, 8201-8211, 8243, 8255-8401, 8453-8520, 8572, 8573, 8576), squamous cell carcinoma (SCC) (8032, 8033, 8051-8074, 8076-8123) and other or unknown histology (8000-8022, 8041-8046, 8075, 8147, 8153, 8200, 8230-

**Figure 1. Study profile**




8242, 8244-8249, 8430, 8530, 8560, 8570, 8574, 8575). Tumors were staged according to the International Union Against Cancer (UICC) TNM classification in use in the year of diagnosis. Vital status was initially obtained from municipal registries, and from 1994 onwards from the nationwide population registries network. These registries provide complete coverage of all deceased Dutch citizens. Follow-up was complete for all patients until December 31st, 2009. The study was approved by the NCR Review Board.

### PATIENTS

Between January 1989 and December 2009, 71,090 patients with esophageal or gastric cancer were diagnosed in the Netherlands (Figure 1). Patients who did not undergo surgical treatment (N = 43,646) and patients without information on the hospital were the diagnosis was established, or where surgery was performed (N = 8), were excluded, leaving 27,436 resections available to calculate annual hospital volumes. After establishing annual hospital volumes, patients with in-situ carcinoma (N = 288), and patients with distant metastases (N = 2902) were excluded, leaving 24,246 patients with non-metastatic invasive carcinoma available for volume-outcome analyses.

### SURGERY

Since the NCR is a topography-based registry, and the type of surgery was not specified for every patient, the distinction between esophageal and gastric cancer surgery was based on tumor location. Esophagectomies were defined as resections for cancers of the

esophagus (C15.0-15.9) and gastric cardia (C16.0), whereas gastrectomies were defined as resections for non-cardia gastric cancer (C16.1-16.9). To ensure this distinction did not influence the results, volume-outcome analyses were repeated with cardia cancer coded as gastric cancer. Yearly resection rates were calculated as the number of resections relative to the number of cancers diagnosed in a year.

### HOSPITAL VOLUMES

Annual hospital volumes were defined as the number of esophagectomies or gastrectomies per hospital per year. Clinically relevant volume categories were defined as very low (1-5 per year), low (6-10 per year), medium (11-20 per year), and high (≥21 per year). From 2005-2009, the hospital where surgery was performed was registered for all patients. Before 2005, the hospital were surgery was performed was only registered in 53% of the cases, and showed an 80% overlap with the hospital of diagnosis. For the remaining 47%, with an unknown surgical hospital, the hospital of diagnosis was used to calculate hospital volume.

### STATISTICAL ANALYSIS

Esophagectomy and gastrectomy were analyzed separately. Resection rates and hospital volumes over time were analyzed with the Chi-square test. Changes in six-month mortality and three-year survival were analyzed with stratified Cox regression, adjusted for sex, age, socio-economic status,[14] stage, morphology, preoperative therapy use, and postoperative therapy use (only for three-year survival). Overall survival (OS) was calculated from the day of diagnosis until death, because the date of surgery was not available before 2005. Six-month OS was calculated unconditionally, while 3-year OS was calculated conditionally on surviving the first six months after diagnosis. Lymph node yields over time were adjusted for sex, age, stage, and morphology.

For volume-outcome analyses, the patient was considered the unit of analysis, with hospital volume as the exposure factor. Differences in survival estimates were calculated with Cox regression, stratified for hospital volume and adjusted for the factors used to analyze changes over time, and for clustering of deaths within hospitals.[15] Differences in lymph node yields were analyzed with generalized estimated equations, adjusted for the factors used to analyze changes over time, and for clustering within hospitals.

Besides analyzing hospital volume in categories, annual volume was analyzed as a linear variable. Analyses were performed with SPSS (version 17.0.2) and R (version 2.12.2).

## RESULTS

### PATIENT CHARACTERISTICS

Between 1989 and 2009, 24,246 patients with resectable, non-metastatic esophageal (N = 10,025) or gastric cancer (N = 14,221) underwent a resection in the Netherlands. Patient characteristics (Table 1 and 2) varied between the different volume categories.

**Table 1. Patient characteristics for all surgically treated patients with non-metastatic invasive esophageal cancer in the Netherlands between 1989 and 2009 (N = 10,025)**

| Annual hospital volume | 1-5 | | 6-10 | | 11-20 | | ≥21 | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | *P* |
| **Total** | 2914 | *100* | 2695 | *100* | 1494 | *100* | 2922 | *100* | |
| **Sex** | | | | | | | | | |
| male | 2213 | *76* | 2058 | *76* | 1130 | *76* | 2249 | *77* | 0.73 |
| female | 701 | *24* | 637 | *24* | 364 | *24* | 673 | *23* | |
| **Age** | | | | | | | | | |
| <60 | 936 | *32* | 956 | *35* | 515 | *34* | 1032 | *35* | 0.002 |
| 60-75 | 1630 | *56* | 1456 | *54* | 814 | *54* | 1632 | *56* | |
| >75 | 348 | *12* | 283 | *11* | 165 | *11* | 258 | *9* | |
| **SES** | | | | | | | | | |
| low | 274 | *9* | 308 | *11* | 165 | *11* | 259 | *9* | < 0.001 |
| medium | 2415 | *83* | 2124 | *79* | 1208 | *81* | 2131 | *73* | |
| high | 135 | *5* | 123 | *5* | 53 | *4* | 115 | *4* | |
| unknown | 90 | *3* | 140 | *5* | 68 | *5* | 417 | *14* | |
| **Morphology** | | | | | | | | | |
| adenocarcinoma | 2288 | *79* | 2006 | *74* | 1113 | *74* | 2134 | *73* | < 0.001 |
| SCC | 554 | *19* | 628 | *23* | 341 | *23* | 732 | *25* | |
| other | 72 | *2* | 61 | *2* | 40 | *3* | 56 | *2* | |
| **TNM stage group** | | | | | | | | | |
| I | 622 | *21* | 512 | *19* | 285 | *19* | 522 | *18* | < 0.001 |
| II | 1161 | *40* | 1093 | *41* | 576 | *39* | 1068 | *37* | |
| III | 988 | *34* | 940 | *35* | 535 | *36* | 1112 | *38* | |
| IV[a] | 30 | *1* | 30 | *1* | 23 | *2* | 25 | *1* | |
| unknown | 113 | *4* | 120 | *4* | 75 | *5* | 195 | *7* | |
| **Preoperative therapy** | | | | | | | | | |
| yes | 165 | *6* | 244 | *9* | 357 | *24* | 938 | *32* | < 0.001 |
| no | 2749 | *94* | 2451 | *91* | 1137 | *76* | 1984 | *68* | |
| **Postoperative therapy** | | | | | | | | | |
| yes | 144 | *5* | 145 | *5* | 91 | *6* | 151 | *5* | 0.43 |
| no | 2770 | *95* | 2550 | *95* | 1403 | *94* | 2771 | *95* | |

SES: socio economic status, SCC: squamous cell carcinoma, preoperative/postoperative therapy: chemotherapy with/without radiotherapy
[a]T4N1-3M0 and T1-4N3M0 gastric cancers were assigned stage IV in the 6th edition TNM-classification

For esophageal cancer, high-volume hospitals treated more patients with squamous cell carcinoma and more advanced tumor stages. For gastric cancer, patients treated in high-volume hospitals were older and had more advanced tumors.

### HOSPITAL VOLUMES OVER TIME

From 1989 to 2009, the annual number of esophagectomies doubled (from 352 to 723), and the annual number of gastrectomies steadily decreased (from 1107 to 495) (Figure 2). The percentage of esophagectomies performed in high-volume hospitals increased from 7% to 64%, while the number of gastrectomies performed in high-volume hospitals decreased from 8% to 5%.

In 2009, 44 of the 92 hospitals (48%) in the Netherlands performed esophagectomies, and 91 of the 92 hospitals performed gastrectomies.

**Table 2. Patient characteristics for all surgically treated patients with non-metastatic invasive gastric cancer in the Netherlands between 1989 and 2009 (N = 14,221)**

| Annual hospital volume | 1-5 | | 6-10 | | 11-20 | | ≥21 | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | P |
| **Total** | 3411 | *100* | 6099 | *100* | 4356 | *100* | 355 | *100* | |
| **Sex** | | | | | | | | | |
| male | 1987 | *58* | 3707 | *61* | 2646 | *61* | 224 | *63* | 0.045 |
| female | 1424 | *42* | 2392 | *39* | 1710 | *39* | 131 | *37* | |
| **Age** | | | | | | | | | |
| <60 | 689 | *20* | 1270 | *21* | 837 | *19* | 53 | *15* | 0.016 |
| 60-75 | 1606 | *47* | 2917 | *48* | 2074 | *48* | 165 | *46* | |
| >75 | 1116 | *33* | 1912 | *31* | 1445 | *33* | 137 | *39* | |
| **SES** | | | | | | | | | |
| low | 378 | *11* | 783 | *13* | 560 | *13* | 53 | *15* | < 0.001 |
| medium | 2665 | *78* | 4846 | *79* | 3559 | *82* | 294 | *83* | |
| high | 118 | *3* | 230 | *4* | 106 | *2* | 8 | *2* | |
| unknown | 250 | *7* | 240 | *4* | 131 | *3* | 0 | *0* | |
| **Morphology** | | | | | | | | | |
| adenocarcinoma | 3336 | *98* | 5985 | *98* | 4287 | *98* | 352 | *99* | 0.11 |
| other | 75 | *2* | 114 | *2* | 69 | *2* | 3 | *1* | |
| **TNM stage group** | | | | | | | | | |
| I | 1299 | *38* | 2279 | *37* | 1687 | *39* | 147 | *41* | 0.014 |
| II | 898 | *26* | 1675 | *27* | 1187 | *27* | 78 | *22* | |
| III | 936 | *27* | 1718 | *28* | 1204 | *28* | 111 | *31* | |
| IV[a] | 181 | *5* | 248 | *4* | 154 | *4* | 11 | *3* | |
| unknown | 97 | *3* | 179 | *3* | 124 | *3* | 8 | *2* | |
| **Preoperative therapy** | | | | | | | | | |
| yes | 167 | *5* | 303 | *5* | 138 | *3* | 8 | *2* | < 0.001 |
| no | 3244 | *95* | 5796 | *95* | 4218 | *97* | 347 | *98* | |
| **Postoperative therapy** | | | | | | | | | |
| yes | 139 | *4* | 236 | *4* | 122 | *3* | 12 | *3* | 0.009 |
| no | 3272 | *96* | 5863 | *96* | 4234 | *97* | 343 | *97* | |

SES: socio economic status, preoperative/postoperative therapy: chemotherapy with/without radiotherapy
[a]T4N1-3M0 and T1-4N3M0 gastric cancers were assigned stage IV in the 6th edition TNM-classification

### RESECTION RATES, MORTALITY, SURVIVAL AND LYMPH NODE YIELDS OVER THE YEARS

Resection rates slightly decreased for esophageal cancer (from 1989-2009: 31% - 29%, $P < 0.01$), and strongly decreased for gastric cancer (56%-37%, $P < 0.01$). Adjusted six-month mortality after esophagectomy decreased from 14.8% in 1989 to 7.1% in 2009 ($P < 0.001$), while adjusted six-month mortality after gastrectomy decreased to a lesser extent: from 15.2% in 1989 to 9.9% in 2009 ($P < 0.001$) (Figure 3a). Adjusted three-year conditional survival significantly increased after esophagectomy: from 41.0% in 1989 to 52.2% in 2009 ($P < 0.001$). Adjusted three-year conditional survival after gastrectomy increased to a lesser extent: from 55.0% in 1989 to 58.4% in 2009 ($P < 0.01$) (Figure 3b). The improvement in six-month mortality and three-year survival over time was significantly stronger after esophagectomy, when compared to gastrectomy (both $P < 0.01$)

**Figure 2. Number of (a) esophagectomies and (b) gastrectomies per hospital volume category**

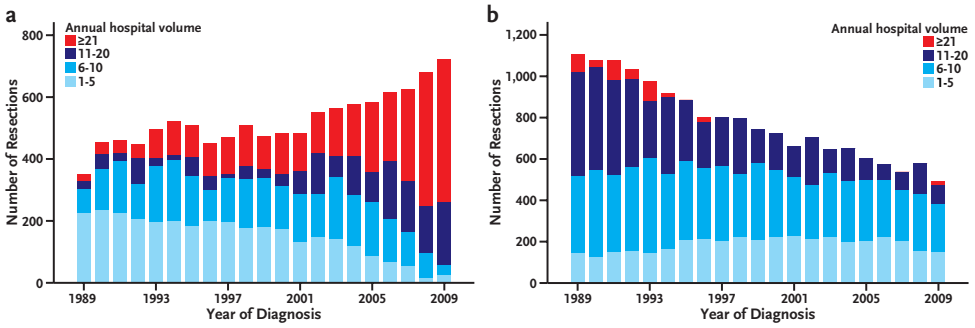
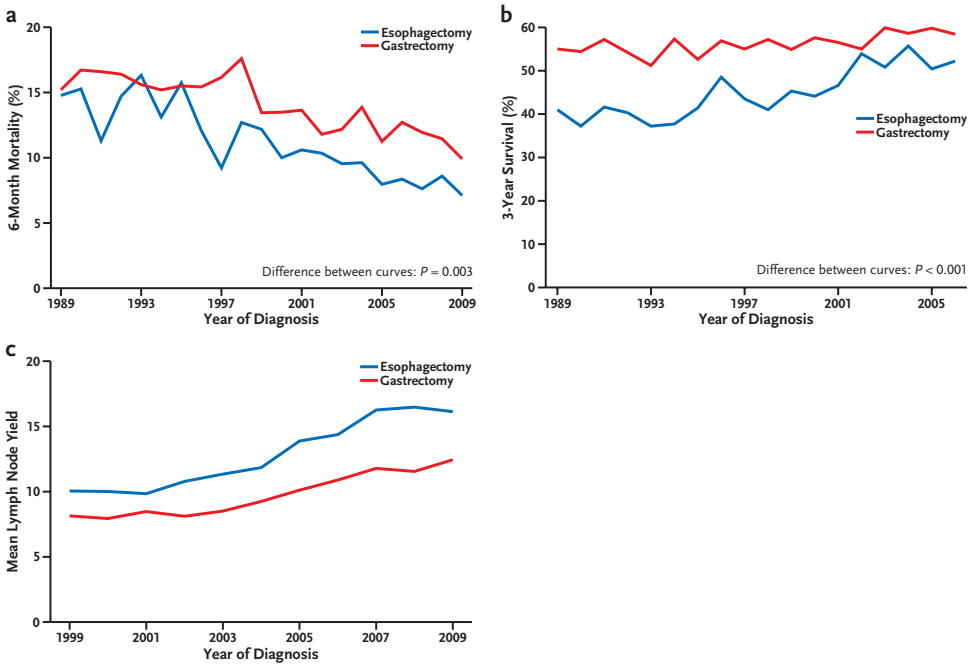



**Figure 3. Adjusted (a) 6-month mortality , (b) 3-year conditional survival, and (c) median lymph node yield for esophagectomy and gastrectomy, 1989-2008**

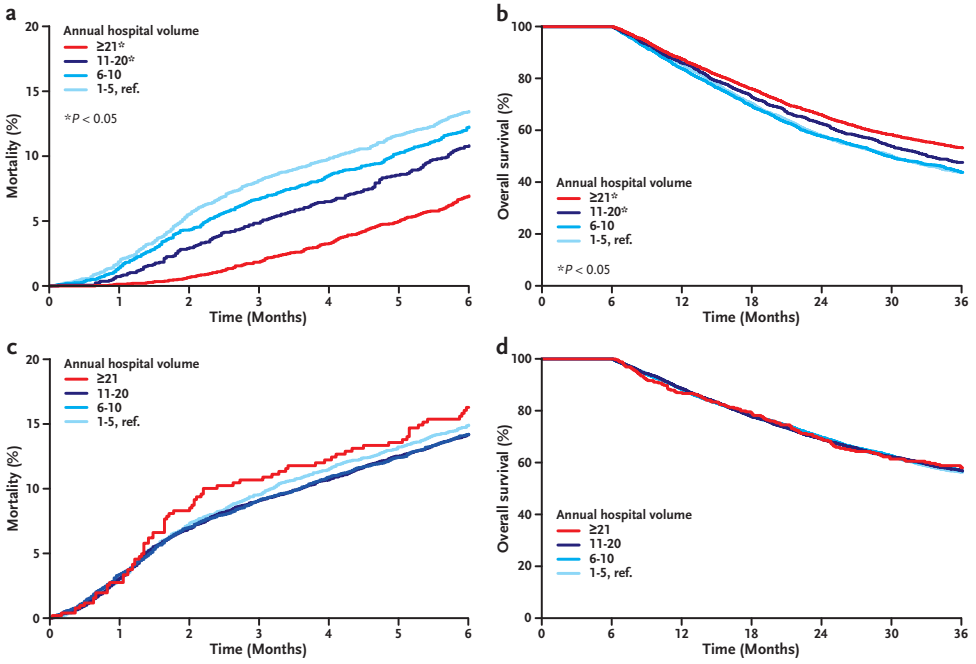



Mean lymph node yield after esophagectomy increased from 10.1 in 1999 to 16.2 in 2009 ($P < 0.001$), and mean lymph node yield after gastrectomy increased from 8.1 in 1999 to 12.4 in 2009 ($P < 0.001$) (Figure 3c).

### VOLUME-OUTCOME RELATIONS

Results from the multivariable analyses on volume-outcome relations are shown in Table 3 and 4. After esophagectomy, medium and high volume hospitals were associated with lower six-month mortality and longer three-year conditional survival when compared

**Figure 4. Adjusted relation between annual hospital volume and (a) 6-month mortality and (b) 3-year conditional survival after esophagectomy, and relation between annual hospital volume and (c) 6-month mortality and (d) 3-year conditional survival after gastrectomy**




to very-low volume hospitals (Figures 4a, 4b). After gastrectomy, neither six-month mortality, or three-year conditional survival were associated with hospital volume category (Figures 4c, 4d). High hospital volume was associated with high lymph node yield both after esophagectomy and gastrectomy.

When analyzing hospital volume as a linear covariate, volume-survival results remained the same. No changes in the results were found when volume-outcome relations were analyzed with surgery for cardia cancer coded as gastrectomy (data not shown).

## DISCUSSION

Over the study period, the number of esophagectomies performed in high volume hospitals considerably increased, while in 2009 most gastrectomies were performed in low volume hospitals. Both six-month mortality and three-year survival improved after esophagectomy, but to a lesser extent after gastrectomy. In the current dataset, a volume-survival relation was revealed for esophagectomy, but not for gastrectomy.

Since Luft et al. published the first study on volume-outcome relations for surgery,[16] many studies have emerged investigating the effect of hospital and surgeons volume on short term and long term outcomes for a variety of diseases, including resections for

**Table 3. Volume-outcome relations for esophagectomy (1989-2009)**

| | 6-month mortality | | 3-year survival[a] | | | LN yield[b] |
|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | OR | 95% CI |
| **Annual hospital volume** | | | | | | |
| 1-5 | 1.00 | | 1.00 | | 1.00 | |
| 6-10 | 0.90 | 0.78-1.03 | 1.01 | 0.94-1.10 | 1.00 | 0.91-1.09 |
| 11-20 | **0.78** | **0.62-0.97** | **0.90** | **0.81-0.99** | 1.10 | 1.00-1.22 |
| ≥21 | **0.48** | **0.38-0.61** | **0.77** | **0.70-0.85** | **1.50** | **1.25-1.80** |
| **Year of diagnosis** | | | | | | |
| 1989-1993 | 1.00 | | 1.00 | | | |
| 1994-1997 | 0.91 | 0.78-1.07 | 0.92 | 0.83-1.01 | | |
| 1998-2001 | **0.82** | **0.68-0.98** | **0.88** | **0.79-0.97** | 1.00 | |
| 2002-2005 | **0.69** | **0.55-0.86** | **0.69** | **0.63-0.75** | **1.18** | **1.10-1.25** |
| 2006-2009 | **0.67** | **0.52-0.85** | **0.75** | **0.67-0.83** | **1.42** | **1.27-1.60** |
| **Sex** | | | | | | |
| male | 1.00 | | 1.00 | | 1.00 | |
| female | **0.75** | **0.66-0.86** | **0.83** | **0.78-0.89** | 1.04 | 1.00-1.08 |
| **Age** | | | | | | |
| <60 | 1.00 | | 1.00 | | 1.00 | |
| 60-75 | **1.83** | **1.56-2.14** | **1.14** | **1.07-1.21** | 0.97 | 0.94-1.00 |
| >75 | **3.10** | **2.54-3.79** | **1.41** | **1.25-1.59** | **0.87** | **0.82-0.92** |
| **SES** | | | | | | |
| low | 1.00 | | 1.00 | | | |
| medium | **0.76** | **0.64-0.90** | 1.05 | 0.96-1.16 | | |
| high | **0.54** | **0.38-0.78** | 1.00 | 0.85-1.17 | | |
| unknown | **0.53** | **0.38-0.74** | 1.04 | 0.86-1.26 | | |
| **TNM stage group** | | | | | | |
| I | 1.00 | | 1.00 | | 1.00 | |
| II | **1.28** | **1.08-1.52** | **2.74** | **2.46-3.04** | **1.15** | **1.09-1.21** |
| III | **1.73** | **1.41-2.13** | **5.20** | **4.46-6.05** | **1.39** | **1.31-1.47** |
| IV | **3.85** | **2.55-5.81** | **9.76** | **7.43-12.81** | **1.93** | **1.70-2.20** |
| unknown | **1.92** | **1.41-2.62** | **2.37** | **2.00-2.81** | 1.04 | 0.92-1.17 |
| **Morphology** | | | | | | |
| adenocarcinoma | 1.00 | | 1.00 | | 1.00 | |
| SCC | **1.26** | **1.11-1.43** | 1.09 | 0.98-1.21 | 1.05 | 0.99-1.11 |
| other | 1.28 | 0.94-1.75 | 1.05 | 0.84-1.33 | 1.00 | 0.88-1.12 |
| **Preoperative therapy** | | | | | | |
| no | 1.00 | | 1.00 | | | |
| yes | **0.32** | **0.23-0.43** | **0.84** | **0.76-0.93** | | |
| **Postoperative therapy** | | | | | | |
| no | | | 1.00 | | | |
| yes | | | 1.07 | 0.94-1.21 | | |

[a]conditional on surviving the first six months, [b]1999-2009
HR: hazard ratio, OR: odds ratio, SES: socio economic status, SCC: squamous cell carcinoma,
95% CI: 95% confidence interval, **Bold:** significant ($P < 0.05$)

esophageal and gastric cancer. Several large studies have shown an association between high hospital volume and low postoperative mortality both for esophagectomy,[17-20] and gastrectomy[17,20-22], but other studies did not find an association[23-25]. In a meta-analysis exploring volume-outcome relations, high volume surgery was associated with lower postoperative mortality after both esophagectomy and gastrectomy.[9] A limited number of studies investigate the relation between hospital volume and *long*-term survival after esophagectomy and gastrectomy, with conflicting results.[7,24,26,27]

**Table 4. Volume-outcome relations for gastrectomy (1989-2009)**

| | 6-month mortality | | 3-year survival[a] | | | LN yield[b] |
|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | OR | 95% CI |
| **Annual hospital volume** | | | | | | |
| 1-5 | 1.00 | | 1.00 | | 1.00 | |
| 6-10 | 0.95 | 0.84-1.07 | 0.99 | 0.91-1.07 | 1.02 | 0.96-1.08 |
| 11-20 | 0.95 | 0.83-1.08 | 0.99 | 0.90-1.08 | 0.99 | 0.90-1.10 |
| ≥21 | 1.10 | 0.82-1.49 | 0.98 | 0.86-1.12 | **1.93** | **1.81-2.04** |
| **Year of diagnosis** | | | | | | |
| 1989-1993 | 1.00 | | 1.00 | | | |
| 1994-1997 | 0.96 | 0.86-1.07 | 0.98 | 0.90-1.05 | | |
| 1998-2001 | 0.89 | 0.79-1.01 | 0.94 | 0.87-1.02 | 1.00 | |
| 2002-2005 | **0.74** | **0.65-0.85** | **0.88** | **0.81-0.96** | **1.08** | **1.02-1.16** |
| 2006-2009 | **0.70** | **0.60-0.81** | **0.78** | **0.72-0.86** | **1.42** | **1.32-1.52** |
| **Sex** | | | | | | |
| male | 1.00 | | 1.00 | | | |
| female | **0.79** | **0.73-0.85** | **0.91** | **0.85-0.97** | **1.10** | **1.05-1.14** |
| **Age** | | | | | | |
| <60 | 1.00 | | 1.00 | | 1.00 | |
| 60-75 | **2.03** | **1.78-2.30** | **1.27** | **1.18-1.37** | **0.88** | **0.82-0.93** |
| >75 | **3.94** | **3.47-4.49** | **1.57** | **1.44-1.71** | **0.75** | **0.69-0.81** |
| **SES** | | | | | | |
| low | 1.00 | | 1.00 | | | |
| medium | 0.92 | 0.81-1.04 | 1.01 | 0.92-1.12 | | |
| high | **0.70** | **0.55-0.91** | 1.00 | 0.84-1.20 | | |
| unknown | 0.94 | 0.73-1.21 | 1.03 | 0.85-1.24 | | |
| **TNM stage group** | | | | | | |
| I | 1.00 | | 1.00 | | 1.00 | |
| II | **1.46** | **1.31-1.63** | **2.99** | **2.78-3.22** | **1.23** | **1.16-1.31** |
| III | **2.15** | **1.93-2.38** | **5.37** | **5.01-5.75** | **1.55** | **1.46-1.66** |
| IV | **3.50** | **3.00-4.08** | **8.45** | **7.43-9.61** | **2.23** | **2.05-2.42** |
| unknown | **1.91** | **1.40-2.60** | **2.36** | **1.96-2.84** | 1.01 | 0.82-1.24 |
| **Morphology** | | | | | | |
| adenocarcinoma | 1.00 | | 1.00 | | 1.00 | |
| other | 1.18 | 0.86-1.64 | **0.58** | **0.44-0.78** | 0.94 | 0.71-1.25 |
| **Preoperative therapy** | | | | | | |
| no | 1.00 | | 1.00 | | | |
| yes | **0.27** | **0.17-0.43** | 1.05 | 0.84-1.31 | | |
| **Postoperative therapy** | | | | | | |
| no | | | 1.00 | | | |
| yes | | | 1.01 | 0.85-1.21 | | |

[a]conditional on surviving the first six months, [b]1999-2009
HR: hazard ratio, OR: odds ratio, SES: socio economic status, 95% CI: 95% confidence interval
**Bold:** significant ($P < 0.05$)

Over the past two decades, the number of esophagectomies in the Netherlands has increased, corresponding with an increasing incidence of esophageal cancer.[28] The decreasing incidence of gastric cancer explains the low number of gastrectomies currently performed in the Netherlands.[29] Furthermore, the resection rate for gastric cancer dropped significantly, most likely the result of improved preoperative staging. Combined with the almost complete disappearance of surgery for reflux disease and ulcers, surgeons are decreasingly exposed to gastrectomies. This might partly be

compensated by increasing volumes of bariatric surgery for obesity, but the surgical techniques used differ significantly.

In the current study, increasing hospital volume was associated with lower mortality and increased long-term survival after esophagectomy, but not after gastrectomy. This observation for gastrectomies might be explained by the low number of high-volume gastrectomies (2.5% of all gastrectomies in the current dataset), and the low threshold for what was considered high volume surgery. In other studies that did find an association between gastrectomy in high volumes and good outcomes, the lower limit of high-volume surgery varied from 20/year up to 264/year.[17,27]

The current study covers an extensive period of two decades of esophagogastric cancer surgery in the Netherlands, and analyzes a significant population of about 25,000 patients. Unlike many of the large volume-outcome studies, the current study uses a clinical database with highly reliable data, providing complete coverage of all diagnosed cancers in the Netherlands. Furthermore, outcomes are case-mix adjusted, increasing reliability of the results.[30] The absence of comorbidity in the current dataset was partly compensated by the use of SES, which can be considered a proxy for comorbidity.[31]

A potential bias when analyzing outcomes over a long period is that preoperative staging and (perioperative) care generally improve over time. For example, endoscopic ultrasound, multislice high resolution computed tomography, and PET computed tomography were introduced resulting in improvement of staging. Hospital volumes for esophagectomy significantly changed during the study period, with most high-volume resections performed in the more recent years. Therefore, high volume resections are intrinsically associated with better outcomes. However, adjusting for year of diagnosis offsets this effect. Another potential weakness is the unavailability of the surgery hospital for part of the patients treated before 2005. Instead, the hospital of diagnosis was used. However, this only happened in the first years of the study, when hospitals less frequently referred patients to another hospital for surgery.

A point of discussion might be that volumes are analyzed on hospital level, rather than surgeon level.[7,27,32] Quality of care, however, consists of more than an individual surgeon's performance. Perioperative care, anesthesia, ICU staffing, experience of the nursery staff, and collaboration between different disciplines all contribute to outcomes associated with the performed procedure.[33] The role of the surgeon is only one, yet important, factor contributing to outcome.

Initiatives to improve medical and especially surgical care are legion. Randomized trials improve care by selecting appropriate treatments for certain indications,[3,34] and by educating surgeons participating in the trial.[35,36] However, the majority of cancer patients are treated outside trials, and especially improvements in the process and structure of care on a nation-wide level will bring benefit to this group of patients. Many studies have advocated the centralization of low-volume, high-risk operations, thereby improving nationwide quality of care.[11,27] Centralization of esophageal and gastric cancer is currently

performed in several European countries, whereas referral to high-volume centers is also advocated in the United States by the Leapfrog group.[37] In Denmark, centralization of gastric cancer surgery from 37 to 5 hospitals leaded to a drop in postoperative mortality from 8.4% to 2.1% over a period of 5 years.[38]

Unlike the Netherlands, which is a relatively small country with good infrastructure, centralization of care in countries with large rural areas might lead to unreasonable travel burdens and problems with continuity of care after surgery. Therefore, others have advocated implementing processes that are related to excellent outcomes in low volume hospitals, but identification of these processes remains challenging.[39]

Meanwhile, using hospital volume as the sole basis for referral to improve outcomes is criticized.[17] Although hospital volume can reliably identify groups of hospitals with better results on average, individual low volume hospitals can have excellent outcomes and vice versa. In contrast to volume-based referral, outcome based-referral avoids this problem and has proven its value for esophagectomy in the Western part of the Netherlands. In this area, a prospective audit was conducted to identify hospitals with excellent performance in esophagectomy. During the five-year audit, a gradual concentration towards centers with excellent performance occurred, leading to a drop in postoperative mortality (12% to 4%) and an improvement in survival.[40]

Combining centralization with auditing substantially adds to improvement of care.[41] With auditing, providers of care are monitored and their performance is benchmarked against their peers. Auditing is performed on a national level for esophagogastric cancer in Denmark,[38] Sweden and the United Kingdom. A nationwide audit for both esophageal and gastric cancer surgery has started in the Netherlands as of 2011 aiming for complete coverage of all esophagectomies and gastrectomies.

In conclusion, enforcing centralization for esophagectomy in the Netherlands has resulted in a shift in annual hospital volumes: most resections are currently performed in high volume centers. For gastrectomy, no minimum number of resections was required, and the majority of gastric cancer resections were performed in low volume hospitals. However, as of 2012 gastrectomies in the Netherlands will be centralized to a minimum of 10/year, and as of 2013 to a minimum of 20/year. Esophagectomy in high volume hospitals is associated with improved outcomes. No such relation for gastric cancer could be established in the current dataset, but only a minority of patients was treated in high volume hospitals. Over the past two decades, short-term mortality and long-term survival after esophagectomy decreased significantly, while outcomes after gastrectomy improved to a lesser extent, indicating an urgent need for improvement in quality of surgery and perioperative care for gastric cancer in the Netherlands.

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