High volume centers for esophagectomy: what is the number needed to achieve low postoperative mortality?

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SUMMARY. Aimed at reducing surgical deaths, several initiatives have attempted to establish volume-based referral strategies in high risk surgery. The detailed analysis of the literature of the last 10 years, comprising 13 papers on esophageal cancer, shows a clear reduction in postoperative mortality with increasing case volumes per year. Single papers have analyzed the main reasons for this phenomenon and showed that postoperative complication rates are lower in high-volume hospitals and management of complications is more successful. Further, long-term prognosis is also correlated to case-volume. In conclusion, the analysis shows that only with the experience of more than 20 esophagectomies per year can a significant reduction of the mortality, down to 4.9%, be achieved. Based on this survey, surgery of esophageal cancer is a task for high-volume hospitals because of decreased postoperative mortality and improved long-term prognosis compared with low volume hospitals.

KEY WORDS: esophageal cancer, esophagectomy, high-volume hospitals, meta-analysis quality control, mortality, prognosis.

INTRODUCTION

Esophagectomy is one of the most demanding surgical procedures performed. Despite substantial advances in preoperative risk evaluation, improved operative techniques and postoperative care, the inhospital mortality for esophageal resection remains high while the prognosis is still poor.1–3 Recent studies examining the relationship of volume and outcome for specific surgical procedures including esophagectomy have demonstrated a consistent improvement in clinical outcomes with increased hospital volumes.4–7 From this body of work a number of authors drew significant conclusions regarding the postoperative mortality of large-scale cancer operations. For example, Dudley et al. evaluated the clinical courses of 121,609 patients with 11 defined surgical conditions. Of these patients, 58,306 were treated in low-volume hospitals. The authors suggested that 602 patient deaths of the total patient cohort could be attributed specifically to the lower number of cases treated in the low-volume hospitals. Birkmeyer’s study, investigated the relationship between decreased mortality and increased volume of cases treated after 14 substantial operations, of which eight were cancer surgeries. In that study, he concluded, ‘Patients undergoing selected cancer procedures can significantly reduce their risk of operative death by selecting a high-volume hospital’.7

Contrary to this, the series of Gillison et al. showed little evidence of an improving trend in 30-day mortality rates with increasing workload, or between workload and long-term survival.9

Besides analysis of mortality, the long-term prognosis of patients as a result of case-volume comparisons has been investigated, as well as post-operative mortality, and cost analyses.9,10

In the present study, we discuss the published data examining the effect of case volume on patient outcome for patients with esophageal cancer treated with esophagectomy. Regarding the term ‘High Volume Center’ we further tried to establish a cut off point for esophagectomy-performing hospitals that makes a significant reduction of postoperative mortality most likely.
MATERIALS AND METHODS

Systematic review

To identify scientific articles to include in the meta-analysis, the researchers followed three steps: First, they conducted a search of several bibliographic databases (i.e. MEDLINE, Current Contents and First Search Social Abstracts) for studies conducted between 1990 and 2003. Keywords were: hospital, volume, outcome, mortality, risk and quality. Second, the investigators reviewed all references in the resulting articles to identify any studies that had not been found in the database search. And third, to ensure that the list of studies included was as complete as possible, the investigators conducted a manual search of the most relevant journals of epidemiology and medicine.

Each article identified by this search process was reviewed and included in the analysis if it reported the total number of esophagectomies and the mortality rate for a specified time span.

As a main outcome measure we used the perioperative mortality rate defined as the 30-day mortality rate or in-hospital mortality. In addition we analyzed the morbidity and long-term outcomes.

Two readers, who received no information on the names and affiliations of the authors of each study, independently determined the eligibility of each article for inclusion in the meta-analysis. When the results of a study were published in more than one article, only the most recent and complete article was included in the analysis.

Data extraction

The remaining articles for each condition were evaluated to identify the study most likely to yield an unbiased estimate of the effect of volume on mortality. This evaluation included consideration of study sample size, range of volume among the hospitals included in the study, risk-adjustment, location of the study and timeliness of data. According to the definitions in the literature we defined four levels of volume:

- Very low volume (VLV): less than 5 esophagectomies per year
- Low volume (LV): 5–10 esophagectomies per year
- Medium volume (MV): 11–20 esophagectomies per year
- High volume (HV): more than 20 esophagectomies per year.

In addition we analyzed the information gathered from the studies referring to the average mortality secondary to case volume. This allowed a continuous description of the relationship between the number of operations per year in each hospital and the mortality rate.

Statistical analysis

Statistical analysis was performed using the results of the mean/median and the lower and upper quartile of frequency in the above-defined groups. The Kruskal–Wallis analysis with a significance level of 0.05 was used to look for differences between the groups. Correlation between volume of cases treated and postoperative mortality was represented graphically by regression analysis. To find out the optimal cut-off point for hospital volume in relation to mortality rate we used the method of Receiver–operator curve (ROC). The area under the curve (AUC) and the 95% confidence-interval have been calculated. These analyses were done using the Statistical Software package SPSS for Windows Version 11 (SPSS Inc. Chicago, Illinois) and the Graphical Software package SigmaPlot 2002 for Windows Version 8.02 (SPSS Inc. Chicago, Illinois).

Meta-analysis

The meta-analysis was done according the proposal for observational studies. Given the obvious heterogeneity of the trials (time-span of surgery, cancer histology, risk-adjustment) we did not consider a fixed effects meta-analysis model to be methodologically sound, even if a test of heterogeneity was acceptable for some outcomes. Instead, a random effects model was used. This gives conservative confidence intervals and minimizes the risk of erroneously assigning benefit to the treatment group, if no benefit really exists. The analysis of variance was done using the Random-effect model according Mantel-Haenszel. As a measurement of effect-size of hospital volume to mortality rate we calculate the odds ratio (OR) and the 95% confidence interval (CI). Odds ratios are calculated as treatment (20 or more esophagectomies per year per institution) versus control (less than 20 esophagectomies per year per institution), so a number less than one favors the treatment group (lower mortality rate). Funnel plot analysis did not suggest publication bias against negative trials. The graphical presentation was done using the Forest-Plot for the selected studies. All calculations were done using the software Package Comprehensive Meta-Analysis, Biostat, Englewood, NJ, USA.

RESULTS

Thirteen studies were included. The study period of these papers included the years 1984–1998 (Table 1). Analyzing the mortality rate for different work-loads according the defined groups we found significantly higher median mortality rates in very...
low volume hospitals (median: 18.0%; LQ-UQ: 12.9–22.1%) and low volume hospitals (13.8%; 12.6–16.5%) compared to median volume (11.0%; 10.2–12.7%) and high volume hospitals (4.9%; 2.8–6.1%) (P < 0.001) (Fig. 1).

In Fig. 2 the distribution of the exact values for mortality rate and case load of esophagectomies per year and institution is shown according to the studies included. We calculated the AUC for different mortality rates using these data to minimize the postoperative mortality. We found the maximum of the AUC (0.94 and 95% CI 0.85–1.0) for mortality rate lower than 10%. The optimal cut-off level was 20 or more esophagectomies per year per institution with a sensitivity of 86% and specificity of 96%. In consequence of this result the meta-analysis was done comparing the mortality rate of hospitals with 20 or more esophageal resections and of hospitals with lower case loads.

Eight studies were usable for meta-analysis. Three studies had no data about the number of patients in each group, two further studies showed no data about hospitals with more than 20 esophagectomies. 

The results of the meta-analysis are shown in Fig. 3. Combining these eight studies yielded data on 18,032 patients with esophagectomy. The odds ratio (95% CI) expressed as hospitals with more than 20 esophageal resections per year versus hospitals with lower case load (treatment versus controls; values < 1 favor high volume hospitals) was 0.43 (0.31–0.58).

Regarding the influence of the case load on the overall prognosis of the patients, preliminary data from Wenner et al. also indicate a better outcome for patients treated in centers with an experienced surgical team.10

**DISCUSSION**

With regard to esophagectomy for patients with esophageal carcinoma, 13 studies between the years 1990 and 2003 were considered. As shown, the mortality rates correlate clearly with the case volume per year. In hospitals with less than five esophagectomies per year, there was a wide distribution of values for postoperative mortality, with a median value of 18.0%. Contrary to this, in hospitals performing more than 20 esophagectomies per year the median value reduced to 4.9%.

Our detailed analysis of the literature confirms the described trend from individual studies with a

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**Table 1** List of characteristics of the 13 selected papers

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<th>Region</th>
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<td>Wenner10</td>
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<td>Finlayson13</td>
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<td>Urbach14</td>
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<td>Dimick15</td>
<td>1994</td>
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<td>Birkmeyer7</td>
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<td>Kuo16</td>
<td>1992</td>
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<td>1984</td>
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clear correlation between case volumes treated and postoperative mortality rates. Moreover, the presented meta-analysis is the first study to show that it is necessary to perform at least 20 esophagectomies per year to reduce mortality to under 5%.

Dimick and Patti investigated the cause for this correlation and came to the following conclusion. Dimick showed that the complications after esophagectomy in high-volume centers in six investigated categories were significantly less severe than complications in the low-volume centers. The six categories observed were pulmonary complications, myocardial infarctions, renal complications, aspirations, re-intubations and surgical complications. Patti analyzed the incidence of infections or hemorrhage after esophagectomy, comparing four categories of case volumes. For both investigated parameters he could show that in the evaluated hospitals, the incidence of both complications was approximately equal. However, in the high-volume hospitals in spite of a similar rate of postoperative infection and hemorrhage as in the low-volume hospitals, there was a significantly decreased rate of mortality. This lead the author to the conclusion that the management of such complications is decidedly better in centers with higher case load, based on better training of the staff, especially in the operating room and the intensive care units, and the complications are therefore recognized earlier and treated more effectively.

Meanwhile there are also data available regarding the correlation between prognosis and case volume of esophagectomies performed per year. Comparing hospitals treating less than five cases, 5–15 cases, or more than 15 cases per year, Wenner observed 5-year survival rates of 17%, 19% and 22%. Between the 5-year survival rate from high-volume centers and low-volume institutions there was a significant statistical difference ($P = 0.02$).

This leads to the question, what should be the limit of cancer operations performed per year required to achieve good results concerning mortality and prognosis? At what level of frequency should a center feel justified to offer patients good quality of care? For esophagectomy, from several specialists in the field, different case volumes per year per institution (ranging from six to 50) were suggested. However, based on the detailed meta-analysis performed in this paper, the evidence indicates that some 20 or more esophagectomies per year per institution are necessary to promise a high probability of decreased postoperative mortality.

CONCLUSIONS

The foregoing analysis, involving operations for esophageal carcinoma, clearly correlated the relationship between case volume per year and postoperative mortality rates. For this type of surgery, there is clear evidence that with increased case volume postoperative complication rates are decreased and the long-term prognosis is improved. However, there is still a need to define a clear frequency cut-off at which a cancer center should feel justified to offer proper surgical treatment for esophageal cancer.

For esophageal carcinoma surgery investigated here, which is highly demanding for the surgeon and the entire team, the recommendation should be that this type of oncologic-surgery should be performed only by specialists who operate in high-volume...
hospitals with at least 20 or more cases per year. Only by consulting specialized teams experienced in esophageal cancer surgery do patients have a chance of decreased postoperative mortality with a better long-term outcome and survival.

References


