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#### Review

# Hospital esophagectomy volume and postoperative length of stay: A systematic review and meta-analysis

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#### ABSTRACT

*Background:* Much attention in the volume-outcomes literature has focused on the empirical impact of surgical caseload on outcomes. However, relevant studies on the association between surgical volume and variables that potentially contribute to healthcare costs are limited. The objective of this study was to systematically elucidate a contemporary analysis of the empirical relationship between hospital esophagectomy volume and postoperative length of stay, a cost-related outcome.

Data sources: OvidSP, PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), ISI Web of Science and OpenGrey were searched for relevant articles published from 2000 to 2016.

Results: High hospital esophagectomy volume was associated with reduced postoperative length of stay (mean: 3 days; 95%CI: 2.8, 3.2) and risk of prolonged length of stay (RR: 0.80, 95%CI: 0.74, 0.87) in a doseresponse fashion.

*Conclusions:* Complex surgeries performed at high surgical volume centers may be associated with overall decrease in postoperative length of stay, a cost-related outcome.

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#### 1. Introduction

Esophageal cancer is a disease of significant public health importance. It is the sixth most common cause of cancer death. Esophageal cancer predominantly affects middle-aged and elderly males, with a substantial burden in most continents of the world. Treatment is typically surgical resection with or without chemoradiation. Despite much technical and technological advancement, esophagectomies continue to represent huge costs to patients and to the healthcare system. 3,4

The volume-outcome field derives from the "practice makes perfect" hypothesis, which suggests that surgical quality may be a derivative of surgical volume. As a result, studies analyzing the empirical impact of surgical caseload have predominantly focused on clinical outcomes<sup>5–8</sup> with lesser academic attention paid to understanding the dynamics between surgical volume and healthcare costs. Relevant studies on the latter interaction are scarce and

The goal of this review was to systematically examine the relationship between hospital esophagectomy volume and postoperative length of stay, a cost-related outcome. An understanding of the magnitude of cost-reduction, if any, as a result of increments in hospital surgical experience may further incentivize health plans, purchasers and policymakers to devote resources towards centralization of high-risk surgical procedures such as esophagectomy. We examined esophagectomy because it has been fairly documented in the literature to be volume-sensitive. <sup>9–13</sup> Along similar lines, length of stay (LoS) and readmissions were examined given their significant relevance to overall hospital costs. 14,15 The differences between hospital charges and insurance reimbursements and the difficulty of ascertaining true hospital costs of surgeries from publicly available information make clinical parameters preferable. Specifically, we evaluated the hypothesis that increased hospital surgical volume may lead to a reduction in postoperative LoS and readmissions.

#### 2. Materials and methods

We followed the PRISMA and Cochrane guidelines in design, analysis and reporting of this study.

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available data have been largely inconsistent.

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#### 2.1. Criteria for considering studies for this review

We identified original research articles through a detailed search in electronic clinical databases such as OvidSP, PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and ISI Web of Science. Grey literatures were searched using OpenGrey (http://www.opengrey.eu). Database searches were conducted in April 2015 using a combination of free text words and medical subject headings (MeSH). The search algorithm combined components of the PICO (patient, intervention, comparator and outcome) question. No restrictions by study design, language or geographical area were done. A search diary was maintained to document keywords, databases and search results. We checked the reference list of included studies for similar studies. We also used the 'related articles' function in the databases, in order to identify primary studies that may have been missed due to indexing inadequacies. A hand search of published abstracts from meetings of the Surgical Research Society, the Society of Academic and Research Surgery, the Association of Surgeons of Great Britain and Ireland, the American College of Surgeons, the Society of Surgical Oncology, the Society for Surgery of the Alimentary Tract, the European Society for Surgical Research, the Association of Upper Gastro-Intestinal Surgeons for Great Britain and Ireland, the Society of American Gastrointestinal and Endoscopic Surgeons were done.

Articles that did not examine the relationship of hospital esophagectomy volume and the length of stay were excluded. In addition, papers that examined only minimally invasive procedures were excluded. Reviews, editorials, letters and opinions as well as articles for which full publications were not available were excluded. Articles that report on single-center or single-surgeon experience were excluded. For articles reporting findings from the same cohort or program around the same time-period, the most recently published article was used. Finally, articles published before January 1, 2000 were excluded to minimize the temporal effect of changes in treatment guidelines, standards of care and health services policy.

Prior to conclusion of the manuscript, a second search was conducted in March 2016 to identify any papers published up until March 2016 but the search returned no relevant papers.

#### 2.2. Selection of studies and data extraction

Two of three authors (FG, AS, AIA) independently screened the title and abstracts for eligibility and examined the full-texts of the articles. Discrepancies were resolved in discussion with the third author. The selection process was documented in accordance with a PRISMA flow chart (Fig. 1).

Data extraction of included studies<sup>6,16–33</sup> was done using a computerized spreadsheet, in accordance with Cochrane recommendations.<sup>34</sup> We extracted data on the characteristics of the study population, including study location, sample size, clinical and demographic information, comorbidities, number, type and volume category of hospitals, tumor stage and histology, treatment protocol, study design, volume thresholds employed, in-hospital mortality, insurance status and outcomes. For continuous outcomes, such as length of stay, we extracted the mean (with standard deviation), or mean differences (with standard errors or confidence intervals). The authors of primary studies were contacted for missing data, although none responded to our requests.

One reviewer each assessed the quality and risk of bias of included studies using a modified Newcastle-Ottawa Scale for non-experimental studies.<sup>35</sup> The risk of bias was not a basis for inclusion or exclusion of studies.

#### 2.3. Statistical analysis

The primary outcome was LoS, which was examined in two ways: (1) LoS in days and (2) prolonged LoS. The secondary endpoint was early (28–30-day) readmission rate. Prolonged LoS was defined in accordance with individual studies, typically post-operative hospital stay beyond 14 days. Effect estimates from the studies were categorized as representing high, medium or low volume in accordance with numerical thresholds reported in the primary papers. Where no numerical thresholds were reported, the mean number of esophagectomies was used to categorize the relevant estimates.

Results were pooled together in unadjusted and adjusted metaanalyses using random effects models, which allow for variability of estimates across populations. Weighted mean differences with 95% confidence intervals were obtained for the postoperative LoS. Relative risks with 95% confidence intervals were obtained for the prolonged LoS and early readmission rates. If two or more studies from the same cohort around the same time-period were identified, they were not included in the same meta-analysis, and the study that was more representative of the population, with a larger sample size or published most recently was preferred for inclusion. For the primary adjusted model, the results with the greatest degree of adjustment for confounding were included.

We investigated the possible dose-response trend of the relationship between esophagectomy volume and LoS using generalized least squares regression for trend estimation (GLST). We also estimated the change in the relative risk of prolonged LoS with respective increments in the esophagectomy volume. We explored the possible linear trend between LoS (y-axis) and the esophagectomy volume (x-axis) visually using a penalized spline plot.

Heterogeneity between studies for the length of stay and prolonged length of stay measures was assessed by means of the Q and  $I^2$  inconsistency test. An  $I^2$  value greater than 50% indicates substantial heterogeneity.<sup>34</sup> Heterogeneity due to study location, study start-year (before or after 2001, the median year for commencement of the studies), age, sex, race, insurance status and in-hospital mortality was further explored through meta-regression (Table 1). Relative risks (with 95% confidence intervals) within each stratum were also estimated. Egger's and Begg's tests were conducted to evaluate publication bias statistically. Influence analysis was conducted to ascertain the effects of omitting individual studies on the estimates. A 2-sided p-value <0.05 was considered significant. Analyses were conducted using Stata version 11 (College Station, TX), SAS v 9.2 (SAS Institute Inc.) and Revman 5.3 (Cochrane).

#### 3. Results

We identified 19 papers reporting on the relationship between hospital esophagectomy volume and LoS among 75,383 patients (See eTable 1 in Supplement). These were observational cohorts that examined esophagectomies published between 2000 and 2015 at international, national and regional hospital programs across the USA, UK, Canada, Netherlands, Australia and Japan. The proportion of male participants varied from 72 to 86%. The mean age also varied from 61 to 74 years. The quality of included studies varied from unclear to low-to-high-risk of bias. The studies presented complication data in a variety of ways. For example, seven studies assessed complications using Charlson Index and the scores varied widely: between 1 and 70% had scores >3; while six papers reported in-hospital mortality which varied from 3 to 10% of the patients who died during the first 30 days. 6.17–19,30,31

We graphically explored the relationship between hospital esophagectomy volume and postoperative LoS in days (Fig. 2) based

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