

INPLASY PROTOCOL

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None declared.

Association between cutoffs for classifying high- and low-volume hospitals and long-term survival after esophagectomy: A systematic review and meta-analysis

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Review question / Objective: It is still unclear about the association between cutoffs for classifying high- and low-volume hospitals and long-term survival after esophagectomy for patients with esophageal cancer.

Condition being studied: It remains controversial whether size of hospital volume influences long-term survival outcomes for patients with esophageal cancer after esophagectomy. In addition, there is still no consensus for defining a reasonable cutoff of esophagectomies per year for classifying high- and low-volume hospitals.

Information sources: After the retrieval of the relevant articles, they were screened to remove the duplicates. Search results were screened by two authors (Q.W. and Z.X.W.) independently according to the titles and abstracts. Next, the retained studies were searched for their full text and further were screened according to the following criteria: surgery for esophageal carcinoma as the theme; primary outcomes included hospital volume and long-term OS; comparison of OS between high- and low-volume hospitals; original articles with informative data; articles reporting adjusted hazard ratios (HRs) in multi-variate analysis; and articles in which procedural volume was an exact cutoff. Any disagreements were resolved through consultation with the third author.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 July 2022 and was last updated on 06 July 2022 (registration number INPLASY202270023).

INTRODUCTION

Review question / Objective: It is still unclear about the association between cutoffs for classifying high- and low-

volume hospitals and long-term survival after esophagectomy for patients with esophageal cancer.

Rationale: Here, the effect of hospital volume on overall survival (OS) of esophageal cancer patients post esophagectomy was assessed, in relation to different cutoff values of hospital volume for classifying high- and low-volume hospitals.

Condition being studied: It remains controversial whether size of hospital volume influences long-term survival outcomes for patients with esophageal cancer after esophagectomy. In addition, there is still no consensus for defining a reasonable cutoff of esophagectomies per year for classifying high- and low-volume hospitals.

METHODS

Search strategy: We conducted a systematic search for all relevant articles on the relationship between hospital volume of esophagectomies and long-term OS. The search was performed in PubMed, Embase, Web of Science, and Cochrane Library. For example, we combined Medical Subject Headings (MeSH) terms and text terms for the search in PubMed. We also searched the references of the included studies to search for potentially eligible articles. The last search was completed on May 30, 2022. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidance (PRISMA).

Participant or population: Patients with esophageal cancer after esophagectomy.

Intervention: High-volume hospital.

Comparator: Low-volume hospital.

Study designs to be included: Cohort study

Eligibility criteria: Surgery for esophageal carcinoma as the theme; primary outcomes included hospital volume and long-term OS; comparison of OS between high- and low-volume hospitals; original articles with informative data; articles reporting adjusted hazard ratios (HRs) in multivariate

analysis; and articles in which procedural volume was an exact cutoff.

Information sources: After the retrieval of the relevant articles, they were screened to remove the duplicates. Search results were screened by two authors (Q.W. and Z.X.W.) independently according to the titles and abstracts. Next, the retained studies were searched for their full text and further were screened according to the following criteria: surgery for esophageal carcinoma as the theme; primary outcomes included hospital volume and long-term OS; comparison of OS between high- and low-volume hospitals; original articles with informative data; articles reporting adjusted hazard ratios (HRs) in multivariate analysis; and articles in which procedural volume was an exact cutoff. Any disagreements were resolved through consultation with the third author.

Main outcome(s): The primary outcome was overall survival at the last follow-up, excluding 30-day mortality, 90-day mortality, in-hospital mortality, and postoperative mortality.

Additional outcome(s): None.

Data management: Two authors independently extracted data from the included studies and collated the following information: author, published year, country, study period, population, the unit of exposure (hospital volume), volume classification for hospitals, and the longest follow-up and clinical outcomes (OS). Cutoffs for classifying high- and low-volume hospitals were recorded. Any disagreements were resolved by discussion with the third author. We also assessed the extent of risk adjustment.

Quality assessment / Risk of bias analysis: All included studies were rigorously assessed for methodological quality and risk of bias by two authors by using the Newcastle-Ottawa Scale [25]. This scale assesses the quality of studies from three aspects: selection of study population (0–4 points), comparability between groups (0–2

points), and outcome measurement (0–3 points). The total score is 9 points.

Strategy of data synthesis: A cutoff value was defined as the threshold number of esophagectomies performed per year to classify high- and low-volume hospitals. A high-volume hospital was considered when the average annual number of esophagectomies matched at least the cutoff value, while a low-volume hospital was considered when the average annual number of esophagectomies was less than the cutoff. We used hazard ratios (HRs) in low-volume groups as the reference. The primary outcome was OS at the last follow-up, excluding 30-day mortality, 90-day mortality, in-hospital mortality, and postoperative mortality. The results were calculated by HRs with 95% confidence intervals (CIs) for long-term outcomes. Regarding the inconsistency in pathological staging, therapeutic regimens, and other confounding factors among the studies, we applied random-effects models for all analyses regardless of heterogeneity.

Subgroup analysis: No subgroup analysis was applied.

Sensitivity analysis: Sensitivity analyses of a leave-one-out method were conducted to verify the results.

Language: In English and Chinese.

Country(ies) involved: Japan.

Other relevant information: None.

Keywords: esophageal carcinoma; esophagectomy; hospital volume; cutoff value; overall survival.

Dissemination plans: This meta-analysis will be submitted within this month.

Contributions of each author:

Author 1 - Qing Wang - Conceptualization, methodology, software, validation, formal analysis, investigation, resources, data curation, writing – original draft preparation.

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