MEASURING AND IMPROVING QUALITY OF CARE IN SURGICAL ONCOLOGY

Michel W.J.M. Wouters

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Colofon

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DEZE UITGAVE IS TOT STAND GEKOMEN MET FINANCIELE STEUN VAN:
KWF Kankerbestrijding, Nederlands Kanker Instituut - Antoni van Leeuwenhoek, Leids Universitair Medisch Centrum, GlaxoSmithKline BV, Roche Nederland BV, Agendia NV, Sanofi-Aventis BV, Jan van der Kroon en Guus Corver (patient tot 2009).

HET ONDERZOEK IN DIT PROEFSCHRIFT IS MEDE MOGELIJK GEMAAKT DOOR:
KWF Kankerbestrijding, Integraal Kankercentrum Nederland (voormalig Integraal Kankercentrum West), Integraal Kankercentrum Zuid, Stichting ZOLEON (voormalig Stichting Samenwerking Oncologie Haaglanden).

The ‘End Result’ Idea

“The common sense notion that **every** hospital should follow **every** patient it treats, long enough to determine whether or not the treatment has been successful, and then to inquire, ‘If not, why not?’ with a view to preventing similar failures in the future”

Ernest Amory Codman, surgeon, 1869-1940

Aan hen die mij al die tijd steunden!
Voor mijn lieve Ouders, Sandra, Alessa en Tim

CONTENTS

Chapter 1

Introduction and outline of this thesis

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Ever since the Institute of Medicine released its report 'Crossing the quality chasm: A New Health System for the 21st Century' in March 2001[1], variation in quality of care between providers has been debated by policymakers, purchasers, health care providers, doctors and their patients. Not only in the United States, but also in Europe improving the quality of Health care is high on the political agenda. In the last 20 years medical science and technology is advancing in an unprecedented rate. This has come with a growing complexity of the care process requiring a multidisciplinary infrastructure in which the full complement of services is provided timely and in a safe, effective, efficient but patient-centered way. Simultaneously, the population is aging with an increase in the incidence and prevalence of chronic conditions, which make these patients especially vulnerable for the risks of medical treatments. Reducing risks, ensuring safety, but also continuous quality improvement are needed to face the challenges in our Health care system.

Measuring quality

A basic way of explaining quality healthcare is that it is the right care, for the right person, in the right setting at the right time. An important mechanism to improve quality of care is to reduce variation and to learn from practices that prove to have excellent outcomes. Though variation in the way care is delivered can be legitimate, there is evidence that differences in outcomes between providers are unconscionably large. To gain insight in the mechanisms leading to variation in quality of care, comparative measurement of performance is essential: clinicians may find out what problems they have, and who else may have solved these problems. In the beginning of the century, data to compare the performance of hospitals were hardly available. The first reports on variation in quality of care were mostly based on information derived from administrative databases. For example, in the Netherlands Caspari et al. published on their analysis of production data from medical insurance companies in 1991. A remarkable variation in amount of ENT procedures per 1000 insured persons were found for 11 partnerships of ENT specialists[2]. Though, in general, these kind of administrative data were thought to be less reliable and were often missing essential characteristics of patients treated by different providers, possibly explaining practice variation. Therefore, in several countries clinical registries were designed to provide detailed and meaningful information concerning the quality of care in different hospitals[3]. This thesis describes the use of detailed clinical data to measure and improve quality of care in surgical oncology.

Volume and outcome

The relationship between procedural volume and outcome was one of the first causes of variation in outcome between providers, reported in the literature. From 2000 until now a plethora of studies has been published evaluating variation in outcome between procedures performed in low and high volume hospitals and by low and high volume surgeons[4]. First, an inverse relation between hospital volume and mortality was shown, especially for high-risk low-volume surgical procedures, like esophagectomies and pancreatectomies[4]. Later on other outcome parameters were studied, like postoperative morbidity, quality of

life and survival[5-7]. In **chapter 2** of this thesis a systematic review and meta-analysis of the relationship between hospital and surgeon volume of esophagectomies for cancer on the one hand and postoperative mortality and survival on the other, is reported[5].

High-risk procedures

Esophagectomies for cancer are high-risk surgical procedures, with considerable morbidity and mortality rates [9,10]. Surgery is the primary curative therapy for esophageal cancer patients, though after esophagectomy overall 5-year survival hardly reaches 50%, even in specialized centers[11]. Next to the technical skills needed to perform the operation, careful patient selection with accurate staging and risk assessment is essential[6]. Moreover experience with the detection and management of complications is needed to prevent the patient from dying postoperatively[7]. These do not only appeal to the competence of the individual surgeon, but also to the infrastructure, experience and expertise available in the institution.

Clinical audit

In 2000, considering the growing evidence for a volume-outcome relationship for esophageal cancer surgery, the professional network of surgical oncologists working in hospitals affiliated with the Comprehensive Cancer Centre Leiden[1] decided to perform a region-wide clinical audit. All patients who underwent an esophagectomy for cancer in the period 1990-1999 were included. Retrospectively, detailed clinical data were retrieved from the original patient files, including information on patient demographics, comorbid diseases, diagnostic procedures, tumor and treatment characteristics as well as outcome. None of the eleven hospitals performed more than 7 esophagectomies a year, consequently all had to be considered low-volume hospitals. To put the data in the right perspective, outcomes were compared with the results of the nearest high volume referral center for esophagectomies. Due to the extensive set of clinical data collected in the audit, important casemix-adjustments could be made in the comparison of outcome in high and low volume hospitals. The results of this study are reported in **Chapter 3**[8].

Centralization

In the audit important variation in outcome between patients operated in different hospitals were revealed. Therefore, the professional network of surgical oncologists decided to concentrate esophageal cancer surgery in three to four hospitals in the region. As none of the hospitals performed more than 7 esophagectomies a year it was agreed on that not differences in procedural volume, but the actual outcome of patients treated in different

1 The **Comprehensive Cancer Centre Leiden** was a network organization of 11 hospitals in the south-west region of the Netherlands, stimulating collaborations between hospitals and health care providers in oncological and palliative care and collecting data for the Netherlands Cancer Registry. In 2010 seven regionally organized comprehensive cancer centres merged into one organization, the comprehensive cancer centre the Netherlands (IKNL).

hospitals in the region, would be leading in the centralization process. From 2000 the audit was continued with prospective data-collection and feedback was given to the professional network every half year. After 5 years of auditing esophagectomies for cancer, these procedures were concentrated in only 4 of 11 hospitals in the region. The effects on patient outcome of this regional centralization project are reported in **Chapter 4**[9].

Volume standards

In 2006 the Netherlands Health Care Inspectorate (IGZ) decided to ban esophageal resections from hospitals with a mean annual volume less than 10. At that time, the number of studies showing a relationship between procedural volume and outcome of high-risk surgical procedures was already extensive. Nevertheless, few changes were seen in referral patterns for esophageal and pancreatic cancer in the other regions in the Netherlands[10]. Therefore we decided to compare the outcome of esophageal resections for cancer before and after the centralization project in the region of the Comprehensive Cancer Centre Leiden, with the outcome in other regions in the Netherlands. For this purpose, the independently collected data of the Dutch National Medical Registry (LMR) were analyzed. In addition, we compared the historic outcome of hospitals which were selected and those that were not selected as future referral center for esophagectomies by the volume cut-off of the Dutch Health Care Inspectorate. The results are reported in **Chapter 5**[11].

Volume or outcome-based referral

The Leapfrog group, a large coalition of private and public purchasers of health insurance in the United States, established minimal volume standards for the contracting of hospitals performing esophagectomies, in the year 2000. In contrast to the results in the region of the Comprehensive Cancer Centre Leiden, no actual improvement in outcome for the Leapfrog patients where reported in the international literature. Therefore, the dramatic improvements in outcome shown in our regional centralization project could not only be based on rising hospital volumes, though also on the feedback given to the surgeons, urging them to improve their performance. The question if concentration of esophageal cancer surgery should be based on a hospitals procedural volume (volume-based referral) or the actual outcome of patients treated (outcome-based referral), was addressed in an editorial published in the Journal of Surgical Oncology (**Chapter 6**)[12].

Quality indicators

The question, which method is more effective in reducing morbidity and mortality after high-risk surgical procedures, like esophagectomies, is still under debate. Many authors state that procedural volume is only a proxy for differences in expertise, processes of care and the subsequent outcome between hospitals and could be a poor predictor of quality of care in individual hospitals. To gain more insight in the variation in quality of care delivered by different institutions, quality indicators are developed in many countries[19,20]. Quality

indicators are measurable aspects of care that discriminate between high and low quality care processes. Adopting the Donebedian paradigm quality indicators are discerned into structure, process and outcome indicators[21,22]. Unfortunately, few quality indicators are supported by solid scientific evidence proving their ability to discriminate high from low quality of care in different institutions. In **Chapter 7** a review of the evidence supporting quality indicators for esophagectomies for cancer available in the literature is reported[23].

Composite measures

In the attempts made to measure the quality of clinical practice, there has been a focus on readily available and easily understandable outcome measures, such as hospital mortality or duration of hospital admission. Another approach has been to use procedural volume as a readily available quality-proxy. However, neither of these simplifying approaches does justice to the multi-dimensional concept of quality. High quality care is safe, effective, patient-centered and cost-efficient, and is the result of high quality (infra)structure, care processes and outcome. Thus, not only at the conceptual but also at a clinical-practical level, quality is a more-dimensional concept and should ideally be measured as such. In **Chapter 8** we present the Exemplary Care and Outcome (ECO) score, that integrates various attributes of quality of care into one overall (composite) measure. Moreover, to obtain a high level of reliability this ECO score is adjusted for differences in case-mix between hospitals and represented graphically in a comprehensive and understandable way, without the loss of information about the quality of different aspects of surgical cancer care.

Variation in quality of care

In cancer care future developments force us to re-evaluate the way care is provided for our patients. The number of cancer patients is increasing and the relative part of elderly cancer patients, with an increased risk of treatment related morbidity and mortality will raise. Moreover, care processes, including diagnostic procedures, multidisciplinary decision making and combined modality treatments, are becoming more and more complex, demanding more specific knowledge, expertise and infrastructure in institutions providing cancer care. This does not only apply to tumors with a low incidence and high treatment-related risk, like esophageal cancer, but also for higher incidence tumors like Non Small Cell Lung Cancer (NSCLC) and Colon cancer care processes become more demanding. In the Netherlands, under the supervision of the Signaling Committee of the Dutch Cancer Society a 'Quality of Cancer Care' taskforce was formed in 2007, which was charged with the evaluation of quality of cancer care in the Netherlands and the development of strategies for improvement. Using the hospital specific data from the Netherlands Cancer Registry, the taskforce investigated variation in quality of care between hospitals in the Netherlands for bladder, non-small cell lung, colorectal and breast cancer and its relationship with a hospitals volume, infrastructure and academic or training status. The results for NSCLC and Colon cancer are reported in **Chapter 9 and 10** respectively[24,25]

Improving quality of care

The 'Quality of Cancer Care report' became available in the summer of 2010 [13]. The taskforce concluded that on a population level, there was significant potential for improvement of outcome for cancer patients in the Netherlands. Especially the concentration of complex high-risk cancer procedures in specialized centres, with the right infrastructure, sufficient volume and adequate expertise, could lead to substantial improvement in outcome. These conclusions are supported by our study in which outcome was compared of patients who underwent esophagectomy or gastrectomy for cancer in the Netherlands, from 1989 tot 2009 (**Chapter 11**) [14]. In this time period, due to regionalisation projects and actions taken by the Dutch Healthcare Inspectorate, esophagectomies were increasingly concentrated in higher volume hospitals. In contrast, the percentage of gastrectomy patients treated in high-volume hospitals decreased. As a result outcome for esophagectomy patients improved to a much greater extent than for gastrectomy patients, indicating an urgent need for improvement in quality of surgery and perioperative care for gastric cancer patients in the Netherlands. Recently, these findings have urged the Dutch Association of Surgical Oncologists to establish quality standards, not only for esophageal but also for gastric cancer surgery, including a minimal hospital volume standard of 20 resections a year. In addition, a nation-wide clinical audit program has been initiated to measure and improve quality of care for gastric and esophageal cancer patients continuously, the Dutch UpperGI Cancer Audit (DUCA).

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Chapter 2

The volume-outcome relationship in the surgical treatment of esophageal cancer: a systematic review and meta-analysis

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Cancer. 2012 Apr 1; 118(7):1754-63.

ABSTRACT

Aims:
To conduct a systematic review and meta-analysis of the literature on the relationship between procedural volume and outcome of esophagectomies.

Methods:
A systematic search to identify articles investigating effects of hospital (HV) or surgeon volume (SV) on short- and long-term outcomes, published between 1995 and 2010. Articles were scrutinized on methodological quality and after inclusion of only high-quality studies a meta-analysis assuming a random effects model was done to estimate the effect of higher volume on patient outcome. Heterogeneity in study results was evaluated with an I^2-test and risk of publication bias with an Egger's regression intercept.

Results:
Forty-three studies were found. Sixteen studies met the strict inclusion criteria for the meta-analysis on HV and postoperative mortality and 4 studies on HV and survival. The pooled estimated effect size was significant for high-volume providers in the analysis of postoperative mortality (OR 2.30; CI 1.89-2.80) and in the survival analysis (OR 1.17; CI 1.05-1.30). The meta-analysis on SV and outcome showed no significant results.
Studies in which the results were adjusted not only for patient characteristics, but also for tumor characteristics and urgency of the operation, showed a stronger correlation between HV and mortality. Also, studies performed on data from the United States showed higher effect sizes.

Conclusions:
The evidence for HV as an important determinant of outcome in esophageal cancer surgery is strong. Concentration of procedures in high volume hospitals with a dedicated setting for the treatment of esophageal cancer, might lead to an overall improvement in patient outcome.

INTRODUCTION

Improving quality and effectiveness of health care is one of the priorities of health policies. In surgical oncology there has been a continuous debate about how to assure that every patient gets the optimal treatment for his or her cancer. Despite improvements in targeted therapies and adjuvant treatments, surgery is still the key to cure cancer patients with solid malignancies. In the past, surgical outcomes and causes of variation were largely unknown, but since the beginning of this century there are an increasing number of population-based studies evaluating differences in practice patterns and outcomes between providers.

Many studies suggest that procedural volume is an important determinant of outcome in cancer surgery[1]. Especially for high-risk, low-volume surgical procedures, like esophagectomies and pancreatectomies, differences in outcomes between high- and low-volume providers have been reported[2,3]. Though the number of volume-outcome studies in the literature is high and continues to increase, there is solid criticism on the methodological quality of these studies. The vast majority of volume-outcome studies in cancer surgery is observational and based on administrative data collected for other purposes. Moreover, potential differences in case mix between high- and low-volume hospitals are not always accounted for and postoperative mortality is often presented as the sole outcome measure. Inadequate reporting of volume-outcome studies restricts the generalizability and credibility of study results, feeds a fruitless debate and hampers the introduction of minimal volume standards for cancer surgery in several countries, for example in the Netherlands[4].

Esophagectomy for cancer is a high-risk, low-volume surgical procedure for which the volume-outcome relationship could be important. In many countries esophagectomies are performed in a low-volume setting. For example, until 2007 approximately 350 of these operations were performed annually in the Netherlands, shared by more than 50 different hospitals[5]. It is believed that concentration of these procedures with high-volume providers could improve overall patient outcome.

The aim of this study was to inform the debate on the volume-outcome relationship in esophageal cancer surgery, by conducting a systematic review of the literature on this subject. The methodological quality of the studies in this review was scrutinized and only high-quality volume-outcome studies were included in a meta-analysis.

METHODS

Systematic Search Strategy

We performed a systematic search to identify all articles describing the association between hospital or surgeon volume of esophagectomies and clinical outcomes (morbidity, mortality, survival, quality of life), published after January 1st 1995. The search was conducted in the

Table 1. Search terms used in the search in the Medline database

Medline (Pubmed)
("Esophagectomy"[MAJR] OR "Esophageal Neoplasms/surgery"[MAJR] OR ("Surgical Procedures, Operative"[MAJR:NoExp] AND "Neoplasms"[MAJR:NoExp])) AND ("hospital volume" OR "surgeon volume" OR "provider volume" OR "Outcome Assessment (Health Care)"[MAJR] OR regionalization[ti] OR regionalization[ti] OR "Health Facility Size"[majr] OR "Workload"[majr] OR (outcome*[ti] AND volume*[ti]) OR (outcome*[ti] AND complication*[ti]) OR (outcome*[ti] AND mortality*[ti]) OR (outcome*[ti] AND morbidity*[ti]) OR (outcome*[ti] AND survival*[ti]) OR (outcome*[ti] AND quality of life*[ti]))

electronic Medline database (Pub med) with a combination of MESH terms and text words (Table 1). Because volume is not well indexed in the electronic databases, we formulated the search terms as sensitive as possible to ensure no publications were missed. The last search was done on July 1st 2010.

Study selection

Two reviewers (MW, GG) independently screened titles and abstracts of all retrieved articles. Studies were selected using the following inclusion criteria:

- The article was in the English language
- The study used primary data (i.e., letters, editorials, and reviews were excluded)
- The subject of the study was the surgical treatment of esophageal cancer.
- The study did not describe the results of a single hospital or surgeon.

After this first selection on titles and abstracts, the remaining articles were obtained in full text and were further selected by the same two reviewers using the following exclusion criteria:

- Lack of comparisons between providers (hospitals or surgeons).
- No definition for procedural volume as a distinct number or cut-off value (i.e., studies that defined volume as 'specialization' were excluded)
- No postoperative morbidity, mortality, survival or quality of life among outcome parameters.

Any discrepancies regarding inclusion or exclusion of a study were solved by consulting a third investigator (RT). In addition, reference lists of relevant articles and recent reviews were hand-searched to identify additional articles, which could have been missed in the initial search[6,7]. We also used the "related articles" function in Pub med.

Assessment of study quality

Two authors (MW, GG) critically appraised each study in the review on methodological quality and risk of bias. Data of the included studies were gathered in a data-extraction form, which was based on the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) criteria (www.strobe-statement.org). From each study, characteristics were collected regarding the unit of analysis (hospital or surgeon), the data source (administrative

or clinical data), study period, the study design (prospective or retrospective), the country of origin, the number of analyzed patients, hospitals and surgeons, volume categories for hospitals and surgeons, outcome parameters (morbidity, mortality, survival, quality of life) and results regarding these outcome parameters (statistically significant or not significant) and the degree of risk adjustment. We noted the case mix factors for which statistical adjustment was done. Case mix factors were categorized as demographic parameters (age, gender, race and income); co morbidities; tumor characteristics (stage, grade, location); treatment characteristics (neo-adjuvant treatments) and urgency of the operation. In addition, some studies adjusted for in-hospital mortality in the survival analyses.
Study inclusion criteria were checked to verify if there was a probability of selection bias. Cut-off values for high- and low-volume were noted per volume group, along with how these cut-off points were determined. The study results were recorded separately for each unit (surgeon or hospital) and for each outcome parameter (postoperative morbidity, postoperative mortality, 2- or 5-year survival and quality of life). The crude outcomes for each volume group were noted (if reported). Subsequently, we noted for each volume group and outcome parameter the estimated effect size after adjustment, expressed as odds ratio's (OR), hazard ratio's (HR) or risk rates (RR) with confidence intervals (CI) and measures of significance.

Synthesis of the data for meta-analysis

A meta-analysis was performed for the relationship between hospital volume and surgeon volume on the one hand and postoperative mortality and survival on the other. No meta-analysis was performed for postoperative morbidity because this outcome parameter was defined too heterogeneous among the included studies. For quality of life, only one study was available.
Only high quality studies were included in the meta-analyses. A high quality study was defined as a multicenter study in which a multivariate analysis was performed including casemix factors, such as demographic parameters (age, gender, race and income); comorbidities; tumor characteristics (stage, grade, location); treatment characteristics (neo-adjuvant treatments) and urgency of the operation. Studies without a multivariate analysis and/or no reporting of OR, HR or RR were excluded from the meta-analysis. The reference category varied between studies. Therefore, we had to convert the effect sizes so that the highest volume group was the reference in all studies. As a result, the OR of mortality or the HR of survival reflected the odds of mortality in the lowest volume group compared to the odds of mortality in the highest volume group.
To determine a pooled estimated effect, we used the random effect model for meta-analyses. The random effects model accounts for expected heterogeneity, which is more appropriate with pooling of observational studies.
Heterogeneity was quantified by the I^2 test. An $I^2 < 40$ was considered homogeneous, between 40 and 60 moderately heterogeneous and > 60 very heterogeneous[8]. We conducted a sensitivity analysis to further explore heterogeneity and to assess the impact

of subgroups. A subgroup analysis was done by data source (administrative versus clinical), adjustments for urgency of the operation (adjusted versus not adjusted), adjustments for tumor characteristics (adjusted versus not adjusted) and by study country (United States versus non-United States). No subgroup analysis by patient characteristics was performed, because all studies were adjusted for age, gender and co morbidities.
Publication bias was assessed with an Egger's regression intercept and shown in a funnelplot[9].
The meta-analysis was conducted with Comprehensive Meta Analysis, professional version 2.2 (©2006, Biostat inc. Englewood, USA).

RESULTS

Search results

Our initial search identified 97 potentially relevant articles regarding the volume-outcome relationship in the surgical treatment of esophageal cancer (figure 1). After the first screening on titles and abstracts we excluded 37 studies. The other 60 articles were retrieved for more detailed evaluation. Among these 35 articles were excluded: in 27 studies, comparisons were made between treatment techniques or patient groups, instead of comparing the outcome between providers (hospitals or surgeons). In 3 studies, degree of specialization (board-certified vs. non-certified surgeons, academic vs. non-academic hospitals) or nurse-to-patient ratio was evaluated, instead of procedural volume[10-12]. And in 5 studies, other outcome parameters than morbidity, mortality, survival or quality of life were evaluated[13-17]. The remaining 25 papers were selected. After this first selection, the related articles feature in Pub med was used and the reference lists of retrieved articles were hand-searched. We identified 18 additional articles which met the predefined criteria for our systematic review.

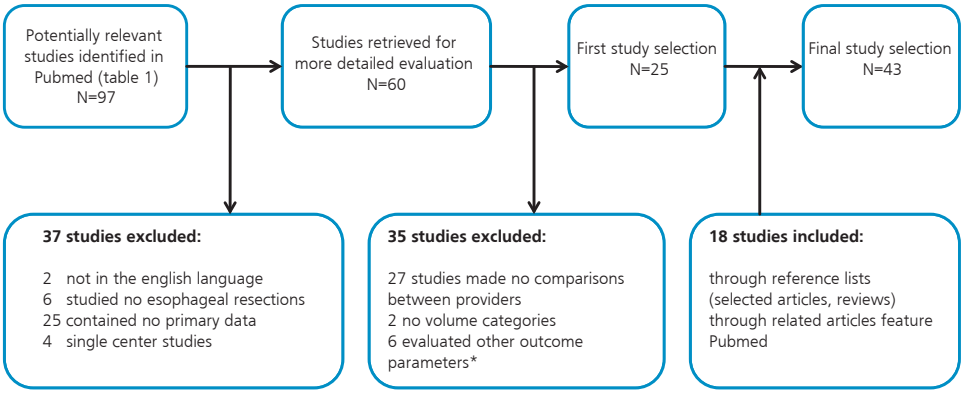

Figure 1. Selection of reviewed studies

Systematic review

Table 2 shows the characteristics of the 43 studies included in the review. Most studies are from the United States and Canada, though the number of European studies has been growing. Study data have been obtained frequently from insurance companies' databases (Medicare, National Inpatient Sample). The number of patients, hospitals and surgeons varied widely between the included studies. In most studies, results were adjusted for differences in case mix between high- and low-volume providers, but the parameters used for adjustments differed largely among studies. In some studies, data were corrected for differences in age and gender only. In other studies, adjustments were made for race, income, co morbidities, ASA-classification, tumor characteristics (stage, grade and location), urgency of the operation, (neo-adjuvant) treatments and (other) hospital characteristics. There was a considerable variation in the cut-off values for the volume groups in the included studies. For hospital volume, cut-off values of the highest volume strata varied between 3 and 87 procedures annually. The cut-off values of the lowest hospital volume strata varied between 1 and 20 procedures per year. The rationale for the cut-off values used was seldom explained in the methodological paragraph of the articles.

Hospital volume

In 36 studies, the relationship between hospital volume and outcome was evaluated. Postoperative mortality was used as an outcome parameter in 32 studies, and in 24 of these studies, a significant inverse relationship between hospital volume and postoperative mortality was found. In 9 studies, hospital volume and postoperative morbidity were investigated; in 4 studies, a statistically significant association was found, favoring high volume. Differences in survival between high- and low-volume hospitals were evaluated in 7 studies of which 4 were positive. Quality of life was evaluated in only one study; in this study, there was no correlation between hospital volume and quality of life[18].

Meta-analysis: hospital volume & postoperative mortality

Of the 32 studies evaluating the relationship between *hospital volume* and *postoperative mortality,* 16 met the inclusion criteria for the meta-analysis. All of these studies had an observational design and only three studies were based on clinical data, often collected in regional or national cancer registries. The other 13 studies were based on administrative data. In all but one study, the results of the multivariate analysis were adjusted for age, gender and co morbidities and in 9 studies the results were adjusted for urgency of the operation. A few studies adjusted for other confounding factors like stage of the disease, type of resection and neo-adjuvant treatments.

Figure 2a shows the forest plot of the included studies regarding hospital volume and postoperative mortality. The pooled estimated effect size was significant in favor of high-volume providers (OR 2.30; CI 1.89-2.80). There was moderate heterogeneity between the studies (I^2=60).

Table 2. Studies included in the systematic review of the literature on the relationship between volume and outcome of esophagectomies for cancer (adjusted from Gruen et al.6).

Study	Country	Data	Patients	Hospitals	Surgeons	Casemix adjustment	Hospital volume
							Volume categories
Leigh 2009 [27]	UK	Adm	9034	n.r.	n.r.	D	<20>
Meguid 2009 [28]	US	Adm	4080	1506	n.a.	D, C, V	<15>
Rutegard 2009 [29]	Swe	Clin	615	n.a.	n.a.	D, C, S, T	-
Gasper 2009 [30]	US	Adm	1210	183	n.a.	D, C	<1-2-4-6>
Yasunaga 2009 [31]	Jap	Adm	642	n.a.	183	n.r.	-
Sundelöf 2008 [32]	Swe	Clin	232	33	n.r.	D, C, S, T	<10>
Reavis 2008 [33]	US	Adm	5236	107	n.a.	n.r.	<6-13>
Wouters 2008 [34]	Neth	Clin	903	12	n.a.	D, C, U, S, T, M	<7>
Ra 2008 [35]	US	Adm	1172	361	n.a.	D, C, S	<.68-2.33>
Rutegard 2008 [18]	Swe	Clin	355	n.a.	n.a.	D, C, S, T	<10>
Hollenbeck 2007 [36]	USA	Adm	421	151	n.a.	D, C, U, S	n.r.
Thompson 2007 [37]	UK	Clin	1079	53	n.a.	D, C, U, S	<13-20-35>
Jensen 2007 [38]	Den	Adm	1152	26	n.a.	none	<5-21>
Allareddy 2007 [20]	US	Adm	2437	717	n.a.	D, C, U, V	<13>
Rodgers 2007 [21]	US	Adm	8075	995	1651	D, C, V	<5-10>
Rouvelas 2007 [39]	Swe	Clin	1199	53	n.a.	D, C, S, T	<10>
Birkmeyer 2007 [19]	US	Adm	822	206	n.a.	D, C, U, S, T, M	<4-14>
Rouvelas 2007 [39]	Swe	Clin	328	n.a.	n.r.	D, C, S, T	-
Simunovic 2006 [40]	Can	Clin	629	n.r.	n.a.	D, C	<8-20-44>
Lin 2006 [41]	Tai	Adm	6674	111	n.a.	D, C	<20-34-59-87>
Urbach 2005 [42]	Can	Adm	613	58	93	D, C	<2.2-7.1-12.1>
Wenner 2005 [43]	Swe	Clin	1429	74	n.a.	D	<5-16>
Birkmeyer 2004 [44]	US	Adm	4350	n.r.	n.a.	none	<13>
Ward 2004 [45]	US	Adm	44	14	n.a.	D, C	<13>
Goodney 2003 [46]	US	Adm	n.r.	n.r.	n.a.	D, C, U	<2-5-8-20>
Elixhauser 2003 [47]	US	Adm	1623	710	n.a.	none	<7>
Dimick 2003 [48]	US	Adm	3023	192	n.a.	D, C, U, T	<3-6-17>
McCulloch 2003 [49]	UK	Clin	955	32	n.a.	D, C, S, T	<11-21>
Dimick 2003 [50]	US	Adm	1226	n.r.	n.a.	D, C, U	<median>
Birkmeyer 2003 [3]	US	Adm	n.r.	n.a.	n.r.	D, C, U	-
Dimick 2003 [51]	US	Adm	366	52	n.a.	D, C, U, T	<8.5>
Urbach 2003 [52]	Can	Adm	613	47	n.a.	D, C	quartiles
Finlayson 2003 [53]	US	Adm	5282	603	n.a.	D, C, U	<4-10>
Gillison 2002 [54]	UK	Clin	1125	n.a.	64	D, U, S	-
Bachmann 2002 [55]	UK	Clin	322	n.a.	23	D, C, U, S	-
Birkmeyer 2002 [2]	US	Adm	6337	1575	n.a.	D, C, U	<2-5-8-20>
Kuo 2001 [56]	US	Adm	1193	64	n.a.	D, C, U	<6>
Dimick 2001 [57]	US	Adm	1136	62	n.a.	D, C, U	<4-16>
vLanschot 2001 [58]	Neth	Adm	1792	100	n.a.	D, S	<11-20>
Swisher 2000 [59]	US	Adm	340	25	n.a.	D,C, U	<5>
Begg 1998 [60]	US	Adm	503	190	n.a.	D, C, S	<6-11>
Patti 1998 [61]	US	Adm	1561	273	n.a.	D, C	<1-2-4-6>
Miller 1997 [62]	Can	Clin	74	n.a.	20	none	-

QoL = Quality of life; Adm = based on administrative data ; Clin = based on clinical data; n.r. = not reported; n.a. =not applicable; D = adjusted for demographic data (e.g. patient age, gender, race, income); C = adjusted for comorbidities (including ASA-classification); U = adjusted for urgency of the operation; S = adjusted for tumor characteristics (e.g. stage, grade, location); T = adjusted for treatment differences (e.g. surgical approach;

				Surgeon volume				
Morbidity	Mortality	Survival	QoL	Volume categories	Morbidity	Mortality	Survival	QoL
-	S	-	-	-	-	-	-	-
-	S	-	-	-	-	-	-	-
-	-	-	-	<2-7>	NS	-	-	-
-	S	-	-	-	-	-	-	-
-	-	-	-	<50-100>	S	-	-	-
NS	NS	S	-	<10>	NS	NS	S	-
S	S	-	-	-	-	-	-	-
-	S	S	-	-	-	-	-	-
-	S	-	-	-	-	-	-	-
-	-	-	NS	<7>	-	-	-	NS
-	NS	-	-	-	-	-	-	-
-	-	NS	-	-	-	-	-	-
-	NS	-	-	-	-	-	-	-
-	S	-	-	-	-	-	-	-
-	NS	-	-	<2-7>	-	S	-	-
-	NS	NS	-	-	-	-	-	-
-	-	S	-	-	-	-	-	-
-	-	-	-	<2-7>	-	NS	-	-
-	NS	NS	-	-	-	NS	NS	-
-	S	-	-	-	-	-	-	-
-	NS	-	-	<2.4-4.6-6.9>	-	NS	-	-
-	S	S	-	-	-	-	-	-
-	S	-	-	-	-	-	-	-
-	NS	-	-	-	-	-	-	-
NS	-	-	-	-	-	-	-	-
-	S	-	-	-	-	-	-	-
-	S	-	-	-	-	-	-	-
NS	S	-	-		-	-	-	-
S	S	-	-		-	-	-	-
-	-	-	-	<2-6>	-	S	-	-
S	S	-	-		-	-	-	-
-	S	-	-		-	-	-	-
-	S	-	-		-	-	-	-
-	-	-	-	<4-12>	-	S	NS	-
-	-	-	-	continuous	-	S	S	-
-	S	-	-	-	-	-	-	-
-	S	-	-	-	-	-	-	-
S	S	-	-	-	-	-	-	-
-	S	-	-	-	-	-	-	-
NS	S	-	-	-	-	-	-	-
-	S	-	-	-	-	-	-	-
NS	S	-	-	S				
-	-	-	-	<6>	NS	S	-	-

(neo)adjuvant treatments); M = survival analysis adjusted for postoperative mortality; V = adjusted for other hospital characteristics (e.g., teaching or academic status); <10-20> = low-volume group less than 10, medium-volume group 10-19 and high-volume 20 or more esophageal resections a year; S = statistically significant; NS = statistically not significant.

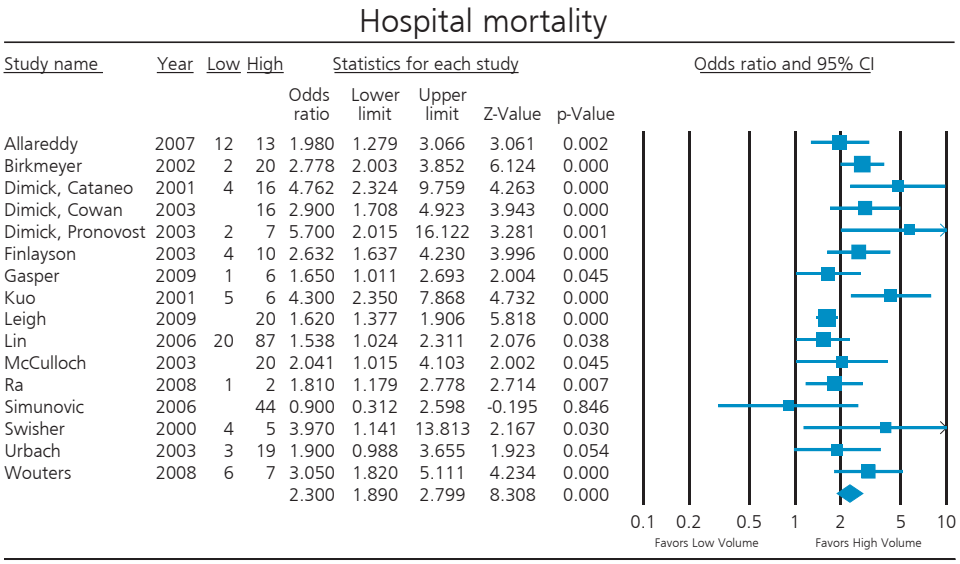

Figure 2a. Forest plot of the included studies in the meta-analysis on hospital volume and postoperative mortality for esophageal resections for cancer. Year = year of publication; Low = highest annual volume of low volume category; High = lowest annual volume of high volume category; CI = confidence interval

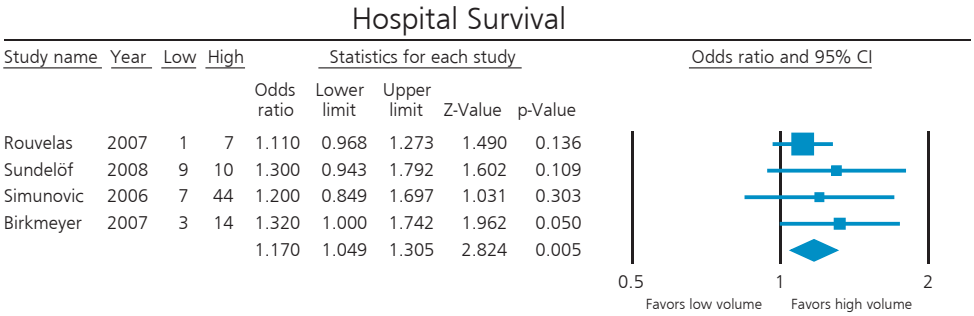

Figure 2b. Forest plot of the included studies in the meta-analysis on hospital volume and survival of esophageal resections for cancer. Year = year of publication; Low = highest annual volume of low volume category; High = lowest annual volume of high volume category; CI = confidence interval

In table 3 the results of the sensitivity analysis of the 16 included studies are depicted. A larger effect size was noted in studies from the United States (OR 2.56; P<0.001), in studies based on clinical data (OR 2.29; P<0.001), in studies with data that were adjusted for urgency of the operation (OR 2.84; P<0.001) and in studies with data that were adjusted for tumor characteristics (OR 2.20; P<0.001).

Figure 4 shows the qualitative analysis of publication bias of all studies regarding hospital volume and postoperative mortality using OR's. The results were suggestive for publication

Table 3. Sensitivity analysis of the 16 included studies on hospital volume and postoperative mortality with Odds ratios as effect size.

Factor	Subgroup	N	OR	CI	P-value
Country	US	10	2.56	2.17-3.00	<0.001
	other countries	6	1.70	1.48-1.94	<0.001
Datasource	Administrative	13	1.99	1.79-2.22	<0.001
	Clinical	3	2.29	1.56-3.37	<0.001
Urgency	Not adjusted	7	1.69	1.49-1.92	<0.001
	Adjusted	9	2.84	2.37-3.40	<0.001
Tumor stage	Not adjusted	13	1.99	1.78-2.22	<0.001
	Adjusted	3	2.20	1.63-2.97	<0.001

N = number of studies; OR = Odds ratio; CI = confidence interval; I2 = result of I square test on heterogeneity of study results8. US = United States

bias, which indicates that smaller negative studies are missing, which to some degree could have influenced the results of this meta-analysis.

Meta-analysis: hospital volume & survival

Of the seven studies evaluating the relationship between *hospital volume* and *survival,* four met the criteria for the meta-analysis. All four studies were observational, though three studies used clinical instead of administrative data. Adjustments for age, gender and co morbidities were made in all four studies; three of them adjusted for tumor characteristics (e.g. stage and grade) and two studies corrected also for (neo)adjuvant treatments in their survival analysis. Figure 2b shows the forest plot of the included studies on hospital volume and survival. Again, the meta-analysis showed a significant pooled estimated effect size in favor of high-volume hospitals (HR 1.17; CI 1.05-1.31). This result was very homogeneous (I^2=0.0).

Surgeon volume

In 12 studies, the relationship between surgeon volume and outcome was investigated. Nine of these studies used postoperative mortality as an outcome parameter and 5 of them showed a significant result favoring high volume. In 4 studies, postoperative morbidity was an outcome parameter; only one study was positive. The relationship between surgeon volume and survival was investigated in 4 studies; in two of them, a significant relationship was found. Quality of life was evaluated in one study; again the result was negative.

Meta-analysis: surgeon volume & postoperative mortality

Of the nine studies evaluating *surgeon volume* and *postoperative mortality,* only three met the inclusion criteria for the meta-analysis. In all three studies age, gender and co morbidities were included in the multivariate analysis. Figure 3a shows the forest plot of the included studies regarding the effect of surgeon volume on postoperative mortality. In the meta-analysis a pooled estimated effect size was detected in favor of high-volume

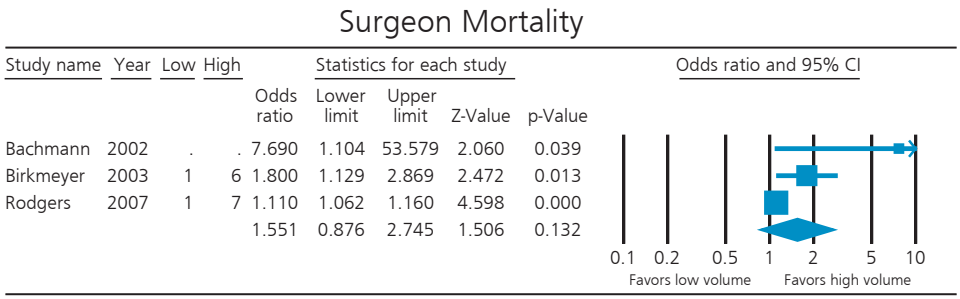

Figure 3a. Forest plot of the included studies in the meta-analysis on surgeon volume and postoperative mortality of esophageal resections for cancer. Year = year of publication; Low = highest annual volume of low volume category; High = lowest annual volume of high volume category; CI = confidence interval

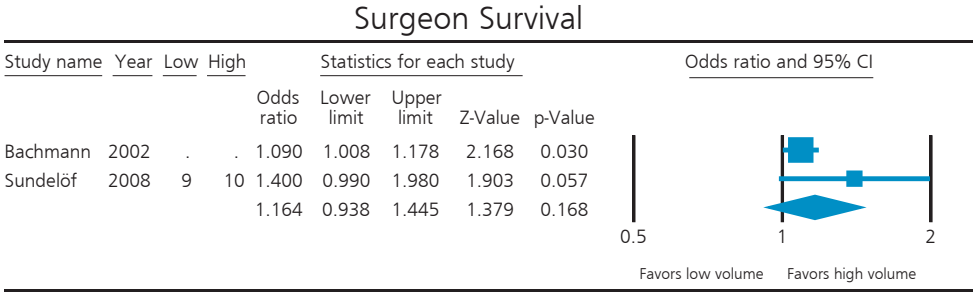

Figure 3b. Forest plot of the included studies in the meta-analysis on surgeon volume and survival of esophageal resections for cancer. Year = year of publication; Low = highest annual volume of low volume category; High = lowest annual volume of high volume category; CI = confidence interval

surgeons, but this effect did not reach statistical significance (OR 1.55; 0.88-2.75) and was very heterogeneous (I^2=75).

Meta-analysis: surgeon volume & survival

Two out of four studies evaluating *surgeon volume* and *survival* were included in the meta-analysis and both adjusted for tumor characteristics in their survival analyses. Figure 3b shows the forest plot of the two included studies regarding the effect of surgeon volume on survival. In the meta-analysis there was a pooled estimated effect size in favor of high-volume surgeons (HR 1.16; 0.94-1.45), which was not significant. The result was moderately heterogeneous (I^2=48).

DISCUSSION

The present study contains the first meta-analysis on the relationship between procedural volume and outcome of esophageal resections for cancer, with strict criteria for

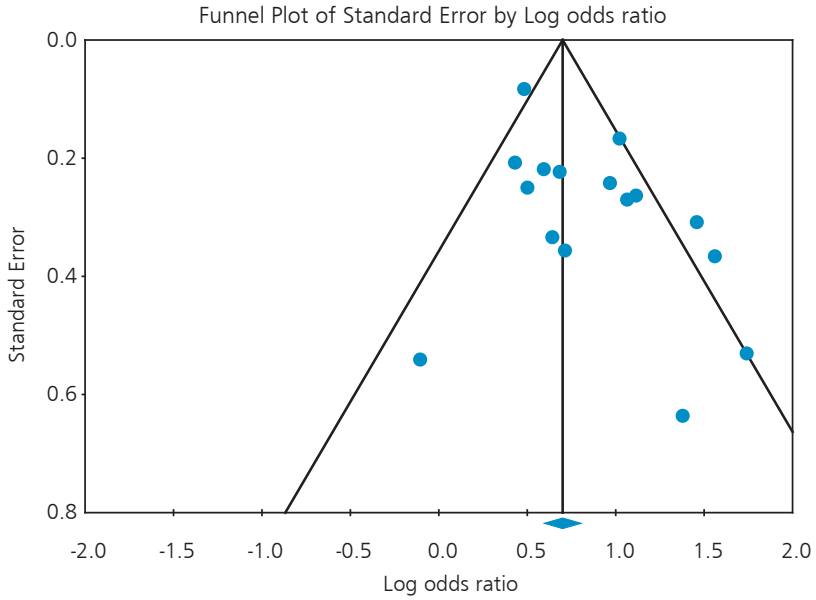

Figure 4. Analysis of risk of publication bias: funnel plot of studies included in the meta-analysis on hospital volume and postoperative mortality using odds ratio's. The funnel plot is asymmetric, missing smaller negative studies, suggesting publication bias. Quantitative analysis with the Egger's regression intercept showed an intercept of 1.7 with a two-sided P value of 0.03, confirming the suggestion of publication bias.

methodological quality. Our systematic review shows that there is an increasing number of studies on this subject originating from different parts of the world and evaluating hospitals' as well as surgeons' procedural volume. Not only short-term outcomes like postoperative morbidity and mortality have been evaluated, but also long-term outcomes like survival and quality of life. Only a minority of these studies met the methodological inclusion criteria for our meta-analysis. We found that hospital volume has a strong inverse relationship with postoperative mortality and that patients operated in high-volume centers have a better survival. This relationship is much stronger than that between surgeon volume and outcome of esophageal cancer resections.

There is solid criticism on the level of evidence for a volume-outcome relationship regarding low-volume, high-risk surgical procedures, like esophagectomies for cancer[10]. Our review confirms that most studies are observational, retrospective and based on administrative data collected for other purposes, instead of carefully designed comparative studies (Table 2). Moreover, studies originate from different health care systems all over the world introducing a large variety in demographical, geographical and epidemiological factors as well as standards of care. For example, our analyses showed larger differences in postoperative mortality between high- and low-volume hospitals identified in the United States than in other countries. In the evaluation of the methodological quality of the available studies substantial heterogeneity was identified. Especially, the choice of volume categories was extremely diverse among all studies. The rationale for specific volume cut-offs was

seldom explained in the methodological paragraphs suggesting a potential selection bias. In addition, the risk of publication bias was calculated for the studies on hospital volume and postoperative mortality, missing the smaller negative studies, which obviously had little chance for publication in peer-reviewed medical journals.

Only high-quality comparative studies were included in our meta-analyses. All but one study included at least age, gender and co morbidity in the multivariate analysis on the relationship between hospital volume and postoperative mortality. Several studies used additional parameters as potential confounders (e.g., neo-adjuvant treatments, urgency of the operation, tumor characteristics). This led to higher effect sizes and less heterogeneity in results between properly adjusted studies, as was shown in our sensitivity analyses (Table 3). Because of these robust effect sizes, the risk of publication bias detected in our analyses (Figure 4), is expected to have influenced the results of this meta-analysis insignificantly.
Adjustments for tumor characteristics not only gave higher effect sizes in studies on hospital volume and postoperative mortality. Also, in three out of four studies on hospital volume and survival in which results were adjusted for tumor stage, a significantly better outcome was found in high-volume hospitals (Table 2).

In the meta-analysis on surgeon volume and outcome, the correlations between volume and postoperative mortality and volume and survival were not significant. This suggests that outcome of esophageal cancer surgery is not only dependent on the experience and skills of individual surgeons. The hospital setting in which they perform their operations seems more important. The above results indicate that - for high-quality of care - experience with esophageal cancer surgery is important on a hospital's level rather than on an individual surgeon's level.

Apart from the methodological shortcomings mentioned above, volume-outcome studies have other important limitations. First, surgery is not the only treatment used in esophageal cancer patients. Differences in treatment patterns, like the use of (neo)adjuvant chemo- and/or radiotherapy may also influence long-term survival. In our meta-analysis on the relationship between hospital volume and survival, data in three out of four studies have been adjusted for differences in the use of (neo)adjuvant therapies. Especially in the study of Birkmeyer, based on the SEER-Medicare database, it is shown that the percentage of patients that receives chemo- and / or radiotherapy besides surgical treatment is not different between low-, medium- and high-volume hospitals[19].
In addition, in only few studies, data have been corrected for (other) provider characteristics[20,21], such as the available infrastructure, teaching or academic status, inner city or private hospital status, experience with other high-risk operations, expertise in multimodality cancer treatments, a hospital's budget, focus and/or referral bias. These factors are often related to, but not identical with procedural volume. In a recent study, Courrech-Staal et al. have reported the results of esophageal cancer surgery in a tertiary

referral center, with a mean annual hospital volume of more than 100 esophageal cancer patients a year[22]. Due to selective referral of patients with higher tumor stages only 20% of them had potentially curable disease, an unfavorable tumor mix when compared to the 50% reported in most series. Nevertheless, the authors have shown excellent results of esophageal cancer surgery despite a low procedural volume (<10 resections/year). The use of procedural volume as the sole measure of quality of care might fall short in identifying high-leverage processes of care in individual institutions. In our opinion policy makers should bare this in mind when efforts are made to centralize complex high-risk surgical procedures.

In the Netherlands, the Quality of Cancer Care taskforce of the Dutch Cancer Society has recently proposed to concentrate specific cancer treatments in those hospitals that meet a set of criteria. These criteria do not only focus on procedural volume, but also on the available infrastructure, specialization of medical professionals and outcome measures, that should be reported by individual institutions[23]. From a patients' perspective outcome information might be more interesting and informative than volume alone. However, also from a professional perspective too much focus on proxy variables like 'volume' is not preferable. Volume standards do have little ability to move the medical field forward[24]. Identifying 'best practices' in patient selection, treatment strategies, technical procedures and peri-operative care is much more important and the central issue in outcomes research and surgical audits[25,26]. Careful analysis of data retrieved from different hospitals, that vary in patterns of care and outcomes, might identify ways to improve the whole field of esophageal cancer treatment.

In conclusion, this meta-analysis has shown that procedural volume is associated with less postoperative mortality and better survival in esophageal cancer surgery. A hospital's annual volume seems more important than the experience of individual surgeons. Although there is no evidence for a specific volume cut-off in the literature, centralization of esophageal cancer surgery in dedicated high-volume centers could lead to better outcome in this patient group.

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Chapter 3

High- versus Low-volume for Esophageal Resections for Cancer: The Essential Role of Case-mix Adjustments based on Clinical data

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ABSTRACT

Background:
Most studies addressing the volume-outcome relationship in complex surgical procedures use hospital mortality as the sole outcome measure and are rarely based on detailed clinical data. The lack of reliable information about comorbidities and tumor stages makes the conclusions of these studies debatable.
The purpose of this study was to compare outcome for esophageal resections for cancer in low- versus high-volume hospitals, using an extensive set of variables concerning case-mix and outcome measures, including long-term survival.

Methods:
Clinical data, from nine hundred and three esophageal resections performed between January 1990 and December 1999, were retrieved from the original patients' files. Three hundred and forty-two patients were operated on in eleven low-volume hospitals (< 7 resections/year) and five hundred and sixty-one in a single high volume center.

Results:
Mortality and morbidity rates were significantly lower in the high-volume center; an in-hospital mortality of 5 versus 13% ($p<0.001$). On multivariate analysis, hospital volume, but also the presence of co-morbidity proved to be strong prognostic factors predicting in-hospital mortality (ORs 3.05 and 2.34). For stage I and II disease, there was a significant better 5-year survival in the high-volume center. ($p = 0.04$) .

Conclusions:
Hospital volume and comorbidity patterns are important determinants of outcome in esophageal cancer surgery. Strong clinical endpoints like in-hospital mortality and survival can be used as performance indicators, only if they are joined by reliable case-mix information.

INTRODUCTION

Since Luft published his study on the inverse relationship between surgical volume and hospital mortality in 1979, a plethora of studies has demonstrated an improvement of clinical outcome with increased hospital volume [1]. Most of these studies use hospital mortality as the sole outcome measure. Often, data are obtained from insurance company's databases and few studies use clinical data for risk-adjustment [2].

The surgical treatment of esophageal cancer is often mentioned as one of the procedures for which concentration in high-volume centers might improve outcome [3,4]. Nevertheless, a clear volume cut-off point at which a cancer center is justified to perform esophageal resections can hardly be defined [5,6]. Also, the volume-outcome literature for esophageal resections is limited to post-operative mortality as the sole determinant of outcome.

Considering the growing evidence for this volume-outcome relationship for esophageal cancer surgery, we decided to investigate the outcome of these procedures in our region from 1990 until 1999. During this study period none of the eleven hospitals, affiliated with the Comprehensive Cancer Center Leiden (CCCL) in the Netherlands, performed more than seven esophageal resections a year, all to be considered as low volume hospitals (LVH).

In contrast to most volume-outcome studies, we decided to use clinical data, obtained from the original patients' files. We retrieved information about comorbid diseases, tumor characteristics, treatment and outcome. Next to hospital mortality, several determinants of outcome were examined, like the number of tumor-free margins and complication rates. Assuming that survival is an essential indicator for quality in cancer surgery, we included a 5 years follow-up. To put our data in the right perspective, we compared these outcomes to the results of the topographically nearest high volume referral center (HVH).

METHODS

All surgically treated esophageal carcinomas in the period 1990-1999 were retrospectively identified through the Leiden Cancer Registry (LCR) of the Comprehensive Cancer Center Leiden (CCCL), in which all cancer patients treated in the mid-western part of the Netherlands are registered (1.7 million inhabitants). All of the eleven hospitals gave consent to participate in this audit and were visited by two investigators to retrieve the original patient files. Patient demographics, pathological notes, data on the surgical and (neo) adjuvant treatments, co-morbidity as well as postoperative morbidity, mortality, length of stay, radicality of the resection, and long-term survival could all be retrieved from the patient's files.

All tumors were staged according to the UICC TNM classification of 1997. This was done by two independent researchers. The obtained pTNM stages were checked with the pTNM stages registered in the LCR. Any discrepancies were discussed between the researchers and a trained data manager from the CCCL. If consensus could not be reached, the pTNM stage was registered as 'unknown'.

In order to make a comparison with the outcomes of the nearest high-volume center, data were categorized according to the database of this center. In this hospital data of patients operated on for an esophageal carcinoma are prospectively collected by a trained data manager.

Differences in patient, tumor and treatment characteristics as well as outcome measurements were assessed using the Kruskal-Wallis test for continuous variables and the chi-square test for categorical variables. Logistic regression was used to determine prognostic factors of in-hospital mortality. Variables were entered in the multivariate model as a prognostic factor when P values < 0.10.

Survival was calculated as the difference between date of surgery and either the date of death or the date of last patient follow up. For both groups follow up of the patients was completed until December 31st, 2005. Observed survival rates were estimated by using the Kaplan–Meier method. The log-rank test was used to assess differences in survival between patients who were operated in LVHs and the HVH. All analyses were conducted using SPSS software (version 12.0; SPSS Inc., Chicago. IL).

RESULTS

Hospital volume

In the period 1990-1999 the evaluation and treatment of patients with an esophageal carcinoma was performed in eleven hospitals in the region of the CCCL (one university hospital, five teaching hospitals and five general hospitals). In 342 patients the tumor was resected with curative intent. Figures 1a and 1b illustrate the distribution of surgical procedures within the studied time period and between the different hospitals. None of the CCCL hospitals performed more than seven esophageal resections a year, what makes them low volume hospitals (LVHs)[7]. In the same period 561 esophageal resections were performed in the nearest high volume referral center (HVH); a mean volume of 56 resections a year.

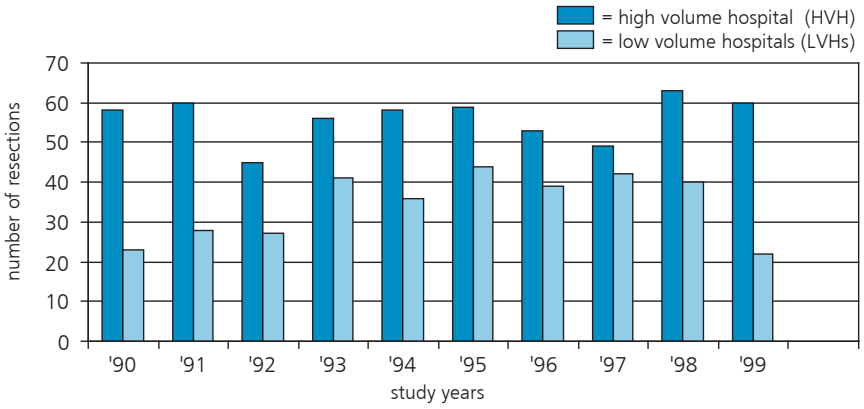

Figure 1a. number of esophageal resections per year in HVH versus LVH group (1990-1999)

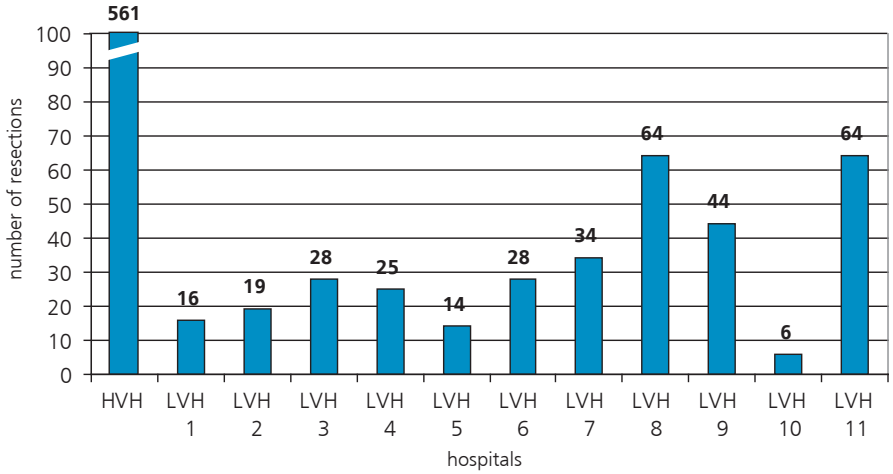

Figure 1b. total number of esophageal resections per hospital for HVH and LVHs (1990-1999)

Patient, tumor and treatment characteristics

Table 1 shows the patient, tumor and treatment characteristics of both groups. More patients from the HVH had a squamous cell carcinoma and an advanced stage of the

Table 1. Patient, Tumor and Treatment Characteristics of Esophageal Resections in LVH* and HVH**

	LVH		HVH		
Characteristics	No. of patients	%	No. of patients	%	P value
Age (years)	65		64		0.240
range (years)	33-87		31-83		
Gender					0.072
male	249	73	438	78	
female	93	27	123	22	
Comorbidity					0.078
no	142	42	273	49	
1 organ system	111	32	179	32	
2 organ systems	51	15	80	14	
≥3 organ systems	11	3	27	5	
Unknown	27	8	2	0	
Histology					0.039
adenocarc	238	69	347	62	
squamous	96	28	193	34	
barrets dysplasia	4	1	6	1	
other	2	1	14	3	
unknown	2	1	1	0	
Tumour localisation					0.740
cervical esoph.	7	2	14	3	
mid esoph.	53	15	86	15	
distal esoph.	114	33	204	36	
ge-junction	166	49	251	45	
unknown	2	1	6	1	

Table 1. Patient, Tumor and Treatment Characteristics of Esophageal Resections in LVH* and HVH** *(Cont).*

	LVH		HVH		
Characteristics	No. of patients	%	No. of patients	%	P value
Stage (pTNM)					< 0.001
0 and I	43	12	61	11	
II	162	47	214	38	
III	107	31	186	33	
IV	21	6	94	17	
Unknown	9	3	6	1	
(Neo)-adj.Treatment					< 0.001
none	316	92	464	83	
chemotherapy	17	5	93	17	
radiotherapy	0	0	2	0	
chemoradiation	4	1	0	0	
unknown	5	2	1	0	
Surgical approach					< 0.001
abdomino-cervical	150	44	466	83	
thoraco-abdominal	97	28	60	11	
abd-thor-cervical	43	13	17	3	
abdominal	52	15	18	3	
Anastomoses					< 0.001
cervical	195	57	541	96	
thoracic	91	27	8	2	
abdominal	56	16	8	2	
unknown	0	0	4	0	
Total no. of patients	342		561		

* LVH = low volume hospitals. ** HVH = high volume hospital

Table 2a. Outcome after resection of esophagus for cancer in LVH* and HVH**

	LVH		HVH		
Outcome	No. of patients	%	No. of patients	%	P value
Margins					0.93
R0	248	72	377	67	
R1	55	16	161	28	
R2	35	11	21	4	
Unknown	4	1	2	1	
Complications					
surgical compl.	144	42	207	37	0.010
general compl.	191	56	207	37	<0.001
no compl.	89	26	247	44	<0.001
Hospital stay					
median (days)	21		14		<0.001
In-hospital					
Mortality	45	13	28	5	<0.001
Survival					
median (months)	21		22		0.90
range (months)	(1-171)		(1-158)		
Total no. of patients	342		561		

* LVH = low volume hospitals. ** HVH = high volume hospital

disease. Operative strategy as well as adjuvant or neoadjuvant treatment varied widely between the groups. The vast majority of resections in the HVH was performed according to the transhiatal technique, with a gastric tube reconstruction and anastomosis to the cervical remnant esophagus. In the LVH-group a substantial number of anastomoses were located in the thoracic cavity, after a (partial) gastro-esophagectomy with either a gastric tube reconstruction or esophago-jejunostomy. In the pathology clear surgical margins (R0) were reported in 72 % and 67 %, respectively for the LVHs and the HVH group.

Morbidity and mortality

A significant higher postoperative morbidity rate was found in the LVH-group, which probably also is reflected by the longer hospital stay (Table 2a). The clinical anastomotic leakage rate differed between both groups: LVHs 17 % versus HVH 5 %. The mortality rate was almost three times higher for patients treated in the LVHs than those who had their operation in the HVH: 13 versus 5 percent respectively ($p < 0.001$). None of the LVHs had a mortality rate lower than the 5 percent of the HVH (Table 2b). Univariate analysis showed that hospital volume, age and co-morbidity are prognostic factors for mortality (table 3a). The mortality risk increased with higher age and the number of organ systems affected. Especially cardiac (OR 3.22, CI 1.91 – 5.44), vascular (OR 2.49, CI 1.45 – 4.27) and respiratory (OR 1.90 CI 1.09 – 3.33) co morbidity were risk factors for postoperative mortality.
Multivariate analysis showed that both hospital volume and co morbidity were independent prognostic factors for hospital mortality (Table 3b).

Table 2b. Mortality after resection of oesophagus for cancer in LVH* and HVH**

Hospitals	In-hospital mortality		
	No. of patients	No. of deaths	%
HVH	561	28	5.0
LVH 1	16	2	12.5
LVH 2	19	2	10.5
LVH 3	28	2	7.1
LVH 4	25	3	12.0
LVH 5	14	1	7.1
LVH 6	28	2	7.1
LVH 7	34	2	5.9
LVH 8	64	12	18.7
LVH 9	44	10	22.7
LVH 10	6	2	33.3
LVH 11	64	7	10.9
Total no. of patients	903	73	8

* LVH = low volume hospitals

** HVH = high volume hospital

Table 3a. Univariate Analysis of In-Hospital Mortality

	Univariate analysis		
	OR	95% CI	P value
Region			<0.001
HVH	1.00	Ref*	
LVH	2.88	1.76 – 4.72	
Age (years)			0.01
< 50	0.19	0.04 – 0.79	
50-59	0.51	0.25 – 1.04	
60-69	1.00	Ref*	
> 70	1.20	0.70 – 2.04	
Gender			0.20
Male	1.00	Ref*	
Female	0.67	0.36 – 1.24	
Co-morbidity			<0.001
No	1.00	Ref*	
1 organ system	2.02	1.06 – 3.86	
2 organ systems	4.51	2.30 – 8.85	
≥ 3 organ systems	4.97	1.92 – 12.83	
Histology			0.97
Adenocarc	1.00	Ref*	
Squamous	0.99	0.60 – 1.65	
Stage			0.24
I	1.00	Ref*	
II	0.50	0.24 – 1.04	
III	0.80	0.39 – 1.63	
IV	0.65	0.26 – 1.61	
Tumor localisation			0.33
cervical / mid esoph	1.00	Ref*	
distal esoph / GE junction	1.41	0.71 – 2.80	
Neo-adj treatment			0.14
No	1.00	Ref*	
Yes	0.49	0.20 – 1.25	
Surgical approach			0.31
Transhiatal	1.00	Ref*	
Transthoracic	1.51	0.90 – 2.54	
Anastomosis			0.46
Cervical	1.00	Ref*	
Thoracic	1.52	0.77 – 3.01	
Abdominal	1.26	0.52 – 3.04	

* Ref = Reference category

Survival

Figure 2a shows the crude 10-year overall survival rate of all patients, in who an esophageal resection for cancer was performed. Survival rates for patients treated in the HVH are significantly better (p=0.01). This survival benefit loses its statistical significance, after exclusion of patients who died postoperatively of complications of the surgical procedure (Figure 2b). Only, when we select patients with stage I and II disease we see a better

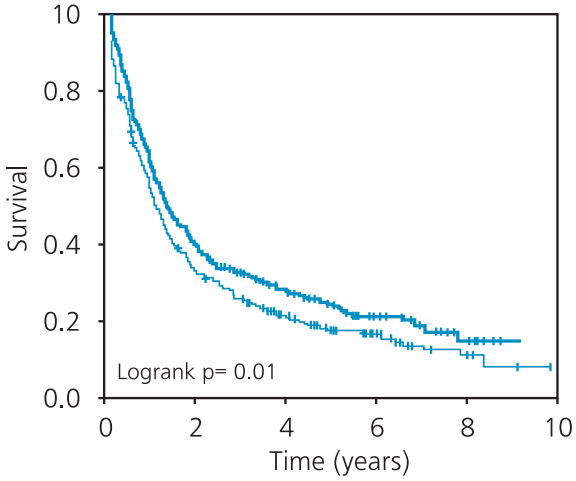

Figure 2a. Overall survival after esophagus resection for cancer: LVHs versus HVH (in-hospital mortality included)

HVH
LVHs

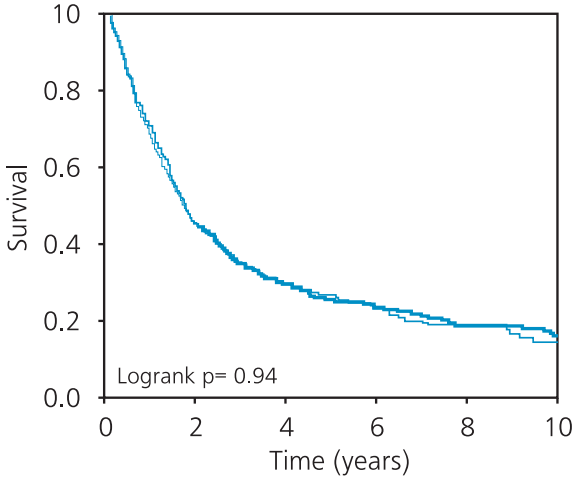

Figure 2b. Overall survival after esophagus resection for cancer: LVHs versus HVH. (in-hospital mortality excluded)

HVH
LVHs

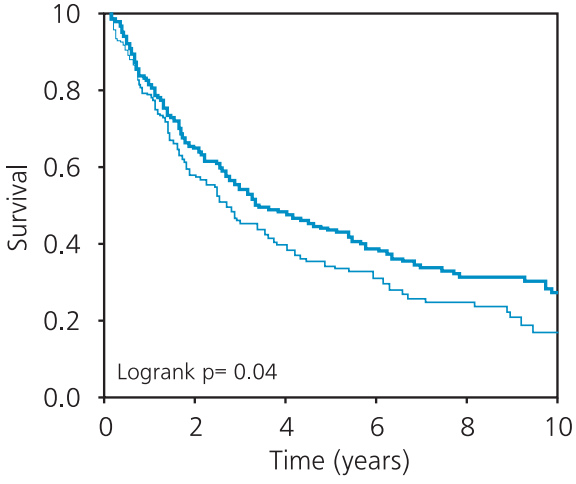

Figure 2c. Overall survival after esophagus resection for stage I and II carcinoma: LVHs versus HVH. (in-hospital mortality excluded)

HVH
LVHs

Table 3b. Multivariate Analysis of In-Hospital Mortality

	Multivariate analysis		
	OR	95% CI	P value
Region			<0.001
HVH	1.00	Ref*	
LVHs	3.05	1.82 – 5.11	
Age (years)			0.10
< 50	0.22	0.05 – 0.96	
50-59	0.60	0.29 – 1.25	
60-69	1.00	Ref*	
> 70	1.07	0.61 – 1.88	
Co-morbidity			0.004
No	1.00	Ref*	
Yes	2.34	1.30 – 4.19	

Ref = Reference category

survival in the HVH (Figure 2c), meaning that its overall results are worsened by the poor survival in the higher stages of the disease, stage III and IV. This can be explained by the unfavorable tumor mix, with significantly more stage IV disease treated in the HVH, than in the LVHs (16.7 versus 6.1%).

DISCUSSION

Currently there is extensive interest in comparing outcome of complex surgical procedures between high- and low-volume providers. Most of the studies are registry-based or relatively small. Our series offers additional proof to the volume-outcome relationship, because it is based on clinical data, retrieved from the original patient files. This allows us to make reliable comparisons for comorbidities and tumor-stage, which proved to be important prognostic factors for in-hospital mortality and survival.

A review of the evidence for a volume-outcome relationship was published by Dudley in 2000 en Halm in 2002 [8] [2]. In the latter publication 135 studies were reviewed, of which only 5 were not from the USA or Canada. The majority of reports were based on state- or national hospital-discharge databases, where only a few studies used clinical data for risk-adjustment. The outcome-measure was 'death' in 79 percent of the studies, without analyzing other dimensions of 'outcome', like morbidity, length of hospital stay, re-operations et cetera. For cancer-related procedures long-term survival was not mentioned. Higher-level methodological issues were rarely addressed. Only five studies concerning cancer treatment adjusted for (neo)-adjuvant therapies or the type of surgical resection, but without any adjustment for tumor stage.
Since 2002 more extensive studies on hospital or surgeon volume appeared in the international literature. Birkmeyer reported a total number of 2.5 million operations concerning 14 different surgical procedures derived from the MEDICARE database [9].

Table 4. Volume-outcome articles for in-hospital mortality after esophagectomy 1998-2006

Author	Journal / Year	Data	Volume 'cut-off'	Conclusion
Dimick [32]	Ann.Thorac.Surg. 2005	Adm	<6>	S
Urbach [33]	BMJ 2004	Adm	<9>	NS
McCulloch [12]	BMJ 2003	Clin	<10-20>	S
Christian [34]	Ann. Surg. 2003	Adm	<22>	S
Finlayson [35]	Arch Surg. 2003	Adm	<4-9>	S
Urbach [36]	CMAJ 2003	Adm	*	S
Dimick [37]	Ann.Thorac.Surg. 2003	Adm	<7>	S
Birkmeyer [9]	N.Engl.J.Med. 2002	Adm	<2-4-7-19>	S
Gillison [11]	Br.J.Surg 2002	Clin	<19>	NS
Bachmann [10]	Br.J.Surg 2002	Clin	*	NS
Dimick [38]	Ann.Thorac.Surg. 2001	Adm	<4-15>	S
vLanschot [7]	Cancer 2001	Adm	<10-20>	S
Kuo [39]	Ann.Thorac.Surg. 2001	Adm	<6>	S
Swisher [40]	J.Thorac.Cardiovasc.Surg.2000	Adm	<5>	S
Gordon [41]	J.Am.Coll.Surg. 1999	Adm	<10-20-50>	S
Begg [42]	JAMA 1998	Mixed	<5-10>	S
Patti [43]	J.Gastrointest.Surg.1998	Adm	<1-2-4-6>	S

* Urbach and Bachmann used equally sized groups and reported only median volumes of these groups. Adm = administrative data; Clin = clinical data; S = significant; NS = not significant

Mortality was the only outcome-measure. Even after risk-adjustment, which decreased the outcome-differences between high- and low-volume hospitals, the differences in results for esophageal and pancreatic resections were highly significant, favoring surgery in a high-volume center. Two more recently published reviews of the volume-outcome relationship for esophagectomies came up with 12 papers addressing this subject [5 4]. Only two of these studies were based on clinical data. Although both showed a decrease in mortality, they failed to show a statistically significant relationship of operative mortality with hospital volume [10,11]. In our own review of the literature we identified another study from the UK using clinical data, in which hospital case volume independently predicted operative mortality [12] (table 4).

In the present study independent data managers collected data retrospectively from the patient files. Not only the (in-hospital) mortality rate was obtained, but also a range of other outcome data, like complication rates, resection margins, length of stay and long-term survival. In our opinion the latter is an important performance indicator in surgical oncology, surprisingly sporadically mentioned in the volume-outcome literature.
The results of patients treated in eleven low-volume hospitals were compared with the results of patients treated in the nearest high-volume referral center. Significant differences in outcome could be revealed. In-hospital mortality was significantly higher in the low-volume hospitals. The retrieved information about co- morbidity and stage of the disease made an extensive preoperative risk- and tumor load comparison possible. Risk-adjustment is an important issue in outcome research, because patients with severe co-morbidity may be

unequally distributed between (groups of) hospitals. Especially, when only administrative data are used to assess hospital performances, a selection-bias could lead to inadvertently penalizing those surgeons who provide excellent care to patients with more severe co morbid disease [7,13]. Administrative data-sets were never designed to predict risk and should probably not be used as such[14]. Therefore, the validity of studies which fail to make case-mix adjustments based on clinical data, has to be questioned.
Nevertheless, a multivariate analysis of our data shows hospital volume to be an independent prognostic factor for in-hospital mortality. Although differences in surgical technique could be detected, with more transthoracic esophagectomies and intrathoracic anastomoses in the low-volume group, these factors are not significantly related to mortality. These findings are confirmed by earlier reports [15-18]. Also, there is little evidence for a beneficial role of neo-adjuvant therapies [19-22]. But, above all, choices made concerning diagnostic strategy, neo-adjuvant treatments and surgical technique are related to the knowledge, experience and judgment of the (team of) specialists.

After exclusion of in-hospital mortality, the survival of patients in the HVH was equal to those treated in the LVHs. But, the results of the HVH were negatively influenced by its case-mix. More patients with stage IV disease were treated in the HVH, corresponding with its status as a tertiary referral center. The very poor survival in this group of patients influences the overall results significantly. Only when we are informed about differences in tumor stage, we are able to detect real differences in survival, between patients treated in different hospitals. Although in this study all pathology reports were reviewed, and the number of lymph nodes resected was equal for both groups, we still have to be cautious suggesting a survival benefit for high-volume surgery. Only when a uniform pathologic evaluation is guaranteed, we can be sure that observed differences in tumor stages are truly characteristic for patient groups. This could be the reason that few studies have attempted to examine the influence of hospital volume on long-term survival in cancer surgery, only one of them concerning esophagectomies [23-27]. A recent study from the Netherlands failed to show a survival benefit in high volume hospitals (>20 resections a year), but did show an improved survival for esophagectomies performed in University compared to non-University hospitals[28]. On the other hand, for pancreatectomies and hepatectomies registered in the MEDICARE-database, Fong showed a significant better survival for procedures performed in high volume centers [25]. In his study administrative data about age, gender, co morbidity, and extent of the resection were included in a uni- and multivariate analysis, but stages of the disease, radicality and intent of the resection (palliative or curative) were not reported.

In conclusion, our study shows that hospital volume is an important determinant of peri-operative morbidity and mortality in esophageal cancer surgery. Nevertheless, volume in itself is no guarantee for high quality of surgical care in a specific institution. Selecting (only) favorable patients can be the basis of superior results. Therefore case-mix adjustments are essential in the assessment of surgical performance of different institutions.

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Chapter 4

Centralization of Esophageal Cancer Surgery: Does It Improve Clinical Outcome?

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ABSTRACT

Background:
The volume-outcome relationship for complex surgical procedures has been extensively studied. Most studies are based on administrative data and use in-hospital mortality as the sole outcome measure. It is still unknown if concentration of these procedures leads to improvement of clinical outcome. The aim of our study was to audit the process and effect of centralizing esophageal resections for cancer by using detailed clinical data.

Methods:
From January 1990 till December 2004, five-hundred fifty-five esophagectomies for cancer were performed in eleven hospitals in the region of the Comprehensive Cancer Center Leiden, 342 patients were operated on before and 213 patients after the introduction of a centralization project. In this project patients were referred to the hospitals which showed superior outcomes in a regional audit. In this audit patient-, tumor- and operative details as well as clinical outcome were compared between hospitals. The outcome of both cohorts, patients operated on before and after the start of the project, were evaluated.

Results:
Despite the more severe comorbidity of the patient group, outcome improved after centralizing esophageal resections. Next to a reduction in postoperative morbidity and length of stay, mortality fell from 12 to 4% and survival improved significantly ($p = 0.001$). The hospitals with the highest procedural volume, showed the biggest improvement in outcome.

Conclusion:
Volume is an important determinant of quality of care in esophageal cancer surgery. Referral of patients with esophageal cancer to surgical units with adequate experience and superior outcomes (outcome-based referral), improves quality of care.

INTRODUCTION

The number of publications that report on the relationship between the volume of high-risk surgical procedures and patient outcome continues to grow[1]. Most studies show better outcome with increasing number of operations performed by a specialized center or surgeon. However, there is still a debate about the level of evidence of these studies and the appropriateness of minimum volume thresholds for high-risk surgical procedures[2 3 4]. For example, there are no randomized controlled trials that have compared outcome for complex surgical procedures between high and low volume hospitals. Despite this "lack of evidence", authors claim that many surgical deaths could be saved by centralizing these high-risk procedures[5]. However, studies that have analyzed the actual effect of centralization (or regionalization) on hospital volumes and outcomes are rare[6].

It has been widely acknowledged that esophagectomy for cancer is a complex surgical procedure and that concentration in high-volume centers could lead to improved outcome [7 8]. However, translation of the conclusions of observational series to clinical practice is difficult. Cut-off values between high- and low volume esophageal surgery vary greatly between studies (Table I). In the Netherlands, van Lanschot *et al.* investigated the volume-mortality relationship for esophageal resections, analyzing data from the Dutch National Medical Registry [9]. They also showed an inverse relationship between hospital volume and mortality. The purpose of our study was to analyze whether centralization of esophageal cancer surgery truly improves clinical outcome. Besides mortality, we were also interested in a more extensive set of outcome measures, including overall survival. As case-mix has also been shown to be an important predictor for treatment outcomes, we included detailed clinical data of individual patient and tumor characteristics[10].

METHODS

Comprehensive Cancer Center Leiden

Eleven hospitals in the mid-western part of the Netherlands are affiliated with the Comprehensive Cancer Center Leiden (CCCL). In this urbanized area travelling distances between hospitals are not more than 45 kilometres (30 miles). In 1997, a Professional Network of Surgical Oncologists (PNSO) involving all affiliated hospitals was established, with the objective to improve the effectiveness and efficiency of surgical care for patients with cancer. Within the light of the increasing number of reports on a volume-outcome relationship for esophagectomies, the Network decided to evaluate the surgical care for patients with esophageal cancer treated in the CCCL region since the year 1990.

Retrospective registration

All surgically treated esophageal carcinomas from 1990 till 1999, were identified through the 'Cancer Registry' of the CCCL, in which all cancer patients diagnosed and treated in the mid-western part of the Netherlands (1.7 million inhabitants) are registered. All eleven hospitals formally gave their consent to participate in this audit and were subsequently visited by two investigators who retrieved the original patient files. Patient demographics, pathological notes, data on surgical and (neo)adjuvant treatments, co-morbidity as well as post-operative morbidity, mortality, length of stay and survival were extracted from the patients' files. Pathological notes were reviewed in detail by two independent researchers and all cancers were staged according to the TNM-staging system of the UICC 1997. The obtained pTNM stages were then cross-checked with the tumor stages in the 'Cancer Registry'. Discrepancies in tumor stage were discussed between the researchers and a trained data manager from the CCCL/Cancer Registry database. If consensus could not be reached, the tumor stage was classified as 'unknown'.

Intervention

In January 2000 the results of this retrospective analysis were presented at the PNSO meeting[10]. Differences in volume and outcome between hospitals were discussed and all surgeons agreed to participate in a prospective registration. Also all surgeons agreed upon the scenario of having to refer esophageal cancer patients to centers with a better outcome if their own results proved to be unfavorable (outcome-based referral). These referrals were on a voluntary basis, however, both for the patient and the surgeon.

Prospective registration

From January 2000 until December 2004 the same data were prospectively collected from the original patient files, and again all affiliated hospitals took part in this exercise. Completeness of the data was cross-checked with the independently collected information from the 'Cancer Registry'. Each year, the interim results were presented and discussed within the group of surgeons at the meeting of the PNSO.

Control group

To put the data of the CCCL in national perspective, we compared the outcome of the CCCL region with the results of the nearest referral center for esophagectomy outside the CCCL region. In this high volume university hospital, information of patients operated on for an esophageal carcinoma is prospectively collected from the original patient files by a data manager.

Statistics

Differences in patient, tumor and treatment characteristics, as well as in outcome measurements were assessed using the Kruskal-Wallis test for continuous variables and

the chi-square test for categorical variables. Patients with an 'unknown' status for a given variable were excluded for the analyses. Duration of survival was calculated as the difference between date of surgery and either the date of death or the date of last patient contact. To prevent the problem of differential follow up, for all groups follow-up was cut-off at two years after surgery. Observed survival rates were estimated by using the Kaplan-Meier method. The log-rank test was used to assess differences in survival between patients who were operated in different time-periods and in low-volume versus high-volume hospitals. The Cox proportional hazard model was used to calculate hazard ratios, adjusting for possible confounding variables. All analyses were conducted using SPSS software (version 12.0; SPSS inc., Chicago.IL).

RESULTS

Hospital volume

Between 1990 and 2004, the evaluation and treatment of patients with esophageal cancer was performed in eleven hospitals in the region of the CCCL (one university hospital, five teaching hospitals and five general hospitals). In 555 consecutive patients, an esophageal tumor was resected with curative intent. Figure 1a illustrates the distribution of surgical procedures within the studied time period for the 11 hospitals and Figure 1b shows the resection rates for esophageal carcinomas diagnosed in the CCCL region in three different time periods.

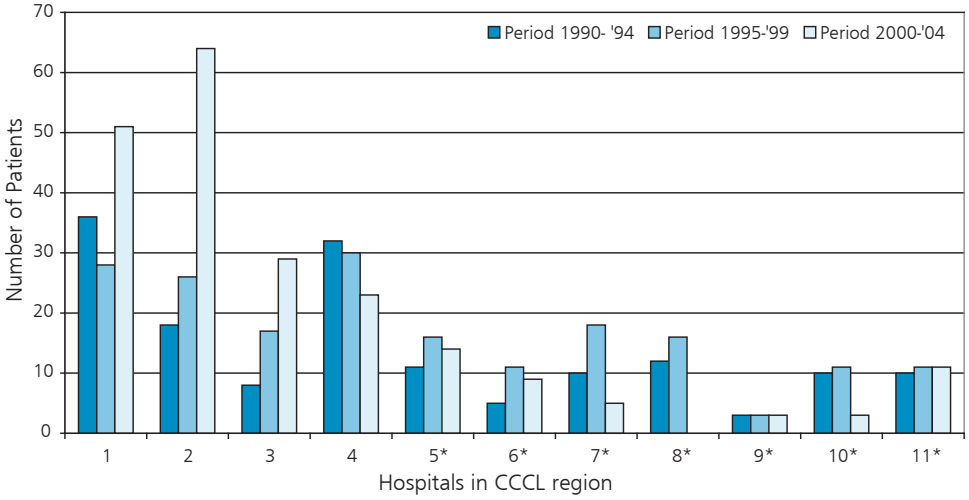

Figure 1a number of esophageal resections in hospitals in region of CCCLeiden per 5-years period (1990-1994, 1995-1999, 2000-2004) * Hospitals that abandoned esophageal resections during 2000-2004 period: 4 Hospital that abandoned esophageal resections after January 1st 2005

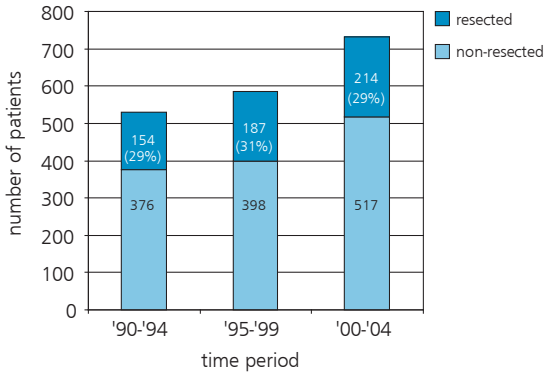

Figure 1b resection rates of newly diagnosed patients with esophagus carcinoma in hospitals in region of CCCL per 5-years period (1990-1994, 1995-1999, 2000-2004)

From 1990 till 1999, none of the hospitals performed more than seven esophageal resections per year (low volume hospitals; LVH). From the year 2000 onwards, a gradual concentration of esophageal resections has occurred, and in two hospitals (I and II) procedural volumes increased to more than 10 resections per year (high volume hospitals; HVH). In the same period of time, a mean annual number of 56 esophageal resections were performed in the nearest high volume center.

Patient, tumor and treatment characteristics

Table 1 shows the patient, tumor and procedural characteristics of esophageal resections performed in three consecutive time periods. There was no significant difference in age, gender, histological type or location of the tumors. However, the number of patients with co-morbidities increased during the study period. Stage I tumors were more frequently seen in the later time periods and an increasing number of transhiatal resections were performed. The number of nodes evaluated by the pathologist changed in time, with a mean number of 6.3, 7.5 and 13.5 nodes reported on in the different time-periods. In the 2000-2004

Table 1. Characteristics of patients who underwent esophageal resection by period of surgery

	1990-1994		1995-1999		2000-2004		
Characteristics	No. of patients	%	No. of patients	%	No. of patients	%	P value
Age (years)							0.19
Median	66		65		64		
Range	37-87		33-85		33-86		
Gender							0.70
Male	109	70.8	139	74.3	159	74.3	
Female	45	29.2	48	25.7	55	25.7	
Co-morbidity							0.25#,*
No	68	44.2	74	39.6	83	38.8	
1 organ system	51	33.1	61	32.6	85	39.7	
2 organ systems	19	12.3	30	16.0	41	19.2	
≥ 3 organ systems	4	2.6	7	3.7	4	1.9	
Unknown	12	7.8	15	8.0	1	0.5	

Table 1. *Cont.*

Characteristics	1990-1994		1995-1999		2000-2004		P value
	No. of patients	%	No. of patients	%	No. of patients	%	
Histology							0.93#,**
Adenocarc	107	69.5	130	69.5	144	67.3	
Squamous carc	45	29.2	51	27.3	52	24.5	
Barrets dysplasia	1	0.6	3	1.6	6	2.8	
Others	-	-	2	1.1	5	2.3	
Unknown	1	0.6	1	0.5	7	3.3	
Tumor localisation							0.97#,***
Cervical esoph.	4	2.6	3	1.6	4	1.9	
Mid esoph.	23	14.9	30	16.0	32	15.0	
Distal esoph./ge-junction	127	82.5	152	81.3	177	82.7	
Unknown	-	-	2	1.1	1	0.5	
Stage (pTNM)							0.65#
0	2	1.3	5	2.7	6	2.8	
I	10	6.5	26	13.9	31	14.5	
II	80	51.9	80	42.8	82	38.3	
III	52	33.8	60	32.1	74	34.6	
IV	9	5.8	12	6.4	15	7.0	
Unknown	1	0.6	4	2.1	6	2.8	
Neo-adj. treatment							<0.001#,****
No	150	97.4	165	88.2	160	74.8	
Chemo +/- radiother.	2	1.3	19	10.1	54	25.2	
Unknown	2	1.3	3	1.6	-	-	
Surgical approach							<0.001#,*****
Abdomino-cervical	53	34.4	97	51.9	156	72.9	
Thoraco-abdominal	62	40.3	34	18.2	11	5.9	
Abd-thor-cervical	16	10.4	27	14.4	27	12.6	
Abdominal	23	14.9	29	15.5	15	7.0	
Unknown	-	-	-	-	5	2.3	
Anastomoses							<0.001******
Cervical	69	44.8	126	67.4	187	87.4	
Thoracic	60	39.0	30	16.0	12	5.6	
Abdominal	25	16.2	31	16.6	15	7.0	
Total no. Of patients	154		187		214		

unknown category was excluded, * linear trend analysis, ** squamous versus adenocarcinoma plus barrets dysplasia, *** distal esophagus / GE-junction versus others, **** no neo-adjuvant therapy versus others, ***** abdomino-cervical versus others, ******cervical versus thoracic plus abdominal

time-period more neo-adjuvant chemotherapy was used, especially in patients with a tumor in the lower esophagus, included in a trial on peri-operative epirubicin, cisplatin and fluorouracil (ECF)[11].

Outcome

The outcome of esophagectomies in the CCCL region improved with time (Table 2). The percentage of patients with a microscopic radical resection (R0) improved from 69 % to

73%. The number of patients who left the hospital without adverse events was highest in the 2000 - 2004 period. Hospital stay was shortened significantly and in-hospital mortality was reduced almost three-fold. As shown in figure 2, a significantly better 2-yrs survival

Table 2. Outcome after esophageal resections in region of CCCLeiden (1990-1994, 1995-1999, 2000-2004)

	1990-1994		1995-1999		2000-2004		
Outcome	No. of patients	%	No. of patients	%	No. of patients	%	P value
Margins							0.57#,*
R0	107	69.5	140	74.9	156	72.9	
R1	34	22.1	21	11.2	39	18.2	
R2	10	6.5	25	13.4	12	5.6	
Unknown	3	1.9	1	0.5	7	3.3	
Complications							0.20#
No	43	27.9	46	24.6	70	32.7	
Yes	106	68.8	140	74.9	143	66.8	
Unknown	5	3.2	1	0.5	1	0.5	
Re-intervention							0.27#,**
None	115	74.4	155	82.9	163	76.2	
1	27	17.5	21	11.2	32	15.0	
2	5	3.2	7	3.7	12	5.6	
≥ 3	2	1.3	3	1.6	3	1.4	
Unknown	5	3.2	1	0.5	4	1.9	
Hospital stay (days)+							0.002
Median	20		21		17		
Range	(9-92)		(9-125)		(8-273)		
In-hospital mortality							0.003#
No	131	85.1	160	85.6	204	95.3	
Yes	22	14.3	23	12.3	10	4.7	
Unknown	1	0.6	4	2.1	-	-	
Total no. of patients	154		187		214		

+ patients who died during hospital stay were not included, # unknown category was excluded, * R0 versus R1 plus R2, ** no re-intervention versus others

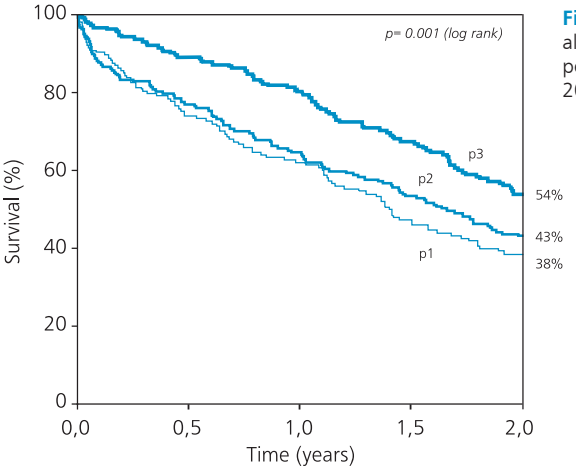

Figure 2. Two year survival after resection for all stages of esophageal carcinoma in 3 time periods (p1:1990-1994, p2: 1995-1999, p3: 2000-2004), incl. hospital mortality

Table 3a. Cox multivariate model adjusted for the impact of covariates on the risk of dying (HR) for patients who underwent esophageal resection for cancer by period of surgery.

	HR	95% CI
Univariate		
1990-1994	1.00	
1995-1999	0.89	0.69–1.14
2000-2004	0.66	0.50–0.86
Adjusted for stage# and co-morbidity#		
1990-1994	1.00	
1995-1999	0.82	0.61–1.11
2000-2004	0.57	0.42–0.77
Adjusted for stage#, co-morbidity# and surgical approach#		
1990-1994	1.00	
1995-1999	0.85	0.62–1.15
2000-2004	0.60	0.43–0.84
Adjusted for stage#, co-morbidity#, surgical approach# and neo-adjuvant treatment#		
1990-1994	1.00	
1995-1999	0.85	0.63–1.16
2000-2004	0.61	0.44–0.86

HR: hazards ratio, 95% CI: 95% confidence interval, # unknown categories were excluded

Table 3b. Cox multivariate model adjusted for the impact of covariates on the risk of dying (HR) for patients who underwent esophageal resection by period of surgery (patients who died in-hospital excluded).

	HR	95% CI
Univariate		
1990-1994	1.00	
1995-1999	0.87	0.64–1.20
2000-2004	0.66	0.48–0.91
Adjusted for stage#		
1990-1994	1.00	
1995-1999	0.90	0.65–1.24
2000-2004	0.67	0.48–0.93
Adjusted for stage#, age and gender		
1990-1994	1.00	
1995-1999	0.88	0.64–1.22
2000-2004	0.67	0.48–0.93
Adjusted for stage#, age, gender and co-morbidity#		
1990-1994	1.00	
1995-1999	0.88	0.64–1.22
2000-2004	0.67	0.48–0.93
Adjusted for stage#, age, gender, co-morbidity# and surgical approach		
1990-1994	1.00	
1995-1999	0.92	0.66–1.29
2000-2004	0.75	0.52–1.07

HR: hazards ratio, 95% CI: 95% confidence interval, # unknown categories were excluded

is seen for the last time-period (p = 0.001). After exclusion of in-hospital mortality, this difference is still significant (p = 0.045).

Table 3a shows the results of a multivariate analysis for the risk of dying after surgery in the three time periods with adjustments for the impact of the covariates: stage, comorbidity, surgical approach and neo-adjuvant treatments. Somewhat higher stages of the disease and more patients with multiple comorbidities were operated in the last time-period. Although there are significant differences in surgical approach and the use of neo-adjuvant chemotherapy between time-periods, the survival benefit in the 2000-2004 period remains significant in multivariate analysis (HR 0.61). An analysis of the data after exclusion of patients who received (neo-)adjuvant treatment showed similar improvements in mortality rates and survival after 2000. Also, a multivariate analysis was performed after exclusion of the patients who died during hospital stay (Table 3b). Improvements in survival stayed (borderline) significant after adjustments for differences in stage, age, gender and comorbidities (p = 0.05), but after introducing surgical approach in the model, significance was lost (p = 0.25).

In table 4 patient, tumor and treatment characteristics of patients operated on in hospitals with less than 10 resections a year (low volume hospitals LVH) and with more than 9

Table 4. Characteristics of patients who underwent esophageal resection by hospital volume in the 2000-2004 time-period

	LVHs		HVHs		
Characteristics	No. of patients	%	No. of patients	%	P value
Age					0.24
Median (years)	64		63		
Range (years)	(33-86)		(43-80)		
Gender					0.53
Male	80	72.1	79	76.7	
Female	31	27.9	24	23.3	
Co-morbidity					0.001#,*
No	56	50.5	27	26.2	
1 organ system	35	31.5	50	48.5	
2 organ systems	18	16.2	23	22.3	
≥ 3 organ systems	1	0.9	3	2.9	
unknown	1	0.9	-	-	
Histology					0.98#,**
Adenocarc	73	65.8	71	68.9	
Squamous	27	24.3	25	24.3	
Barrets dysplasia	3	2.7	3	2.9	
Other	2	1.8	3	2.9	
Unknown	6	5.4	1	1.0	
Tumor localisation					0.61#,***
Cervical esoph.	2	1.8	2	1.9	
Mid esoph.	18	16.2	14	13.6	
Distal esoph./ge-junction	90	81.1	87	84.5	

Table 4. Characteristics of patients who underwent esophageal resection by hospital volume in the 2000-2004 time-period *(Cont).*

	LVHs		HVHs		
Characteristics	No. of patients	%	No. of patients	%	P value
Unknown	1	0.9	-	-	
Stage (pTNM)					0.90#
0	3	2.7	3	2.9	
I	15	13.5	16	15.5	
II	43	38.7	39	37.9	
III	39	35.1	35	34.0	
IV	6	5.4	9	8.7	
Unknown	5	4.5	1	1.0	
Neo-adj. treatment					0.27#,****
No	90	81.1	70	68.0	
Chemo +/- radioth.	21	18.9	33	32.0	
Surgical approach					<0.001#,*****
Abdomino-cervical	66	59.5	90	87.4	
Thoraco-abdominal	10	9.0	1	1.0	
Abd-thor-cervical	17	15.3	10	9.7	
Abdominal	14	12.6	1	1.0	
Unknown	4	3.6	1	1.0	
Anastomoses					<0.001******
Cervical	86	77.5	101	98.1	
Thoracic	12	10.8	-	-	
Tbdominal	13	11.7	2	1.9	
Total no. of patients	111		103		

LVHs: Low Volume Hospitals (< 10 resections/yr) HVHs: High Volume Hospitals (≥ 10 resections/yr), # unknown category was excluded, ** adenocarcinoma / barrets dysplasia versus squamous and others, *** distal esophagus / GE-junction versus cervical / mid esophagus, **** no neo-adjuvant therapy versus others, ***** abdomino-cervical versus others, ****** cervical anastomoses versus others

resections a year (high volume hospitals HVH) are shown. Only patients operated in a year in which the procedural volume of the hospital concerned, exceeded 9 resections, were included in the HVH group. In this group more patients with more comorbidity were operated and the transhiatal approach was used more often, than the transthoracic approach. Significantly more adverse events occurred in the LVH group, with a mortality rate of 6.3% in the LVH group and 2.9% in the HVH group (table 5). After exclusion of the patients who died in-hospital, the median hospital stay was 8 days shorter in the HVH group. Survival analysis did not show a difference in 2-year survival between the LVH and HVH group (p = 0.63).

DISCUSSION

In the last decade, many studies have been published that have addressed the volume-outcome relationship for complex surgical procedures[1,12]. The results of these studies focus

Table 5. Outcome after esophageal resections by hospital volume in the 2000-2004 time-period

	LVHs		HVHs		
Characteristics	No. of patients	%	No. of patients	%	P value
Margins					0.35#,*
R0	77	69.4	79	76.7	
R1	19	17.1	20	19.4	
R2	10	9.0	2	1.9	
Unknown	5	4.5	2	1.9	
Complications					
No	24	21.6	46	44.7	0.001#
Yes	86	77.5	57	55.3	
Unknown	1	0.9	-	-	
Surgical complications					0.05#
No	54	48.6	64	62.1	
Yes	56	50.5	39	37.9	
Unknown	1	0.9	-	-	
General complications					0.001#
No	44	39.6	65	63.1	
Yes	66	59.5	38	36.9	
Unknown	1	0.9	-	-	
Re-intervention					0.39#,**
None	82	73.9	81	78.6	
1	19	17.1	13	12.6	
2	7	6.3	5	4.9	
≥ 3	1	0.9	2	1.9	
Unknown	2	1.8	2	1.9	
Hospital stay (days)+					<0.001
Median	22		14		
Range	(10-273)		(8-104)		
In-hospital mortality					0.24
No	104	93.7	100	97.1	
Yes	7	6.3	3	2.9	
Total no. of patients	111		103		

LVHs: Low Volume Hospitals (< 10 resections/yr) HVHs: High Volume Hospitals (≥ 10 resections/yr), + patients who died during hospital stay were not included, # unknown category was excluded, * R0 versus R1 plus R2, ** no re-intervention versus others

on the rather high difference in mortality rates between high- and low-volume providers for esophageal resections for cancer[7]. As a consequence, these authors speculate that concentration of these high-risk surgical procedures in centres with adequate experience could avoid thousands of preventable deaths[5,13]. However, the present study is the first that shows an actual improvement in outcome after the process of centralization of esophageal resections for cancer.

Chowdhury *et al.* reviewed 163 studies that looked at the volume-outcome relationship for complex surgical procedures[1]. Seventy-three percent of these studies showed significant better outcomes in high volume hospitals and for high-volume surgeons. However, most

studies are registry-based and omit important case-mix adjustments from clinical data. Moreover, hospital mortality is often presented as the sole outcome measure, without presenting other dimensions of quality of care. Therefore, there is solid criticism on the methodological issues, which hampers centralization initiatives for complex surgical procedures, especially in the Netherlands. Despite the expected benefits of centralizing complex surgical procedures at high-volume providers, there are few studies that show an actual improvement in clinical outcome after centralization of a specific procedure[14]. As a part of a broader initiative, The Leapfrog group, a large coalition of private and public purchasers of health insurance in the United States, is referring their patients to high volume providers of esophagectomies since 2000. Although expectations about the beneficial effects of this intervention were high, no results have been published yet[5,13].

Our study adds clinical proof to the effectiveness of concentrating complex surgical procedures: not only hospital mortality was reduced to a third of the original value, but also other outcome indicators, like the number and severeness of adverse events, showed a significant improvement after centralization of esophagectomies in the CCCL region in the Netherlands. This was also reflected in a lower number of reinterventions and a lower length of stay. Remarkable is the significant improvement in survival that is already demonstrated after a limited concentration of esophageal resections (Figure 2). To our opinion overall survival, adjusted for differences in tumor stages, should be the most important performance indicator in surgical oncology, being even more valuable than operative mortality.
In an earlier article from our group we showed that case-mix is an important determinant of outcome and should be part of every study comparing outcome between providers[10]. Therefore, we tried to study the effect of differences in case-mix between the hospitals. The identification of more patients with multiple comorbid diseases and more patients with stage IV disease in the last time period (Table 1), supports our conclusion that outcome improved with centralization of esophageal resections.

However, our study has several limitations. First, the accuracy of the registry database should be confirmed. This was done by comparing the results with the data of the independently retrieved information in the Cancer Registry of the CCCL. Only 3% of the patients operated on for esophageal cancer in our region were missing from our prospective database. The treatment and outcome characteristics of this small group of patients did not differ significantly from the original group. An earlier report on a detailed medical audit confirms the accuracy of clinical outcomes databases on major fields like operative mortality, major complications, and significant factors in risk stratification[15].

Secondly, our dataset is still limited, though more (co)variables were included than in most volume-outcome studies. In contrast to the available data on case-mix variations, no information on structural changes in perioperative care was available. To our knowledge no important improvements in the treatment of esophageal cancer are known from the

literature nor within the region of the CCCL. Nevertheless, progress in anesthesiologic techniques and postoperative care within the study period, could have interfered with our findings. In addition, limited data were available on the survival of patients in the later time-period (2-year survival). This could be insufficient to evaluate differences in disease control obtained by transthoracic and transhiatal procedures. Recently, the 5-year survival data of the Dutch randomized controlled trial comparing these surgical approaches were published[16]. No survival benefit was shown for either approach. Nevertheless, after introducing surgical approach in our multivariate analyses (Table 3b), the statistical difference in survival between the time-periods was lost, suggesting an important role for the choice of operative approach. To our opinion, the choice for a transhiatal or transthoracic procedure is made in a decision making process in which careful interpretation of diagnostic images and surgical experience is combined. The increase in hospital volumes, as a result of the concentration of esophagectomies in our study, might have lead to better surgical decision making, especially in the choice of operative approaches.

The beneficial effects of the centralization-process conducted in the last time-period is further supported by the comparison of outcome between LVHs and the hospitals that acquired the status of HVH (> 10 resections/ year) in the last time-period (Table 5). Although differences in operative mortality are not significant, they strongly suggest that the most important improvement in outcome is made in the HVHs, which now parallel the outcome in the nearest high-volume referral center (data not shown). Differences in case-mix, especially comorbidities, are also in favour of the HVHs (Table 4). A continuation of the centralization process and the outcome registration in our region will elucidate the mechanisms behind these improvements in patient outcome. From January 1st 2005 esophagus resections in the region of the CCCL are concentrated in three hospitals with a mean annual volume of more than 15 esophagus resections.

Finally, the feedback we gave to individual surgeons and hospital organizations on their performance (mirror-information) could in itself have influenced practice patterns and dedication of the professionals. When outcomes data are used for internal peer review within institutions, changes in the process of care can be initiated by surgeons or hospitals themselves. A good example is the Veterans Affairs National Surgical Quality Improvement Program (NSQIP) in which feedback to providers and managers lead to a decrease in the relative risk for postoperative mortality of 27% and a 45% decrease in postoperative morbidity[17]. However, this program was more detailed consisting of outcome-based annual reports, periodic assessment of performance, self-assessment tools, structured site visits and dissemination of best practices. Nevertheless, the observed improvements in outcome in our study could not only be a result of the concentration of services, but also of the introduced feedback on surgical performance. This could be the explanation for the improved outcome that was also demonstrated in the LVHs, though of a lesser magnitude than the improvements in HVHs (Table 5).

Some authors believe that procedural volume, as a proxy for quality, is preferable above direct outcomes measurement [18,19]. The availability and easy access of these data and the avoidance of the statistical 'problem of small sample size' are mentioned as important advantages [20]. However, in a study from our own country, van Heek *et al.* showed that, despite a 10-year lasting 'evidence-based' plea for centralization of pancreatic surgery, no reduction of mortality or change in referral pattern was seen in the Netherlands [21]. The problem is that provider volume as a quality measure only holds true on average, and is a poor predictor of quality in individual hospitals or surgeons [22 23] .

In our opinion, a continuous monitoring of clinical outcomes has not only the ability to assess quality of care, but can actually improve surgical performance. A number of methods for surgical monitoring, that take into account different levels of prior risk, have been described in the literature [24,25]. A routinely conducted clinical audit, providing hospitals and surgeons with individualized and pooled outcome-information, can be a stimulus to the introduction of a range of improvements in hospital and surgical care [26-28]. In addition, a national or regional approach, like the example for esophageal cancer surgery in our study, clarifies important differences in quality of care. In a peer review environment or when reliable, hospital specific outcome information is made available to the public, actual changes in referral patterns can be made (outcome-based referral).

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Chapter 5

Volume- or Outcome-based Referral to Improve Quality of Care for Esophageal Cancer Surgery in the Netherlands

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ABSTRACT

Recently, in the Netherlands esophageal resections for cancer are banned from hospitals with an annual volume less than ten. In this study we evaluate the validity of this specific volume cut-off, based on a review of the literature and an analysis of the available data on esophagectomies in our country. In addition, we compare the expected benefits of volume-based referral to the results of a regional centralization process based on differences in outcome (outcome-based referral).

INTRODUCTION

For high-risk surgical procedures, variation in outcome between hospitals and surgeons, has been the subject of a large number of studies performed in different countries[1]. Most studies are from the United States, but also in European countries outcomes research has become a subject of major interest. In the Netherlands differences in outcome for esophagectomies and pancreatectomies between high- and low volume hospitals have been the subject of a continuing debate in the last decade[2]. In 2001 van Lanschot et al. reported the effect of hospital volume on hospital mortality after esophagectomy in the Netherlands on data from the Dutch National Medical Registry[3]. In the 1993-1998 study period mortality rates varied from 5 to 12 percent between high- and low volume providers. Despite extensive discussions within the Association of Surgeons in the Netherlands about the consequences this volume-based variation should have, there were few changes in referral patterns. In 2006 this lead to a decision of the Netherlands Health Care Inspectorate to ban esophageal resections from hospitals with a mean annual volume less than ten.

In the mid-western part of the Netherlands eleven hospitals are affiliated with the Comprehensive Cancer Center West (CCCL), one of the nine regional comprehensive cancer centers in the country. Based on the volume-outcome literature the Professional Network of Surgical Oncologists (PNSO) in this region decided to start a surgical outcome registration (clinical audit) for esophageal cancer surgery in 2000. Detailed clinical data were retrieved retrospectively from the 1990 -1999 time-period. In this period no hospital performed more than six esophagectomies a year and the overall in-hospital mortality rate was 13 percent, much higher than the national average and the results of high-volume referral centers in our country[4].
Based on these results the PNSO decided that esophageal resections had to be concentrated in 2 to 3 hospitals in the region. Because concentration of services could not be based on historical differences in procedural volume, all surgeons agreed upon a prospective outcome-registration, with a scenario of having to refer patients to hospitals with better outcome if their own results proved to be unfavorable (outcome-based referral).

The primary purpose of our study is to evaluate variations in outcome for esophageal cancer surgery in a nation-wide cohort of hospitals, in a larger time-period. By reviewing the volume-outcome literature and analyzing hospital specific data on esophagectomies performed in the Netherlands, we investigate the proportion of hospital variation that can be attributed to differences in volume and the validity of a specific cut-off value of 10 resections a year.
In addition, we evaluate outcome-based referral as an instrument to concentrate esophageal cancer surgery in a situation where historical hospital volumes are insufficient for the selection of referral centers.

METHODS

Review of the Volume-outcome Literature

A search of the medical literature was performed in Medline for the period 1998-2008. The search was limited to publications in the English language and original articles. The medical subject headings (MeSH) 'esophagectomy' and 'hospitals' were combined with the key words 'volume' or 'mortality'. Also the related articles feature of PubMed was used. A manual search was performed for references mentioned in the first selection of articles, to identify all publications considerable for inclusion.

All original articles comparing mortality rates after esophagectomy between hospitals with a lower and higher procedural volume, were selected. Reports on data from less than 10 hospitals or less than 500 patients were excluded. Two authors (MW and GG) performed the search independently. Disagreements were resolved by discussion with a third author (RT). From the selected articles 'study period', 'country of origin', 'number of patients', 'number of hospitals', 'volume categories' and 'outcome measures' being 'hospital mortality' or '30-day mortality' were retrieved. The relation between the different hospital volume categories and the corresponding mortality rates was graphically displayed.

A meta-analysis of the data provided by these studies was not considered feasible because of the heterogeneity in study populations and volume categories. In addition, several sources of bias, like selection- and publication bias can not be controlled for without the availability of the primary data.

Esophagectomies in the Netherlands

Patients

Data of all esophageal resections for cancer that were performed in Dutch hospitals from January 1991 to January 2005 were retrieved from the Dutch National Medical Registry (DNMR) administered by Prismant, the Dutch Center for Health Care Information, Utrecht, the Netherlands. This register is a (near) complete database of hospital discharge data for all in-hospital and day-care treatments in Dutch hospitals (general and academic). The DNMR collects data on diagnosis and treatments performed during hospital admission. In addition, demographic (age and gender) and outcome data (length of stay, mortality) are available. Only esophageal resections that were followed by reconstruction with a gastric tube or colon interposition were included in our study. Though individual patients and hospitals could not be identified, the number of resections performed per calendar year could be calculated for each hospital code. Hospital volume was defined as the average number of resections performed in that hospital in the three preceding calendar years. Hospitals were divided in three volume categories according to an earlier publication of vLanschot et al [3]: low volume, less than 10 resections a year, medium volume, 10 to 20 resections a year, and high volume, more than 20 resections a year.

CCCLeiden: hospital identification

To identify the data from the hospitals affiliated with the CCCL we asked the representing surgeons for a written consent to break their hospital code. The region of the CCCL has 1.7 million inhabitants and is served by eleven hospitals (one university hospital, five teaching hospitals and five general hospitals). The results of these hospitals were analyzed separately to be able to compare their results historically and in relation to the national averages.

Statistics

Differences in patient and hospital characteristics as well as in outcome were assessed using the chi-square test for categorical variables and ANOVA and Kruskall-Wallis test for continuous variables.

To study the difference in performance between hospitals and the relation between volume and mortality, logistic regression models with a random hospital effect were used. To study the difference in performance in the CCCL region before and after 2000, a logistic regression model with the independent variables age, sex, region, time-period and a random hospital effect was used.

To visualise the relation between hospital volume and mortality and show the variation in outcome among hospitals, funnel plots were made[5]. Therefore the observed mortality rates were compared to expected numbers, based on gender, age and operation year of the patients within the hospital. The expected numbers were obtained by fitting a logistic regression model with mortality as dependent and sex, age and year of operation as independent variables. Then standardized mortality rates (SMR) were computed (SMR = observed/expected).The SMRs and the control limits were then multiplied by the average mortality rate in the population in the study period to obtain adjusted mortality rates. As target the average mortality in the high volume hospitals was used, with the 95 and 99 % limits from the Possoin distribution.

Analyses were conducted using SPSS software (version 14.0; SPSS inc., Chicago.IL), SAS PROC NLMIXED (SAS Institute Inc., Carey, North Carolina) for the random effect logistic regression or R for Funnelplots (www.r-project.org).

RESULTS

Review of the Volume-outcome Literature

The initial two search strategies yielded 96 articles, of which 75 did not meet the inclusion criteria: 58 had a different subject, 6 where not original studies (reviews or comments), 9 studies reported the results of less than ten hospitals, 1 study was published twice and 1 article was not in the English language. The other 21 articles where included in our review. On these articles the related articles feature of PubMed was used and a manual reference search was performed. Four additional articles were found that met the inclusion criteria. The assessment of the 25 candidate articles led to exclusion of one article, which reported only the results of the lowest volume decile and the top volume decile of hospitals performing

Table 1. Studies evaluating the volume-outcome relationship for esophagectomies 1998-2008.

Year	Author	Country	Study period	Patients	Hospitals	Volume cut-offs*	Outcome measures	Result
1998	Begg [7]	USA	1984-1993	503	190	<6-11>	Mortality	S
1998	Patti [8]	USA	1990-1994	1561	273	<30>	Mortality	S
1999	Gordon [9]	USA	1989-1997	518	51	<11-21-51>	Mortality	S
2000	Swisher [10]	USA	1994-1996	n.k.	101	<5>	Mortality	S
2001	Kuo [11]	USA	1992-2000	1193	64	<6>	Mortality	S
2001	Lanschot [3]	Netherlands	1993-1998	1792	n.k.	<10-20>	Mortality	S
2001	Dimick [12]	USA	1984-1999	1136	52	<4-16>	Mortality	S
2002	Birkmeyer [13]	USA	1994-1999	6337	1575	<2-5-8-19>	Mortality	S
2003	Finlayson [14]	USA	1995-1997	5282	603	<4-10>	Mortality	S
2003	Urbach [15]	Canada	1994-1999	613	47	<3-9-17-19>	Mortality	S
2003	McCulloch [16]	UK	1999-2002	955	23	<10-21>	Mortality	S
2003	Dimick [17,18]	USA	1995-1999	3023	200	<3-6-16>	Mortality	S
2004	Urbach [19]	Canada	1994-1999	613	47	<9>	Mortality	NS
2005	Wenner [20]	Sweden	1987-1996	1429	74	<5-16>	Mortality	S
2005	Dimick [21]	USA	1997-2000	3031	n.k.	<6>	Mortality	S
2006	Simunovic [22]	Canada	1990-2000	629	68	<8-20-44>	Mortality	NS
2006	Lin [23]	Taiwan	2000-2003	6674	111	<20-34-59-86>	Mortality	S
2007	Rodgers [24]	USA	1988-2000	8075	n.k.	<5-10>	Mortality	NS
2007	Rouvelas [25]	Sweden	1987-2000	1199	n.k.	<10>	Mortality Survival	S NS
2007	Al-Sarira [26]	UK	2002-2003	3229	111	<10-20-30-40>	Mortality	S
2007	Allareddy [27]	USA	2000-2003	2473	717	<13>	Mortality	S
2008	Ra [28]	USA	1997-2003	1172	361	<1-2>	Mortality	S
2008	Wouters [4]	Netherlands	1990-1999	903	12	<7>	Mortality Survival	S S
2008	Pal [29]	UK	1999-2005	8874	144	<11-21-39>	Mortality	S

S = Significant. NS = Not significant. n.k. = not known. * = Volume categories are represented by '<x-y>' meaning: lowest volume category with hospitals performing less than x resections a year, medium volume category with x to less than y resections a year, high volume category with y or more resections a year.

esophagectomies[6]. The remaining 24 articles are listed in Table 1 [3 4 7 8 9 10 11 12 13 14 15 16 17,18 19 20 21 22 23 24 25 26 27 28 29].

A total number of 61,214 esophagectomies performed between 1984 and 2005 were studied. Most studies are from the USA and Canada, but more recently several European studies have been published. The median number of patients per study was 1429 and the median number of hospitals 106. Volume cut-offs between (very) low volume, median and (very) high volume differed widely. Twenty-one studies reported a statistically significant difference in hospital mortality between low- and high volume providers, with a median difference in mortality between the lowest and highest volume category of 7.2 percent. Two studies also report a difference in long-term survival.

Figure 1 shows the mortality rate found for each volume category in these studies. Mortality rates are high and vary widely, especially for hospital volume categories beneath 20 resections a year.

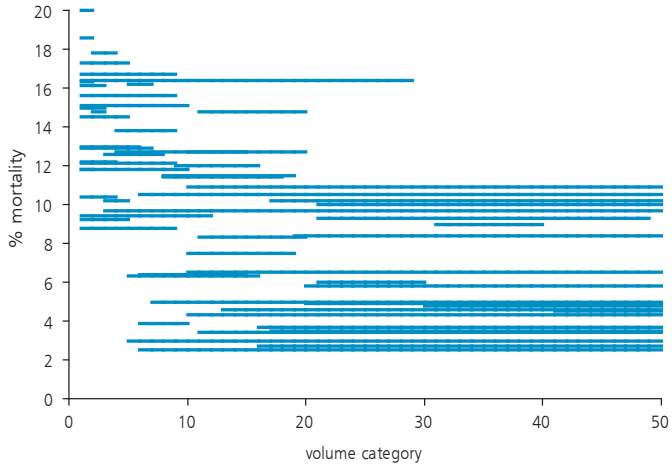

Figure 1. Mortality after esophageal resections for different hospital volume categories as reported in the literature

Esophagectomies in the Netherlands

In the period 1991-2004, a total of 4939 esophageal resections for cancer were performed in 104 Dutch hospitals. Patient, hospital and procedural characteristics of the resections are described in Table 2. Over time, no relevant differences were found in the distribution of age and gender. The hospital volume of esophageal resections increased since the mid 1990's and the length of hospital stay decreased during the study period (p<0.0001). In the most recent time-period (2000-2004) forty-seven percent of esophageal resections were performed in low volume hospitals, with a mean annual volume less than 10.

Nation-wide, the in-hospital mortality decreased from 9.7% in the period 1991-1994 to 7.3% in 2000-2004 (p=0.04). Figure 2 shows that in-hospital mortality decreased in high volume

Table 2. Patient, hospital and procedural characteristics of esophageal resections for cancer between 1991-2004 in the Netherlands by calendar period. (Data are presented as number (%), unless stated otherwise.)

	1991-1994 N=1377	1995-1999 N=1702	2000-2004 N=1860	P value
Patient age (yrs)				
mean ±SD	62.1 ±10.3	63.1 ±10.1	62.6 ±9.8	**0.02**
Gender				
male	1035 (75)	1290 (76)	1436 (77)	0.37
female	342 (25)	412 (24)	424 (23)	
Hospital volume *				
low (<10 /yr)	200 (54) **	802 (47)	884 (48)	**<0.0001**
medium (10-20 /yr)	0 (0)	150 (9)	265 (14)	
high (>20 /yr)	168 (46)	750 (44)	711 (38)	
Hospital stay (days)				
median (range)	18.4 (0.4-206)	17.6 (0-215)	16.4 (0.1-212)	**<0.0001**
In-hospital mortality	133 (9.7)	130 (7.6)	136 (7.3)	**0.04**

* Hospital volume was calculated as the average number of resections in a specific hospital in the three preceding calendar years. ** Available for calendar year 1994 (n=368). Hospital volume could not be calculated for 1991-1993, because the resection volume in the 3 preceding years was not (completely) known.

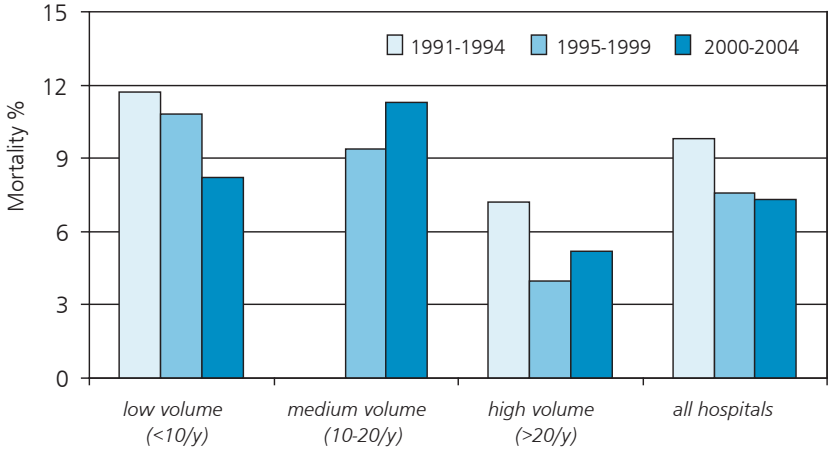

Figure 2. Mortality after esophageal resections in the Netherlands for low, medium and high volume hospitals in three time-periods: 1991-1994, 1995-1999, 2000-2004.

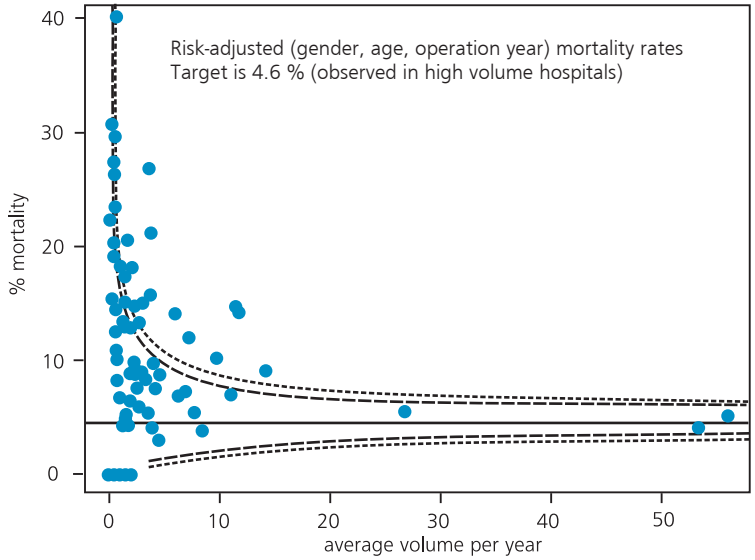

Figure 3. In-hospital mortality in relation to the average annual volume of esophageal resections, for each hospital in the Netherlands. (Mortality is adjusted for age, sex and year of operation. The straight line indicates the average mortality in the high volume hospitals, the dotted lines the 95 and 99 percent limits)

hospitals as well as in low-volume hospitals. A growing number of patients were treated in medium volume hospitals (10-20 resections / year) during the study period, from none during 1991-1994 period to 265 during the 2000-2004 time period. Mortality was high in these medium-volume hospitals; 11% during the most recent time period.

Figure 3 shows the mortality after esophageal resections for all hospitals performing esophagectomies in the Netherlands. Individual hospital volumes ranged from 1 to 682

esophagus resections in the 14 years study period. Targeting the outcome as was identified in the three high volume hospitals (>20 resections / year) mortality proved to be significantly worse in four out of five of the hospitals in the medium volume category (10-20 resections a year). Several low volume hospitals with a mean annual volume between five and ten, showed an in-hospital mortality similar to the mortality rate identified in the high volume hospitals. Logistic regression with mortality as dependent variable and a random hospital effect showed that after adjusting for age, gender and year of operation, there was a highly significant difference in performance between hospitals (hospital variation was

Table 3. Results of logistic regression for in-hospital mortality with random hospital effect

	Multivariate Analysis								
	for age, gender and operation year			for age, gender, operation year and volume			for age, gender, operation year, volume and region		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Age (years)	1.05	1.04-1.07	**<0.0001**	1.05	1.04-1.07	**<0.0001**	1.05	1.04-1.07	**0.0001**
Gender	0.78	0.58-1.04	0.09	0.78	0.58-1.04	0.09	0.78	0.58-1.04	0.09
Operation year	0.96	0.92-0.99	**0.02**	0.96	0.92-1.00	**0.03**	0.97	0.93-1.01	0.10
Hospital volume									
medium vs low				1.01	0.66-1.55	0.95	1.00	0.66-1.54	0.98
high vs low				0.49	0.30-0.79	0.004	0.48	0.30-0.77	**0.003**
CCCLeiden									
before 2000							1.35	0.75-2.43	0.31
after 2000							0.31	0.09-1.08	0.07
Hospital variation									
(on logit scale)		**0.27**			**0.14**			**0.13**	

OR = Odds ratio. 95% CI = 95 percent confidence interval. CCCL = region of Comprehensive Cancer Center West. Bold values indicate that p-values are statistically significant.

0.27). The hospital volume accounted for 50% of this variation; after adjusting for hospital volume, hospital variation reduced to 0.14 (Table 3). There was no difference in mortality risk between median volume and low volume hospitals (odds ratio median volume versus low volume was 1.01, 95%CI (0.66;1.55). The high volume hospitals performed significantly better (OR compared to low volume 0.49, 95%CI (0.30;.079).

Esophagectomies in the CCCL region

Of the 4939 esophageal resections, 312 (6.3%) were performed in the hospitals of the CCCL region. In this region, a centralization process for esophageal cancer surgery was started in the year 2000. The in-hospital mortality rates decreased from 11.6% before 2000 to 3.1% in the period afterwards (Figure 3). In a logistic model, adjusting for age, gender and between hospital variation, with a separate effect for the period before and after 2000 the odds of dying in the CCCL decreased 4.68 times (95% CI (1.26;17.3), p=0.02). In the other regions of the Netherlands, the in-hospital mortality rate was stable: 8.3% in the period 1991-1999 and 7.5% in 2000-2004, with a decrease in OR of 1.09 (95% CI (0.84; 1.41), p=0.50). This

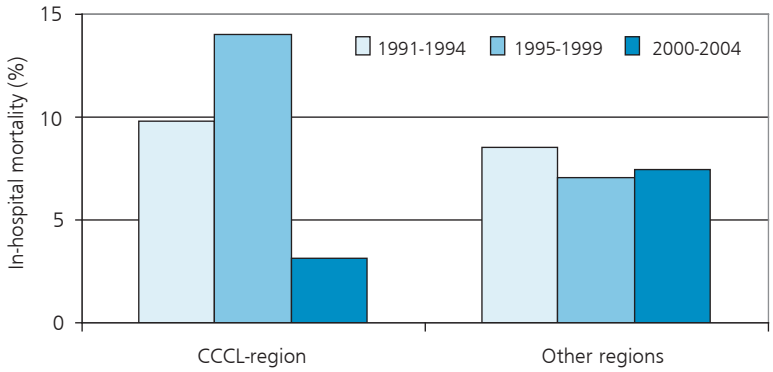

Figure 4. In-hospital mortality rates following esophageal resections in the CCCL region and in the other regions of the Netherlands by calendar period.

considerable decrease in the odds of dying in the CCCL region is not caused by an increase in hospital volumes; after adjustments for volume, the improvements in the CCCL region are still statistically significant: OR 4.76 (1.30;17.48).

DISCUSSION

In the last decade, esophagectomies for cancer have been the subject of many volume-outcome studies, addressing differences in mortality between high- and low volume providers. In the Netherlands, only recently esophagus resections were banned from hospitals with a mean annual volume below ten resections a year. In the literature there is little evidence for this specific volume-cut-off. In addition, our study based on the best available data on esophagectomies in our country, shows that hospitals with an annual volume between 10 and 20 resections a year, on average do not perform better than lower volume hospitals (less than 10 resections a year). Therefore, expectations about quality improvements as a result of this volume standard of 10 resections a year, have to be moderate. Procedural volume is not the only factor determining the variation in outcome between institutions. A strategy that directs patients to hospitals showing superior outcomes (outcome-based referral) could be more effective in improving quality of care than the current strategy of volume-based referral.

Volume standards for Esophageal Cancer Surgery

In 2004 a review by Metzger et al. showed 13 papers on the volume-outcome relationship for esophagectomies, showing a clear reduction in postoperative mortality with increasing case volumes[30]. The majority of these series originate from the United States, with several studies analyzing data from the same databases in overlapping time-periods. Nevertheless,

the authors concluded: "only with the experience of more than 20 procedures a year a significant reduction of mortality can be achieved".
In the present, more recent review of the literature we found 24 original articles concerning the inverse volume-mortality relationship for esophageal resections for cancer, on an institutional level. Some series describe procedures in more than 2000 hospitals (Table 1). Between studies, the choice of volume categories differs widely, with the lowest volume categories varying from less than 1 to less than 30 resections a year. In our study, we didn't perform a meta-analysis, because of heterogeneity in methodology and the choice of volume categories, with possible publication- and selection biases that can not be controlled for. Instead, a graphical representation of mortality rates found for the different volume categories in the literature is given in Figure 1. This figure also suggests that a volume cut-off for esophagectomies should at least be 20 resections a year. However, mortality rates found in several of these high volume categories exceed 10 percent, which in our opinion is still unacceptably high for non-emergency surgical procedures.

Our population-based study on patients that underwent an esophagus resection in the Netherlands in the period 1991-2004, shows an overall improvement in mortality rates over time. The introduction of relatively new anesthesiologic techniques, like the increasingly widespread use of thoracic epidurals, and better staffed ICU departments can be the cause of decreasing mortality rates. Some authors suggest that differences in quality of care between high and low volume hospitals could be based on the earlier adoption of new diagnostic tools and surgical or anesthesiologic techniques in high volume hospitals[31]. Nevertheless, differences in hospital mortality between high- and low volume providers proved to be persistent in the three consecutive time periods investigated in our study (Figure 2).
Since 2000, the evidence for these differences in mortality rates is available to the Dutch surgical community[3]. Despite, the remarkable variation in outcome, no changes in referral patterns were made in the most recent time-period. Only 38 percent of esophagectomies were performed in high volume hospitals, between 2000 and 2004 (Table 2). This information supports the decision of the Netherlands Health Care Inspectorate to ban esophageal resections from hospitals with low procedural volumes: the safety of patients surgically treated for esophageal cancer is at stake and quality improvements are certainly needed.
However, the present study does *not* support the cut-off value of ten resections a year that was chosen to concentrate esophagectomies in hospitals with historically higher procedural volumes. Our data show that only 3 centers have procedural volumes of more than 20 resections a year, with an in-hospital mortality of approximately 5%. On the other hand, the group of hospitals performing 10 to 20 resections a year, has significantly worse results than the outcome shown by these three high volume centers. On average they do not perform better than the low-volume group, but *are* selected as future referral centers for esophageal cancer surgery, under the current provision. Besides, there are several low volume hospitals, performing 5 to10 resections a year which do perform better, with similar results to those of the high volume centers (Figure 3). To our opinion, the effectivity of the current volume

standard (10 resections a year) as an instrument to improve quality of care for esophageal resections in the Netherlands is questionable, considering the presented data.

In addition, we found that volume accounted for only 50 percent of the variation in mortality between hospitals performing esophagectomies (Table 3). Probably, differences in infrastructure, patient selection, (surgical) expertise and dedication of multidisciplinary teams taking care of esophageal cancer patients are at least as important. Volume standards do not take these differences into account, bearing the risk of selecting the 'wrong' hospitals to become future referral centers for esophageal cancer surgery.
For example, recently the Netherlands Cancer Institute, a tertiary referral center for esophageal cancer patients with advanced stages of the disease, evaluated the outcome of patients treated in their hospital in the last thirteen years (1995-2007). The annual number of esophageal cancer patients referred to and treated in this hospital is high, more than 70 patients a year. However, the number of patients with an indication for surgical resection is below the volume standard of ten resections a year. Although most of these patients were downstaged with neoadjuvant therapies before surgery (65%), outcome in this patient group was remarkably good, with an in-hospital mortality of 1% and a five-year survival of 42% [unpublished data. Volume standards for operative procedures do not take in to account the experience with advanced tumor stages and multimodality treatments accumulated in the multidisciplinary setting of specialized cancer centres[32].
Moreover, few studies have been published that show an actual improvement in outcome after the introduction of minimal volume standards[29]. The leapfrog group, a large coalition of private and public purchasers of health insurance in the United States, is referring their patients to high volume providers of high-risk surgical procedures (esophagectomies, pancreatectomies etc.) since 2000[33]. Although expectations were high, no beneficial effects of this 'volume-based referral' initiative have been published yet[34].

Outcome-based Referral

In the region of the CCCL concentration of esophageal cancer surgery has started in 2000, with a scenario in which region-wide outcome registration was linked to a commitment to refer patients to hospitals with superior outcomes (outcome-based referral). In a recent article from our group we describe the results of this regional centralization project, in which detailed clinical data of the patients operated in the region were reported regularly to the participating surgeons. In a five years time period esophagus resections were concentrated in three of the original eleven hospitals. The data analyzed in the present study were retrieved from an independent data-source and validate the conclusions about quality improvements in the CCCL region. The dramatic fall in mortality after the intervention in this region differs significantly from the national trend (Figure 4). Moreover, this considerable decrease in the odds of dying in the CCCL region is not only caused by an increase in hospital volumes. After adjustments for differences in hospital volume between time-periods, the mortality rate in the CCCL region was still statistically significant (Table 3).

In the literature we find several examples of multi-institutional outcome registration programs, in which case-mix adjusted data are fed back to those personally involved in the clinical process of diagnosis, treatment planning, surgical intervention and peri-operative care[35 36]. In Europe, the Nordic countries like Norway and Sweden started a 'national audit' for the surgical treatment of rectal cancer more than 10 years ago. They focussed on the optimalization of the surgical technique for rectal cancer resections (Total Mesorectal Excisions). A nation-wide rectal cancer registry was established and results of rectal cancer resections were fed back to individual institutions and surgeons. In both countries the rate of local recurrence and overall survival improved within a few years[37]. Simultaneously, referral patterns changed with more patients treated in specialized surgical units which continued to show excellent results. Recently, national audit programs for colorectal cancer surgery have been started in the United Kingdom, the Netherlands and Belgium, to improve quality of care on a national level.

Transforming Outcomes into Health Care Policy

The present study is based on the best available data on esophageal cancer resections in the Netherlands. Unfortunately, these data have several limitations. First, few data were available on patient and tumor characteristics like co morbid diseases and stages of the disease. Adjustments for differences in case-mix can lead to considerable changes in results. Detailed clinical data of patients who underwent esophagectomy in the region of the CCCL were analyzed in a recently published study by Wouters et al[4]. Only minor differences in co morbid diseases and stages of the disease were identified between patients operated on in low and high volume hospitals in our country.
Second, in this study only in-hospital mortality and length of stay could be evaluated. In our opinion, more dimensions of outcome should be assessed to evaluate and compare the quality of care in different institutions. Unfortunately, few data collection systems that deliver comprehensive and reliable (case-mix adjusted) outcome data are available, at this moment.
Moreover, our analysis of differences in outcome between institutions is based on data from a 14 years time period. Presuming that concentration of esophageal cancer surgery in the Netherlands should ideally be based on differences in outcomes between providers (outcome-based referral), volumes of the hospitals performing esophageal resections should be sufficient to find statistical differences in quality of care in a more limited time-period [38]. Apparantly, outcome-based referral as an instrument to improve quality of care for esophageal resections for cancer is only feasible in a combination with minimal volume standards.

In conclusion, our study could not provide the evidence for a specific volume cut-off of ten resections a year as was established for esophageal cancer surgery by The Netherlands Health Care Inspectorate. Our data suggest that the use of 'volume' as a proxy for quality of care bears the risk of selecting hospitals with unfavorable outcomes as future referral centers for esophagectomies. Outcome-based referral could be a safer and more effective instrument for procedure-specific quality improvement, but the data needed to transform outcomes

in to policy are not available in most countries. In our opinion, (minimal) volume-standards should at least be accompanied by some sort of outcome registration (clinical audit), not only assessing hospital mortality, but a more extensive set of outcome parameters.

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Chapter 6

Outcome-based Referral to Improve Quality of Care in Upper GI Surgery

Editorial Journal of Surgical Oncology

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"……..adequate hospital caseloads are important for achieving safe pancreatic resection, but not necessarily sufficient. To ensure acceptable operative mortality rates, high-volume surgeons and hospitals should actively monitor their outcomes and benchmark their performance against their peers. They should also look for opportunities to learn from each other and improve."

Sonnenday C.J. and Birkmeyer J.D., Annals of Surgical Oncology 2010

In most western countries quality of care is high on the political agenda. In different health care systems various methods are used to improve patient safety and outcome in surgical oncology. The potential benefits of concentrating high-risk surgical procedures in high volume hospitals or with high volume surgeons are often mentioned in this context. Nevertheless, studies that show an actual improvement in outcome after centralization of complex surgical procedures are still rare. In the United States the Leapfrog group, a large coalition of private and public purchasers of health insurance, is referring their patients to high volume providers of high-risk surgical procedures (esophagectomies, pancreatectomies etc.) since 2000. Although expectations were high, no beneficial effects of this 'evidence based referral' initiative have been published yet. Also in the Netherlands, van Heek et al. showed no reduction in mortality or change in referral patterns, despite a 10-year lasting plea for centralization of pancreatic resections [1].

A plethora of articles has been published about the inverse relationship between hospital volume and mortality in high-risk surgical procedures. Chowdhury *et al.* reviewed 163 studies that looked at the volume-outcome relationship for complex surgical procedures. Seventy-three percent of these studies showed significant better outcomes in high volume hospitals and for high-volume surgeons[2]. However, most studies are registry-based and omit important case-mix adjustments from clinical data[3]. Moreover, hospital mortality is often presented as the sole outcome measure, without presenting other dimensions of quality of care.
Nevertheless, the differences in operative mortality between high- and lowvolume providers are remarkably high for upper GI procedures, like pancreatectomies and esophagectomies. Reviewing the volume-outcome literature for these procedures we find more recent studies that not only provide evidence for reduced operative mortality, but also for a survival-benefit in patients operated on in specialized or high-volume centers.

Despite the overwhelming number of publications, in many countries the level of evidence of these studies and the appropriateness of minimum volume thresholds is under debate. Not only the lack of unambiguous cut-off values between high- and low volume hampers the introduction of volume-standards. Many doubt if 'volume' is an appropriate proxy for quality of care. In one of his many publications on the subject John D. Birkmeyer considers the relative merits of different approaches to measuring and ultimately improving the quality of surgical care, adopting the Donabedian paradigm of structure, process and outcome. He concludes that focusing on proxy variables like 'volume' does not move the medical field forward in improving the quality of care[4]. A better understanding of the complex clinical processes that lead to success or failure has much more potential to improve outcomes of medical treatments.

Identifying highleverage processes of care is the central issue in outcomes research that includes not only volume, but carefully analyzes individual patients, their comorbidities,

tumor and treatment characteristics. The way the surgeon and his/her team select their patients, make use of neo-adjuvant treatments, provide pre-, peri- and postoperative care and manage complications, determines the quality of the clinical process and its outcome. The ultimate challenge for outcomes researchers is to transfer the 'excellence' achieved in 'best practices' to all hospitals performing these procedures[5].

To date, more large-scale data collections are needed to perform solid outcomes research[6]. There are several reports from countries in which a nation-wide registry of cancer treatment lead to a significant improvement in outcome. In Norway, for example, surgeons are obliged to include all surgical cases of rectal cancer in the Rectal Cancer Registry. Each department regularly receives its own results together with the national average for comparison and quality control. In 2006, Wibe et al. described a nation-wide improvement in the risk of local recurrence and overall survival for rectal cancer treatment as a result of this registry and monitoring treatment standards throughout the country[7].

In 2001 the American College of Surgeons (ACS) adopted the National Surgical Quality Improvement Program (NSQIP) that was founded twenty years before in the Veterans Affairs hospitals in the United States. The ACS NSQIP facilitates surgeons and medical centers to reliably collect and analyze risk-adjusted outcome-data, and act on them by making improvements in quality of care. Recently, an impressive number of multi-institutional outcome studies from the NSQIP was published in one issue of the Journal of the American College of Surgeons. One of these articles showed that the clinically rich NSQIP database is an effective instrument for local quality improvement programs to significantly reduce postoperative adverse event rates [8].

Outcome-based referral

The question which method is most effective in reducing morbidity and mortality rates of high-risk surgical procedures, like esophagectomies and pancreatectomies, is still under debate. On one hand concentration of services seems to improve outcome significantly, but on the other hand the introduction of volume-standards doesn't empower surgeons to improve quality of care. In the Netherlands a regional intervention to concentrate esophagectomies for cancer was accompanied by a routine data collection system, to monitor performances of the different hospitals in the region. Risk-adjusted outcome data were fed back to the participating surgeons and hospitals. Important differences in quality of care were revealed and lead to actual changes in practice, but also in referral patterns in this 'peer review environment'. Directing patients to hospitals with superior outcomes (outcome-based referral) showed to have a dramatic improvement in overall morbidity, mortality and survival for esophagectomy patients. This composite model, in which good performers (best practices) are empowered with higher case-loads, could be an effective instrument to improve quality of care in high-risk surgical procedures, like esophagectomies and pancreatectomies and deserves further exploration.

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Chapter 7

Quality-of-care indicators for esophageal cancer surgery: a review

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ABSTRACT

Background:
Quality-of-care indicators are measurable elements of practice performance that can assess the (change in) quality of the care provided. To date, the literature on quality-of-care indicators for esophageal cancer surgery has not been reviewed.

Methods:
We performed a review of the literature on quality-of-care indicators for esophageal cancer surgery. The indicators were classified by their nature of care provision (structural, process, or outcome).

Results:
One hundred thirty articles were included. For structural measures, most evidence was found for the inverse relationship between hospital or surgeon volume and postoperative mortality. Few articles described the required infrastructural and organisational elements for esophageal cancer surgery. Regarding process measures, the most common indicators were determinants of patient selection for surgery. Other process indicators with considerable evidence were found (e.g., multidisciplinary team management), though the number of studies was small. For outcome indicators, the level of evidence for pathological outcome measures was strong. Data on postoperative complications as outcome indicators varied widely.

Conclusion:
Since there is considerable variation in the evaluation of quality of care, the uniform use of well-defined quality-of-care indicators to measure and document practice performance holds the promise of improving outcome in patients who undergo esophageal cancer surgery.

INTRODUCTION

Quality assurance in the treatment of cancer is gaining importance since many studies have shown variation in outcome between different providers. In Europe, quality assurance programmes have been introduced in the field of radiotherapy as well as for medical oncology, however, surgical quality control has received less attention[1;2]. Only recently, the European Society for Surgical Oncology (ESSO) has started an international audit program for rectal cancer treatment[3;4]. Few attempts have been made to spread the merits of quality assurance programmes to other tumor types.

Evidence-based guidelines that have been developed for a large variety of cancer treatments worldwide are seldom accompanied by well-defined standards for the evaluation of the quality of surgical care. Donabedian has conceptualized the evaluation of patient care in terms of structure, process, and outcome measures[5].

Esophageal cancer ranks sixth on the list of cancer mortality worldwide[6]. In 2008, the incidence in the Netherlands was around 1850 new patients per year[7]. It has been recommended to concentrate the surgical treatment of esophageal cancer in high-volume centers. The effectiveness of such measures in raising the whole level of care has been questioned[8]. Preferably, the concentration of esophageal cancer treatment is accompanied by a national quality assurance program, evaluating the different dimensions of quality of care in all hospitals taking care of these patients[9]. A practical definition of quality of care would be the degree to which health services achieve a level of care deemed adequate by evidence-based quality measures[10].

We have performed a review of the literature to identify evidence-based standards for high-level quality of care for esophageal cancer patients who are candidates for surgical therapy. We used the Donabedian quality-of-care model to categorize the identified standards. Furthermore, we aimed to construct a minimum dataset of evidence-based quality-of-care indicators for future registration and benchmarking.

METHODS

Search strategy

A search of the literature on PubMed was performed to find articles published between January 1990 and October 2009 on quality of care in the surgical treatment of esophageal cancer. Three Medical Subject Heading (MeSH) terms were used: 'esophageal neoplasms', 'surgery' and 'esophagectomy'. Studies describing aspects of quality of care were searched by combining these three MeSH terms with the following keywords: 'benchmarking', 'health care', 'hospital mortality', 'hospitals', 'medical audit', 'outcome and process assessment (health care)', 'postoperative complications', 'quality assurance', 'quality indicators', 'referral and consultation'. Articles were selected on the basis of their relevance using pre-defined in- and exclusion criteria (Figure 1). Many studies were excluded because they were non-comparative studies. Only original articles were considered for inclusion. Selection was

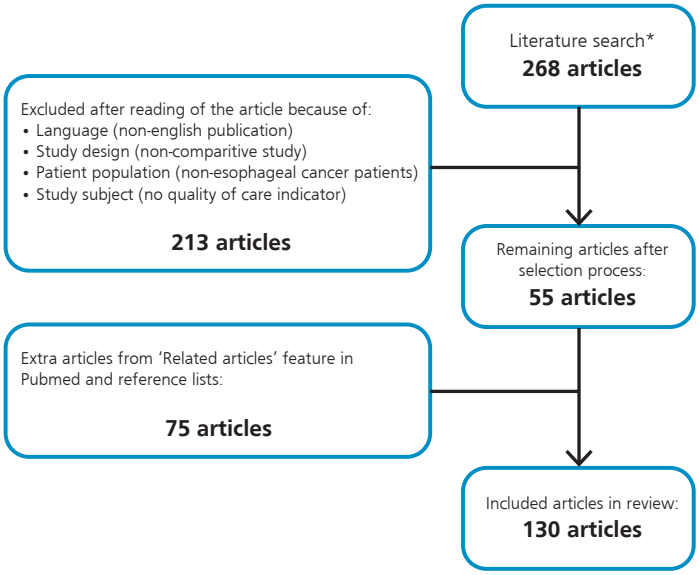

Figure 1. Flow chart of included articles on quality of care in the surgical treatment of esophageal cancer.
* For MeSH terms and keywords: see Methods

performed independently by two investigators (ECS and MW). A third reviewer (JvS) was consulted in case of disagreement. One hundred thirty articles were included.

Classification of studies

Articles were categorized according to the primary subject of the study: structural, process or outcome measures. *Structural* components of care are characteristics of the provider, reflecting the setting in which care is delivered. These may be related to the physical or organizational characteristics of a hospital, but also include staff expertise and experience. *Process* components of care refer to the interactions between the provider (i.e., physician) and the patient. An example is the delivery of adequate staging investigations to detect distant metastases in patients who are considered to be candidates for esophagectomy. *Outcome* characteristics are measurable short-term outcomes affecting the final outcome of patients (e.g., radicality of resection).

Level of evidence

Of 130 included articles 13 studies were randomised controlled trials, 26 were prospective (cohort) studies and 91 were retrospective studies. Because of the comparable level of evidence for most of these included studies, we classified results of evidence according to a scoring system used in a previous article by Lagarde *et al*: none (no evidence), minor (only evidence from univariate analysis), considerable (evidence from uni- and multivariate analysis), strong (evidence from several multivariate analyses or evidence from univariate analysis in at least ten articles)[11].

Only characteristics with strong evidence or those with considerable evidence based on at least three articles were entered into a minimum dataset of 'evidence-based' quality-of-care indicators for esophageal cancer surgery.

RESULTS

Structural measures

Structural variables with corresponding articles are listed in Table 1.

Volume

A wide variation in the definitions of hospital volume was found in the various studies on hospital volume and mortality rates (e.g., the definition of high-volume ranged from 6 to 40 resections per year). Besides the clear association between high hospital volume and low mortality rates, also lower complication rates and shorter admission times have been found in high-volume hospitals as compared to low-volume hospitals. Consequently, treatment in high-volume hospitals has been associated with a decrease in hospital charges. Other clinical endpoints, such as long-term survival and quality of life, have been studied less often. Two out of three studies could not demonstrate a survival benefit in high-volume hospitals and one other study did not find an improved quality of life.

As in studies on the influence of hospital volume, higher annual case volume per surgeon has been associated with lower postoperative mortality rates.

Specialization

Volume is related to, but does not equal specialization. Three studies have reported on the influence of subspecialty training of the surgeon on outcome (Table 1). In two studies, a lower postoperative mortality rate has been found in patients operated on by cardiothoracic surgeons as compared to that in patients operated on by a general surgeon. The third study reported no significant differences in outcome between general and thoracic surgeons with regard to postoperative mortality, morbidity, ICU stay and hospital stay. To date, no comparisons between dedicated upper gastrointestinal and general surgical oncologists have been made.

Organization

Few studies specifically addressed the impact of organization of care on the outcome of surgically treated esophageal cancer patients. In one study, daily rounds by an ICU physician were associated with shorter lengths of stay, lower hospital cost, and less postoperative complications after esophageal resection, but not with a lower in-hospital mortality rate. In an other large study, a comparison between 225 patients with a night-time nurse-to-patient ratio of 1:1 or 1:2 and 128 patients with a night-time nurse-to-patient ratio of 1:3 or more (one nurse caring for three or more patients) was made. Patients in the second group

Table 1. Structural measures for quality of care in esophageal cancer surgery

Structural measure	End point	Favoring	Nr of articles favoring	Level of evidence	References
Hospital volume *(high versus low)*	Postoperative mortality	High-volume hospital	22 out of 25	strong	1-25
	Postoperative morbidity	High-volume hospital	5 out of 8	considerable	1;2;7;8;13;17;26;27
	Postoperative ICU-stay	High-volume hospital	1 out of 1	minor	10
	Postoperative hospital stay	High-volume hospital	6 out of 8	considerable	1;2;7;10;12;17;24;26
	Survival	High-volume hospital	1 out of 3	minor	18;28;29
	Quality of life	--	0 out of 1	none	30
	Costs	High-volume hospital	5 out of 5	considerable	1;7;10;12;24
Surgeon volume *(high versus low)*	Postoperative mortality	High-volume surgeon	9 out of 10	strong	6;15;18;31-37
	Postoperative morbidity	High-volume surgeon	1 out of 1	considerable	26
	Postoperative hospital stay	High-volume surgeon	1 out of 1	considerable	26
	Anastomotic leakage	High-volume surgeon	1 out of 2	considerable	32;34
	Survival	High-volume surgeon	2 out of 4	considerable	15;18;35;36
	Quality of life	--	0 out of 1	none	30
Specialty training *(general versus thoracic surgeon)*	Postoperative mortality	Thoracic surgeon	2 out of 3	considerable	9;38;39
	Postoperative morbidity	--	0 out of 1	none	38
	Postoperative ICU-stay	--	0 out of 1	none	38
	Postoperative hospital stay	--	0 out of 1	none	38
ICU physician staffing *(daily rounds versus no daily rounds)*	Postoperative mortality	--	0 out of 1	none	40
	Postoperative morbidity	Daily ICU rounds	1 out of 1	considerable	40
	Postoperative hospital stay	Daily ICU rounds	1 out of 1	considerable	40
	Costs	Daily ICU rounds	1 out of 1	considerable	40
ICU nurse-to-patient ratio *(1 or 2 versus ≥3 patients per nurse)*	Postoperative mortality	--	0 out of 1	none	41
	Postoperative morbidity	1 or 2 patients /nurse	1 out of 1	minor	41
	Postoperative hospital stay	1 or 2 patients /nurse	1 out of 1	minor	41
	Costs	1 or 2 patients /nurse	1 out of 1	minor	41
Centralization *(referral versus regional centre)*	Postoperative mortality	Referral centre	3 out of 3	considerable	1;42;43
	Postoperative morbidity	Referral centre	1 out of 2	minor	42;43
	Survival	--	0 out of 1	none	42

Abbreviations: ICU: Intensive Care Unit None: no evidence; minor: only evidence from univariate analysis; considerable: evidence from uni- and multivariate analysis; strong: evidence from several multivariate analyses or evidence from univariate analysis in 10 or more articles.

had an increased risk of postoperative complications after esophageal resection which was associated with an increased use of resources.

Centralization

Following the relationship between volume/specialization and outcome, one may expect that centralization of esophagectomies at high-volume providers improves outcome. Few studies have actually demonstrated this. Recently, we have shown a dramatic improvement in mortality and survival after centralization of esophageal cancer surgery in a region of the Netherlands[9]. This centralization process was accompanied by feedback of detailed clinical data to individual hospitals and surgeons (surgical audit).

Process measures

Process variables with corresponding articles are listed in Table 2.

Table 2. Process measures: patient selection, staging and treatment choices for quality of care in esophageal cancer surgery

Process measure	End point	Favoring	Nr of articles favoring	Level of evidence	References
Age					
(< 70 years versus > 70 years)	Postoperative mortality	No age limit	11 out of 11	strong	44-54
	Postoperative morbidity	< 70 years	4 out of 11	minor	44-54
	Survival	No age limit	11 out of 11	strong	44-54
(< 80 years versus > 80 years)	Postoperative mortality	< 80 years	1 out of 4	minor	44;53;55;56
	Postoperative morbidity	< 80 years	2 out of 4	considerable	44;53;55;56
	Survival	< 80 years	1 out of 4	minor	44;53;55;56
Use of risk score					
(yes versus no)	Postoperative mortality	Use of risk score	1 out of 1	minor	57
Nutritional status					
(normal weight versus cachexia)	Postoperative mortality	Normal weight	1 out of 2	minor	58;59
	Postoperative morbidity	Normal weight	1 out of 3	minor	58-60
(normal weight versus obesity)	Postoperative mortality	--	0 out of 2	none	58;59
	Postoperative morbidity	--	0 out of 4	none	58-61
Socio-economic status					
Race	Surgical resection	White race	3 out of 3	considerable	62-64
Income	Surgical resection	Higher income	1 out of 1	considerable	65

Table 2. Process measures: patient selection, staging and treatment choices for quality of care in esophageal cancer surgery. *(Cont)*.

Process measure	End point	Favoring	Nr of articles favoring	Level of evidence	References
Preoperative quality of life *(good versus bad score)*	Postoperative mortality	Good preoperative QoL score	1 out of 1	minor	66
	Postoperative morbidity	--	0 out of 1	none	66
	Survival	Good preoperative QoL score	4 out of 5	considerable	66-70
Staging					
CT-scan	Detection of metastases	Experienced radiologist	1 out of 1	considerable	71
FDG-PET	Detection of metastases	Additional value of PET	8 out of 8	strong	72-79
EUS	Detection of metastases	High-volume EUS centre	1 out of 1	minor	80
Neoadjuvant chemoradiation *(yes versus no)*	Postoperative mortality	No effect	12 out of 13	strong	81-93
	Postoperative morbidity	No effect	9 out of 10	strong	81-90
	Overall Survival	Neoadjuvant chemoradiation	2 out of 11	minor	83;86;88-90;92-97
	Disease Free Survival	Neoadjuvant chemoradiation	2 out of 6	minor	88;93-97
MDT management *(yes versus no)*	Survival	MDT management	1 out of 1	considerable	98
Surgical approach *(transhiatal versus transthoracic)*	Postoperative mortality	Transhiatal	1 out of 4	minor	99-102
	Postoperative morbidity	Transhiatal	3 out of 4	considerable	99-102
	Overall Survival	Transthoracic	1 out of 4	minor	99;100;102;103
Thoracic Epidural *(yes versus no)*	Postoperative mortality	Thoracic epidural	1 out of 2	minor	104;105
	Postoperative morbidity	Thoracic epidural	2 out of 2	considerable	104;105
	Hospital stay	Thoracic epidural	1 out of 1	minor	106
Pathology reporting	Accurateness of reporting	Proforma reporting	2 out of 2	minor	107;108

Abbreviations: QoL: quality of life; CT: computed tomography; FDG-PET: fluorodeoxyglucose positron emission tomography; EUS: endoscopic ultrasonography; MDT: multidisciplinary team. None: no evidence; minor: only evidence from univariate analysis; considerable: evidence from uni- and multivariate analysis; strong: evidence from several multivariate analyses or evidence from univariate analysis in 10 or more articles.

Patient selection

In several studies, the influence of old age was investigated. In a minority of studies, older age was associated with an unfavorable postoperative outcome.

The *use of a risk score* may be a quality indicator. Bartels *et al* evaluated a risk scoring model in a prospective setting and found a marked reduction in post-operative deaths due to better patient selection[16].

The relationship between the preoperative *nutritional status* and the outcome of surgery in patients with esophageal carcinoma has shown conflicting results. In one study,

underweight patients who underwent major intra-abdominal surgery, e.g., esophagectomy, had a five-fold increased risk of postoperative mortality. Though, other studies including exclusively esophageal cancer patients have not confirmed this. In four studies, complication rates for obese patients equalled those for non-obese patients.
The role of *race* and *socio-economic* status on patient selection has received some attention. In the United States, African-American patients with esophageal cancer were less likely to undergo surgical resection compared to Caucasian patients. In the Netherlands, low socio-economic status proved to be associated with a lower chance of resection. These disparities are not fully explainable by differences in medical factors. It has been suggested that patients' but possibly also physicians' preferences might differ among different socio-economic groups of patients.
In one study, there was a relationship between better pretreatment *quality of life* and lower postoperative mortality. Especially reduced physical function as an aspect of pretreatment quality of life was predictive of lower survival in several studies.

Staging
For high-risk surgical procedures, it is important to select only those patients who can be cured. For computed tomography (CT) examination, the level of experience of the radiologist appeared to influence the detection of metastases in patients with esophageal cancer. Fluorodeoxyglucose positron emission tomography (FDG-PET) has shown its incremental value with the identification of 5 to 17% additional patients with metastases. Van Vliet *et al* studied the results of endoscopic ultrasonography (EUS) performed in low-volume EUS-centers and found unfavorable results in comparison with those in high-volume EUS-centers[12].

Treatment choices
- Multimodality treatment
  Several studies have compared the use of neoadjuvant chemoradiation with surgery alone for patients with esophageal cancer. Although a negative effect of neoadjuvant treatment on postoperative morbidity and mortality was found in two separate studies, most studies could not demonstrate these differences. Regarding overall survival, there was a benefit of neoadjuvant chemoradiation in two out of 11 studies.

- Multidisciplinary team
  It is generally believed that a multidisciplinary approach in cancer treatment results in the best achievable outcomes. The added value is hardly measurable. Nevertheless, in a study by Stephens *et al*, the selection, staging and treatment of patients eligible for esophagectomy by a multidisciplinary team resulted in a better survival as compared to the survival of patients treated by surgeons alone.

- Surgical approach
  Four randomized trials have compared the outcome of a limited transhiatal approach versus an extended transthoracic approach. Differences in postoperative morbidity were in favor of a limited transhiatal approach. Differences in post-operative morbidity were in favor of a limited transhiatal approach, and one trial showed a trend towards better survival in patients operated via an extended transthoracic approach. Complete 5-year survival data suggested that patients with a tumor in the distal esophagus had benefitted from an extended transthoracic resection.

- Peri-operative care
  Watson *et al* showed that respiratory complications decreased from 30 to 13% and death due to these complications from 5 to 0%, after introducing the routine use of thoracic epidural analgesia (TEA)[13]. In an other series, TEA lowered the anastomotic leakage rate[14]. The authors suggested a causal relationship between hypoxemia and hypotension due to respiratory hypofunction in patients undergoing esophagectomy without the use of TEA. It has also been shown that the use of TEA enables early discharge of patients after esophagectomy.

- Pathology reporting
  Histopathological assessment of the resection specimen plays an important role in patient management, in confirming whether complete excision has been achieved and in providing essential information on pathological tumor-node-metastasis (TNM) staging. The need to improve the quality of pathology reporting in esophageal cancer management has been recognised.

Outcome measures

Outcome variables with corresponding articles are listed in Table 3.

ICU stay
Length of ICU stay did not influence patients' survival and long-term quality of life.

Postoperative complications
The occurrence of postoperative complications after esophageal cancer surgery has not only been associated with higher postoperative mortality rates and increase use of resources, but also with worse long-term survival.

Radicality of resection
Multiple studies have shown the independent prognostic value of a microscopically radical (R0) resection.

Table 3. Outcome measures for quality of care in esophageal cancer surgery

Outcome measure	End point	Favoring	Nr of articles favoring	Level of evidence	References
Duration of ICU-stay *(≤ 5 days versus ≥6 days)*	Survival	--	0 out of 1	none	109
	Quality of life	--	0 out of 1	none	109
Postoperative complication *(yes versus no)*	Postoperative mortality	No complication	2 out of 2	considerable	27;110
	Postoperative ICU stay	No complication	1 out of 1	minor	110
	Postoperative hospital stay	No complication	1 out of 1	minor	110
	Costs	No complication	1 out of 1	considerable	110
	Survival	No complication	2 out of 2	considerable	111;112
(technical versus no complication)	Postoperative mortality	No complication	3 out of 4	minor	113-116
	Medical complications	No complication	3 out of 3	minor	113;114;116
	Postoperative hospital stay	No complication	2 out of 2	minor	113;116
	Survival	No complication	1 out of 2	considerable	113;114
(pneumonia versus no pneumonia)	Postoperative mortality	No pneumonia	3 out of 3	considerable	117-119
	Survival	No pneumonia	1 out of 1	considerable	117
Radicality of resection *(R0 versus R1 and R2)*	Survival	R0 resection	7 out of 8	strong	120-127
Number of resected lymph nodes *(high versus low)*	Survival	Higher nodal count (ranging from >23 to >40)	3 out of 3	strong	128-130

Abbreviations: ICU: Intensive Care Unit; R0: microscopically radical resection, R1: microscopically irradical resection; R2: macroscopically irradical resection. None: no evidence; minor: only evidence from univariate analysis; considerable: evidence from uni- and multivariate analysis; strong: evidence from several multivariate analyses or evidence from univariate analysis in 10 or more articles.

Number of resected lymph nodes

The number of identified lymph nodes is an independent predictor of survival after esophagectomy for cancer. According to Peyre *et al*, a minimum of 23 lymph nodes should be resected[15].

'Evidence-based' quality indicators for esophageal cancer surgery

A minimum dataset of 'evidence-based' quality-of-care indicators for the surgical treatment of esophageal cancer was created based on the identified standards with strong evidence or those with considerable evidence in at least three articles. This dataset is presented in Table 4.

Table 4. 'Evidence-based' quality-of-care indicators for esophageal cancer surgery

Quality Indicator	End point	Favoring	Level of evidence
Structural measures			
Hospital volume (high- versus low-volume)	Postoperative mortality	High-volume hospital	Strong
	Postoperative morbidity	High-volume hospital	Considerable
	Postoperative hospital stay	High-volume hospital	Considerable
	Costs	High-volume hospital	Considerable
Surgeon volume (high- versus low-volume)	Postoperative mortality	High-volume surgeon	Strong
Centralization (referral versus regional center)	Postoperative mortality	Referral center	Considerable
Process measures			
Age	Postoperative mortality	No age limit	Strong
(< 70 years versus > 70 years)	Survival	No age limit	Strong
Preoperative quality of life	Survival	Good preoperative score	Considerable
(good versus bad score)			
Staging	Detection of metastases	Additional value of PET	Strong
(FDG-PET versus no FDG-PET)			
Neoadjuvant chemoradiation	Postoperative mortality	No effect	Strong
(yes versus no)	Postoperative morbidity	No effect	Strong
Surgical approach	Postoperative morbidity	Transhiatal	Considerable
(transhiatal versus transthoracic)			
Outcome measures			
Postoperative complication			
(yes versus no)	Survival	No complication	Considerable
(pneumonia versus no pneumonia)	Postoperative mortality	No pneumonia	Considerable
Radicality of resection	Survival	R0 resection	Strong
(R0 versus R1 and R2)			
Number of resected lymph nodes	Survival	Higher nodal count	Strong
(high versus low)		(ranging from >23 to >40)	

Abbreviations: FDG-PET: fluorodeoxyglucose positron emission tomography ; R0: microscopically radical resection; R1: microscopically irradical resection; R2: macroscopically irradical resection. Considerable: evidence from uni- and multivariate analysis in 3 or more articles; strong: evidence from several multivariate analyses or evidence from univariate analysis in 10 or more articles.

DISCUSSION

This has been the first review of the literature to identify evidence-based standards for high-level quality of care for esophageal cancer patients who are candidates for surgery. Results show that (1) there is strong evidence that both hospital and surgeon volume are important determinants for postoperative mortality, (2) other structural measures, e.g., infrastructure and organization of esophageal cancer surgery, have been less frequently investigated, (3) the most commonly reported process measures were determinants of patient selection for surgery (e.g., patients' age), (4) other process indicators with considerable evidence were found (e.g., multidisciplinary team management), though the number of studies was small, and (5) the level of evidence for pathological outcome measures was high.

Structural measures

A plethora of studies concerning the volume-outcome relationship for esophageal cancer surgery was found. High-volume and specialized care were mostly related to a decreased postoperative mortality, and, in a lesser extent, to lower postoperative morbidity, shorter hospital stay, better survival and lower costs. Volume is only a surrogate for high-level processes of care and does not reveal the mechanisms behind the better outcomes. There is evidence that centralization of esophageal cancer resections leads to substantial improvements in outcome. Such efforts have been accompanied by continuous measurement and feedback of process and outcome indicators to individual surgeons and their referring colleagues. Only then, improvements in outcome are to be expected[9]. Data on infrastructural or organizational characteristics that lead to success or failure, were very limited (e.g., ICU staffing) or absent (e.g., ICU level).

Process measures

Evidence was found that teams using a risk score for the selection of surgical patients can decrease their postoperative mortality rates[16]. Several risk-prediction models have been proposed for this purpose, such as the Physiologic and Operative Severity Score for the enumeration of Mortality and morbidity (O-POSSUM)[17]. The O-POSSUM has only been studied retrospectively showing a two- or three-fold overprediction of in-hospital mortality[18-20]. Steyerberg *et al.* developed a more simple risk score, that also included the excess risk on postoperative mortality introduced by operations performed in low-volume hospitals[21]. Again, this risk score could not be validated by others[22;23].

Age, nutritional or socio-economic status should not be used as selection criteria for esophageal cancer surgery. On the other hand, in assessing resection rates or surgical outcome as indicators for quality of care, these factors are to be included as case-mix variables. Preoperative feeding to prevent further deterioration of the nutritional state of patients presenting with obstructive symptoms and weight loss could be a valid quality indicator, but the level of evidence for a better outcome is low[24].

We found evidence –although limited- that volume and experience play a role in the staging process of patients with esophageal cancer[25;12]. It would be better to assess the whole staging process by calculating the percentage of patients in whom a futile operation has been performed due to inadequate staging.

Neoadjuvant chemoradiation followed by surgery was associated with similar postoperative mortality rates as surgery alone in all studies, and survival rates improved in two studies[26;27]. If neoadjuvant chemoradiation becomes standard of care, there is a need to formulate quality indicators for its use (e.g., toxicity criteria).

Diagnosis and treatment of esophageal cancer patients by a dedicated multidisciplinary team could be an important quality indicator, but this is supported by only one paper[28]. Not only the expertise of the surgeon, but also that of the radiologist, anaesthesiologist, ICU-physician and nurses contribute to the outcome of surgery.

There is considerable evidence that the transhiatal approach leads to a reduced postoperative morbidity rate[29-32]. Presumed that the transthoracic approach with an extended lymphadenectomy is technically more challenging, one could propose that the performance of transthoracic esophagectomies in patients with a tumor located in the distal esophagus should be regarded as a quality indicator. No studies were found on other process indicators such as waiting times or psychological guidance during treatment.

Outcome measures

Outcome measures, like postoperative complication rates, tumor negative surgical margins, and number of retrieved lymph nodes are plausible measures of quality of care for physicians and their patients. Further investigation is warranted to look for additional valid outcome parameters of quality of care (e.g., hospital readmission rates, pain scores, number of anastomotic dilatations).

Limitations

A major limitation to this review is that there is no MESH term for "quality of care". We have tried to give an overview of the available literature on evidence-based determinants for high-leverage quality of care, but our review may have been biased by the choice of our search terms. Secondly, case-mix plays an important role in evaluating differences in outcome after esophageal cancer surgery. Consequently, for many studies, with a lack of information on patients' co-morbidity, tumor stage distribution, and patient selection criteria, the conclusions are debatable.

Future directions

The uniform use of well-defined quality-of-care indicators to measure and document practice performance holds the promise of improving outcomes in patients who undergo surgical treatment for esophageal cancer. Recently, another evidence-based review of esophageal cancer surgery was published[33]. In this review, non-surgical issues were not addressed. The present review places esophageal cancer surgery in a broader perspective. Improving the level of care for surgical esophageal cancer patients is a team effort from diagnosis, staging and risk assessment to follow-up and management of late sequelae of treatment. Ideally, each step is monitored by a set of measurable elements which reflect the quality of care.
Several projects have been started in which quality indicators are to be developed, not only based on evidence from the literature, but also on consensus of experts in the field. In Denmark, the Danish National Indicator Project has shown that continuous performance and outcome measurement,
using clinical indicators is possible and fruitful in terms of quality improvement[34]. Recently, Bilimoria *et al* presented an extensive set of quality indicators for pancreatic cancer[35]. After reviewing the literature for potential quality indicators, a Delphi method was used to develop quality indicators consulting several expert panels. In our opinion, a similar procedure should

be pursued for esophageal cancer care. To benchmark the outcome of consensus-based quality indicators, multi-centred data-collection, data-analysis and feedback of individual data is essential to provide physicians with actionable information about their quality of care.

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Chapter 8

Exemplary Care and Outcome (ECO): a composite measure for quality assessment in cancer surgery

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ABSTRACT

Background:
There is on-going interest in measuring quality in clinical practice. Though quality of care is a multi-dimensional concept, it is often assessed using singular outcomes. The purpose of this study is to provide a multi-dimensional assessment of quality, using esophageal cancer surgery as an example.

Methods:
Two methods for multi-dimensional quality assessment were tested. A relevance-weighted quality score (RWQS) and a cumulative quality profile, in which relevant quality parameters are ordered by their relevance for long-term outcome. Subsequent higher levels in the profile represent progressively more strict quality-standards; the proportion of patients meeting all standards is called the Exemplary Care and Outcome (ECO) measure. The two methods were used both unadjusted and adjusted for case-mix. Both methods were tested on outcome data from 12 hospitals that performed 1439 esophagectomies between 1991 and 2004.

Results:
No hospital scored best on more than one Observed/Expected quality score. O/E scores varied between hospitals from 0.65 to 1.05 for hospital survival, from 0.1 to 1.69 for profile-ECO, and from 0.88 to 1.03 for RWQS. Both multidimensional quality scores differed significantly between high and low volume hospitals, and between academic and non-academic hospitals, while O/E-scores for single-dimension of hospital survival did not differ significantly.

Conclusion:
Quality of care can be measured by more than one parameter only. We designed two methods of combining multiple quality parameters and a top-quality measure of ECO. Both methods seemed feasible, and results suggest that these methods may better discriminate between higher and lower quality of care.

INTRODUCTION

Ever since the publication of the Harvard Medical Practice Study,[1] and of the Institute of Medicine report "To Err is Human",[2] public attention has focused upon quality and safety in health care, or on the lack of it. The Institute of Medicine (IoM) has defined quality as a multi-dimensional concept, encompassing the dimensions effectiveness, safety, timeliness and patient centeredness. The Agency for Healthcare Research and Quality (AHRQ) described quality health care as "doing the right thing, at the right time, in the right way, for the right person, and having the best possible results". In recent years, the IOM, AHRQ and other institutions such as the Institute of Health Care Improvement, the Leapfrog Group and the UK department of Health, have pioneered initiatives on quality assessment, improvement and transparency. However, although quality is conceptually clear, there is an on-going debate on how to measure quality in clinical practice. One approach has been to use simple and readily available outcomes, such as hospital mortality or duration of hospital admission, another approach to use procedural volume as a readily available quality-proxy[3;4]. However, neither of these simplifying approaches has adequate content validity, as it does no justice to the multi-dimensional concept of quality. High quality care is safe, effective, patient-centered and cost-effective, and its good outcomes are the result of high quality (infra)structure and process[5]. Thus, as quality is a multi-dimensional concept, it should be measured as such.

For esophageal cancer surgery, quality assessment has so far focused almost exclusively on in-hospital mortality. Although this mortality has declined in recent years,[6] marked differences between institutions still exist, ranging from 2 to 10%.[7;8] In a recently published study we were able to show that concentration of esophageal resections by outcome-based referral dramatically reduced hospital mortality[9]. However, high-quality esophageal cancer care encompasses more than in-hospital survival only. Anastomotic leakage (occurring in 10-25% of the patients) and other adverse outcomes may severely affect esophageal cancer patients' quality of life[10]. In addition, treatment effectiveness (radicality of cancer resection, long-term survival) is no less important than treatment safety.

There is a need for quality frameworks that encompasses and combines different dimensions or aspects of health care quality. If such frameworks are to be used to compare the quality of care between hospitals, they should take into account differences in patient, disease- and procedure-mix between hospitals. In the present study we designed and piloted multi-dimensional quality assessment that aims at providing a more valid insight into the quality of surgical oncological care than mortality alone. In general, such studies are hampered by the absence of a 'golden standard' for quality of care. In the absence of a clear reference standard, we used hospitals' academic status as a proxy. In addition, we investigated whether multidimensional quality assessment could have potential to

discriminate better between hospitals with different levels of care than mortality alone. Thus, in this study, we addressed the following three research questions:

1. In cancer surgery, which parameters can be used to assess the quality of care provided to patients?
2. How can these parameters be combined into multidimensional assessment of quality, that could provide more insight than a singular quality measure (such as mortality) alone?
3. Is it plausible that multidimensional quality assessment, after correction for case-mix, better (or less good) discriminates between hospitals with higher and lower quality of care than a singular quality measure?

To test the framework's feasibility, we used it to assess the (differences in) quality of care between hospitals that provided surgical treatment to patients with esophageal cancer between 1991 and 2004 in the Netherlands, and on which we reported one-dimensional outcome information in an earlier paper.[11]

METHODS

Patient data were derived from a database that was created to assess the quality of esophageal cancer surgery in 12 hospitals (2 academic hospitals, indicated by A1 and A2, and 10 general hospitals, G3 - G12) in the mid-western part of the Netherlands (1.7 million inhabitants). Through the 'Cancer Registry' of the Comprehensive Cancer Center Leiden we identified 1438 patients that were treated between 1990 and 2004.[11;12] Patient and disease characteristics, and information on treatment and outcome were extracted and analyzed from patient records and hospital information systems. In our earlier study, we reported on a few separate outcomes only and thus could not provide a broader assessment on the quality of care that patients experienced. The quality framework we now propose aims at addressing these limitations.

Constructing and testing multidimensional quality assessment

Design and testing of multidimensional quality assessment was done in 3 phases; being a) the choice of relevant quality dimensions and parameters, b) design of two methods of combining different parameters into multidimensional assessment (a cumulative quality profile that provides insight, and a relevance-weighted quality score that supports choice), and c) testing these assessments on the dataset described above, both without and with case-mix adjustment.

In the first phase, we used the four main quality dimensions (safety, effectiveness, efficiency and patient-centeredness) to guide the selection of appropriate quality parameters (from those that were available in our retrospective database).[13] To assess safety, 4 categories of adverse outcomes were selected from the Dutch surgical adverse outcome registry that is

Table 1. Patient, tumor, treatment, outcome and hospital characteristics

	Overall		Academic		General		
Characteristics	No. of patients	%	No. of patients	%	No. of patients	%	P value
Age							
median (yrs)	62.4		62.0		63.3		0.02
range (yrs)	28-89		28-89		32-87		
Gender							
Male	1099	76.4	775	77,9	324	72.9	0.04
Female	340	23.6	220	22.1	120	27.1	
Co-morbidity							
None	636	44.2	450	45,2	186	41.9	0.26
1 organ system	467	32.5	317	31.9	150	33.7	
2 organ systems	202	14.0	141	14.2	61	13.7	
≥ 3 organ systems	91	6.3	71	7.1	20	4.5	
Stage (pTNM)							
I	228	15.8	155	15.6	73	16.4	0.001
II	569	39.6	380	38.2	189	42.7	
III	463	32.2	313	31.4	150	33.6	
IV	179	12.4	147	14.8	32	7.3	
Esophagectomy							<0.001
Transthoracic	304	21.1	178	17.9	126	28.4	
Transhiatal	1101	76.5	787	79.1	314	70.7	
Adverse outcome							
None	509	35.4	400	40.2	109	24.5	<0.001
Grade 1	587	40.8	407	40.9	180	40.5	
Grade 2	172	12.0	97	9.7	75	16.9	
Grade 3	62	4.3	38	3.8	24	5.4	
Grade 4 (mortality)	102	7.1	53	5.3	49	11.0	
Length of stay							
mean (days)	22		20		28		<0.001
range (days)	5-273		5-173		9-273		
Radical resection	1054	73.2	729	73.3	325	73.2	0.98
1-year survival	1003	69.7	700	70.4	303	68.2	0.42
Hospital volume							
Low (<20/y)	566	39.3	122	12.3	444	100	<0.001
High (>20/y)	873	60.7	873	87.7	0	0.0	
Total no. of patients	1439		995		444		

Academic = academic hospitals; general= general hospitals; yrs = years; adverse outcome: Grade 1 = minor complications without re-intervention or permanent damage leading to hospital stay > 14 days; Grade 2 = complications needing re-intervention; Grade 3 = complications with permanent damage; Grade 4 = complications leading to in-hospital mortality

carried by most Dutch hospitals.[14] In decreasing order of severity these adverse outcomes were 'in-hospital death' (grade 4 adverse outcome), 'major complications with permanent/ long term morbidity' (grade 3 adverse outcome), 'major complications requiring re-operation' (grade 2 adverse outcome) and 'minor complications leading to delayed discharge (> 14 days) from hospital' (grade 1 adverse events). To assess effectiveness, 2 treatment goals were chosen, one short-term and one longer term: 'tumor free margins of cancer resection' (R0-resection) and '1-year survival'. No information was available on the dimensions

Table 2. The 6 quality parameters chosen and their correlation

	avoiding adverse outcomes				achieving goals		
	SurvHosp	No long-term AO	No Reop	Hosp <14 days	R0	Surv1YR	
SurvHosp	1.000	-0.047	**-.089***	0.045	0.031	**.433***	pearson corr.
No long-term AO	0.076 (ns)	1.000	**-.078***	**.138***	0.013	-0.033	
No Reop	**0.001**	**0.003**	1.000	**.236***	**-.053***	0.005	
Hosp<14 days	0.088 (ns)	**<0.001**	**<0.001**	1.000	0.019	**.086***	
R0	0.244 (ns)	0.613 (ns)	**0.045**	0.475 (ns)	1.000	**.242***	
Surv1YR	**<0.001**	0.205 (ns)	0.864 (ns)	**0.001**	**<0.001**		
	2-sided chi-square						

SurvHosp = no complications leading to in-hospital mortality (grade IV adverse outcome); No Long-term AO = no complications with permanent damage (grade III adverse outcome) ; No Reop = no complications needing re-intervention (grade II adverse outcome); Hosp<14 days = no minor complications leading to hospital stay > 14 days (Grade I adverse outcome); R0 = microscopically radical resection; Surv1YR = patient alive one year after resection; ns = not significant. For Pearson correlation coefficients (upper right table-half) stars (*) indicate statistical significance (at alpha 0.05). In the lower-left table-half, significance of correlations is quantified by p-value of chi-square test

efficiency and patient-centeredness. For each of these (4 + 2 =) 6 quality parameters, a favorable quality standard was defined, being the absence of adverse outcome for the first four, and achieving the treatment goal for the latter two.

In the second phase we combined the 6 quality parameters into two methods of multidimensional quality assessment. The first method is a cumulative quality profile (CQP) in which each subsequent profile-level indicates whether the quality standards of the present and all preceding levels are met (scored 1) or not (scored 0). Higher levels represent progressively more strict standards for health care quality, their order being determined by their relevance for long term outcome (using Cox regression for survival). The second method is a relevance-weighted quality score (RWQS), being the sum of products of relevance weights and parameter outcomes. Relevance weights represent the extent to which each of the 6 parameters is considered relevant for choosing a high quality hospital. For the present study, these weights were obtained by questionnaire (shown in appendix) from 18 members of the Dutch Association of Surgical Oncologists who have special expertise in (the quality of) esophageal cancer care. At hospital level, the relevance weighted quality score is quantified as the average of scores for all patients.

For both multidimensional assessments (CQP and RWQS) 0 is the lowest score per patient and stands for (total) quality failure, while a score of 1 signifies that all predefined quality standards are met, i.e. that the patient has experienced exemplary care and outcome (ECO). Intermediate quality levels are represented on the quality profile by a score of 1 on lower profile only, and using the relevance weighted quality score by values between 0 and 1.

In the third phase we tested both these multidimensional quality assessment on the database of esophageal cancer patients, and compared them with the single-dimension quality measure of hospital survival. For all hospital comparisons, case-mix correction was applied by logistic regression for the covariates age, gender, co-morbidity and cancer stage to predict patient-specific outcomes for each parameter. For patient level-analysis,

a case-mix corrected O/E-score is the quotient of the observed (0 or 1) and expected (between 0 and 1) patient-outcome. For hospital level-analysis, a case-mix corrected hospital score is the quotient of the observed and expected proportion of patients in whom the desirable outcome is achieved. The hospital ECO-score is the proportion of patients in whom all predefined quality standards are met. Hospital performance was analyzed both per hospital, and for specific categories of hospitals (high versus low volume, and academic versus non-academic), using O/E-scores for survival, ECO and RWQS respectively.

Statistics

Differences in patient, tumor and treatment characteristics and outcome measurements were assessed using Kruskal-Wallis and Mann Whitney U test for continuous variables, and chi-square testing for categorical variables. Spearman rank and two-sided chi-square test were used to test correlations between outcomes. Survival was analyzed using Cox regression for the period between the date of first surgery to either death or the last patient contact, with follow up monitoring being continued until December 31st 2006. Prediction of events was calculated using multivariate logistic regression. All analyses were conducted using SPSS software (version 18.0; SPSS inc., Chicago.IL), using an alpha of 0.05 as the significance-threshold.

RESULTS

Results are reported per phase (parameters, multidimensional assessment, and hospital comparisons. Table 1 provides the characteristics of all patients.
Correlations between patient-outcomes for the 6 quality parameters are shown in table 2. Interestingly, reoperation is not only associated with increased length of stay, but also with R0-resection, hospital survival and the absence of permanent or long term morbidity. 1 Year survival is not only (unsurprisingly) associated with hospital survival, but also with R0 resection and timely discharge. Table 3 shows the proportions and O/E-scores of patients meeting the 6 separate quality standards (i.e. having a favorable outcome on a quality parameter) in each of the 12 hospitals. No hospital scored best on more than 1 case-mix corrected parameter. That quality parameters are not always positively associated is illustrated by hospital G8, that scored best on (both absolute and case-mix corrected) hospital survival (97%, 1.05)

For the first multidimensional assessment, the cumulative quality profile, the order of the various parameters (on the basis of their relevance for long term outcome, by Cox regression) is shown in table 4. The most basic parameter is hospital survival, followed by 1-year survival, R0-resection, no reoperation, timely discharge, and no permanent/long term morbidity respectively. Case-mix corrected hospital ECO-scores varied from 0.24 (G10) to 1.63 (A2) and 1.69 (A1) for the two university hospitals. Figure 1 shows the quality profiles of the 12 hospital profiles graphically, both without (1a) and with (1b) case-mix correction.

Table 3. Hospital performance on each of the 6 separate quality parameters, both uncorrected (expressed as the proportion of patients meeting the quality standard), and with correction for case-mix (expressed as observed/expected ratio for each parameter)

Hospitals		Outcome measures											
		SurvHosp		No Long-term AO		No Reop		Hosp <14 days		R0		Surv1YR	
Id	Volume	%	O/E	%	O/E	%	O/E	%	O/E	%	O/E	%	O/E
A-1	873*	94%	1.02	97%	1.01	91%	1.03	53%	1.16	72%	1.00	69%	1.01
A-2	122	93%	1.01	91%	0.95	85%	0.97	54%*	1.17*	80%	1.04	79%*	1.07
G-3	108	87%	0.94	96%	1.00	79%	0.90	48%	1.03	76%	1.01	76%	1.05
G-4	88	83%	0.90	94%	0.99	82%	0.93	27%	0.61	68%	0.94	56%	0.80
G-5	54	93%	1.01	94%	0.99	78%	0.88	15%	0.32	81%	1.03	70%	0.95
G-6	39	95%	1.02	100%*	1.04	92%	1.05	33%	0.72	67%	0.94	74%	1.08*
G-7	37	95%	1.03	92%	0.96	86%	0.98	3%	0.06	62%	0.86	70%	1.04
G-8	33	97%*	1.05*	94%	0.98	82%	0.93	36%	0.80	61%	0.83	73%	1.04
G-9	28	82%	0.89	100%*	1.05	100%*	1.11*	25%	0.52	75%	0.94	68%	0.91
G-10	25	92%	1.03	76%	0.80	80%	0.90	12%	0.30	84%	1.15	64%	0.98
G-11	21	90%	0.97	100%*	1.04	81%	0.91	19%	0.42	95%*	1.25*	71%	0.97
G-12	10	60%	0.65	100%*	1.05*	90%	1.01	40%	0.94	80%	1.05	50%	0.71

Id = hospital identification G = general hospital; A = academic hospital; SurvHosp = no complications leading to in-hospital mortality (grade IV adverse outcome); No Long-term AO = no complications with permanent damage (grade III adverse outcome) ; No Reop = no complications needing re-intervention (grade II adverse outcome); Hosp <14 days = no minor complications leading to hospital stay > 14 days (Grade 1 adverse outcome); R0 = microscopically radical resection; Surv1YR = patient alive one year after resection; * = highest score for separate measures

Table 4. Hospital performance on the cumulative quality profile, both uncorrected (expressed as the percentage of patients that meets each of the 6 progressively stricter cumulative quality levels), and with correction for case-mix (expressed as observed/expected ratio for each level).

Hospitals		Cumulative standards satisfied (in O/E)											
		SurvHosp		+ Surv1YR		+ R0		+ NoReop		+ No Long-term AO		+ Hosp <14days (= ECO)	
Id	Volume	%	O/E	%	O/E	%	O/E	%	O/E	%	O/E	%	O/E
A-1	873*	94%	1.02	69%	1.08	56%	1.21	51%	1.25	49%	1.25	31%	1.69*
A-2	122	93%	1.01	79%*	1.19*	65%	1.26	56%	1.23	50%	1.14	32%*	1.63
G-3	108	87%	0.94	76%	1.14	59%	1.21	44%	1.00	43%	1.03	27%	1.37
G-4	88	83%	0.90	56%	0.90	45%	0.97	33%	0.76	31%	0.75	10%	0.60
G-5	54	93%	1.01	70%	1.04	59%	1.12	43%	0.94	37%	0.82	9%	0.39
G-6	39	95%	1.02	74%	1.17	54%	1.18	51%	1.18	51%	1.23	21%	1.11
G-7	37	95%	1.03	70%	1.12	49%	1.09	41%	1.04	41%	1.09	3%	0.10
G-8	33	97%*	1.05*	73%	1.12	52%	0.96	39%	0.78	33%	0.70	12%	0.49
G-9	28	82%	0.89	68%	0.96	54%	0.88	54%	0.98	54%	1.03	4%	0.14
G-10	25	92%	1.02	64%	1.08	56%	1.26	44%	1.16	28%	0.80	4%	0.24
G-11	21	90%	0.96	71%	1.06	71%*	1.43*	62%*	1.37*	62%*	1.43*	14%	0.74
G-12	10	60%	0.66	50%	0.75	50%	0.96	40%	0.85	40%	0.90	10%	0.56

O/E = observed / expected ratio; Id = hospital identification G = general hospital; A = academic hospital; SurvHosp = no complications leading to in-hospital mortality (grade IV adverse outcome); No Long-term AO = no complications with permanent damage (grade III adverse outcome) ; No Reop = no complications needing re-intervention (grade II adverse outcome); Hosp <14 days = no minor complications leading to hospital stay > 14 days (Grade 1 adverse outcome); R0 = microscopically radical resection; Surv1YR = patient alive one year after resection; * = highest score for separate measures without and with casemix correction.

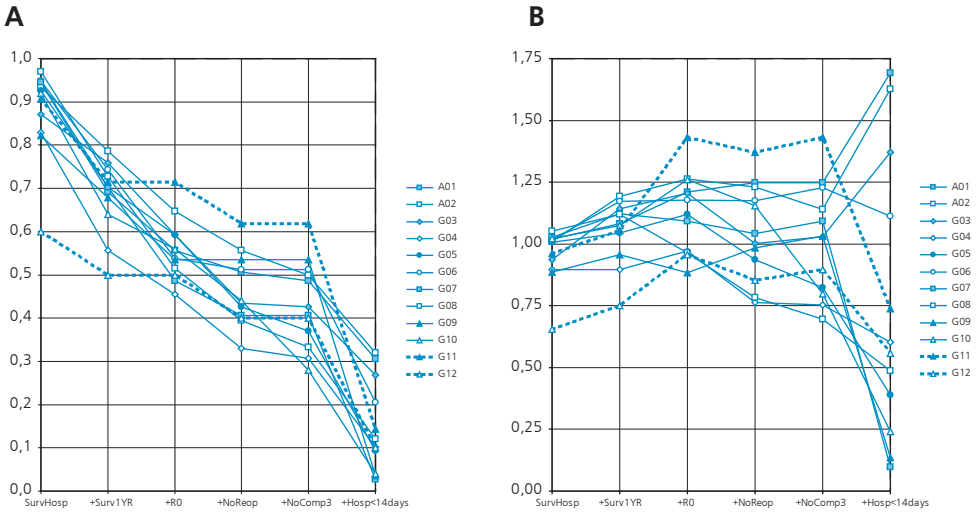

Figure 1. Cumulative outcome profile for 12 hospitals performing esophagectomy for cancer: **A.** shows the percentage of patients meeting the present and all preceding quality standards. **B.** shows the observed/expected percentage, based on gender, age, cancer stage and number of co-morbidities. G = general hospital; A = academic hospital; SurvHosp = no in-hospital mortality; Surv1YR = 1 year survival; R0 = microscopically radical resection;NoGrade2 = no complications needing re-intervention; NoGrade3= no complications with permanent damage; NoGrade1= no minor complications leading to hospital stay > 14 days.

For the second assessment, the multidimensional weighted quality score, we used relevance weights that were obtained from the 18 surgeons-experts, and that are shown in table 5. Hospital quality scores are shown in table 6, varying from 0.88 for G12 to 1.03 for G11.

Correlations between case-mix corrected hospital quality scores on single dimension hospital survival, and on multidimensional ECO-score and RWQS were compared, and yielded modest to low correlations, varying from 0.022 (Pearson correlation between hospital scores on O/E-survival and O/E-ECO), to 0.526 (for O/E-hospital survival and O/E-RWQS) and 0.276 (for O/E-ECO and O/E-RWQS). This is not surprising, as these scores deal with failure (mortality/survival), perfection (ECO) and the whole quality range (RWQS) respectively.

Table 5. Results of assessment of relevance for quality of care by 18 surgeon-experts.

Outcome	SurvHosp	R0	No Long-term AO	Surv1YR	No Reop	Hosp <14days
parameter						
Mean	26.7	24.8	19.2	14.7	11.5	3.2
Stdev	7.9	8.4	5.2	8.9	7.9	2.9
Max	45	45	30	35	25	5
Min	10	10	10	0	0	0

SurvHosp = no complications leading to in-hospital mortality (grade IV adverse outcome); No Long-term AO = no complications with permanent damage (grade III adverse outcome) ; No Reop = no complications needing re-intervention (grade II adverse outcome); Hosp <14 days = no minor complications leading to hospital stay > 14 days (Grade 1 adverse outcome); R0 = microscopically radical resection; Surv1YR = patient alive one year after resection; stdev = standard deviation; max = maximum; min = minimum

Table 6. Hospital performance on the relevance-weighted quality score, both uncorrected (expressed as hospital averages for absolute quality scores), and with correction for case-mix (expressed as averages of observed/expected ratios for quality).

Hospitals		Outcome measures													
Relevance weights		26.7		24.8		19.2		14.7		11.5		3.2		100	
Id	Volume	SurvHosp		R0		No Long-term AO		Surv1YR		No Reop		Hosp <14days		Weighted total	
		O	O/E	O	O/E	O	O/E	O	O/E	O	O/E	O	O/E	O	O/E
A-1	873*	94%	1.02	72%	1.00	97%	1.01	69%	1.01	91%	1.03	53%	1.16	84%	1.02
A-2	122	93%	1.01	80%	1.04	91%	0.95	79%*	1.07	85%	0.97	54%*	1.17*	85%	1.01
G-3	108	87%	0.94	76%	1.01	96%	1.00	76%	1.05	79%	0.90	48%	1.03	82%	0.98
G-4	88	83%	0.90	68%	0.94	94%	0.99	56%	0.80	82%	0.93	27%	0.61	76%	0.91
G-5	54	93%	1.01	81%	1.03	94%	0.99	70%	0.95	78%	0.88	15%	0.32	83%	0.97
G-6	39	95%	1.02	67%	0.94	100%*	1.04	74%	1.08*	92%	1.05	33%	0.72	84%	1.01
G-7	37	95%	1.03	62%	0.86	92%	0.96	70%	1.04	86%	0.98	3%	0.06	79%	0.96
G-8	33	97%*	1.05*	61%	0.83	94%	0.98	73%	1.04	82%	0.93	36%	0.80	80%	0.97
G-9	28	82%	0.89	75%	0.94	100%*	1.05	68%	0.91	100%*	1.11*	25%	0.52	82%	0.96
G-10	25	92%	1.03	84%	1.15	76%	0.80	64%	0.98	80%	0.90	12%	0.30	79%	0.97
G-11	21	90%	0.97	95%*	1.25*	100%*	1.04	71%	0.97	81%	0.91	19%	0.42	87%*	1.03*
G-12	10	60%	0.65	80%	1.05	100%*	1.05*	50%	0.71	90%	1.01	40%	0.94	74%	0.88

Id = hospital identification G = general hospital; A = academic hospital; SurvHosp = no complications leading to in-hospital mortality (grade IV adverse outcome);No Long-term AO = no complications with permanent damage (grade III adverse outcome) ; No Reop = no complications needing re-intervention (grade II adverse outcome; Hosp <14 days = no minor complications leading to hospital stay > 14 days (Grade 1 adverse outcome); R0 = microscopically radical resection; Surv1YR = patient alive one year after resection; * = highest score for separate measures without and with casemix correction;

Table 7. Comparisons of different categories of hospitals (high versus low volume, academic versus non-academic) by single dimension patient O/E-scores for hospital survival, and by multidimensional patient O/E-scores for ECO and RWQS

Hospital categories	n (patients)	HospSurv		ECO		RWQS	
		average	stdev	average	stdev	average	stdev
High volume	873	1.020	0.255	1.692	2.970	1.021	0.247
Low Volume	565	0.968	0.335	0.911	2.131	0.970	0.242
p (Mann Whitney U)		0.114		< 0.001*		< 0.001*	
Academic	995	1.019	0.257	0.168	2.928	1.021	0.243
Non-academic	443	0.957	0.350	0.713	1.933	0.956	0.248
p (Mann Whitney U)		0.095		< 0.001*		< 0.001*	

Comparison of the quality provided to patients treated in different categories of hospitals (high versus low volume, academic versus non-academic) is shown in table 7, and shows that O/E-hospital survival scores did not differ (p=0.114 for high vs. low volume, and p=0.085 for academic vs. non-academic by Mann Whitney U-test), while O/E-ECO and O/E-RWQS did, highly significantly (p<0.001).

DISCUSSION

Our study addresses the fact that quality of care should be measured by more than one outcome only, and illustrates this point by introducing multidimensional assessment for the quality of esophageal cancer surgery. We introduce 6 quality parameters, including the traditional measure of hospital mortality, and combine these parameters into a cumulative quality profile and a relevance-weighted quality score. Both the finding that the separate quality parameters may be negatively correlated (table 2) and that no hospital scored best on all parameters, supports the relevance of such a multidimensional approach.

For both frameworks we introduce the concept of ECO, exemplary care and outcome. Per patient, this signifies the provision of care that meets all of the predefined quality standards, while at hospital level, the ECO score is the proportion of patients treated with ECO-quality. We tested the feasibility of multidimensional quality assessment on the performance of 12 hospitals providing esophageal cancer surgery to patients treated in the west of the Netherlands between 1991 and 2004. Although no hospital performed best on more than 1 parameter, overall scores of the two university hospitals (A1 and A2) and one low-volume hospital (G11) tended to have higher scores in many assessments. Finally, we clustered hospitals in categories expected to provide different levels of esophageal cancer care (high versus low volume hospitals, and academic versus non-academic) and assessed quality between these categories. The results are shown in table 7, and demonstrate that differences in case-mix corrected O/E-ECO and O/E-RWQS between hospital categories are highly significant, whereas O/E-hospital survival does not differ significantly. This demonstrates that both multidimensional methods can provide a broader assessment of quality (suggesting better construct validity) but could also be more sensitive to differences in the quality of care provided (i.e. better criterion validity)

In recent years, a plethora of articles describing variation in outcome between different institutions has been published. Most studies are population-based and assess differences in outcome between large groups of hospitals, without evaluating quality of care on the level of individual institutions. Adopting Donabedian's paradigm of structure, process and outcome, Birkmeyer et al. mentioned the relative merits of different approaches to measuring the quality of surgical care.[3] More recently, Porter made a strong case for multidimensional outcome measurement, and for taking the point of view of the care-seeker, not the care-provider.

However, comparison of health outcomes between hospitals is not without its problems, the most obvious problems being data-quality and case-mix correction[11]. In addition, for rare outcomes, there is 'the problem of small sample size'. Dimick et al. investigated the minimum hospital caseloads necessary to detect a doubling of the mortality rate for different procedures, and found that an annual volume of 77 esophageal resections is necessary to detect significant mortality differences.[15] He concluded that most operations are not performed frequently enough to use surgical mortality as an indicator of hospital quality.

Multidimensional quality assessment aims at better construct validity (by taking a greater proportion of relevant quality aspects into account) and (hopefully) at better criterion validity (being better able to discriminate between hospitals with better and lower overall quality). However, it also adds a new challenge to existing ones; the question of how to combine different quality parameters. O'Brien, analyzing quality measurement of adult cardiac surgery on behalf of the Quality Measurement Task Force of the Society of Thoracic Surgeons, tested four methods of composite scoring (1 – an opportunity-based approach, 2 - [weighted or un-weighted] averaging of item-specific estimates, 3 - all or none scoring, and 4 - latent trait analysis), and concluded that none is without flaws or limitations.[16]
In the present study, we use two ways of composite scoring. One, the relevance-weighted quality score, is a specific example of O'Brien's second method. The parameters weights we used were obtained from 16 oncological surgeons-experts. They were asked to image that they were esophageal cancer patients choosing the most appropriate hospital, or that they were asked for such advice by a family member. Their relevance weights would thus represent both their professional insight, and their "as-if"-patient perspective.
The other way, the cumulative quality profile, is new and combines advantages of transparency and integration. In another study from our institution, we found that such a summary measure is very well received by patients.[17]

Our study has several limitations. The first was mentioned in the introduction and is hampering quality assessment in general: the absence of a 'golden standard' for quality of care. We selected six parameters available in our database and gave them weights representing the extent to which each of the 6 parameters is considered relevant for choosing a high quality hospital. We used substitutes for patient preferences, obtained from surgeons-experts by an "as-if" questionnaire. However interesting and valid their stated preferences may be, they are no substitute for real patients' preferences. The models presented in this study are therefore no more than a 'proof of principle', and the appropriateness of relative importance, either by sequence or by weights, requires more in-depth study in real patients.
The second limitation is the low number of institutions evaluated and there is the obvious problem of low patient numbers per institution and the ensuing lack of statistical power for rare outcomes. The fact that the Dutch Health Care Inspectorate has recently banned esophageal surgery in low volume hospitals, will provide part of the solution to this problem.[4] Another part of the solution may be our finding that multidimensional measures of quality may be more sensitive to quality differences, than single dimensional outcomes that rarely occur. In addition, following examples in our neighboring countries, nation-wide clinical audits for oncological and other care have recently been started in the Netherlands (www.clinicalaudit.nl).[18] In 2011, the Dutch Upper Gastro-intestinal Cancer Audit has been initiated in which all patients in who an esophageal or gastric resection for cancer has been performed are registered. The results of the present study suggest that multidimensional quality assessment may be a valid tool to analyze differences in quality of care in these clinical audits. It may provide broader and more relevant information on quality to patients,

doctors and society, but also may have better power to identify those hospitals that provide care of appropriate quality. The data from these much larger and detailed clinical databases may give us, or other researchers, the opportunity to refine and validate multi-dimensional frameworks for the assessment of quality of care, like the Exemplary Care and Outcome (ECO) concept presented in this study.

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APPENDIX

Evaluation of quality of care for esophageal resections for cancer: a survey *(this survey is translated from the original Dutch version)*

Publications regarding the inverse relationship between hospital volume and postoperative mortality have initiated an extensive debate on the quality of care for patients undergoing esophagectomy for cancer. However, in-hospital mortality is not the only factor that's important in the evaluation of quality of care for this patient group. Preferably, a more extensive set of measures would be used for the assessment of quality of care in individual institutions. Though, the data needed for this quality assessment are not always available and are usually limited to data regarding the outcome after surgery, like postoperative complications, re-operations, radicality of the resection and survival. In addition, it's not always clear how these quality aspects have to be weighed. Through this survey we would like to investigate how medical specialists treating patients with esophageal cancer value different outcomes of esophageal cancer surgery, their selves.

"Suppose that you, or a member of your family should be treated for esophageal cancer and you had to make a choice from a number of hospitals. From every hospital only a limited set of data regarding 6 quality aspects is available, collected by an independent authority. The differences in 'case-mix' of these hospitals do not have to be taken into consideration. The 6 quality aspects are:

	Quality aspect	Definition
1	In-hospital mortality	The percentage of patients that dies postoperatively during the same hospital admission.
2	Complications	The percentage of patients that has complications with permanent damage concerning functional loss or handicaps (for example: hoarseness, dysphagia, dependence on feeding tubes after failure of gastric tube reconstruction, cardiac failure after myocardial infarction)
3	Re-operations	The percentage of patients in who one or more re-operations have been performed due to complications after esophagectomy.
4	Length of stay	Percentage of patients with a length of stay longer than 2 weeks.
5	Radicality	Percentage of patients with a radical resection (R0).
6	1-year survival	Percentage of patients alive 1 year after the operation

"If there was a hospital that scores perfect on every quality aspect, you would obviously choose for that hospital. Unfortunately, there's no perfect hospital and hospitals score better or worse on different quality aspects. Therefore it's necessary to make a choice based on a combination of different quality aspects. Would you be so kind to answer the 2 questions best as you can:

Question 1

Please select which quality aspect is most important for you, and which aspects gradually would be less important.

Quality aspect	Ranking*
- In-hospital mortality	
- Complications	
- Re-operations	
- Length of stay	
- Radicality	
- 1-year survival	

* give ranking from "1" = most important to "6" = least important.

Question 2

You get 100 weight points. Can you divide these between the 6 quality aspects in such a way that the number of points represents the weight that you assign to the different aspects.

Quality aspect	Points*
- In-hospital mortality	
- Complications	
- Re-operations	
- Length of stay	
- Radicality	
- 1-year survival	
Total	100

* divide 100 points between 6 quality aspects

Examples

- Answers in the two examples beneath are intentionally chosen at random -

Answer 1

Quality aspect	Ranking*
- In-hospital mortality	4
- Complications	6
- Re-operations	2
- Length of stay	1
- Radicality	5
- 1-year survival	3

* Rank from "1" = most important to "6" = least important.

Answer 2

Quality aspect	Points*
- In-hospital mortality	8
- Complications	7
- Re-operations	20
- Length of stay	30
- Radicality	10
- 1-year survival	25
Total	100

* divide 100 points between 6 quality aspects

Chapter 9

Variation in treatment and outcome in patients with Non-small cell lung cancer by region, hospital type and volume in the Netherlands

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ABSTRACT

Background:
Care processes for patients with NSCLC can vary by provider, which may lead to unwanted variation in outcomes. Therefore, in modern health care an increased focus on guideline development and implementation is seen. It is expected that more guideline adherence leads to a higher number of patients receiving optimal treatment for their cancer which could improve overall survival. The aim of this study was to evaluate variations in treatment patterns and outcomes of patients with NSCLC treated in different (types of) hospitals and regions in the Netherlands. Especially, variation in the percentage of patients receiving the optimal treatment for the stage of their disease, according to the Dutch national guideline of 2004, was analyzed.

Methods:
All patients with a histological confirmed primary NSCLC diagnosed in the period 2001-2006 in all Dutch hospitals (N=97) were selected from the population-based Netherlands Cancer Registry. Hospitals were divided in groups based on their region (N=9), annual volume of NSCLC patients, teaching status and presence of radiotherapy facilities. Stage-specific differences in optimal treatment rates between (groups of) hospitals and regions were evaluated.

Results:
In the study period 43,544 patients were diagnosed with NSCLC. The resection rates for stage I / II NSCLC patients increased during the study period, but resection rates varied by region and were higher in teaching hospitals for thoracic/lung surgeons (OR 1.5; 95%CI 1.2 - 1.9, p=0.001) and in hospitals with a diagnostic volume of more than 50/year (OR 1.3; 95%CI 1.1 – 1.5, p=0.001). Also the use of chemoradiation in stage III patients increased, though marked differences between hospitals in the use of chemoradiation for stage III patients were revealed. Differences in optimal treatment rates between hospitals led to differences in survival.

Conclusion:
Treatment patterns and outcome of NSCLC patients in the Netherlands varied by region and the hospital their cancer was diagnosed in. Though resection rates were higher in hospitals training thoracic/lung surgeons, variation between individual hospitals was much more distinct. Hospital characteristics like a high diagnostic volume, teaching status or availability of radiotherapy facilities proved no guarantee for optimal treatment rates.

INTRODUCTION

In literature a plethora of studies describes hospital volume as an important predictor of surgical outcomes. Most of these studies evaluate the inverse relationship between volume and adverse surgical outcomes, like postoperative complications and mortality[1]. Only few authors address the mechanisms which lead to these differences. Intermediate outcomes, like the percentage of patients receiving potentially curative treatment for their cancer, could explain differences in survival. Moreover, other hospital characteristics reflecting the setting in which care is delivered to cancer patients, could be equally important predictors of outcome as hospital volume.

The variation of care processes by caregiver is widely recognized and can sometimes lead to unwanted variation in patients outcomes. Therefore, in modern health care an increased focus on guideline development and implementation is seen. It is expected that more guideline adherence leads to a higher number of patients receiving optimal treatment for their cancer which could improve overall survival. Moreover, evaluating differences in guideline adherence between hospitals can reveal the reasons behind the differences in outcome and can identify best practices with better outcomes.

Differences in guideline adherence have been described for patients with Non small cell lung cancer (NSCLC) in several countries[2-5]. In the Netherlands, lung cancer is the second common tumor in men and the third in women, with an incidence of 71 and 31 per 100,000 person years in 2007, respectively (European Standardized Rate)[6]. In 2007, 10,533 patients were diagnosed with lung cancer and in eighty percent it concerned NSCLC. Only 14% of patients diagnosed with NSCLC in the Netherlands survive 5 years. Unfortunately, these survival figures have not improved in the last decades[6]. While the incidence of NSCLC in men is decreasing since the early eighties, it has been rising in women until 1999. Fortunately, recent reports predict the end of this lung cancer epidemic in women, meaning an overall decrease in lung cancer patients in the near future[7].

In 2004 the first Dutch National Guideline on NSCLC was introduced (www.oncoline.nl). The main reasons for development of this evidence-based guideline were the introduction of PET-scanning in staging NSCLC, induction chemotherapy in locally advanced NSCLC, and concurrent chemoradiation in stage III NSCLC. According to this guideline surgical resection is the preferred treatment in patients with stage I or II NSCLC, who are fit to undergo surgery. Under the guidelines valid in our study period, surgery is also the treatment of choice in patients with limited stage III disease (T1-3N1). Patients with more advanced stage III NSCLC (cT4 and/or cN2 or cN3) should be treated with a combination of radiation therapy and chemotherapy (chemoradiation), if their performance score is sufficient (WHO-score 0-1). Chemoradiation is given in a concurrent regimen or sequentially. In general, stage III patients with malignant pleural effusions or tumor volumes too extensive for radiation treatment are no candidates for this combined modality therapy and are treated like stage IV patients with a platinum based chemotherapy regimen and / or best supportive care.

The aim of this study was to evaluate variations in treatment patterns and outcomes of patients with NSCLC treated in different (types of) hospitals and regions in the Netherlands. Especially, variation in the percentage of patients receiving optimal treatment for the stage of their disease, according to the Dutch national guidelines, was analyzed.

METHODS

Netherlands Cancer Registry

In the Netherlands, all newly diagnosed malignancies are registered in the nationwide population-based Netherlands Cancer Registry (NCR). The automated pathological archive (PALGA) and the Hematology Departments are the main sources of notification. The National Registry of Hospital Discharge Diagnosis is an additional source, which accounts for up to 8% of new cases.[8] Data are collected from the medical records by specially trained registrars and are coded according to a national manual. Information on patient characteristics, tumor characteristics, treatment, hospital of diagnosis, hospital of treatment and follow-up is recorded. For coding tumor site and morphology the International Classification of Diseases for Oncology (ICD-O) is used.[9] Cancers are staged according the TNM classification.[10] Quality of the data is high[11] and completeness is estimated to be at least 95%.[12]

Patients

All patients with a histological confirmed primary NSCLC diagnosed in the period 2001-2006 were selected from the NCR. Excluded from analysis were clinical diagnosis (no pathology), autopsy findings, sarcomas, lymphomas, neuro-endocrine and carcinoid tumors. Moreover, patients living abroad and cases with an incomplete registration status in the NCR (<1%) were excluded from analyses. Stage grouping was done according to TNM classification, 6th edition.

Hospitals and regions

Patients treated in all 97 hospitals in the Netherlands were included in this analysis. Hospitals were divided in groups based on their teaching status, availability of radiotherapy facilities, annual amount of NSCLC diagnoses (hospital volume) and their region. For the analyses concerning treatment, type of hospital was based on the hospital where the tumor was diagnosed reasoning that referral of patients is good care as well. For the analyses on postoperative mortality and survival, type of hospital was based on the hospital where the resection was performed.

Hospitals were categorized in three groups: non-teaching, teaching and academic. A teaching hospital was defined as a hospital which provides medical training to residents. A distinction was made between a teaching hospital for chest physicians and thoracic/lung surgeons. In the group of teaching hospitals for thoracic/lung surgeons all academic hospitals were included in the teaching hospital group. Academic hospitals are teaching

hospitals affiliated with a university. The one specialized oncology center in the Netherlands was also classified as an academic hospital as well.
Radiotherapy is an essential part of the treatment of patients with stage III NSCLC. In the Netherlands there are 24 hospitals with radiotherapy facilities and 73 hospitals without a radiotherapy department. These hospitals are affiliated with a radiotherapy department on a different location. All radiotherapy departments treat patients with NSCLC. Hospitals were categorized as having radiotherapy facilities in the same location or not.
Hospital volume stands for the mean number of NSCLC diagnoses per year or for the mean number of lung resections per year. Hospital volume was categorized in 3 groups: less than 50, 50-100 and more than 100 diagnoses per year. In the period 2005-2006, 88% of the patients were operated in the hospital were the tumor was diagnosed.

In addition, hospitals were categorized according to their Comprehensive Cancer Center region (9 groups). These Comprehensive Cancer Centers (CCCs) are non-hospital organizations that facilitate provision of consultancy services, implementation of national guidelines, coordinate organization of cancer care, palliative care and host the cancer registry. Each CCC serves a region that includes five to twenty hospitals. Hospitals are affiliated to one CCC.

Stage grouping

Since clinical stage determines treatment policies for NSCLC, the cTNM was used in the analysis concerning the treatment policies. For the analysis concerning the outcome after resection the pathological stage (pTNM) was applied. During the study period PET-scanning was introduced gradually as an addition to traditional clinical staging in NSCLC patients. Effectiveness and stage migration effects of PET-scanning were reported in a Dutch randomized study [13]. A report on cost-effectiveness and availability of PET-scanning showed an unequal distribution across the Netherlands in 2005-06 of mobile units aimed especially for staging of localized lung cancer [14].

Treatment

Treatment was categorized by resection (pneumonectomy, lobectomy or segmentectomy), radiation therapy, chemotherapy or combined modality treatment (chemoradiation). Chemoradiation was defined as radiation therapy combined with chemotherapy given concurrent or sequentially. Treatment was described as percentages per clinical stage and age group (<75 years and ≥75 years).
The optimal treatment ratio was defined as the percentage of patients receiving optimal treatment by stage of the disease according to the Dutch guideline of 2004 [15]: resection for stage I and II patients, chemoradiation (possibly followed by resection) for stage III patients and chemotherapy for stage IV patients. Resection ratios of stage IIIa patients, usually part of combined modality therapy was investigated separately.

Statistical analyses

Logistic regression analysis was performed to examine the influence of age at diagnosis (<60, 60-74, 75+), gender, tumor size and invasion (cT), type of hospital of diagnosis (academic, teaching, general), radiotherapy facilities (same versus different location), hospital volume (<50, 50-100, >100), CCC-region and year of diagnosis on the odds of receiving optimal treatment per stage as described above.
Performance of the individual hospitals for these optimal treatment rates was exhibited in funnel plots using 95% control limits calculated around the mean.[16] Each hospital was displayed as a scatter point presenting the rates of optimal treatment, i.e. resection for patients with stage I and II disease (adjusted for age, gender and tumor size) and chemoradiation for those with stage III disease (adjusted for age, gender, tumor size and nodal involvement).

Furthermore, logistic regression analysis was used to investigate the influence of age at diagnosis (<60, 60-74, 75+), gender, tumor size and invasion (cT), type of hospital of surgery (academic, teaching, general), hospital volume of resections (<10, 10-19, 20-29 and ≥30/year) and CCC-region on the odds of postoperative mortality, defined as death within 30 days after resection. Patients with stage IV disease were excluded from this analysis. Postoperative mortality was determined for patients diagnosed in 2005 and 2006 only.
Follow-up was calculated as the time from diagnosis to death or to 1st January 2008. Cox proportional hazard modeling was used to investigate the relation between resection and survival in patients with stage I and II disease, adjusted for age at diagnosis, gender, T-stage and year of diagnosis. Furthermore, this analysis was used to determine the relation between the resection rate of hospitals and overall survival. The hospitals were split into 3 groups based on their resection rate in the funnel plot: higher than the 95% control limit, within the 95% control limits or below the 95% control limit.
STATA (version 10.0) was used and a p-value of 0.05 was considered as being significant.

RESULTS

In the period 2001-2006, 43,544 patients (69% male) were diagnosed with primary NSCLC (table 1) . During the study period the annual number of new NSCLC diagnoses increased from 6,774 patients in 2001 to 7,853 in 2006 (16%). The rise in incidence was much higher in women than in men, 45 and 5% respectively and occurred largely at middle age, contrasting the situation in males. Twenty-five percent of NSCLC patients were older than 75 years at the time of diagnosis. During the study period there has been a minor shift from clinical stage I and II disease to the more advanced stages, especially stage IV (Figure 1a). Table 2 shows the distribution of patients between the different types of hospitals and their CCC region. The majority of the patients with NSCLC were diagnosed in general hospitals without training status for chest physicians (68%) or thoracic surgeons (84%). Only 18% of

Table 1. Patient and tumor characteristics of patients diagnosed with Non Small Cell Lung Cancer in the Netherlands 2001-2006

	N	%
Total		
Patients	43 544	100%
Age (years)		
< 60	11 357	26%
60-74	21 403	49%
≥ 75	10 784	25%
Gender		
Male	30 172	69%
Female	13 372	31%
Year of diagnosis		
2001	6 774	16%
2002	6 954	16%
2003	7 108	16%
2004	7 395	17%
2005	7 460	17%
2006	7 853	18%
Histology		
Adenocarcinoma	14 454	33%
Squamous cell carcinoma	14 310	33%
Large cell carcinoma	14 332	33%
Other histology	448	1%
Clinical stage		
In situ	78	0%
Stage I	9 544	22%
Stage II	1 930	4%
Stage III	13 715	32%
Stage IV	17 231	40%
Unknown	1 046	2%
Pathological stage (in case of surgery)		
In situ	13	0%
Stage I	5 681	13%
Stage II	2 002	5%
Stage III	1 749	4%
Stage IV	389	1%
Unknown	56	0%

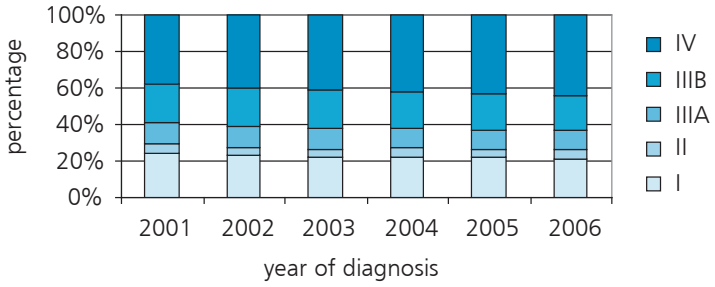

Figure 1a. Stage migration in patients diagnosed with Non Small Cell Lung Cancer during the study period 2001-2006

Table 2. Number of Non Small Cell Lung Cancer patients per hospital volume category, teaching status, radiotherapy facility and region 2001-2006.

	N	%
Total		
Patients	43 544	100%
Hospital volume		
<50 (23 hospitals)	3 910	9%
50-100 (44 hospitals)	16 209	37%
>100 (32 hospitals)	23 425	54%
Teaching status (chest physician)		
Non-teaching hospital	29 582	68%
Teaching hospital	9 889	23%
Academic hospital	4 019	9%
Teaching status (lung- / thoracic surgery) physician)		
Non-teaching hospital	36 622	84%
Teaching hospital (incl. academic hospitals)	6 922	16%
Radiotherapy facilities		
No	35 538	82%
Yes	8 006	18%
Regions		
I	5 888	13%
II	3 732	9%
III	3 172	7%
IV	7 868	18%
V	4 245	10%
VI	6 271	14%
VII	6 411	15%
VIII	2 908	7%
IX	3 049	7%

Hospital characteristics in this table are based on the hospital where the patient is diagnosed with NSCLC.

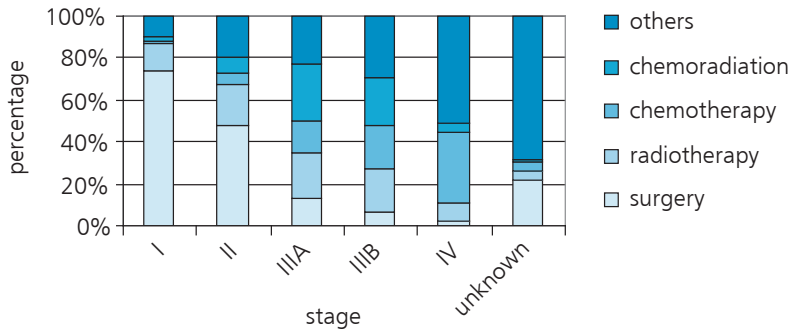

Figure 1b. Treatment characteristics according to stage of Non Small Cell Lung Cancer Patients (all age groups).

the patients were diagnosed in a center with radiotherapy facilities and 9% in an academic center. About 54% of the patients were diagnosed in 32 hospitals with an annual diagnostic volume of more than 100 cases with NSCLC.

Treatment

Primary surgery i.c. resection of the tumor through pneumonectomy, lobectomy or segmentectomy, was performed in 23% of all NSCLC patients, being 60% for patients with clinical stage I or II (Figure 1b). The others received radiotherapy, either with or without chemotherapy. A substantial number of patients received no oncological therapy at all, being 25% in stage I and II patients older than 75 years. In only 43% of these elderly the tumor was resected. This percentage increased only slightly during the study period. In the younger patient group (<75 years), a resection was performed in 79% of the patients.

Stage I and II

Logistic regression confirmed this role of age in the chance of a resection; in stage I and II patients older than 75 years the OR of a resection is 0.09 (95%CI 0.08 – 0.11, p=0.000). Also, the size of the tumor, expressed in T stage, was important. Nevertheless, the chance of resection did not only depend on patient- and tumor-characteristics. Patients with clinical stage I or II disease more often had a resection of their tumor in hospitals with a teaching status for thoracic surgeons (OR 1.5; 95%CI 1.2 - 1.9, p=0.001) and in hospitals with a diagnostic volume of more than 50 NSCLC patients a year (OR 1.3; 95%CI 1.1 – 1.5, p=0.001). Marked differences in resection rates appeared between groups of hospitals and regionally. The chance of a resection for stage I or II NSCLC ranged from an OR of 2.0 in one region (95%CI; 1.6 – 2.4, p=0.000) to 0.77 in another (95%CI 0.63 – 0.91; p=0.004).

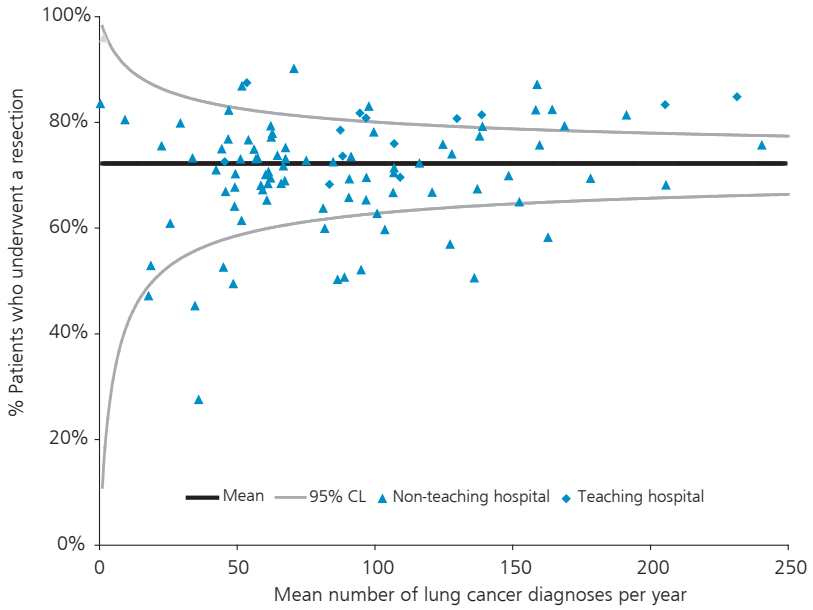

Figure 2. Percentage of stage I or II NSCLC patients in who a resection is performed for non-teaching and teaching hospitals (adjusted for differences in age, gender and T-stage).

Figure 2 shows differences in resection rates between *individual* hospitals from 75 to 93% for hospitals with accredited training of thoracic surgeons and from 54 to 97% for hospitals without training facilities.

Table 3. Multivariate analysis for the odds of resection for stage I and II NSCLC in the Netherlands during 2001-2006

	OR	95% CI	p-value
Age (years)			
< 60	ref		
60-74	0.40	0.35-0.46	< 0.001
≥ 75	0.09	0.08-0.11	< 0.001
Gender			
Male	ref		
Female	1.00	0.90-1.12	0.896
Year of diagnosis			
2001	ref		
2002	1.2	1.01-1.39	0.030
2003	1.53	1.31-1.78	< 0.001
2004	1.53	1.32-1.78	< 0.001
2005	2.04	1.75-2.37	< 0.001
2006	1.99	1.71-2.31	< 0.001
T-stage			
T 1	ref		
T 2	0.48	0.43-0.54	< 0.001
T 3	0.21	0.18-0.25	< 0.001
Hospital volume			
<50	ref		
50-100	1.40	1.17-1.68	< 0.001
>100	1.69	1.40-2.04	< 0.001
Teaching status (chest physician)			
Non-teaching hospitals	ref		
Teaching hospitals	0.91	0.80-1.05	0.212
Academic hospitals	1.02	0.74-1.42	0.741
Teaching status (lung- / thoracic surgery)			
Non-teaching hospitals	ref		
Teaching hospitals (incl. academic hospitals)	1.58	1.28-1.94	<0.001
Radiotherapy facilities			
No	ref		
Yes	0.92	0.77-1.05	0.304
Region			
I	0.94	0.82-1.12	0.452
II	1.52	1.23-1.76	< 0.001
III	0.82	0.69-1.01	0.045
IV	ref		
V	0.95	0.81-1.14	0.634
VI	0.97	0.85-1.17	0.729
VII	1.08	0.92-1.25	0.324
VIII	1.46	1.24-1.82	< 0.001
IX	1.02	0.83-1.23	0.794

Hospital characteristics based on hospital of diagnosis.

The postoperative mortality rates after a resection for NSCLC were based on data from 2005 and 2006. Within 30 days after the resection 111 of 3206 patients died (3.3%), being 7.5% for patients older than 75 years. Tumor size (pT) and operative procedure also proved important factors. Patients operated in the 63 hospitals with less than 20 resections a year exhibited a similar postoperative mortality rate as in a higher volume hospital with 20 or more NSCLC resections annually (34 hospitals). Patients with stage I or II NSCLC operated in the academic centers had a significantly lower postoperative mortality (1.3%, p=0.012). Logistic regression showed that this reduced risk of dying postoperatively in academic centers is only borderline significant (OR 0.25; 95%CI 0.06 – 0.93, p=0.038).

Stage III

During the study period 13,744 patients were diagnosed with stage III NSCLC, 4,938 stage IIIa and 8,806 stage IIIb patients. In the whole group of stage III patients 24% received combined modality treatment (figure 1b), 30% of the younger patients (<75 years, n=10,069) and 9% of the older patients (>75 years, n=3,675). The percentage of patients receiving chemoradiation went from 18% in 2001 to 29% in 2006 (p<0.001). Higher age and advanced tumor size were the most important factors to abandon chemoradiation (Table 4).The odds of receiving chemoradiation were lower when a patient was diagnosed in an academic center. Chemoradiation rates were not higher in high volume hospitals (>100 diagnoses a year) or in hospitals with radiotherapy facilities, except for hospitals training thoracic or lung

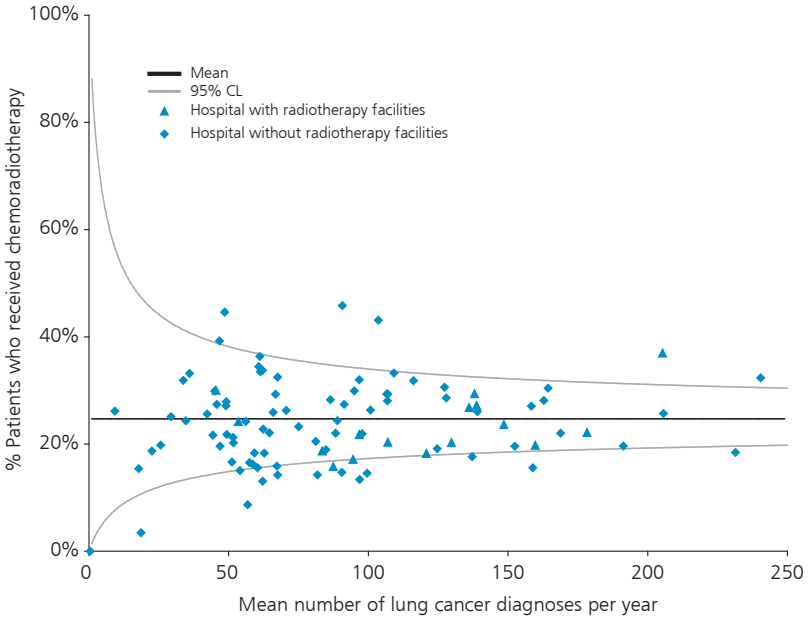

Figure 3. Percentage of stage III patients who received chemoradiation according to mean number of lung cancer diagnoses per year.

Table 4. Multivariate analysis for the odds of receiving combined modality therapy for stage III NSCLC

	OR	95% CI	p-value
Age (years)			
< 60	ref		
60-74	0.63	0.58-0.70	< 0.001
≥ 75	0.16	0.14-0.18	< 0.001
Gender			
Male	ref		
Female	0.92	0.84-1.02	0.101
Year of diagnosis			
2001	ref		
2002	1.21	1.03-1.42	0.019
2003	1.53	1.31-1.79	< 0.001
2004	1.54	1.32-1.79	< 0.001
2005	2.03	1.74-2.36	< 0.001
2006	1.99	1.71-2.31	< 0.001
T-stage			
T 1	ref		
T 2	1.03	0.87-1.22	0.732
T 3	1.00	0.81-1.22	0.967
T 4	0.87	0.74-1.03	0.107
N-stage			
N 0	ref		
N 1	0.56	0.42-0.75	<0.001
N 2	1.77	1.54-2.04	<0.001
N 3	1.64	1.40-1.93	<0.001
Hospital volume			
<50	ref		
50-100	0.77	0.66-0.91	0.002
>100	0.89	0.76-1.05	0.169
Teaching status (chest physician)			
Non-teaching hospitals	ref		
Teaching hospitals	0.90	0.79-1.03	0.128
Academic hospitals	0.64	0.48-0.86	0.003
Teaching status (lung- / thoracic surgery)			
Non-teaching hospitals	ref		
Teaching hospitals (incl. academic hospitals)	1.59	1.29-1.96	< 0.001
Radiotherapy facilities			
No	ref		
Yes	0.93	0.79-1.09	0.345
Region			
I	0.96	0.82-1.12	0.589
II	1.54	1.29-1.84	< 0.001
III	0.84	0.69-1.02	0.081
IV	ref		
V	0.97	0.82-1.16	0.755
VI	1.00	0.85-1.17	0.978
VII	1.12	0.96-1.31	0.145
VIII	1.49	1.23-1.81	< 0.001
IX	1.04	0.86-1.27	0.678

Hospital characteristics based on hospital of diagnosis.

surgeons (OR 1.6, CI 1.3-1.9). Also, regional differences in the use of chemoradiation were revealed, but they seemed larger between individual hospitals, independent of their region, volume of NSCLC patients, teaching status or radiotherapy facilities (Figure 3).
Patients younger than 75 years diagnosed with stage IIIa in an academic hospital (26%), teaching hospital (26%) or in radiotherapy center (22%) had a resection of their tumor more often than patients in non teaching (15%) or hospitals without radiation facilities (16%). Resection rates in stage IIIa declined slightly during the study period (not significant), while combined treatment of stage IIIa disease with chemoradiation increased, from 24% in 2001 to 43% in 2006 (p=0.001). A multivariate analysis revealed marked regional differences in the percentage of patients having surgery for their stage IIIa NSCLC, varying between 9 and 25%.

Stage IV

The percentage of patients with stage IV NSCLC at primary diagnosis gradually increased during the study period from 38% in 2001 to 44% in 2006. The use of chemotherapy in the primary treatment of stage IV patients younger than 75 years also increased in this period, from 31% to 50% (p=0.001), but approximately 40% of stage IV patients received no active treatment. Hospital differences in the palliative use of chemotherapy in stage IV NSCLC were not a part of the current study.

Survival

Patients who underwent a resection for stage I or II disease had a significantly higher survival than patients without a resection (Figure 4). Adjusted for age, gender, T-stage and year of diagnosis, overall survival of stage I and II patients was significantly higher in hospitals with a higher resection rate and significantly lower in hospitals whose resection rate was lower than the group of hospitals within the 95% control limits of the funnel plot of figure 2 (HR

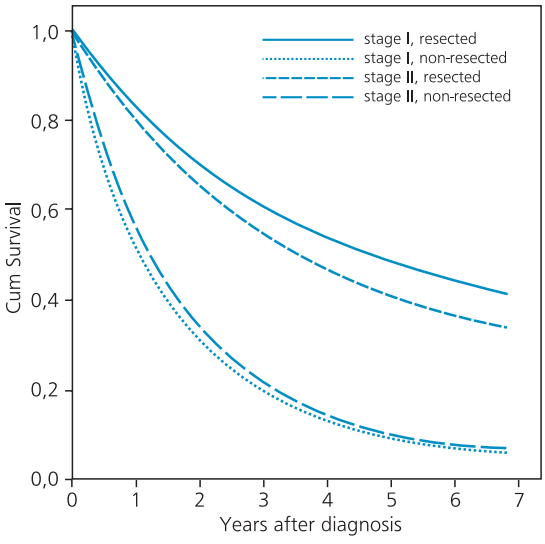

Figure 4. Survival of stage I and II NSCLC patients with or without surgical resection.

0.88, 95%CI 0.83-0.93 and HR 1.15, 95% CI 1.07-1.24, respectively). Though, no differences were found in overall survival for patients who underwent resection in the hospitals with high and with low resection ratios.

DISCUSSION

The introduction of a national evidence-based guideline in 2002, appears to have had several effects on staging and patterns of care for NSCLC patients in our country. Especially the routine use of PET-scanning in the work-up of patients for curative therapy led to an increased number of patients with stage IV at diagnosis. In addition, recommendations on the use of chemoradiation for stage III patients led to an increased utilization of radiotherapy combined with chemotherapy, concurrent or sequentially. Nevertheless this study reveals marked variation in treatment patterns and outcome of patients with NSCLC in our country. Not only are these differences influenced by patient or tumor characteristics, also the hospital of diagnosis seems to affect the treatment given. On the level of the individual hospital resection rates in stage I / II patients varied between 54 and 97 percent. The administration of potentially curative chemoradiation in stage III patients varied from less than 10 to more than 40 percent. These differences were only sporadically explained by structural differences between hospitals, like their teaching status or the availability of radiotherapy facilities. Nevertheless, the variation in optimal treatment rates identified in this study could mean that there's room for further improvement in the treatment of NSCLC patients in our country, possibly leading to actual survival benefits.

Inequality in the treatment of NSCLC has been addressed in many publications. Several patient factors are associated with lower odds of undergoing a potentially curative treatment for lung cancer. Higher age is the most important factor, but in studies from the United States as well as Europe gender, comorbidity, race, socio-economic status, region or country of origin have also proven to be predictive [17-22]. These inequalities are not only due to decreased access to care, but also differences in physicians' treatment choices and differences in guideline implementation and adherence are believed to be of influence. Whereas active treatment of NSCLC patients appeared to be strongly associated with better survival, studies from Yorkshire and the Southeast of England [15,16] demonstrated wide regional variations in the use of active treatments like surgery and radiotherapy [23;24]. In one of these studies the use of any active treatment in NSCLC patients, independent of stage, ranged from 15% in one area to 42% in another. Despite corrections for case-mix the reasons behind this variation stayed unclear, but if the first hospital visited was a radiotherapy center, patients were more likely to receive any active treatment.

In the present study, we analyzed the treatment compliance according to the Dutch evidence-based guidelines, not only at the regional level, but also on the level of the individual hospital. For early stage NSCLC (stage I and II) surgical resection by (bi)lobectomy or pneumonectomy

is treatment of choice and for advanced stage NSCLC (stage III) a combined treatment with radiotherapy and chemotherapy (sequentially or concurrent) is the advised treatment.
After adequate staging, the best chances for survival in early stage NSCLC are obtained by surgical resection. Despite, our study showed marked differences in resection rates between individual hospitals and regions. Patients who were diagnosed in a (specialized) center, with a training status for thoracic/lung surgery, seem to have higher chances for resection. These results confirm the findings of a regional study from the Netherlands showing that patients diagnosed with stage I or II disease at specialized centers or higher volume hospitals are more likely to receive surgical therapy. These differences were seen in all age groups and led to a better survival of patients diagnosed in specialized centers than those that initially went to a community hospital [25]. Our study confirms these observations, but we cannot exclude that selective referral of patients with a good performance status has taken place before their NSCLC was diagnosed. Moreover, variation was most prominent on the individual hospital level, with resection rates for early stage NSCLC varying between 55 and 100%. Also among teaching hospitals and specialized centers a wide range of variation was exhibited, between 64 and 89% and 75 and 93% respectively. Considering the results of our study, the choice for a teaching hospital or specialized hospital does not guarantee better care and guideline compliance.
In literature many reports have shown that resection rates and surgical outcome of patients with early stage NSCLC can be improved by treatment in experienced and specialized multidisciplinary teams [2;3;26;27]. The combination of heightened awareness, more adequate staging, improved surgical skill and postoperative care might lead to better outcome. In this context, the inverse relationship between procedural volume and mortality has been studied extensively [24;28]. In our study half of the resections for early stage NSCLC were performed in low volume hospitals with an annual volume less than 20. Mortality hardly differed between low- and high volume hospitals, but ranged from 1% in the younger (< 60 years) to 8% in the oldest group (> 75 years). Opposite to our findings in high volume hospitals, a lower mortality rate was found in the specialized centers (1%). This is remarkable, considering the higher resection rates we found in elderly patients diagnosed with stage I and II NSCLC in the same centers. Patient selection for operative treatment as well as peri-operative management of the older patient could thus be better in specialized centers. Future 'in depth' studies could reveal the aspects of these care processes (best practices) that lead to these better outcomes and can be used to improve the care for older NSCLC patients in the whole field.
In contrast with the plethora of studies investigating the differences in surgical outcome, only a few studies have investigated institutional differences for non-surgical treatments. In stage III patients with a favorable performance status, a potentially curative treatment by a combination of radio- and chemotherapy is recommended. In our study the use of this chemoradiation increased for stage IIIa as well as for stage IIIb patients. Nevertheless, our study showed a wide variation in the use of chemoradiation between regions and individual hospitals (figure 3), without a clear explanation based on their (infra)structural

characteristics. For example, the use of chemoradiation was not different between hospitals with or without radiotherapy facilities. With the data available in the NCR, we can only suggest that differences in experience with the complex radiotherapy techniques and the nontrivial toxicity encountered in patients undergoing these treatments, is causing hospital variation in the use of chemoradiation.

Our study has several limitations. First, only a limited set of (infra)structural characteristics of hospitals was available. For example, during the study period PET-scanning was introduced gradually for the staging of NSCLC in the Netherlands from 2000 on[14]. Improved clinical staging in hospitals using PET-scans could have influenced outcome for different stages of the disease. The addition of PET to conventional workup can improve staging and prevents unnecessary surgery in one out of five patients with suspected non-small-cell lung cancer[13]. Though, in our study only a minor shift from early to advanced stages NSCLC was detected (Figure 1a), the differential introduction of PET-scanning in the Netherlands can be a confounding factor for the survival analyses performed.
Furthermore, data on comorbidities and performance status of patients diagnosed with NSCLC were not available in the NCR. Lung cancer is predominantly a disease of the elderly. Physician treatment decisions can be guided by a patients' age and general medical condition, in all stages of the disease[29;30]. On the other hand, in the Dutch setting there are no indications that patient groups of individual hospitals are truly different. Nevertheless, remarkable variation in resection rates (stage I-II) and the use of combined modality treatment (stage III) was shown. These differences are relevant, because they led to differences in survival, as was shown for stage I-II patients diagnosed in groups of hospitals with low- and high resection rates.
In conclusion, treatment patterns and outcome of NSCLC patients vary by region and the hospital their cancer is diagnosed in. Though, resection rates are higher in hospitals training thoracic surgeons, variation between individual hospitals is much more distinct. Hospital characteristics like a high diagnostic volume, teaching status or availability of radiotherapy facilities proved no guarantee for optimal treatment compliance. Therefore, initiatives to improve quality of care for NSCLC patients should focus on actual differences in treatment patterns and outcome between hospitals, instead of using hospital characteristics as proxies for high quality of care. In addition, 'in depth' prospective documentation studies or clinical audits could reveal high leverage processes of care that lead to the better outcomes. This information creates the opportunity to optimize treatment of NSCLC patients and move the medical field forward.

Acknowledgements

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Chapter 10

Variation in treatment and outcome of colon cancer patients between hospitals in the Netherlands

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ABSTRACT

Background:
Aim of this study was to describe treatment patterns and outcome according to region, and according to hospital types and volumes among patients with colon cancer in the Netherlands.

Methods:
All patients with invasive colon carcinoma diagnosed in the period 2001-2006 were selected from the Netherlands Cancer Registry. Logistic regression analyses were performed to examine the influence of relevant factors on the odds of having adequate lymph node evaluation, receiving adjuvant chemotherapy and postoperative mortality. Relative survival analysis was used to estimate relative excess risk of dying according to hospital type and volume.

Results:
In total, 39 907 patients were selected. Patients diagnosed in a university hospital had a higher odds (OR 2.47; 95% CI 2.19-2.78) and patients diagnosed in a hospital with >100 colon carcinoma diagnoses annually had a lower odds (OR 0.70; 95% CI 0.64-0.77) of having ≥10 lymph nodes evaluated. The odds of receiving adjuvant chemotherapy was lower in patients diagnosed in teaching hospitals (OR 0.85; 95% CI 0.73-0.98) and university hospitals (OR 0.56; 95% CI 0.45-0.70) compared to patients diagnosed in non-teaching hospitals. Funnel plots showed large variation in these two outcome measures between individual hospitals. No differences in postoperative mortality were found between hospital types or volumes. Patients diagnosed in university hospitals and patients diagnosed in hospitals with >50 diagnoses of colon carcinoma per year had a better survival.

Conclusions:
Variation in treatment and outcome of patients with colon cancer in the Netherlands was revealed, with differences between hospital types and volumes. However, variation seemed mainly based on the level of the individual hospital.

INTRODUCTION

Ever since the Institute of Medicine reviewed variations in the quality of cancer care in their 1999 report[1], there is an ongoing debate on this issue, not only in the United States, but also in European countries. Especially, the differences in surgical outcome of patients treated in high and low volume hospitals and between specialized and non-specialized providers, have been studied extensively.[2-4] Most of these studies focus on adverse outcomes like complications and postoperative mortality; few describe differences in the proportion of patients getting optimal treatment for their cancer.

In the Netherlands, colon cancer is one of the most frequent cancers with more than 7 500 new diagnoses in 2007.[5] It is also one of the most frequent causes of cancer death with more than 3 800 deaths in 2007.[6] According to the current Dutch guideline, the primary treatment for colon cancer is surgery, while adjuvant chemotherapy should be considered for patients with lymph node metastasis. Therefore, adequate lymph node evaluation is important in patients with colon cancer;[7-9] 10 or more lymph nodes should be evaluated for accepting N0 status.[10] However, regional population-based studies in the Netherlands showed large variation on the level of lymph nodes evaluated by pathologists and in the proportion of patients receiving adjuvant chemotherapy.[11;12]

Currently, colon cancer patients are treated in every hospital in the Netherlands. These patients are treated in different settings: university, teaching and non-teaching hospitals; high- and low-volume hospitals, situated in urbanized or more rural regions. It is unknown, to what extent these structural differences between hospitals lead to differences in patterns of care and outcome. A number of studies demonstrated better patient outcomes in teaching versus nonteaching hospitals.[13-15] Others found lower mortality with increasing hospital or surgeon volume.[16;17] However, studies on mortality among patients with colon cancer showed conflicting results: some demonstrated an association between mortality and hospital volume or teaching status, while others did not.[18-24]

Aim of this study was to describe variation in staging, treatment patterns and outcome according to region and, according to type and volume of individual hospitals among patients with colon cancer in the Netherlands.

METHODS

Netherlands Cancer Registry

In the Netherlands, all newly diagnosed malignancies are registered in the nationwide population-based Netherlands Cancer Registry (NCR). The automated pathological archive (PALGA) and the Haematology Departments are the main sources of notification. The National Registry of Hospital Discharge Diagnosis is an additional source, which accounts

for up to 8% of new cases.[25] Data are collected from the medical records by specially trained registrars and are coded according to a nationally used manual. Information on patient characteristics, tumor characteristics, treatment, hospital of diagnosis, hospital of treatment and follow-up is recorded. For coding tumor site and morphology the International Classification of Diseases for Oncology (ICD-O) is used.[26] Cancers are staged according the TNM classification.[27] Quality of the data is high[28] and completeness is estimated to be at least 95%.[29]

Patients

All patients with an invasive colon carcinoma, diagnosed in the period 2001-2006 were selected from the NCR. Diagnoses without histological confirmation, diagnoses based only on autopsy findings, patients living abroad and incomplete records were excluded from analyses. Tumor site was classified as ascendens (C18.0-C18.2), transversum and descendens (C18.3-C18.6), sigmoid (C18.7) and overlapping/unknown (C18.8-C18.9). Pathological stage was used to classify the extent of the disease. In cases where pathological stage was unknown, clinical stage was used.

CCC-regions and hospitals

The Netherlands are divided in 9 regions, each served by a Comprehensive Cancer Center (CCC). Activities of CCCs are facilitation of consultancy services, development and implementation of guidelines, improving organisation of cancer care, coordinating palliative care and the population-based cancer registry. Each CCC serves an area covering five to twenty hospitals. All hospitals are affiliated to one center. Within each CCC-region, treatment policies are discussed within multidisciplinary meetings which may lead to differences in oncologic care between the regions. Patients of all 97 hospitals in the Netherlands were included in the analyses.

A teaching hospital was defined as a hospital which provides medical training to residents. A distinction was made between a teaching hospital for surgery and a teaching hospital for internal medicine. All teaching hospitals for surgery were also teaching hospitals for internal medicine. University hospitals were teaching hospitals affiliated to a medical university. The one specialized oncology center in the Netherlands was also classified as a university hospital. Hospital volume was based on the mean number of diagnoses of colon carcinoma per year or on the mean number of colon resections for cancer per year. In the Netherlands, resections for colon cancer are in general performed in the hospital of diagnosis. Hospital volume was categorized into <50 , 50-100 and >100 diagnoses/resections per year.

For the analyses of treatment and relative survival, type of hospital was based on the hospital where the tumor was diagnosed reasoning that referral of patients for treatment in another hospital can also be considered as a good standard of care. For the analyses of postoperative mortality, type of hospital was based on the hospital where the surgery was performed.

Statistical analyses

Treatment was described as percentages per stage and age group (<75 years and ≥75 years).

Variation in lymph node evaluation and adjuvant chemotherapy

Logistic regression analysis was performed to examine the influence of age at diagnosis, gender, depth of invasion, nodal involvement, type of hospital of diagnosis, hospital volume, CCC-region and year of diagnosis on the odds of having an adequate lymph node evaluation (defined as ≥10 or more evaluated lymph nodes). Patients whose tumor was removed by polypectomy and patients with distant metastasis (M1) were excluded from this analysis. Moreover, the influence of age at diagnosis, gender, type of hospital of diagnosis, hospital volume, CCC-region and year of diagnosis on the odds of receiving adjuvant chemotherapy in patients with stage III disease colon cancer was analyzed using logistic regression analysis. To compare the performance of the individual hospitals for these two outcome measures, funnel plots were made using 95% control limits calculated around the mean of the 20% best performing hospitals.[30;31] The proportion of resections involving 10 or more evaluated lymph nodes was adjusted for age, gender, depth of invasion (pT) and nodal involvement (pN). The proportion of resected patients receiving adjuvant chemotherapy was adjusted for age and gender. Each hospital was displayed as a scatter point presenting the adjusted rate for the outcome and the hospital volume.

Variation in postoperative mortality

Logistic regression analysis was used to investigate the odds of postoperative mortality by age at diagnosis, gender, depth of invasion, type of hospital of surgery, resection volume of hospital of surgery and CCC-region. Postoperative mortality was defined as death within 30 days after surgery. Patients with distant metastasis (M1) and acute surgery (date of surgery = date of first pathological examination) were excluded from this analysis. Postoperative mortality was analysed for tumors diagnosed in 2005 and 2006, because date of surgery was not registered in the NCR until 2005.

Variation in survival

Relative excess risks (RER) of dying according to hospital type and volume were estimated by means of multivariate relative survival analyses. Relative survival, an estimation of disease-specific survival, was calculated as the ratio of the observed rates in cancer patients to the expected rates in the general population using the Ederer method.[32] Results of the multivariate relative survival analyses were stratified by pathological stage of the tumor, because interaction was found between stage and hospital type. Length of follow-up was calculated as the time from diagnosis to death or to 1st January 2008. Only first tumors were included in the multivariate relative survival analyses.

Table 1. Description of study population (N=39 907)

	N	%
Gender		
Male	19 882	49.8
Female	20 025	50.2
Age at diagnosis		
< 60	7 269	18.2
60-74	16 553	41.5
75+	16 085	40.3
Year of diagnosis		
2001	6 016	15.1
2002	6 127	15.4
2003	6 487	16.3
2004	6 840	17.1
2005	7 077	17.7
2006	7 360	18.4
Tumor location		
Ascendens	14 434	36.2
Transversum and descendens	9 318	23.4
Sigmoid	15 091	37.8
Overlapping/Unknown	1 064	2.7
Pathological stage		
I	6 209	15.6
II	13 812	34.6
III	10 024	25.1
IV	8 662	21.7
Unknown	1 200	3.0
Teaching hospital surgery		
No	16 808	42.1
Yes	20 651	51.8
University hospital	2 448	6.1
Teaching hospital internal medicine		
No	12 231	30.7
Yes	25 228	63.2
University hospital	2 448	6.1
Annual volume of hospital of diagnosis		
<50 diagnoses colon carcinoma	7 484	18.8
50-100 diagnoses colon carcinoma	19 816	49.7
>100 diagnoses colon carcinoma	12 607	31.6
Comprehensive Cancer Center region		
1	6 900	17.3
2	5 496	13.8
3	3 529	8.8
4	2 930	7.3
5	4 044	10.1
6	5 632	14.1
7	5 651	14.2
8	2 485	6.2
9	3 240	8.1

STATA (version 10.0) was used for the analyses. A p-value below 0.05 was considered statistically significant.

RESULTS

In the period 2001-2006 39 907 patients were newly diagnosed with colon carcinoma in the Netherlands, with an annual increase from 6 016 in 2001 to 7 360 in 2006. The male/female ratio was 1:1 and 40% of the patients was aged 75 years or older. Most frequent were stage II tumors (35%). Stage was unknown for 3% of the patients. Six percent of the patients were diagnosed in a university hospital and half of the patients were diagnosed in a hospital with 50 to 100 diagnoses per year (Table 1).

Treatment

Almost all patients with stages I-III disease underwent surgical resection. Around 10% of the stage I tumors were removed by endoscopic polypectomy. Of the patients younger than 75 years with stage III disease 76% received adjuvant chemotherapy. Among patients 75 years and older this proportion was 17%. Around 60% of patients with stage IV disease underwent surgical resection of the primary tumor. The surgery of the primary tumor was combined with chemotherapy in 39% of the patients younger than 75 years and in 10%

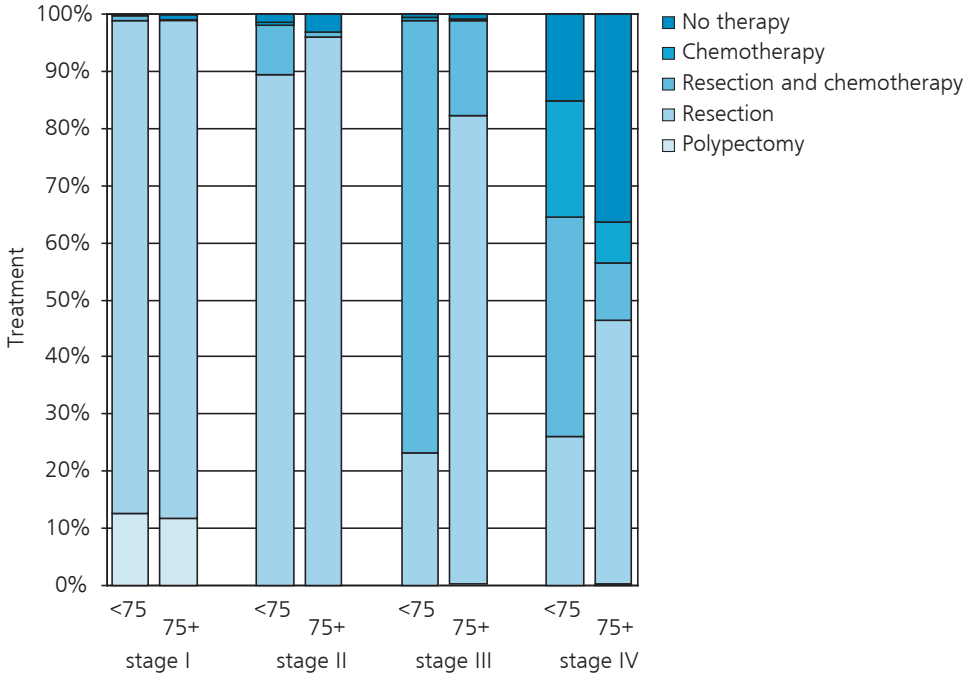

Figure 1. Treatment according to stage and age at diagnosis

of the patients 75 years and older. The proportion of patients with stage IV who did not receive any treatment was 15% among patients younger than 75 years and 37% among patients 75 years and older (Figure 1).

Table 2. Odds ratio of having 10 or more lymph nodes evaluated in patients with stage I-III (multivariate logistic regression analysis)

	OR	95% CI
Gender		
Male	1.00	Reference
Female	1.14*	1.08-1.20
Age at diagnosis		
< 60 years	1.00	Reference
60-74 years	0.74*	0.69-0.79
≥ 75 years	0.54*	0.50-0.58
Year of diagnosis		
2001	1.00	Reference
2002	1.16*	1.06-1.28
2003	1.30*	1.18-1.43
2004	1.61*	1.47-1.77
2005	2.57*	2.34-2.81
2006	3.29*	3.00-3.60
Depth of invasion		
pT1	1.00	Reference
pT2	3.06*	2.64-3.55
pT3	5.02*	4.38-5.76
pT4	4.62*	3.97-5.38
Nodal involvement		
pN0	1.00	Reference
pN+	1.27*	1.20-1.34
Hospital of diagnosis		
Non-teaching hospital	1.00	Reference
Teaching hospital for surgery	1.04	0.97-1.11
University hospital	2.47*	2.19-2.78
Annual volume of hospital of diagnosis		
<50 resections colon carcinoma	1.00	Reference
50-100 resections colon carcinoma	0.97	0.91-1.04
>100 resections colon carcinoma	0.70*	0.64-0.77
Comprehensive Cancer Center region		
1	1.00	Reference
2	1.22*	1.11-1.34
3	1.32*	1.19-1.47
4	1.38*	1.24-1.55
5	1.19*	1.08-1.32
6	0.92	0.84-1.01
7	0.70*	0.64-0.78
8	0.85*	0.75-0.97
9	1.28*	1.15-1.42

* $p<0.05$

Lymph node evaluation

The proportion of patients with 10 or more evaluated lymph nodes after resection increased from 31% in 2001 to 58% in 2006, with an odds ratio of 3.29 (95% CI 3.00-3.60) in 2006 compared to 2001. Female patients were more likely to have had 10 or more lymph nodes evaluated after resection. The odds ratio decreased with older age at diagnosis. The odds of having an adequate lymph node evaluation increased by year of diagnosis, up to 3.29 (95% CI 3.00-3.60) in 2006 compared to 2001. Patients with a larger depth of invasion and with nodal involvement were more likely to have had 10 or more lymph nodes evaluated. Patients diagnosed in a university hospital were more likely to have an adequate lymph node evaluation (OR 2.47; 95% CI 2.19-2.78). Patients diagnosed in a hospital with more than 100 resections per year were less likely to have an adequate lymph node evaluation (OR 0.70; 95% CI 0.64-0.77). There was variation between CCC-regions in the odds of having 10 or more lymph nodes evaluated (Table 2). In the funnel plot, the adjusted proportion of patients with 10 or more evaluated lymph nodes is depicted for each hospital by mean number of colon resections per year, showing a large variation between the individual hospitals (Figure 2). The proportion of patients with an adequate lymph node evaluation ranged from more than 70% to less than 20% per hospital.

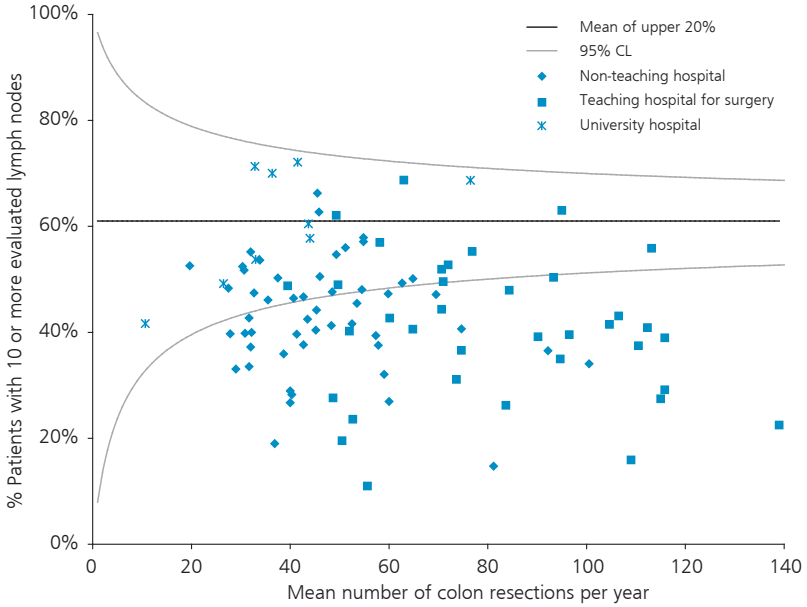

Figure 2. Funnel plot of proportion of patients of whom 10 or more lymph nodes were evaluated after resection in the period 2001-2006 according hospital type and mean number of colon resections per year

Adjuvant chemotherapy

In table 3 the odds of receiving adjuvant chemotherapy in patients with stage III tumors are shown. The use of adjuvant chemotherapy in patients with stage III tumors increased from 49% in 2001 to 58% in 2006, with an odds ratio of 1.66 (95% CI 1.40-1.97) in 2006 compared to 2001. Female patients had a lower odds of receiving adjuvant chemotherapy (OR 0.88; 95% CI 0.80-0.98). The odds of receiving adjuvant chemotherapy decreased with increasing age, with an odds ratio of 0.03 (95% CI 0.03-0.04) in patients 75 years and older compared to those younger than 60 years. Patients diagnosed in a teaching hospital for internal medicine or in a university hospital had a lower odds of receiving adjuvant chemotherapy, compared to patients diagnosed in a non-teaching hospital. No significant

Table 3. Odds ratio of receiving adjuvant chemotherapy in patients with stage III disease (multivariate logistic regression analysis)

	OR	95% CI
Gender		
Male	1.00	Reference
Female	0.88*	0.80-0.98
Age at diagnosis		
< 60 years	1.00	Reference
60-74 years	0.40*	0.34-0.46
≥ 75 years	0.03*	0.03-0.04
Year of diagnosis		
2001	1.00	Reference
2002	1.05	0.88-1.25
2003	1.22*	1.02-1.46
2004	1.34*	1.13-1.59
2005	1.44*	1.21-1.71
2006	1.66*	1.40-1.97
Hospital of diagnosis		
Non-teaching hospital	1.00	Reference
Teaching hospital for internal medicine	0.85*	0.73-0.98
University hospital	0.56*	0.45-0.70
Annual volume of hospital of diagnosis		
<50 diagnoses colon carcinoma	1.00	Reference
50-100 diagnoses colon carcinoma	1.04	0.89-1.22
>100 diagnoses colon carcinoma	0.91	0.74-1.11
Comprehensive Cancer Center region		
1	1.00	Reference
2	0.84	0.70-1.02
3	0.73*	0.59-0.90
4	0.86	0.69-1.07
5	0.76*	0.63-0.93
6	0.98	0.82-1.18
7	0.88	0.73-1.06
8	1.66*	1.29-2.12
9	0.84	0.68-1.05

* p<0.05

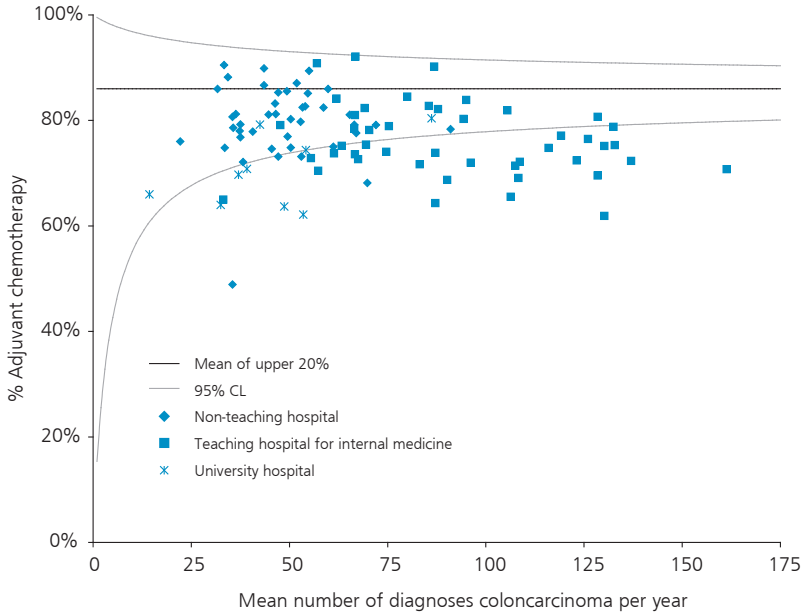

Figure 3. Funnel plot of proportion of patients receiving adjuvant chemotherapy in patients <75 years with stage III disease receiving adjuvant chemotherapy in the period 2001-2006 according hospital type and mean number of diagnoses per year

difference in adjuvant chemotherapy administration between hospitals with different volumes was found. The administration of adjuvant chemotherapy differed between CCC-regions. However, there was also a wide variation between hospitals within the regions (data not shown). The funnel plot shows, for each hospital, the adjusted proportion of patients younger than 75 years with stage III disease receiving adjuvant chemotherapy by mean number of diagnoses per year, demonstrating some variation between the hospitals (Figure 3). The proportion of patients who received adjuvant chemotherapy varied from less than 50% to more than 90% for individual hospitals.

Postoperative mortality

Overall, 4.2% of the patients without distant metastasis at diagnosis undergoing an elective resection died within 30 days after surgery. Female patients had a lower odds of dying within 30 days after resection (OR 0.74; 95% CI 0.58-0.93). The odds of dying within 30 days increased with increasing age, up to 11.61 (95% CI 6.13-21.98) for patients aged 75 years and older compared to those younger than 60 years. The odds was higher for T4-tumors compared with T1-T3 tumors (OR 1.87; 95% CI 1.37-2.56). No differences in postoperative mortality were found between hospital types, hospital volumes and CCC-regions (Table 4).

Table 4. Odds ratio of death within 30 days after resection in patients without distant metastasis (multivariate logistic regression analysis)

	OR	95% CI
Gender		
Male	1.00	Reference
Female	0.74*	0.58-0.93
Age at diagnosis		
< 60 years	1.00	Reference
60-74 years	2.55*	1.30-5.00
≥ 75 years	11.61*	6.13-21.98
Depth of invasion		
T1-T2-T3	1.00	Reference
T4	1.87*	1.37-2.56
Unknown	1.58	0.37-6.81
Hospital of surgery		
Non-teaching hospital	1.00	Reference
Teaching hospital for surgery	0.95	0.71-1.28
University hospital	1.06	0.63-1.80
Annual volume of hospital of surgery		
<50 resections colon carcinoma	1.00	Reference
50-100 resections colon carcinoma	1.33	0.93-1.88
>100 resections colon carcinoma	1.23	0.77-1.98
Comprehensive Cancer Center region		
1	1.00	Reference
2	0.69	0.44-1.08
3	0.84	0.51-1.38
4	0.95	0.58-1.57
5	0.95	0.61-1.47
6	0.83	0.54-1.27
7	1.07	0.71-1.63
8	0.61	0.32-1.16
9	0.83	0.50-1.38

* $p < 0.05$

Multivariate relative excess risks (RER) of dying

In the multivariate model for all patients with colon cancer, patients diagnosed in a university hospital had a lower risk of dying compared to patients diagnosed in a non-teaching hospital (RER 0.76; 95% CI 0.69-0.83). Patients diagnosed in hospitals with 50-100 diagnoses colon carcinoma per year and with more than 100 diagnoses colon carcinoma yearly had a lower risk of dying compared to patients diagnosed in a hospital with less than 50 diagnoses colon carcinoma yearly (RER 0.90; 95% CI 0.85-0.95 and RER 0.86; 95% CI 0.80-0.93, respectively).

For stage I, survival was worse in patients diagnosed in a university hospital (RER 1.87; 95% CI 1.02-3.42). No differences in survival of patients with stage II disease were found between hospital types or between hospital volumes. Both among patients with stage III disease and among patients with stage IV disease, patients diagnosed in a university hospital

had a lower risk of dying compared to patients diagnosed in a non-teaching hospital (RER 0.70; 95% CI 0.57-0.87 and RER 0.77; 95% CI 0.69-0.86, respectively). For stage IV, patients diagnosed in hospitals with 50-100 diagnoses colon carcinoma yearly and more than 100 diagnoses colon carcinoma yearly had a better survival (RER 0.88; 95% CI 0.82-0.95 and RER 0.85; 95% CI 0.77-0.94, respectively) (Table 5).

DISCUSSION

In this nationwide population-based study, analyzing Netherlands Cancer Registry data of 39 907 patients with colon carcinoma diagnosed in the period 2001-2006, considerable variation in treatment patterns and outcome was identified. The proportion of patients receiving optimal postoperative staging with adequate lymph node evaluation and accurate treatment for their cancer increased considerably over time, but differed widely between individual hospitals.
Being diagnosed in a hospital with a large patient volume or in a university hospital was positively related with the odds of having an adequate lymph node evaluation, and being diagnosed in a teaching hospital or in a university hospital had a negative relation with the odds of receiving adjuvant chemotherapy. Differences in relative survival were found between the various types and volumes of hospitals. In total, patients diagnosed in a university hospital or patients diagnosed in a hospital with a large volume had a better survival.

In literature, the number of studies evaluating differences in quality of care between various types of providers is overwhelming. Most studies show an inverse relationship between hospital volume and mortality, especially for high risk surgical procedures.[2;16;17] However, few studies have focused on other dimensions of quality of care besides differences in morbidity and mortality after surgery. In our study two important aspects of high leverage colon cancer treatment were investigated, lymph node evaluation and the administration of adjuvant chemotherapy. The choice for these specific process measures is supported by evidence from literature.[9;33]

Lymph node evaluation

Lymph node evaluation is crucial for staging and planning treatment in patients with colon cancer. Since adjuvant chemotherapy should be considered for patients with positive lymph nodes, inadequate lymph node examination might lead to understaging and undertreatment.[7;8] On the other hand, according to Dutch treatment guidelines, adjuvant chemotherapy should be considered for patients with stage II disease who had less than 10 evaluated lymph nodes, which could lead to overtreatment.[10] In our study we found that patients diagnosed in a university hospital were more likely to have more lymph nodes examined. This confirms the results of earlier studies from Canada and France.[34;35] The

Table 5. Relative excess risks (RER) of dying for patients with colon cancer diagnosed in the period 2001-2006, according to stage (multivariate relative survival analysis)

	Total[1]		Stage I[2]	
	RER	95 % CI	RER	95 % CI
Type of hospital of diagnosis				
Non-teaching hospital	1.00	Reference	1.00	Reference
Teaching hospital surgery	1.03	0.98-1.09	1.11	0.70-1.76
University hospital	0.76*	0.69-0.83	1.87*	1.02-3.42
Annual volume of hospital of diagnosis				
<50 diagnoses colon carcinoma	1.00	Reference	1.00	Reference
50-100 diagnoses colon carcinoma	0.90*	0.85-0.95	0.92	0.56-1.51
>100 diagnoses colon carcinoma	0.86*	0.80-0.93	0.84	0.44-1.61

[1] Adjusted for gender, age at diagnosis, grade, year of diagnosis, tumor location, stage, surgery, chemotherapy and CCC-region

[2] Adjusted for gender, age at diagnosis, grade, year of diagnosis, tumor location, depth of invasion, surgery and CCC-region, * p<0.05

available resources in university hospitals to provide high quality multidisciplinary cancer care could be an explanation for this result. Other studies found a positive correlation between hospital volume and number of evaluated lymph nodes.[36;37] The current study, however, found an inverse relationship and showed that patients diagnosed in high-volume hospitals were less likely to have 10 or more lymph nodes examined. This suggests that an increased workload for pathology staff might lead to a less extensive lymph node evaluation, although a high-volume hospital not necessarily has to be served by a high-volume pathology laboratory. Furthermore, the workload per pathologist depends on the number of pathologists in a staff. Unfortunately, data on individual pathologists was not available in the NCR. However, the differences found between individual hospitals are remarkable.

Adjuvant chemotherapy

Ever since a randomized trial in the early nineties showed that patients with stage III colon carcinoma treated with adjuvant chemotherapy had a significant survival benefit33], chemotherapy after surgery has been the standard of care for stage III patients with an adequate performance status.[10] However, not all patients with stage III disease receive adjuvant chemotherapy.[12] There are several explanations why elderly patients receive adjuvant chemotherapy less often than younger patients, such as the presence of comorbidities, unfavourable performance status or patient refusal.[38-40] Our study is hampered by the lack of information about comorbidities and performance status of the patient at time of diagnosis. Nevertheless marked differences in performance status of patients between hospitals in the Netherlands have not been reported.

University hospitals and teaching hospitals proved more restraint in the use of adjuvant chemotherapy compared to general hospitals. A French regional study showed the opposite: a lower relative risk for receiving adjuvant chemotherapy in patients treated in non-teaching hospitals compared to a single university center.[34] An American study demonstrated that

	Stage II[2]		Stage III[3]		Stage IV[4]	
	RER	95 % CI	RER	95 % CI	RER	95 % CI
	1.00	Reference	1.00	Reference	1.00	Reference
	1.14	0.99-1.31	0.96	0.86-1.07	1.05	0.98-1.12
	0.74	0.54-1.00	0.70*	0.57-0.87	0.77*	0.69-0.86
	1.00	Reference	1.00	Reference	1.00	Reference
	0.98	0.83-1.16	0.90	0.80-1.02	0.88*	0.82-0.95
	0.87	0.70-1.07	0.88	0.75-1.03	0.85*	0.77-0.94

[3] Adjusted for gender, age at diagnosis, grade, year of diagnosis, tumor location, depth of invasion, surgery, chemotherapy, number of positive nodes and CCC-region

[4] Adjusted for gender, age at diagnosis, grade, year of diagnosis, tumor location, depth of invasion, surgery, chemotherapy and CCC-region

patients treated by surgeons practicing in a teaching hospital were more likely to see a medical oncologist.[41] Our contrasting findings suggest a more severe selection of patients for administering adjuvant chemotherapy in university hospitals.

Postoperative mortality

In our study, age was an important predictor for postoperative mortality. According to a review of the Colorectal Cancer Collaborative Group, the increased proportion of elderly patients undergoing emergency surgery, together with multiple co morbidities, could contribute to this increased risk of postoperative mortality.[42] However, in our study only elective procedures were included, with a very high risk of postoperative mortality in the elderly patient group compared to the younger patient group. Elderly patients undergoing major surgery can have similar outcomes as younger patients if carefully selected.[42;43]However, the risk of obstruction or even perforation in colon cancer patients forces surgeons to perform surgery in elderly patients with an unfavourable physical status. Apparently, colon resections in elderly people are high risk procedures, in which specific experience and expertise is needed.

Nevertheless, no association between postoperative mortality and the volume or teaching status of hospitals was found in our study. This confirms the results of earlier Dutch and Canadian studies, in which no association between type or volume of hospitals and postoperative mortality was found.[18;44] For other high-risk operations, like pancreatic or esophageal resections, clear differences between low- and high-volume hospitals were demonstrated, also in the Netherlands.[2;3;45] Due to the high incidence of colon carcinoma, hospital volumes are substantially higher than the hospital volume of, for example, pancreas or esophageal cancer, which might explain our results. Nevertheless, despite the lack of an inverse relationship between hospital volume and postoperative mortality, our study

identified important differences in quality of care between hospitals in the Netherlands, as shown above.

Survival

Some consider survival as the most important performance indicator for cancer treatments. Process measures, like the number of lymph nodes evaluated and the use of adjuvant chemotherapy investigated in the current study, are futile, when a relationship with direct outcome measures, like survival, is lacking. Survival was analyzed in the present study and significant differences between hospital types and volumes were found. Survival of patients diagnosed in university hospitals was better than in other hospitals, especially those with a high volume of colon cancer diagnoses. This finding does not parallel the restrained use of adjuvant chemotherapy in stage III patients diagnosed in these university hospitals, although it could be related to a better patient selection for adjuvant chemotherapy. Furthermore, one might speculate about a more aggressive and multidisciplinary approach in case of recurrence. Unfortunately, information on incidence and treatment of recurrences is lacking in the Netherlands Cancer Registry. The relatively low survival of patients diagnosed in low volume hospitals was reported before by a nested cohort study form the US.[46] Another American population-based study found an association between both surgeon and hospital volume and outcome, but hospital volume had a stronger effect.[47]

Comparing quality of care between hospitals on the basis of structural characteristics like volume and teaching status might have important disadvantages. Investigating acknowledged measures of quality of care, our study shows that variation was largest on the level of the individual hospital. Characterisations of hospitals by, for instance, volume, do not necessarily correspond with quality of care and do not reveal the differences in patterns of care that lead to poor or better outcomes. The advantage of direct measurement of the care process and its outcome, is the possibility to feed this information back to individual hospitals. Several studies have stressed the beneficial effects of quality assurance and outcome analysis in the evaluation of the quality of cancer care.
In conclusion, we found variation in treatment and outcome of patients diagnosed with colon cancer in the Netherlands, with differences based on hospital types and volumes. However, variation in quality of care seemed mainly determined on the level of the individual hospital.

Acknowledgements

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Chapter 11

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 multi-modality 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.

Conclusion:
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, 5-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 Association of Surgeons in the Netherlands, 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 Association of Surgeons in the Netherlands 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.

METHODS

The 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, 8230-8242,

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

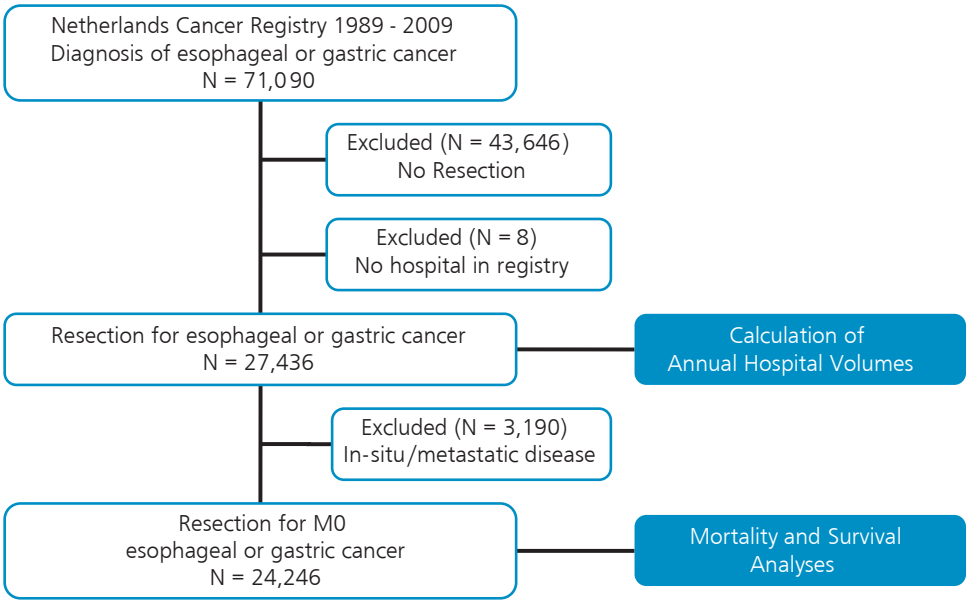

Figure 1. Study profile.

(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/year), low (6-10/year), medium (11-20/year), and high (≥21/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)

	VLV (1-5)		LV (6-10)		MV (11-20)		HV (≥21)		P
	N	%	N	%	N	%	N	%	
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 Category									
<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									
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*	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	

VLV: Very Low Volume (1-5 resections/year) LV: Low Volume (6-10 resections/year), MV: Medium Volume (11-20 resections/year), HV: High Volume (≥21 resections/year). SES: Socio Economic Status, SCC: Squamous Cell Carcinoma, Preoperative/postoperative therapy: chemotherapy with/without radiotherapy. * 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 2a and b).

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%.

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)

	VLV (1-5)		LV (6-10)		MV (11-20)		HV (≥21)		P
	N	%	N	%	N	%	N	%	
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 Category									
<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									
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*	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	

VLV: Very Low Volume (1-5 resections/year) LV: Low Volume (6-10 resections/year), MV: Medium Volume (11-20 resections/year), HV: High Volume (≥21 resections/year). SES: Socio Economic Status, Preoperative/postoperative therapy: chemotherapy with/without radiotherapy. * T4N1-3M0 and T1-4N3M0 gastric cancers were assigned stage IV in the 6th edition TNM-classification

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

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

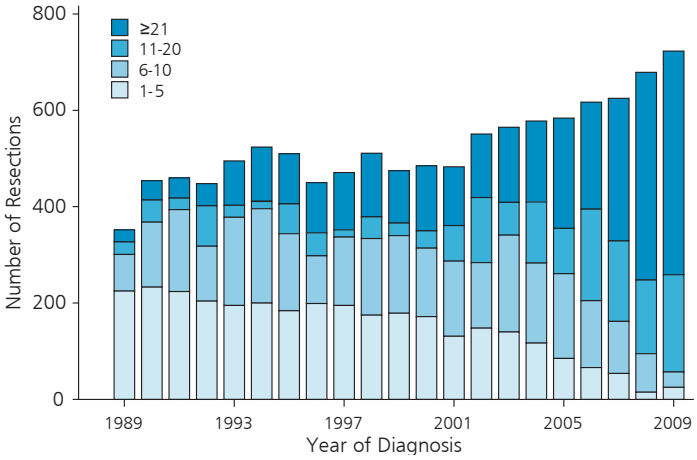

Figure 2a. Number of esophagectomies per hospital volume category.

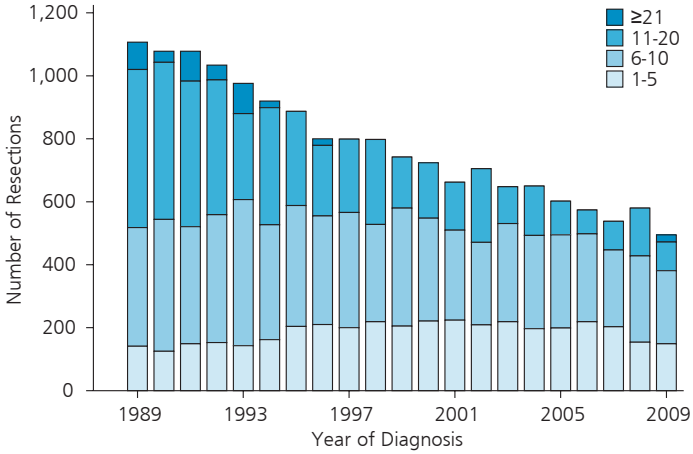

Figure 2b. Number of gastrectomies per hospital volume category.

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 $P < 0.01$).

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 ($P < 0.001$).

Volume-outcome relations

Results from the multivariable analyses on volume-outcome relations are shown in Table 3. After esophagectomy, medium and high volume hospitals were associated with lower

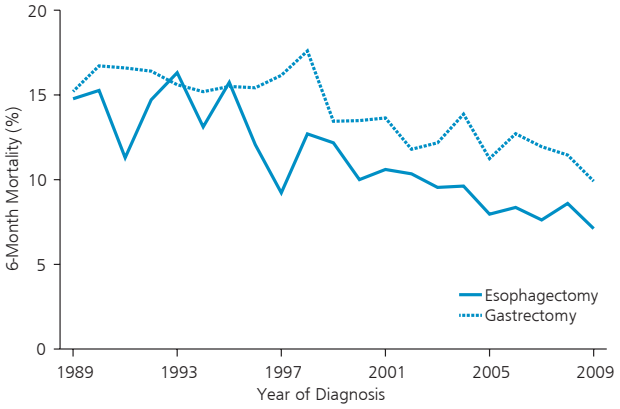

Figure 3a. 6-Month mortality for esophagectomy and gastrectomy, adjusted for sex, age, socio-economic status, stage, morphology, and use of preoperative therapy (1989-2009). Esophagectomy, HR 0.96 for each year, P < 0.001. Gastrectomy, HR 0.98 for each year, P < 0.001. Difference between esophagectomy and gastrectomy: P = 0.003

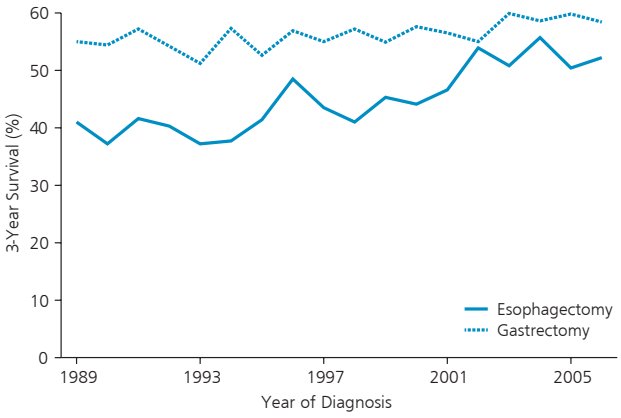

Figure 3b. 3-Year survival rate conditional on surviving the first 6 months for esophagectomy and gastrectomy, adjusted for sex, age, socio-economic status, stage, morphology, and use of preoperative and postoperative therapy (1989-2006). Esophagectomy, HR 0.97 for each year, P < 0.001. Gastrectomy, HR 0.99 for each year, P < 0.001. Difference between esophagectomy and gastrectomy: P < 0.001

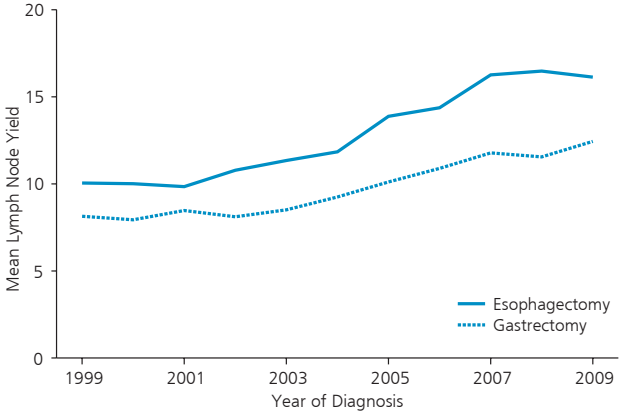

Figure 3c. Median lymph node yield for esophagectomy and gastrectomy, adjusted for sex, age, stage and morphology (1999-2009). Esophagectomy: P < 0.001. Gastrectomy: P < 0.001

Table 3. Volume-outcome relations for esophagectomy and gastrectomy (1989-2009). Mortality and survival were calculated with multivariable Cox regression, nodal yield was calculated with generalized estimated equations.

	Esophagectomy					
	6-month mortality		3-year survival*		LN yield**	
	HR	95% CI	HR	95% CI	OR	95% CI
Hospital Volume						
Very Low (1-5/yr)	1.00		1.00		1.00	
Low (6-10/yr)	0.90	0.78-1.03	1.01	0.94-1.10	1.00	0.91-1.09
Medium (11-20/yr)	**0.78**	**0.62-0.97**	**0.90**	**0.81-0.99**	1.10	1.00-1.22
High (≥21/yr)	**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 category						
<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						
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		1.00			
Yes			1.07	0.94-1.21		

*conditional on surviving the first six months. **1999-2009. HR: Hazard Ratio, OR: Odds Ratio, SES: Socio Economic Status, SCC: Squamous Cell Carcinoma, CI: Confidence Interval, Bold: significant ($P < 0.05$)

Gastrectomy					
6-month mortality		3-year survival*		LN yield**	
HR	95% CI	HR	95% CI	OR	95% CI
1.00		1.00		1.00	
0.95	0.84-1.07	0.99	0.91-1.07	1.02	0.96-1.08
0.95	0.83-1.08	0.99	0.90-1.08	0.99	0.90-1.10
1.10	0.82-1.49	0.98	0.86-1.12	**1.93**	**1.81-2.04**
1.00		1.00			
0.96	0.86-1.07	0.98	0.90-1.05		
0.89	0.79-1.01	0.94	0.87-1.02	1.00	
0.74	**0.65-0.85**	**0.88**	**0.81-0.96**	**1.08**	**1.02-1.16**
0.70	**0.60-0.81**	**0.78**	**0.72-0.86**	**1.42**	**1.32-1.52**
1.00		1.00			
0.79	**0.73-0.85**	**0.91**	**0.85-0.97**	**1.10**	**1.05-1.14**
1.00		1.00		1.00	
2.03	**1.78-2.30**	**1.27**	**1.18-1.37**	**0.88**	**0.82-0.93**
3.94	**3.47-4.49**	**1.57**	**1.44-1.71**	**0.75**	**0.69-0.81**
1.00		1.00			
0.92	0.81-1.04	1.01	0.92-1.12		
0.70	**0.55-0.91**	1.00	0.84-1.20		
0.94	0.73-1.21	1.03	0.85-1.24		
1.00		1.00		1.00	
1.46	**1.31-1.63**	**2.99**	**2.78-3.22**	**1.23**	**1.16-1.31**
2.15	**1.93-2.38**	**5.37**	**5.01-5.75**	**1.55**	**1.46-1.66**
3.50	**3.00-4.08**	**8.45**	**7.43-9.61**	**2.23**	**2.05-2.42**
1.91	**1.40-2.60**	**2.36**	**1.96-2.84**	1.01	0.82-1.24
1.00		1.00		1.00	
1.18	0.86-1.64	**0.58**	**0.44-0.78**	0.94	0.71-1.25
1.00		1.00			
0.27	**0.17-0.43**	1.05	0.84-1.31		
		1.00			
		1.01	0.85-1.21		

six-month mortality and longer three-year conditional survival when compared to very-low volume hospitals (Figure 4). After gastrectomy, neither six-month mortality, or three-year conditional survival were associated with hospital volume category (Figure 5). 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).

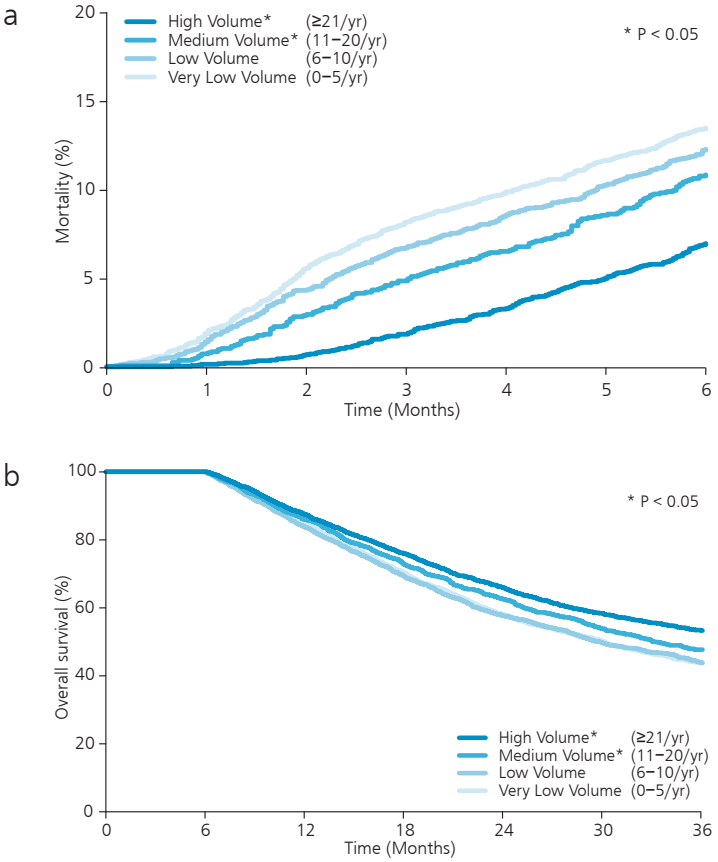

Figure 4. Volume-outcome relations for esophagectomy. a. Relation between volume and 6-month survival, adjusted for year of diagnosis, sex, age, socio-economic status, stage, morphology, and preoperative therapy use. * P < 0.05 compared to Very Low Volume. b. Relation between volume and 3-year survival, conditional on surviving the first 6 months, adjusted for year of diagnosis, sex, age, socio-economic status, stage, morphology, and preoperative and postoperative therapy use. * P < 0.05 compared to Very Low Volume.

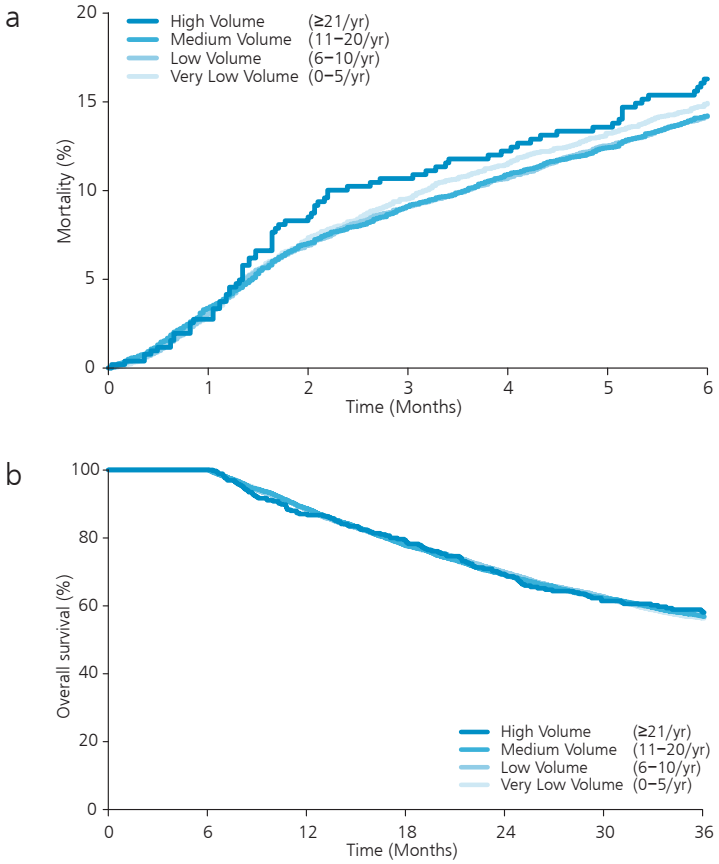

Figure 5. Volume-outcome relations for gastrectomy. a. Relation between volume and 6-month survival, adjusted for year of diagnosis, sex, age, socio-economic status, stage, morphology and preoperative therapy use. * P < 0.05 compared to Very Low Volume. b. Relation between volume and 3-year survival, conditional on surviving the first 6 months, adjusted for year of diagnosis, sex, age, socio-economic status, stage, morphology, and preoperative and postoperative therapy use. * P < 0.05 compared to Very Low Volume.

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 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]

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 esophago-gastric 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.[27,32,33] 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.[34] 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,[3,35] and by educating surgeons participating in the trial.[36,37] However, the majority of cancer patients are treated outside trials, and especially improvements in the process and structure of care on a nationwide 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.[38] 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.[39]

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.[40]

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.[41]

Combining centralization with auditing substantially adds to improvement of care.[42] 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,[39] 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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Chapter 12

Discussion and future perspectives

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Clinical Audit

“the systematic critical analysis of the quality of medical care, including the procedures used for diagnosis, treatment and resulting outcome for the patient, carried out by those personally engaged in the activity concerned”.

Ernest Amory Codman, Surgeon, 1869 - 1940

In most modern health care systems the quality as well as the costs of health care are high priority. This is especially so in cancer care where recent developments force us to constantly re-evaluate the way we provide care to our patients. The number of cancer patients is rising and will continue to do so with, concurrently, a rise in the number of elderly patients leading to a greater risk of treatment-related morbidity and mortality. Moreover, the processes of care, including diagnostic procedures, multidisciplinary decision making, combined modality and targeted treatments, are becoming more and more complex, demanding specific knowledge, expertise and infrastructure in the institutions that provide such care.

Volume and outcome

Simultaneously, there is a growing concern about the quality and safety of health care. Much has been said about the harmful effects of care that fails to deliver the desired benefits[1]. A plethora of articles have reported on variation in patient safety and quality of care delivered by different types of hospitals[2-4]. The differences in operative mortality between high and low volume providers can be striking, especially for high-risk low-volume cancer procedures, like pancreaticoduodenectomy and esophagectomy. The first reports on this issue were published at the end of the 20th century. Initially there was solid criticism on the methodological quality of these volume-outcome studies: the majority was based on administrative instead of clinical data, lacking important information on differences in hospitals' casemix and limited to postoperative mortality as the sole determinant of outcome. Our study from the region of the Comprehensive Cancer Centre Leiden **[this thesis]** emphasized the role of casemix-adjustments in comparing outcomes between hospitals, though showed substantial differences in outcome between high- and low-volume providers[5]. During the last decade more than 40 studies on the volume-outcome relationship for esophageal cancer surgery have been added to the literature, including extensive casemix-adjustments and using several outcome parameters, like morbidity, mortality, long-term survival and quality of life. Our meta-analysis of these studies shows that hospital volume is an important determinant of outcome in esophageal cancer surgery **[this thesis]**[6]. Other reports show the same for other low-volume high-risk procedures and other attributes of hospitals, like their teaching status or specialized setting (e.g. cancer centers)[2,7,8].

This suggests substantial opportunities for improving outcome through the selective referral of patients to centers with high procedural volumes of these high-risk operations[9]. On the other hand, doubts remain about actual improvement in outcome after concentrating high risk cancer operations in centers selected exclusively on their procedural volume **[this thesis]**[10,11]. The differences found in volume studies between high- and low-volume providers might only be true for groups of hospitals on average, without adequate discrimination in quality of care between individual hospitals c.q. future referral centers for complex surgical procedures like esophagectomies.

Variation in quality of care

In 2010, the 'Quality of Cancer Care taskforce' of the Dutch Cancer Society published its report on variation in quality of care between hospitals in the Netherlands[12]. Considering the reports on variation in quality for high-risk cancer procedures, the question was raised how extensive or wide-spread hospital-based quality differences could be? An initial review and meta-analysis of the volume-outcome literature, performed by the taskforce, showed substantial provider variation in the whole field of cancer procedures (Figure 1) [13-17]. Despite these results, the taskforce found several impediments translating these results into policy. No evidence-based cut-offs between low- and high volume could be identified and most studies originated from essentially different health care systems, hampering the extrapolation of their results to the Dutch setting.

Figure 1. Meta-analyses: odds ratio (OR) plots for postoperative mortality (fig 1a) and survival (fig 1b) after pancreatic, breast, bladder, lung, and colorectal resections for cancer, in high volume versus low volume hospitals The center of the square represents the pooled OR and its extremities represent its 95% confidence interval.

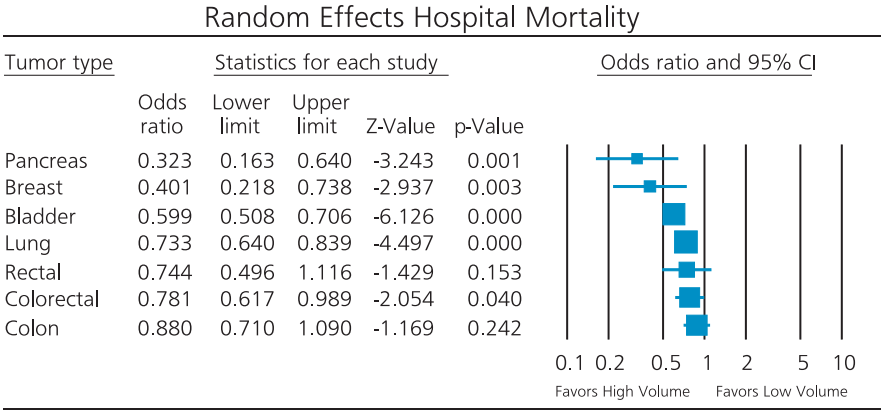

Figure 1a. Hospital volume versus postoperative mortality

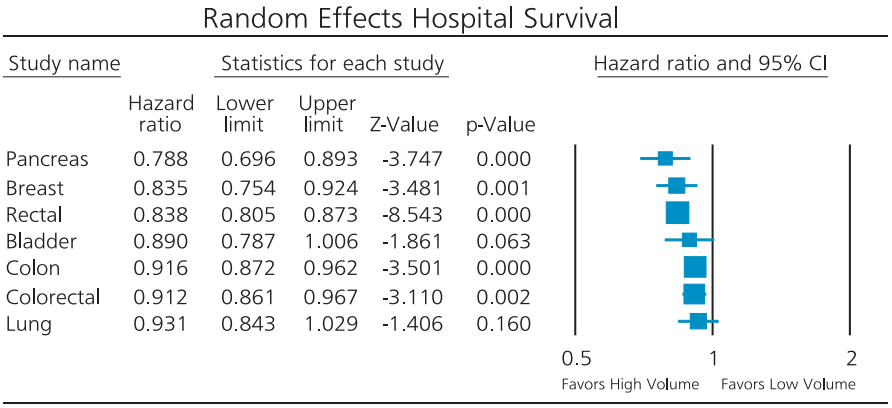

Figure 1b. Hospital volume versus long-term survival

Therefore, the taskforce selected four tumor types based on their varying risk profiles (Table 1), to investigate actual differences in quality of cancer care between hospitals in the Netherlands. For this study the best available data at that moment, those of the Netherlands Cancer Registry, were used. Investigations were not limited to the quality of surgical treatment; instead different quality parameters in the whole treatment process of cancer patients were analyzed. In these studies, substantial differences in quality of care were revealed for the treatment of bladder-, colorectal-, non-small cell lung (NSCLC) and breast cancer[18-23]. For NSCLC patient's treatment patterns and outcome varied by region and the hospital their cancer was diagnosed in. Though resection rates were on average higher in hospitals training thoracic surgeons, variation between individual hospitals was much more distinct. Hospital characteristics like volume, teaching status or on-site availability of radiotherapy facilities proved no guarantee for optimal treatment rates **[this thesis]**[23]. For colon cancer, patients treated in high-volume hospitals had lower odds to have more than 10 lymph nodes examined – an important quality indicator for colon cancer treatment - than patients in low-volume hospitals **[this thesis]**[19]. Similar results from the other studies performed by the taskforce, emphasized that quality varies widely between individual hospitals and that hospital attributes alone are inadequate predictors for high quality care.

Table 1. Profile of tumors investigated by the 'Quality of Cancer Care' taskforce

Tumor	Number / year	Morbidity	5- year survival
Invasive bladder cancer	1 300 / year	High	33%
Non-small cell lung cancer	6 400 / year	High	15%
Colorectal cancer	10 000 / year	High	59%
Breast cancer	13 000 / year	Low	86%

Data-source: Netherlands Cancer Registry 2009

Also in literature, despite multiple efforts to investigate the root causes of variation in outcomes, the underlying mechanisms remain largely unknown[24]. Analyzing variation, it's important to understand that variation in outcome is not synonymous with variation in quality. There are legitimate causes of variation. According to Iezzoni's *'algebra of effectiveness'* there are three contributing factors: patient characteristics, quality of the care process and chance[25]. Consequently, only after adequate corrections for differences in characteristics of patients treated by hospitals (casemix adjustments) and chance variations (reliability adjustments), real differences in quality of care can be revealed[5,26].

Quality of the care process

In surgical oncology eight different phases of the clinical process can be distinguished: diagnosis and staging, pre-operative work-up (including neo-adjuvant treatment), surgical procedure, pathology, postoperative care and adjuvant treatment and follow-up (Figure 2). Variation in quality of care can originate from every phase of the care process and interact with the outcome of the other phases. For example, in rectal cancer surgery inadequate

Patients	- 3000 patient/year - 85% resection - 15% irresectable	**Quality indicators DSCA**	**Indicator results DSCA**
Diagnosis	- coloscopy, colography on indication - tumor biopsy - tumor marker CEA - MRI/CT pelvis - endoscopic ultrasound on indi indication - CT thorax or X thorax - CT abdomen or ultrasound liver - multidisciplinary meeting (MDT)	% full visualization of colon % fully staged % preoperative MRI % discusses in MDT	88% fully staged 89% MRI 88% MDT
Neo-adjuvant treatment	- short-course pre-operative radiotherapy - long-course pre-operative radiotherapy - pre-operative chemoradiation	% neo-adjuvant treatment (cT3-T4) % neo-adjuvant treatment (cT0-T1)	87% neoadjuvant treatment - short course RTx 47% - long course RTx 7% - chemoradiation 28%
Surgery	- intake/informed consent surgeon - consultation anaesthesiologist - consultation stoma-nurse - other consultations (e.g. cardiologist) - open or laparoscopic resection - Low Anterior Resection, APER or Hartmann - colostomy: end- or defunctioning	% treatment-start <5weeks % laparoscopic resections % APER % blood transfusion % colostomies	- 43% started treatment <5weeks - 37% laparoscopic - 29% APER - 79% colostomy: - end 44% - deviating 35%
Pathology	- histology, grade - radicality (R0) - Circumferential Resection Margin - lymph node examination	% irradical (R1-R2) % CRM unknown % CRM tumorpositive % >10 lymph nodes examined	4% irradical (R1-R2) 42% CRM unknown 11% CRM tumor positive 61% >10 lymph nodes
Postoperative recovery	- fast track recovery program - length of stay - adverse events - re-interventions - mortality	median length of stay % complications % serious complications % re-interventions % mortality % failure to rescue	9 days median length of stay 41% complications 28% serious complications 18% re-interventions 10% re-operations 2 % mortality

Figure 2. Different phases of the care process for patients in who rectal cancer surgery is performed, with quality indicators for each phase according to the Dutch Surgical Colorectal Audit (www.clinicalaudit.nl).

pre-operative imaging of the pelvis can lead to inadequate neo-adjuvant treatment and irradical circumferential resection margins as an outcome of the surgical procedure. On the other hand, complications occurring after surgical cancer procedures, like colorectal resections, are associated with omission of or a delay in the administration of adjuvant chemotherapy, possibly affecting the long term outcomes of these patients[27]. These downstream effects of quality issues in preceding phases of the care process underline the importance to evaluate the whole process of diagnosis and treatment in quality improvement

initiatives and not focus on surgical treatment alone. Hence, it's remarkable that few volume-outcome studies have evaluated non-surgical issues, like differences between providers in the quality of diagnostic procedures. In esophageal cancer treatment van Vliet et al. compared the diagnostic sensitivity of pre-operative metastasis detection in a high volume referral center and regional referring centers. The better CT scanning equipment and more experienced radiologists in the referral center prevented futile esophagectomy in 1 in 20 patients[28]. Patient selection, the ability to give a patient the optimal treatment in his or her situation is the essence of surgical oncology. This process has benefitted largely from pre-operative multidisciplinary decision making that was introduced in practically all hospitals in the Netherlands. Still, the limited experience of a multidisciplinary team with low-volume tumor types can hamper the quality of such decisions.

Measuring quality of care

According to the definition of the Institute of Medicine, quality of care is a multidimensional concept, encompassing safety, effectiveness, timeliness, efficiency and patient centeredness. In this thesis only two domains of quality have been addressed, the safety and effectiveness of cancer surgery, not meaning that the other determinants of quality are less important. The way quality is measured depends largely on the availability of reliable data. Only recently, large and detailed multicenter clinical databases have become available, mainly from north-western Europe and the United States[29-31]. In general, simple and readily available clinical outcomes have been used to evaluate the quality of surgical care. This does not do justice to the multidimensional construct of quality and the complexity of care processes described above. The framework in which quality is measured is evaluated by research groups around the world seeking for better ways to measure quality.

As mentioned, to reveal real differences in quality of care, measurements of variation between providers have to be adjusted for casemix and chance variation. Subsequently, to

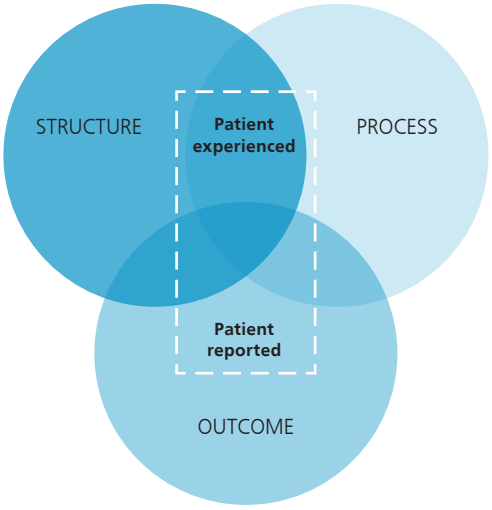

Figure 3. Donabedian paradigm for health care quality; adjusted by the author to emphasize the patients persective in the evaluation of quality of care.

understand variation, it is important to consider relationships between structure, process of care and clinical outcomes as was described by Donabedian[32]. Though, quality should be viewed from different perspectives, not only that of the health care provider, but preferably also from a patients' and social perspective. Therefore, the integration of patient reported experiences (PREMs) and outcomes (PROMS) in quality measurement models is of utmost importance (Figure 3).

Structure

Structural variables describe the setting in which care is provided, which can be attributes of the hospital (infrastructure, volume), multidisciplinary teams or individual physicians. These structural variables, for instance procedural volume, availability of a plastic surgeon, high-level ICU or on-site radiotherapy department, can be related to patient outcomes, especially by the influence they have on the process of care. Hospital volume is a structural measure that has been related to outcome of surgical procedures in an overwhelming number of studies [33]. Though, the extent of this relationship varies widely by type of procedure[2]. In their landmark publication in the New England Journal of Medicine in 2002, *Birkmeyer et al.* reported on the inverse relationship between hospital volume and surgical mortality for different types of cancer procedures. For low-volume high-risk procedures like esophagectomy and pancreatectomy a 3- to 4-fold higher mortality was seen in very low-volume hospitals compared to high-volume hospitals. Though, for cancer procedures that are more frequently performed and/or have a lower risk profile, like colectomies or lung resections, mortality was only 1.2 to 1.4 times higher. Moreover, as argumented above, the relationship between hospital volume and outcome has proven to be true on average, however as a quality measure it may fall short in identifying highleverage processes of care in hospitals with excellent outcomes. Focusing on 'procedural volume' has few ability to move the medical field forward in better understanding the complex clinical processes that lead to success or failure **[this thesis]**[34].

Process of care

Process components of care refer to the interactions between the provider (i.e. physician) and the patient, for example the delivery of adequate staging investigations to detect distant metastases in patients considered for curative surgery. To use process measures to evaluate quality levels in different institutions, it has to be determined which care processes lead to the better outcomes. The development of evidence-based guidelines has provided standards for diagnostic and treatment policies used by clinicians[35]. Measuring the implementation of these standards in routine patient care, could give insight in the quality provided by an institution. Regretfully, the empirical evidence of relationships between measurable process variables and outcome is limited **[this thesis]**[33]. Many components of the clinical process are not evidence-based and guidelines often provide evidence only for a selected group of patients. Especially in elderly, current guidelines can fall short in guiding clinicians in their decision process. The absence of a clear clinical guideline for a certain group of patients

(e.g. elderly) can be an important cause of variation in patterns of care. Moreover, there are no studies available that provide evidence for process indicators really discriminating between high- and low quality of care (construct validity). Therefore, comparing quality by oversimplifying the clinical process using a few measurable aspects of care might not be feasible. On the other hand, process characteristics can have an intrinsic value for patients, without a direct relationship with *clinical* outcome, e.g. limited waiting times, assistance by case managers, shared decision making. As mentioned above, a multi-dimensional approach of quality, in which patient preferences and experiences are combined with clinical outcomes, might give a more sound view on health care quality (Figure 3).

Clinical outcome

The ultimate outcome in (surgical) oncology is survival, in which also the 'quality of survival' has to be taken into account. In cancer surgery irradical resections can reduce survival and adverse events do affect patients' quality of life. Unfortunately, patient reported outcomes after cancer surgery are not yet available on such a scale that they can be used in routine outcome monitoring. Nevertheless, direct outcome measurements are preferable in the evaluation of quality, not in the least because they are face-valid for physicians as well as patients. Though, there are several limitations to direct outcome measurement. First, relevant casemix-factors should be available to make reliable outcome comparisons between institutions **[this thesis]**[5]. Recently, we published data from the Dutch Surgical Colorectal Audit in which an extensive set of casemix-factors is collected to be able to adjust hospital-specific complication and mortality rates for colorectal cancer surgery[36]. The expected mortality, based on patient- and tumorcharacteristics of groups of patients treated in Dutch hospitals ranged from 1.5 to 14 percent[36]. Surprisingly, in the Netherlands the majority of high-risk coloncancer patients, with an unfavorable expected mortality, are not treated in high-volume, but in low-volume hospitals. And high-risk rectal cancer patients are treated in non-teaching instead of academic hospitals. These findings underline the need for proper casemix-adjustments in the evaluation of quality of care. Second, when evaluating differences in outcome between institutions, the reliability of these comparisons is largely dependent on sample sizes. For low-volume cancer procedures the number of cases per hospital (denominator) and the number of complications (nominator) can be too small to evaluate quality of care within a reasonable period of time[37]. Moreover, in quality assessment various outcome parameters can interact. For example, complication rates after colorectal surgery can be reduced substantially by omitting a primary anastomosis and performing a colostomy in the majority of patients. Likewise, local recurrence rates of patients with advanced rectal cancer can be improved with neo-adjuvant chemoradiation, though radiation may lead to more perineal wound complications. Such improvements in outcome on one parameter (anastomotic leakage and local recurrence rates) at the expense of another (colostomy and wound complication rate) asks for a more comprehensive approach in outcome assessment. The combination of different case-mix adjusted outcomes in quality measurement can provide a better construct validity, by taking a greater proportion of relevant quality

measures into account and possibly also a better criterion validity, being better able to discriminate between hospitals with better and worse overall quality **[this thesis]**.

Improving quality

Acknowledging the differences in the quality of (infra)structure, care processes and outcome for cancer patients, efforts to reduce undesired variation could lead to real benefits for the whole patient group. Traditionally, improvement of quality of surgical care on a national level is the domain of professional organizations like the Association of Surgeons in the Netherlands. Until recently, quality improvement efforts were based on the transfer of knowledge and skills through surgical education and training, the development of evidence-based guidelines and the organization of scientific meetings. In addition, periodical consultation of teaching hospitals was performed to guarantee the quality of surgical training.

Guideline adherence

Despite these initiatives, actual information on variation in quality of care in routine practice is generally lacking. The implementation process following development of evidence-based guidelines is seldom monitored and reasons for non-adherence are largely unknown. The gradual introduction of studies comparing outcomes between providers has changed this situation and gave rise to more and more research groups evaluating hospital-variation in quality of care, also in the Netherlands[38,39]. Despite important variation in outcomes identified for high-risk cancer procedures performed in high- and low-volume hospitals, for a long time no changes in referral patterns were seen in our country[40]. The regionalization project for esophageal cancer surgery described in this thesis proved to be an exception, showing actual changes in referral patterns and marked improvements in outcome in comparison to the national average **[this thesis]**[11]. The major difference of this successful regional intervention with other centralization initiatives was that it was accompanied by a routine data collection system, to monitor guideline adherence and outcomes of participating hospitals in the region (clinical audit). Risk-adjusted outcome data were fed back to the participating surgeons and hospitals. Important differences in quality of care were revealed which led to actual changes in referral patterns and marked improvements in outcome **[this thesis]**[41].

Selective referral

The potential benefits of selective referral of patients to hospitals with better outcomes has been speculated upon by many authors[10]. In response to an Institute of Medicine report on building a safer healthcare system[1], in 2000, several large employers in the United States formed the Leapfrog group. The objective of Leapfrog is to improve the quality and safety of medical care and steering surgical patients to hospitals likely to have the best results, is one of their instruments. Since 2003 Leapfrog has a volume standard for esophagectomy (>13/year), which was recently evaluated in Washington state. This investigation showed

that on average Leapfrog hospitals had lower risk-adjusted mortality rates, though between hospitals meeting the Leapfrog standard there was still important variation in outcomes, including a 5-fold variation in mortality[42]. Apparently, procedural volume as a proxy for quality of care falls short in identifying hospitals providing 'excellent' care. Recently, Simunovic et al. published the results of centralization of pancreatic surgery in two provinces in Canada, Ontario and Quebec[43]. In a 10 years period, pancreatic surgery was concentrated in high-volume hospitals in both provinces to the same extent. However, only in Ontario this resulted in actual improvement in outcomes of pancreatic surgery patients. The difference was that in Ontario centralization was accompanied by an audit of results, which were fed back to participating surgeons. The parallel with the outcome-based centralization project for esophagectomies described in this thesis is striking and was noticed by *Birkmeyer et al.* who concluded that adequate hospital caseloads are important for achieving safe surgery, but not necessarily sufficient: *'to ensure acceptable mortality rates, high volume surgeons and hospitals should actively monitor their outcomes and benchmark their performance against their peers'* [44].

Quality assurance

An alternative approach to selective referral, are strategies that aim to improve quality of care in *all* hospitals treating a certain patient group. Such an approach seems most appropriate for high-volume cancer surgery performed in significant volumes by almost all hospitals, like breast and colorectal cancer surgery. Though, given the remarks of *Birkmeyer et al.* mentioned above, also low-volume cancer surgery might benefit from a strategy that sets quality standards that are continuously monitored.

Quality assurance is such a strategy and focuses on the implementation and monitoring of a complete set of systematic actions that is required to achieve a certain standard of care. Since variability in skills and techniques performed by surgeons can lead to irreproducible results, quality assurance is used in clinical trials, in which the quality of surgery is essential for the outcome[45]. Therefore, to reduce variation, participating surgeons are trained to perform the procedure in an identical way. Yet, quality assurance is not necessarily limited to the surgical aspects of treatment; it is a complete set of measures required to achieve a treatment result that meets a certain standard[46]. For example, quality assurance was integrated in the Dutch TME trial, in which a new surgical technique was used in rectal cancer resections by all participating surgeons[47]. It was considered crucial that the study was quality controlled. To train the surgeons, workshops, videotapes and instructors supervising the first 5 operations were used. Also, for radiotherapy exact descriptions of dose, volume, fields and simulation techniques were used and for pathology a strict protocol was dictated, which gave the surgeons immediate feedback on their performance. The quality assurance in this trial proved to be very successful: local recurrence rates were reduced by 50% compared to historical data[48]. The association between circumferential resection margin (CRM) involvement and outcome (local recurrence, survival) demonstrated

the importance of this parameter in evaluating surgical performance, not only in trials, but also in daily practice[49].
The question is: shouldn't adequate quality control on how diagnostic procedures and treatments are performed be an integrated part of daily medical practice?

Clinical audit
An instrument that combines the relative merits of monitoring guideline adherence, quality assurance, outcome measurement and selective referral is clinical audit. Clinical audit as a quality improvement tool was first defined by Ernest Amory Codman, a surgeon at the Harvard university hospital in 1912: *'the systematic critical analysis of the quality of medical care, including the procedures used for diagnosis, treatment and resulting outcome for the patient, carried out by those personally engaged in the activity concerned'.* In Healthcare, clinical audits can be carried out on different levels, on the level of a clinical department, on a hospital, regional or national level. There are different types of audits. First, those that focus on individual cases, with an unexpected or adverse outcome, which are peer-reviewed by a multidisciplinary team to reflect on the way the team functioned and to learn from in the future. An example of such a 'significant event audit', though on a national level, is the Dutch Surgical Adverse Outcomes Registry (Landelijke Heelkundige Complicatie Registratie)[50]. Another type, is the 'standards-based audit', using an audit-cycle that involves the definition of quality standards, collecting data to measure current practice, setting benchmarks and implementing improvements (Figure 4). This concept of auditing is closely related to quality assurance and provides continuous feedback on a set of quality standards and outcomes to the participating clinicians.
Recently, we performed a systematic review on the outcome of clinical audits reported in the literature, that showed that audit and feedback of quality information has a positive effect on the quality of surgical care [51]. This conclusion is supported by the results of nationwide clinical audit programs that have been developed in the United States and Western Europe in the last two decades[52,53]. In Norway local recurrence rates dropped from 28 to 7% as a result of a national audit program for rectal cancer surgery [54]. In the United States the National Surgical Quality Improvement Program (NSQIP) that began more than 20 years ago in the Veterans Affairs hospitals, reported marked reductions in morbidity (45%) and mortality (27%) after surgery in the participating hospitals[52]. This is accomplished by a peer-controlled program of continuous and timely feedback of case mix adjusted outcomes of surgical care. Recently, similar results have been shown after adoption of the NSQIP program by the private sector[55].
The reason for clinical auditing being a powerful instrument for quality improvement is found in the combination and integration of several quality improvement tools. First, the peer-controlled development of datasets covering a set of quality standards based on evidence-based guidelines, explicates which aspects of the care process are believed to be essential for optimization of clinical outcome. Through the data-collection as well as the -reporting process these sets of standards are spread within the surgical community

Figure 4. Audit cycle in a standards-based clinical audit

(knowledge transfer). The continuous data-collection, often executed or supervised by the clinicians themselves, gives constant attention to these quality aspects. In addition, clinicians are provided with rigorous feedback of their outcomes relative to those of their peers (benchmarking). That feedback itself can be very effective in improving outcome was shown in New England, United States, were mortality after CABG fell with 25%, almost immediately after feedback was given to thoracic surgeons[56]. This surgical "Hawthorn effect" has been observed by many of the starting clinical audits, though can be strengthened if feedback is accompanied with benchmark information and meaningful suggestions for improvement[51]. The remarkable success of the centralization process, linked to a regional audit for esophagectomy, as was described in **this thesis**, can be considered as additional proof for this concept[41].

Understanding variation

Next to its direct influence on quality of care, one of the most important side-effects of the development of nationwide data-collection systems, is the detailed clinical information that is retrieved by these clinical audits. Apart from quality assurance and the initiation of local improvement initiatives, reliable databases with essential information on (differences in) care processes and outcome may move the whole medical field forward. Recognizing groups of patients at risk for adverse outcome, revealing the underlying mechanisms and identifying processes of care with better outcomes, are the central issues in outcomes research (Figure 5). The ultimate goal is to transfer best practices found in centers with excellent results to all hospitals treating these patients. For example, Ghaferi et al. reported recently on hospital differences in mortality after esophagectomy, gastrectomy and pancreatectomy[57]. They found that complication rates did not differ largely between hospitals. Instead, differences seemed to be associated with the ability of a hospital to effectively rescue patients once

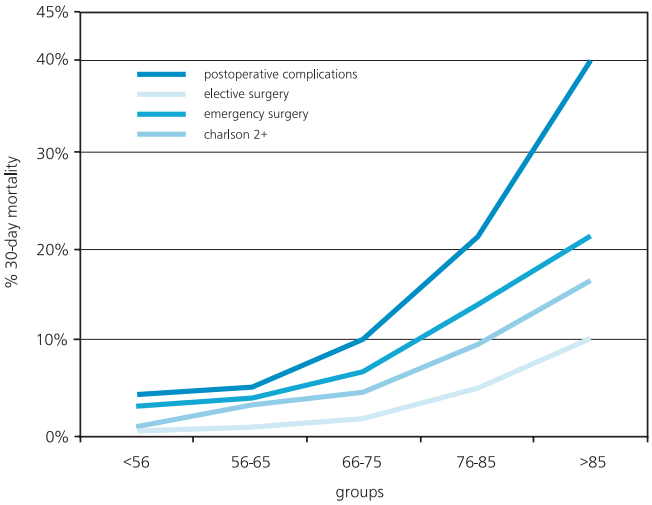

Figure 5. The merits of clinical auditing: identifying high risk patients for postoperative mortality after colorectal cancer resection (source: Dutch Surgical Colorectal Audit)

complications occur (failure to rescue). The adequate way clinical teams in hospitals with low mortality rates react on symptoms or signs of complications, may be of benefit for all patients having this kind of surgery.

Transparency

It is generally believed that transparency in hospital-specific quality information, catalysts quality improvement. Additional to the benefits of clinical auditing, public reporting of a hospitals' outcomes could stimulate improvement initiatives in under- as well as good performing hospitals. Moreover, transparency could steer patients to the hospitals with better outcomes for certain kinds of procedures, given these the opportunity to specialize in treating such a group of patients.

A recent report of the *Boston Consulting Group* has compared the availability and transparency of reliable quality information between Sweden and the Netherlands[58]. In Sweden, there are 82 national registries collecting detailed data on quality of care for a broad spectrum of diseases, on average covering 70% of patients diagnosed. With these registries, developed and controlled by medical specialists, Sweden is the worlds' front runner in the transparency of hospital-specific outcome-information.

The transparency paradigm

Transparency has different levels, first hospital-specific outcome information can not be available at all, also for the clinicians involved. Second, clinicians know their own results, though do not share it with their environment. Third, clinicians share this information with patients in their daily practice to inform them on the morbidity and mortality of medical procedures. Fourth, clinicians have outcome-information and share that with their peers, within or outside the hospital, for example in regional networks like that of the comprehensive cancer Leiden **[this thesis]**, though also sharing information with referring centers or family physicians is possible. Fifth, clinicians share their outcome information with the management

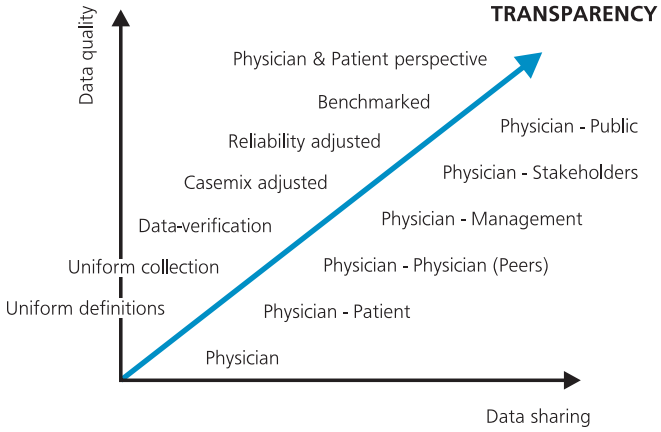

Figure 6. Transparency paradigm for hospital-specific outcome-information: degree of data-quality and data-sharing determines transparency level.

of their institution . And sixth, with (external) stakeholders like their professional organization or payers; for example in the negotiations with insurance companies. Finally, hospital-specific (or clinician-specific) outcome information is publicly available.

These 7 levels of transparency are meaningless if they are not accompanied with an appreciation of the quality of information. Good outcome information is meaningful, reliable and comparable. It's generally believed that the relevance of outcome-indicators is best appreciated by those directly involved in the clinical process: patients and their doctors. Therefore, most successful outcome-registries are developed by clinicians and their professional organizations, though often lack direct patient involvement. Consequently, patient reported outcomes (PROMS) are seldom collected. Reliable outcome information is best retrieved using uniform definitions and preferably data is quality controlled. As stated before, in the comparison of providers, adjustments for differences in casemix **[this thesis]** and chance variation are essential. Moreover, to be meaningful, outcome-information has to be compared (benchmarked) with information of other providers treating the same patient group.

These criteria for good outcome information can be combined with the levels of transparency identified above, into a transparency-paradigm (Figure 6). According to the *Boston Consulting Group* report, Swedish healthcare is at the highest transparency level for several diseases, though a clear insight in the quality of quality information is not provided by the authors[58]. The alleged benefits of open reporting are closely associated with the quality of the outcome information presented to the public. Since, transparency can very easily turn into a risk for quality of care, when inaccurate data wrongly stigmatize and demoralize hospital staffs and unnecessarily decrease patients' confidence in a particular hospital or healthcare in general[59].

Transparency in the Netherlands

In the Netherlands, the Healthcare Inspectorate introduced performance indicators for hospitals in 2003, which are publicly reported. In addition, a nation-wide quality indicator program, Zichtbare Zorg Ziekenhuizen, has been launched by the Dutch government, to reveal hospital-specific quality information for patients and payers. Only a minority, 16 %, of

these indicators is outcome-based, the quality of self-reported hospital-data is not controlled and the lack of information on differences in casemix undermines the reliability of indicator results[58]. Nevertheless, these government-initiated efforts to enhance transparency in quality of care in the Netherlands, has raised awareness of clinicians and their professional organizations which led to a number of bottom-up initiatives. For example, a Dutch Surgical Colorectal Audit was initiated by the Dutch College of Surgeons to collect reliable data on all patients in who a resection of a primary colorectal cancer was performed in our country[60]. This nation-wide peer-reviewed quality-controlled outcome-based and casemix-adjusted clinical audit program, feeds back benchmarked information on the quality of colorectal cancer treatment to the participating surgeons. All hospitals participate and data are validated by the Netherlands Cancer Registry, suggesting a 95% completeness on a population-level in 2011[36]. An extensive set of outcome indicators is reported, including radicality of resections, complications and mortality after colorectal surgery. However, in addition care processes are monitored by process indicators to identify shortcomings as well as best practices. At this moment, three other clinical audits, for breast-, lung- and upper-gastrointestinal cancers, have been initiated in the Netherlands, consistent with the formula of this colorectal audit[51]. A number of quality indicators from these reliable data-sources are reported publicly through the Zichtbare Zorg Ziekenhuizen program, improving transparency of Dutch healthcare.

Measuring improvement

Through the improvement-cycle and transparency of hospital-specific quality information, clinical auditing can reduce variation and lead to an overall improvement in quality of care. In its first 3 years, feeding back benchmarked information on guideline adherence lead to remarkable reduction of variation between hospitals in the Dutch Surgical Colorectal Audit (Figure 7). The quality improvement curve did not only shift right, but also narrowed, meaning that high quality care – based on evidence-based guidelines - was optimized for the whole group of colorectal cancer patients (Figure 8). In addition, significant improvements in outcome after colon cancer surgery were shown, with a more than 20 percent drop in the risk for postoperative mortality and 14 percent reduction in the risk for severe postoperative morbidity.

Health care costs

In many western countries the costs of healthcare are rising exponentially, as a consequence of demographic developments, technological advancements and increased healthcare consumption. Consequently, finding more efficient ways to provide high-quality care is high on the political agenda. Although, clinicians tend to avoid discussions about the costs of their medical actions, quality and costs of care are closely related. Improvement of patient care, by reducing complication rates proves to reduce costs[61]. Pay-for-performance initiatives in the United States are aimed at process compliance to achieve rapid and significant quality improvement. For example, in Michigan, a financial incentive to promote that every

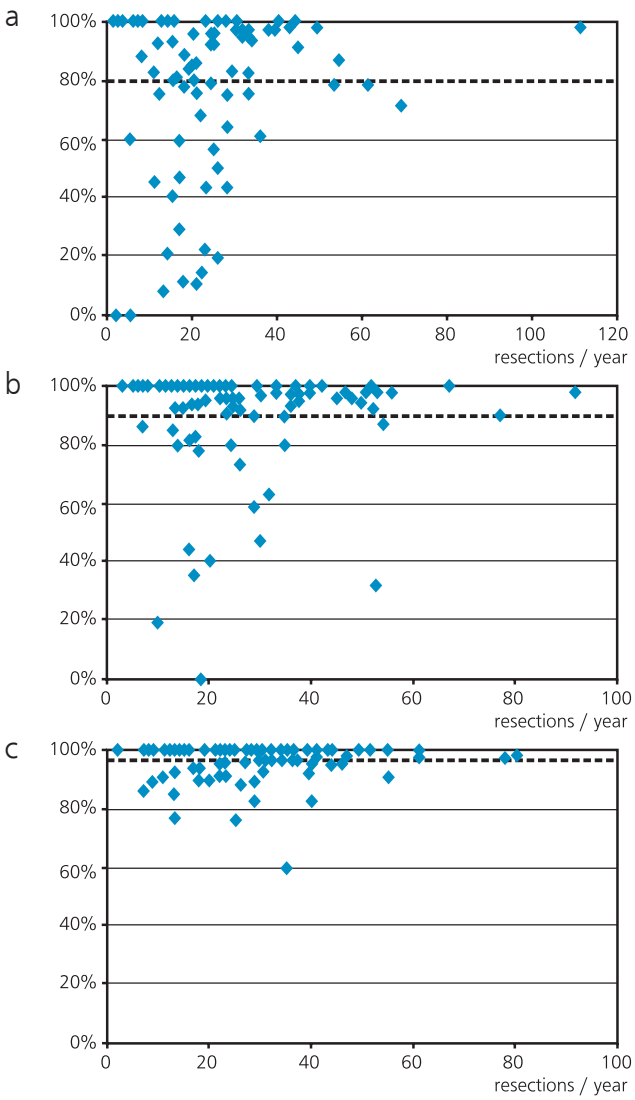

Figure 7. Improvement in guideline adherence: reduction of hospital variation and improvement of average hospital performance on the quality indicator ' percentage of rectal cancer patients discussed in a pre-operative multidisciplinary meeting ' in the Dutch Surgical Colorectal Audit in 2009 (Figure 7a), 2010 (Figure 7b) and 2011 (Figure 7c).

colorectal surgery patient received an appropriate antibiotic within 60 minutes before incision, increased from 70 to more than 95%, virtually over night[24]. Despite, empirical proof that paying for quality leads to actual improvement in outcome, is lacking[62].

To discover how a limited health care budget is spent best, we need information on the value of health services for patients. *Porter et al.* defined *value* in health care as outcomes relative to costs. The proper unit for measuring *value* should encompass the whole process of care, completed with short-term as well as long-term outcome information. According to *Porter*, outcome measurements should include risk-adjustments and in the complexity of the clinical process competing outcomes should be weighed against each other. This calls for an integrated approach, in which quality information for the whole care process – from a

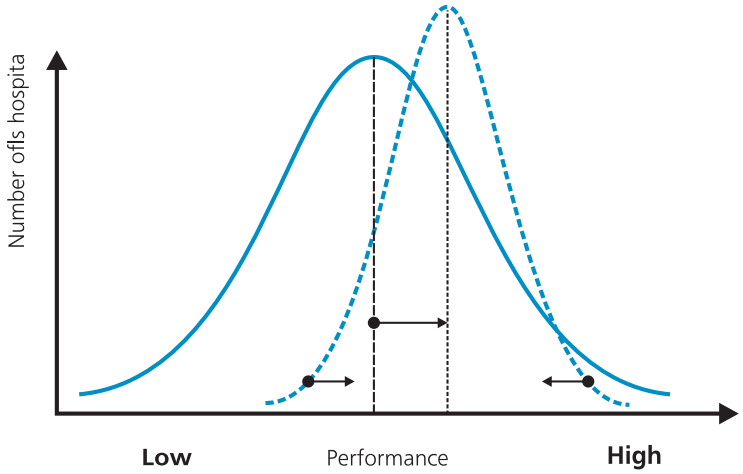

Figure 8. Quality improvement curve: reduction in hospital variation and improvement o f average hospital performance

physicians as well as a patients' perspective - becomes available and can be weighed against costs. Combining cost-information with the risk-adjusted outcomes acquired in clinical audits can provide a transparent view on the value of health services in the Netherlands.

Conclusion

This thesis shows that quality of care in surgical oncology varies by provider and is partly based on differences in procedural volume and other attributes of hospitals. Especially for low-volume high-risk surgical procedures concentration of services in hospitals with better outcomes (outcome-based referral) can lead to dramatic improvement in short- as well as long-term outcomes. Casemix- and reliability adjustments are essential in the evaluation of quality of care. In addition, an integrated approach, in which several determinants of outcome are combined, might provide a more valid instrument to assess the quality of complex clinical processes.

Clinical audit combines several ways to improve quality of care. It stimulates guideline adherence and provides clinicians with continuous and timely feedback on their performance, in relation to a national benchmark. Feedback itself has proven to be very effective, though the most important benefits of clinical audit can be found in the identification and appreciation of clinical processes that lead to better outcomes. This knowledge can be transferred to all practices treating such patient groups, improving outcome on a population-level. In addition, transparency of reliable, meaningful, hospital-specific outcome information, can catalyst the continuous process of quality improvement, steer patients to the right hospitals and reduce the costs of healthcare.

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Samenvatting

Meten en verbeteren van kwaliteit van zorg in de Chirurgische Oncologie

De Nederlandse gezondheidszorg staat voor grote uitdagingen. In de afgelopen twintig jaar zijn de medische wetenschap en technologie met sprongen vooruit gegaan, maar is de zorg ook in toenemende mate multidisciplinair en complex geworden. Dit geldt bij uitstek in de kankergeneeskunde, waar de snelheid van de ontwikkelingen een voortdurende evaluatie van de zorg nodig maakt. Het aantal kankerpatiënten neemt snel toe met tegelijkertijd een toename van het percentage ouderen met kanker. Doordat zij naast hun ziekte, vaak ook meerdere chronische aandoeningen hebben, nemen de risico's van kankerbehandelingen fors toe. Daarnaast worden de zorgprocessen steeds ingewikkelder, bijvoorbeeld door toegenomen diagnostische mogelijkheden, multidisciplinaire samenwerking, multimodaliteits behandelingen, en zogenoemde 'targeted drugs'. Deze toegenomen complexiteit vraagt om specifieke kennis, ervaring en infrastructuur in de ziekenhuizen die deze moderne kankerzorg verlenen. Bovendien is er meer en meer aandacht voor de veiligheid, effectiviteit en patientvriendelijkheid waarmee de zorg geleverd wordt, waarbij ook de beheersing van de stijgende zorgkosten hoog op de politieke agenda staat.

Volume en uitkomst

Aan het eind van de vorige eeuw verschenen er in de medische literatuur een aantal artikelen die verschillen in postoperatieve sterfte rapporteerden tussen ziekenhuizen waarin bepaalde kankeroperaties vaak (hoogvolume ziekenhuizen) en minder vaak, of zelfs zelden uitgevoerd werden (laagvolume ziekenhuizen). Aanvankelijk was er veel kritiek op deze volume-uitkomst studies omdat zij gebaseerd waren op administratieve in plaats van klinische gegevens en niet corrigeerden voor verschillen in zorgzwaarte tussen de onderzochte ziekenhuizen (casemix-correcties). Bovendien werden alleen verschillen in postoperatieve sterfte onderzocht, terwijl ook lange-termijn overleving en kwaliteit van leven belangrijke uitkomsten van kankerzorg zijn.

Onze studie naar de kwaliteit van slokdarmkanker operaties in de regio van het Integraal Kankercentrum West, welke destijds 11 ziekenhuizen in de regio Leiden, Den Haag, Delft en Gouda omvatte, toonde aan dat er inderdaad aanzienlijke verschillen in zorgzwaarte zijn tussen ziekenhuizen die slokdarm kankerpatiënten behandelen **(Hoofdstuk 3).** Omdat voor dit onderzoek gebruik werd gemaakt van klinische gegevens, verkregen uit de statussen van patiënten die tussen 1990 en 1999 behandeld werden in deze 11 ziekenhuizen, was het mogelijk om voor deze zorgzwaarte verschillen te corrigeren. Bovendien konden naast postoperatieve sterfte, ook andere zorguitkomsten worden onderzocht, zoals complicaties, heroperaties, opnameduur, radicaliteit van de resectie en lange termijn overleving van patiënten.

Er bleken aanzienlijke verschillen in zorguitkomsten tussen de 11 ziekenhuizen in de regio. Een vergelijking met het dichtstbijzijnde hoogvolume centrum voor slokdarmchirurgie

toonde bovendien aan dat er ook in zuid-west Nederland sprake was van een relatie tussen hoog volume en betere zorguitkomsten.

Literatuurstudie

Ook in de wetenschappelijke literatuur nam het aantal studies dat een volume-uitkomst relatie onderzocht snel toe. Vooral complexe hoog-risico operaties, zoals slokdarm- en alvleesklieroperaties, waren het onderwerp van deze onderzoeken. Onze literatuurreview en meta-analyse van studies naar ziekenhuis- en chirurg-volume voor slokdarmoperaties enerzijds en uitkomsten zoals postoperatieve sterfte en overleving anderzijds, was de eerste die alleen onderzoeken van hoge kwaliteit includeerde **(Hoofdstuk 2)**. Alleen als er gecorrigeerd werd voor verstorende factoren, zoals verschillen in casemix tussen ziekenhuizen, werden studies in de meta-analyse meegenomen. De meta-analyse leverde het bewijs dat ziekenhuisvolume een belangrijke determinant is van goede uitkomsten van operaties voor slokdarmkanker.

Centralisatie

De gegevens uit de regio van het Integraal Kankercentrum West (IKW) suggereerden dat het verwijzen van patiënten naar een hoogvolume ziekenhuis voor slokdarmoperaties zou kunnen leiden tot betere zorguitkomsten. In de regio waren er echter geen ziekenhuizen die meer dan 7 slokdarmoperaties per jaar verrichtten. Het professioneel netwerk van kankerchirurgen besloot daarom een 'clinical audit' uit te voeren, waarbij gedurende 5 jaar de patiënten-, tumor-, behandelingsgegevens en uitkomsten van zorg van alle slokdarm kankerpatiënten in de regio verzameld, geanalyseerd en teruggekoppeld zouden worden binnen het netwerk. Deelname aan deze audit was vrijwillig, maar niet vrijblijvend: wanneer er verschillen in zorguitkomsten zouden worden geconstateerd, zouden patiënten voortaan verwezen worden naar de ziekenhuizen met de betere uitkomsten (uitkomst-gestuurde centralisatie).

De uitkomst van deze interventie in de IKW regio was uitermate onzeker. In de literatuur waren er verschillen tussen groepen hoogvolume en laagvolume ziekenhuizen aangetoond, maar het was destijds onvoldoende duidelijk of het verwijzen van de patiënten uit laagvolume naar hoogvolume ziekenhuizen ook daadwerkelijk betere uitkomsten voor de gehele groep op zou leveren. In de periode 2000 tot 2004, werden de resultaten van de slokdarmchirurgie halfjaarlijks teruggekoppeld aan de slokdarmchirurgen in de regio, waarbij men inzicht had in elkaars resultaten. Er waren aanzienlijke verschillen in percentages complicaties, heroperaties, opnameduur, radicaliteit en sterfte. Dit leidde binnen 5 jaar tot het centraliseren van slokdarmoperaties in 4 en later 3 van de 11 ziekenhuizen in de regio. De uitkomsten verbeterden in deze periode aanzienlijk, waarbij de postoperatieve sterfte werd verlaagd van 12 naar 4 procent, maar ook de lange-termijn overleving van patiënten significant verbeterde **(Hoofdstuk 4)**.

Volume of uitkomst-sturing

Het succes van deze 'clinical audit' voor slokdarmoperaties in de IKW regio riep de vraag op of concentratie van zorg op basis van volume-criteria zou moeten gebeuren, of dat patiënten verwezen zouden moeten worden naar de ziekenhuizen met de beste uitkomsten. De bekende volume-uitkomst studies lieten zien dat ook binnen de groep ziekenhuizen in de hoogvolume categorie, er veel variatie in uitkomsten was tussen individuele ziekenhuizen. Volume is dus geen garantie voor kwaliteit! Om er zeker van te zijn dat centralisatie leidt tot betere uitkomsten zou men dus niet alleen op volume, maar ook op aantoonbaar goede uitkomsten van zorg moeten sturen.
Op basis van de volume-uitkomst studies in de literatuur, waarvan er ook enkele uit Nederland afkomstig waren, besloot de Inspectie voor de Gezondheidszorg in 2006 als prestatie-indicator een volumenorm voor slokdarmresecties in te stellen. Ziekenhuizen met minder dan 10 resecties per jaar moesten stoppen met slokdarmchirurgie en hun patiënten verwijzen naar ziekenhuizen die meer dan 10 resecties per jaar deden. Om een uitspraak te kunnen doen of deze specifieke volumenorm effectief zou kunnen zijn in het verbeteren van de uitkomsten van zorg voor slokdarmkanker patiënten in Nederland, deden wij een validatiestudie op basis van de literatuur en de gegevens van de Landelijke Medische Registratie. De resultaten in de verschillende volume categorieën onderzocht in de literatuur lieten zien dat vooral boven de 20 resecties per jaar een verlaging van postoperatieve sterfte verwacht mocht worden. Bovendien konden wij aantonen dat slokdarmresecties verricht in Nederlandse ziekenhuizen met 10 tot 20 van deze operaties per jaar, significant slechter waren dan de gemiddelde uitkomst in ons land **(Hoofdstuk 5)**.
Hier tegenover werden de resultaten in de IKW regio gezet in drie tijdsperiodes van 5 jaar. De eerste twee periodes, 1991-1994 en 1995-1999, gingen vooraf aan de 'clinical audit' in de regio. In de periode 2000-2004 vond de audit plaats. De IKW regio bleek in de eerste twee periodes aanzienlijk slechtere resultaten te hebben dan de andere regio's in ons land. Na 2000, ten tijde van de audit, verbeterden de resultaten echter zodanig dat de regio juist betere resultaten had dan het landelijk gemiddelde. Samenvattend legde deze studie bloot, dat 'volume' als afgeleide van kwaliteit, het risico met zich meebrengt dat patiënten worden verwezen naar ziekenhuizen met suboptimale uitkomsten. Het combineren van een minimale volumenorm met uitkomstnormen op basis van gegevens verzameld in een 'clinical audit', lijkt veel effectiever in het verbeteren van de zorg, dan het hanteren van een op zich staand volumecriterium.

Variatie in kwaliteit van kankerzorg

De eerste studies die variatie in kwaliteit van zorg tussen ziekenhuizen aantoonden, onderzochten de verschillen bij weinig voorkomende hoog-risico operaties, zoals slokdarm- en alvleesklierresecties. De logische vragen die vervolgens opkwamen zijn:

- Is variatie in kwaliteit van zorg ook aantoonbaar voor *hoog*-risico *hoog*volume operaties, of zelfs *laag*-risico *hoog*volume operaties?

- Is de variatie in kwaliteit van zorg alleen aantoonbaar voor het chirurgische deel van kankerbehandelingen of geldt het ook voor andere onderdelen van de behandeling zoals radio- en chemotherapie?
- Is de variatie beperkt tot ongewenste uitkomsten zoals complicaties en operatiesterfte, of betreft het ook andere aspecten zoals het percentage patiënten dat de optimale behandeling voor zijn/haar stadium van de ziekte krijgt?

Deze vragen werden onderzocht door de werkgroep Kwaliteit van Kankerzorg van de Signaleringscommissie van het Koningin Wilhelmina Fonds (KWF). De werkgroep voerde een uitgebreide literatuurstudie uit naar de relatie tussen volume en kwaliteit, maar onderzocht ook voor het eerst op landelijk niveau de variatie in kwaliteit van kankerzorg geleverd door Nederlandse ziekenhuizen. Hiervoor werden de op dat moment best beschikbare gegevens gebruikt, die van de Nederlandse Kanker Registratie (NKR). Variatie in kwaliteit werd onderzocht voor vijf tumorsoorten: borst-, darm-, endeldarm-, long- en blaaskanker. In dit proefschrift zijn twee van deze studies opgenomen, die voor long- en darmkanker, respectievelijk **Hoofdstuk 9** en **10.**

Voor patiënten met een laagstadium longkanker is een chirurgische resectie de optimale behandeling, met de grootste kans op lange-termijn overleving. Toch bleek er aanzienlijke variatie tussen Nederlandse ziekenhuizen, in het percentage laagstadium longkankerpatiënten dat een resectie onderging. Wanneer de diagnose werd gesteld in een ziekenhuis dat longchirurgen opleidt, of dat meer dan 50 longkankerpatiënten per jaar diagnosticeert, bleek de kans op een resectie groter dan in niet-opleidings of laagvolume ziekenhuizen.
Ook voor patiënten met een gevorderd stadium van de ziekte, bij wie een combinatie van chemo- en radiotherapie de grootste kans op overleving geeft, bestaan er ziekenhuisverschillen in het percentage patiënten dat de optimale behandeling krijgt.

Voor patiënten met darmkanker werden vergelijkbare kwaliteitsverschillen tussen Nederlandse ziekenhuizen gevonden. Bijvoorbeeld varieerde het aantal patiënten waarbij na de darmkankerresectie meer dan 10 lymfeklieren werd onderzocht en het percentage patiënten dat aanvullende chemotherapie kreeg. Patiënten die werden gediagnosticeerd in een academisch ziekenhuis of een ziekenhuis met meer dan 50 darmkankerdiagnoses per jaar, hadden een betere overleving.

Op basis van vergelijkbare resultaten gevonden bij de andere tumorsoorten die de KWF-werkgroep bestudeerde, concludeerde men dat er aanzienlijke variatie is in de kwaliteit van kankerzorg in Nederlandse ziekenhuizen. Die variatie was echter niet goed te duiden, omdat in de NKR onvoldoende gegevens aanwezig zijn ten aanzien van patiënt- en tumorkarakteristieken, zoals comorbiditeit, tumorcomplicaties en de urgentie waarmee de patiënt zich presenteert. Het rapport van de KWF-werkgroep ‘Kwaliteit van

Kankerzorg' werd gepubliceerd in de zomer van 2010. Het advies van de werkgroep was dat concentratie van kankerzorg plaats zou moeten vinden op basis van kwaliteitsnormen, betreffende de infrastructuur, het minimale volume en de specialismen die nodig zijn om in een ziekenhuis optimale kankerzorg te verlenen. Daarnaast zouden kankerspecialisten voortdurend op de hoogte moeten zijn van de resultaten van de kankerzorg die zij leveren, gecombineerd met landelijke spiegelinformatie, zodat verbeterpunten aangepakt kunnen worden ('clinical audit').

Kwaliteitsindicatoren

Om (verschillen in) kwaliteit van zorg zichtbaar te maken, zijn parameters nodig die iets zeggen over de kwaliteit van de geleverde zorg. In **hoofdstuk 7** wordt een systematische review van de literatuur beschreven, waarin wij zochten naar 'evidence-based' kwaliteitsindicatoren voor de behandeling van slokdarmkanker. De indicatoren werden onverdeeld in indicatoren betreffende de (infra)structuur van het ziekenhuis, de kwaliteit van het zorgproces en de zorguitkomsten. Het meeste bewijs werd gevonden voor structuurparameters, maar ook voor het optimale zorgproces waren een aantal indicatoren te definiëren, zoals het multidisciplinair bespreken van de behandelingsstrategie, voorafgaand aan de operatie. Voor uitkomstindicatoren was er sterk bewijs voor de uitkomsten die vastgesteld worden met pathologisch onderzoek, zoals de radicaliteit van een tumorresectie. Veel andere kwaliteitsaspecten zijn echter nauwelijks onderbouwd, en vooral gebaseerd op consensus binnen de beroepsgroep.

Afgezien van het feit dat het bewijs voor specifieke kwaliteitsindicatoren zeer beperkt is, kan er getwijfeld worden aan het concept van een enkele kwaliteitsindicator die de kwaliteit van een complex zorgproces weerspiegelt. Bovendien heeft het begrip kwaliteit meerdere dimensies: het gaat niet alleen om effectieve zorg, maar ook om zorg die veilig is, op tijd verleend wordt, op een patiëntvriendelijke manier, maar ook kosten-efficiënt. Vervolgens kan de kwaliteit van de zorg ook nog bekeken worden vanuit verschillende perspectieven, niet alleen vanuit die van de dokter, maar vooral ook vanuit het perspectief van de patiënt en zijn/haar omgeving.

Kwaliteit meten

De manier waarop kwaliteit van zorg gemeten wordt, wordt van oudsher bepaald door de gegevens die daar min of meer toevallig voor beschikbaar zijn. Door de introductie van klinische registraties ('clinical audits') in de Verenigde Staten en de landen in Noord-west Europa, is daar echter verandering in gekomen. In deze registraties worden gegevens verzameld met het specifieke doel om kwaliteit te meten en kwaliteitsverschillen tussen ziekenhuizen aan te tonen. Het gaat hierbij over het gehele zorgproces, waarbij een set van kwaliteitsaspecten wordt gedefinieerd die het gehele proces van diagnostiek en behandeling beslaat (quality assurance). Daarnaast worden zorguitkomsten geregistreerd, zowel voor wat betreft de *gewenste* (radicale resectie, overleving) als voor wat betreft de *ongewenste*

uitkomsten (complicaties, sterfte), van het zorgproces. Daarbij wordt er gecorrigeerd voor casemixverschillen tussen ziekenhuizen en de toevalsvariatie die vooral optreedt als het gaat om kleine aantallen patiënten per ziekenhuis of weinig voorkomende uitkomsten.

De gemeten uitkomsten worden vaak opzichzelfstaand gepresenteerd, wat geen recht doet aan het multidimensionele karakter van kwaliteit, zoals hier boven beschreven. Idealiter zijn verschillende aspecten van kwaliteit te combineren in een samengestelde uitkomstmaat, gecorrigeerd voor casemix en gewogen voor datgene wat patiënten belangrijk vinden, patientenpreferenties.
In **hoofdstuk 8** worden twee van deze samengestelde uitkomstmaten gepresenteerd. We laten enerzijds zien dat het mogelijk is om verschillende uitkomsten van zorg zodanig te rangschikken dat per ziekenhuis bepaald kan worden hoe vaak de *gewenste* uitkomsten gehaald en *ongewenste* uitkomsten vermeden worden. Het percentage patiënten bij wie alle uitkomsten positief zijn, wordt de 'Exemplary Care and Outcome' score genoemd. Daarnaast, wordt er een samengestelde maat geïntroduceerd waarin de uitkomsten gewogen kunnen worden op basis van patiënten- of dokterspreferenties. In beide gevallen is er een kwaliteitsmaat ontwikkeld die meerdere kwaliteitsaspecten combineert, en tegelijkertijd beter onderscheid maakt tussen de kwaliteit geleverd in individuele ziekenhuizen, dan op basis van een enkele uitkomstmaat mogelijk is.

Kwaliteit verbeteren

In Nederland spelen Wetenschappelijke Verenigingen van Medisch Specialisten een belangrijke rol bij het verminderen van variatie en verbeteren van kwaliteit van zorg, onder andere in de Oncologie. Er staan hen verschillende kwaliteitsinstrumenten ter beschikking. Voorheen beperkten die zich tot scholing, richtlijnontwikkeling en periodieke (kwaliteits) visitaties van klinieken. Na het verschijnen van het Kwaliteit van Kankerzorg rapport, heeft een aantal Wetenschappelijke Verenigingen, waar onder de Nederlandse Vereniging voor Heelkunde, het voortouw genomen om kwaliteitsnormen te formuleren, onder andere voor de Chirurgische Oncologie. Recent zijn die kwaliteitsnormen door de Samenwerkende Oncologische Specialismen (SONCOS) aangevuld tot multidisciplinaire normen. Bovendien hebben de 'clinical audits', die inmiddels opgezet zijn voor borstkanker-, darmkanker-, slokdarm-maag- en longkanker, de kwaliteitscirkel gesloten. Waar voorheen met opleiding, nascholing en richtlijnen, 'evidence based' kennis werd overgedragen, maar nauwelijks bekend was wat er in de dagelijkse praktijk gebeurde, is dit nu veranderd. Er is sprake van een geïntegreerd kwaliteitsbeleid (zie figuur 1), waarin van de 'evidence-based' richtlijn kwaliteitsnormen en –indicatoren worden afgeleid, die vervolgens op ziekenhuisniveau worden gemeten om de kwaliteit van het zorgproces te waarborgen ('quality assurance'). Bovendien worden ook verschillen in uitkomsten van zorg zichtbaar, en voor casemix gecorrigeerd teruggekoppeld aan de behandelaars, vergezeld van een landelijke benchmark ('clinical audit'). Dit leidt tot een continue verbetercyclus, die bovendien versterkt wordt door het 'surgical Hawthorne effect': een snelle verbeterimpuls geobserveerd in veel van

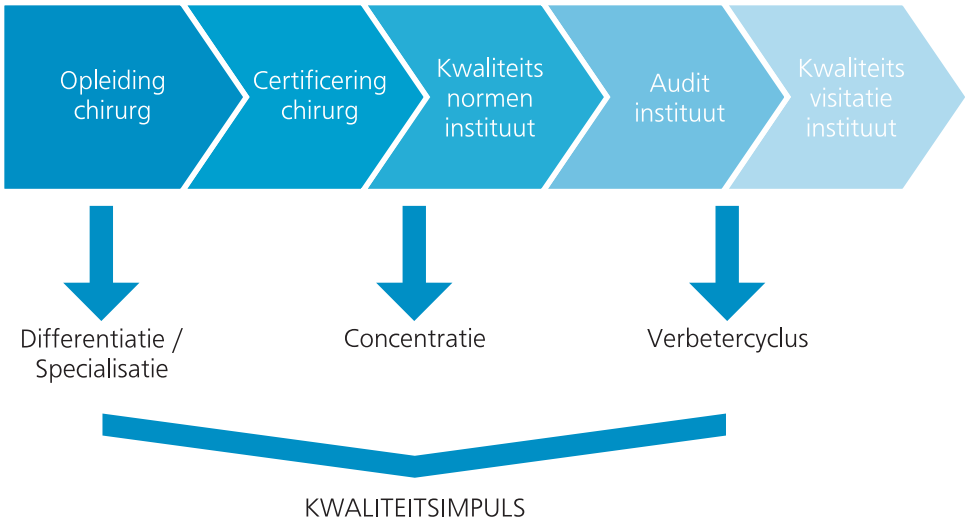

Figure 1. Geintegreerd kwaliteitsbeleid van de Nederlandse Vereniging voor Heelkunde

de startende audits. Dit effect wordt veroorzaakt door de aandacht die er ontstaat voor de kwaliteit van het zorgproces, en 'awareness' van groepen patiënten met een hoog risico op ongewenste uitkomsten.

Transparantie

Naast een interne verbetercyclus, is er ook een externe -cyclus gedreven door transparantie van ziekenhuisspecifieke kwaliteitsinformatie. Het publiek rapporteren van indicatorresultaten op ziekenhuisniveau is een krachtige stimulans voor ziekenhuizen om zichzelf te verbeteren. Bovendien kan deze informatie patiëntenstromen buigen naar de ziekenhuizen met de betere uitkomsten, wat hen weer de kans geeft zich verder te specialiseren in de desbetreffende behandeling.

In Nederland staan we echter nog maar aan het begin van echte transparantie. De mate waarin er sprake is van kwaliteitstransparantie is namelijk niet alleen afhankelijk van de bereidheid van medisch specialisten om hun resultaten te delen met collega's, patiënten, de ziekenhuisdirectie, zorgverzekeraars of patiëntenverenigingen, maar ook van de betrouwbaarheid van de verzamelde kwaliteitsinformatie. Het gaat dan om eenduidig verzamelde gegevens, met uniforme definities en inclusiecriteria, geverifieerd en gecorrigeerd voor casemix en toevalsvariatie, en gespiegeld aan de resultaten van anderen met een overeenkomstige patiëntengroep. Dat dit kan leiden tot snelle verbeteringen in de kwaliteit van de geleverde zorg, wordt bewezen door het audit-project voor slokdarmchirurgie beschreven in dit proefschrift **(Hoofdstuk 4, 5 en 6),** maar ook de resultaten van de Dutch Surgical Colorectal Audit, die sinds 2009 aanzienlijke verbeteringen in de uitkomsten van darmkankerchirurgie in Nederland laat zien. Niet alleen zijn de gemiddelde scores op een aantal kwaliteitsindicatoren landelijk aanzienlijk verbeterd, ook

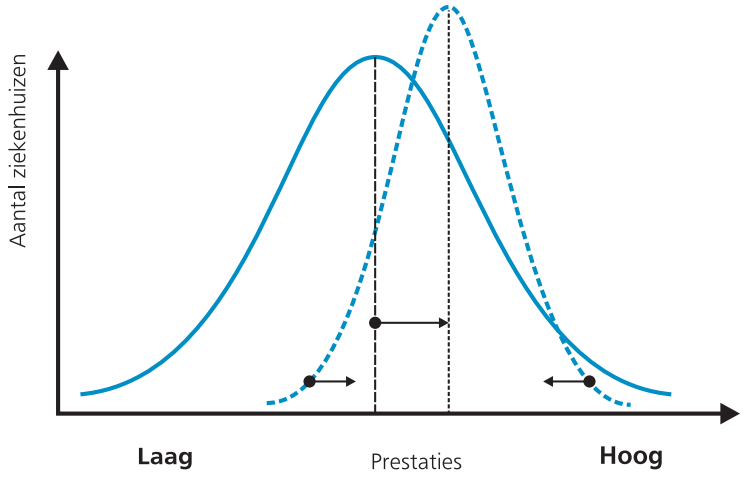

Figure 2. Klassieke kwaliteit verbetermodel: reductie in ziekenhuisvariatie en verbetering van gemiddelde ziekenhuisprestaties

de variatie in indicatorresultaten tussen ziekenhuizen is fors afgenomen. Dit is een voorbeeld van het klassieke kwaliteitsverbetermodel, waarbij de Gausse kromme niet alleen naar rechts verschuift, maar ook smaller wordt (figuur 2).

Conclusie

Dit proefschrift laat zien dat kwaliteit van zorg in de Chirurgische Oncologie varieert tussen ziekenhuizen, en deels gebaseerd is op volumina en andere structurele kenmerken van die ziekenhuizen. Vooral voor laagvolume hoog-risico ingrepen kan concentratie in ziekenhuizen met aantoonbaar goede resultaten een sterk kwaliteitsverbeterend effect hebben (outcome-based referral). Correcties voor verschillen in casemix en toevalsvariatie zijn essentieel voor het vergelijken van kwaliteit van zorg tussen ziekenhuizen. Bovendien zou een geïntegreerde benadering, waarin verschillende kwaliteitsaspecten gecombineerd worden tot een samengestelde uitkomstmaat, een meer valide instrument op kunnen leveren en kwaliteitsverschillen beter aan kunnen tonen.
Clinical audit combineert verschillende instrumenten om kwaliteit van zorg te verbeteren. Het stimuleert richtlijncompliance en voorziet clinici van continue en snelle feedback op hun prestaties, gespiegeld aan een landelijke benchmark. Daarnaast zorgt het voor transparantie van betrouwbare en betekenisvolle kwaliteitsinformatie op ziekenhuisniveau waarmee een continu proces van kwaliteitsverbetering tot stand wordt gebracht.

Curriculum Vitae

CURRICULUM VITAE

Michel Wouters was born in Rilland-Bath on May 4th 1967. He graduated from the St Willibrord College (Atheneum) in Goes in 1985. In the same year he started with his study Medicine at the Leiden University and passed his medical Masters degree in 1995, after writing a paper on 'Cost considerations in Health care' at the department of Medical Ethics of the Leiden University, supervised by professor dr Heleen Dupuis.

With this strong basis for a medical career he started his internships in 1995 and graduated *cum laude* in 1997. He performed his graduation project on 'Rationing health care: the role of costs in physicians treatment decisions', supervised by dr Danielle Timmermans and professor dr Job Kievit of the department of Medical Decision Making of the Leiden University Medical Center.

In 1997 he worked as a surgical resident in the IJsselland ziekenhuis in Capelle aan den IJssel with dr Eelco de Graaf, dr Geert Tetteroo and dr Imro Dawson. After six months he switched to the Leijenburg hospital in the Hague, were he worked under the supervision of dr Boy Bruijninkx and dr Willem Hans Steup. With dr Steup he developed the first ideas on a region-wide clinical audit for esophageal cancer surgery in 1998, which started in the region of the Comprehensive Cancer Center Leiden in 2000.

In 1999, he started his surgical training in the Leiden University Medical Center under the supervision of professor dr Onno Terpstra and after two years he continued his training in the Bronovo hospital in The Hague, where he acquired his surgical skills, teached by dr Bob van Rijn, dr Jisk Heslinga, dr Harm Smeets and dr Arthur Niggebrugge. In his last year of training, he specialized in surgical oncology and lung surgery, under the supervision of dr Onno Guicherit, dr Jisk Heslinga and dr Bob van Rijn.
During his surgical training he was a member of the board of the Association of Surgical Trainees in the Netherlands (VAGH). On behalf of the VAGH he organized two symposia in 2004, on 'Concentration of low-volume high risk surgical procedures' and 'Quality indicators for surgical procedures' respectively.

In 2005, after his registration as a general surgeon, he was offered a position as a surgical fellow in the Erasmus University Medical Center – Daniel den Hoed kliniek, under the supervision of professor dr Alexander Eggermont. He acquired additional skills and expertise in surgical oncology, working with dr Bert van Geel, dr Marian Menke-Pluijmers, dr Kees Verhoef and professor dr Hans de Wilt. In this period, his interest in surgical oncology, especially in the diagnosis and treatment of melanoma and chest wall tumors, was raised.

In January 2006, he decided to spent half a year on analyzing the results of the regional clinical audit for esophageal cancer surgery in the region of the Comprehensive Cancer

Center Leiden. He worked in the Leiden University Medical Center with dr Henrike Karim-Kos and wrote two articles on centralization of esophageal cancer surgery in the Leiden region, under supervision of professor dr Rob Tollenaar. One of these articles, the first in literature showing actual improvement in patient outcome after centralizing esophagectomies in specialized high volume centers, was awarded with the IQ scientific award of the Radboud University in 2010.
During this period, working with dr Eric-Hans Eddes and professor dr Rob Tollenaar, he also took part in the development of the first nation-wide clinical audit for colorectal cancer surgery in the Netherlands, the Dutch Surgical Colorectal Audit (DSCA), which was initiated in January 2009.

He started as a fellow in the department of surgical oncology of the Netherlands Cancer Institute – Antoni van Leeuwenhoek hospital in July 2006. Under the supervision of dr Houke Klomp and working with dr Johanna van Sandick he was trained in the surgical treatment of thoracic malignancies for a period of 2 years, after which he was offered a position in the staff of the department of surgical oncology lead by professor dr Bin Kroon. After professor Kroon emerited in 2008, he took over his position as a melanoma surgeon in the surgical staff of Netherlands Cancer Institute, presided by prof dr Emiel Rutgers. Until today, he works closely with his colleagues dr Omgo Nieweg and dr Jos van der Hage in the field of melanoma surgery.

Ever since his appointment in the Netherlands Cancer Institute, he continued his scientific work at the departments of Surgery and Medical Decision Making of the Leiden University Medical Center for one day a week, supervised by professor dr Rob Tollenaar en professor dr Job Kievit. In 2007 he was nominated in the working party 'Quality of cancer care' of the Signalling Committee Cancer of the Dutch Cancer Society, directed by professor dr Cornelis van der Velde. As a member of this working party he performed meta-analyses on the volume-outcome relationship in cancer treatments, together with drs Gea Gooiker, drs Willem van Gijn and dr Piet Post. In addition, working with epidemiologists of the Netherlands Cancer Registry, he analyzed variations in quality of care between hospitals in the Netherlands, especially the relation between hospital volume, teaching status and infrastructure on the one hand and patient outcome on the other.
Together with dr Marlies Jansen and dr Freke Kloosterboer he wrote the Quality of Cancer Care report of the Dutch Cancer Society, which was published in 2010. This report provided a road map for the concentration of complex cancer treatments in the Netherlands through the development of quality standards on infrastructure, minimal procedural volume, degree of specialization and organization and the realization of hospital-specific outcome monitoring in clinical audits.

To realize these goals set by the Dutch Cancer Society, he was appointed in the board of the Association of Surgical Oncologists in the Netherlands (NVCO) in 2010. With prof dr Jean

Klinkenbijl and prof dr Laurents Stassen he worked on the first quality standards for surgical cancer treatments, which were published by the Association of Surgeons in the Netherlands (NVvH) in January 2011.
In November 2010, he was elected President of the Association of Surgical Oncologists in the Netherlands and entered the board of SONCOS, a multidisciplinary cooperation of medical oncologists, radiotherapists and surgical oncologists. Together with prof dr Koos van der Hoeven (NVMO) and prof dr Marcel Verheij (NVRO), he established multidisciplinary quality standards for cancer treatments, the 'SONCOS kwaliteitsnormen', which were written down by dr Paul de Jong and published in December 2012.

In 2010, together with prof dr Rob Tollenaar and dr Eric-Hans Eddes he founded the Dutch Institute for Clinical Auditing (DICA). The objective of this organization is to initiate and facilitate web-based clinical audits for the monitoring, feedback, benchmarking and improvement of the care process and outcome of medical treatments. The blueprint of the Dutch Surgical Colorectal Audit was used to establish clinical audits in the field of upperGI cancer surgery, lung surgery, pediatric surgery, breast cancer treatment, melanoma treatment, vascular surgery, et cetera [www.clinicalaudit.nl]. As Chief of the Scientific Bureau of DICA, he leads a dedicated team of young investigators and bears responsibility for the development of quality indicators, web-based data-collection, analyses and feedback in the various clinical audits. He was the chief-editor of the DSCA reports in 2009 and 2010 and the annual DICA reports in 2011 and 2012.

In May 2012 he was elected in the board of the Association of Surgeons of the Netherlands, as the successor of dr Marie-Jeanne Baas-Vrancken Peeters as Quality Secretary, a position he holds until today.

Dankwoord

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Bij het onderzoek dat heeft geleid tot dit proefschrift heb ik samen mogen werken met een enthousiaste groep chirurgen, statistici, epidemiologen en arts-onderzoekers. Vooral de bereidheid van de chirurg-oncologen in de regio van het Integraal Kankercentrum West om kritisch te (laten) kijken naar de kwaliteit van hun dagelijkse werk, en daar ook consequenties aan te verbinden, heeft indruk op mij gemaakt. In die tijd is bij mij een passie voor kwaliteit en wetenschap ontstaan, die ik tot op de dag van vandaag deel met een aantal even bevlogen collega's.
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