BJA Advance Access published September 17, 2014

British Journal of Anaesthesia Page 1 of 12
doi:10.1093/bja/aeu294

BJA

Predicting perioperative mortality after oesophagectomy: a systematic review of performance and methods of multivariate models

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Editor's key points

- The authors systematically reviewed the prediction of mortality risk after oesophagectomy for cancer.
- They found generally unsatisfactory performance in commonly used models, and recommend further work in developing and validating new prediction models via large data sets.

Summary. Predicting risk of perioperative mortality after oesophagectomy for cancer may assist patients to make treatment choices and allow balanced comparison of providers. The aim of this systematic review of multivariate prediction models is to report their performance in new patients, and compare study methods against current recommendations. We used PRISMA guidelines and searched Medline, Embase, and standard texts from 1990 to 2012. Inclusion criteria were English language articles reporting development and validation of prediction models of perioperative mortality after open oesophagectomy. Two reviewers screened articles and extracted data for methods, results, and potential biases. We identified 11 development, 10 external validation, and two clinical impact studies. Overestimation of predicted mortality was common (5–200% error), discrimination was poor to moderate (area under receiver operator curves ranged from 0.58 to 0.78), and reporting of potential bias was poor. There were potentially important case mix differences between modelling and validation samples, and sample sizes were considerably smaller than is currently recommended. Steyerberg and colleagues' model used the most 'transportable' predictors and was validated in the largest sample. Most models have not been adequately validated and reported performance has been unsatisfactory. There is a need to clarify definition, effect size, and selection of currently available candidate predictors for inclusion in prediction models, and to identify new ones strongly associated with outcome. Adoption of prediction models into practice requires further development and validation in well-designed large sample prospective studies.

Keywords: oesophagectomy; postoperative complications, mortality; risk assessment

The UK government has put the provision of information to facilitate patient choice of treatment and provider at the centre of its vision for the NHS.[1 2] For oesophagectomy, perioperative morbidity and mortality rates are likely to feature in this information as reported in-hospital mortality is around 5%,[3 4] major complication rates up to 60%, and there is a possibility of reduced quality of life in the postoperative period.[5] Unadjusted mortality rates for individual surgeons, who carry out oesophagectomy, are also now publicly available.[6] Risk prediction models may allow a risk-stratified and more suitable comparison of service providers and also assisting individual choice of treatment. However, these stratifiers can only be considered for general use if they have been shown to be reliable, can contribute clinical benefit to patient care, and are 'transportable' to new settings.[7 8] Currently, available prediction models of perioperative mortality for oesophagectomy are not widely used, because it is not clear that they fulfil the above criteria.

Clinicians assess a range of potential comorbidities when providing prognostic information, and therefore, successful prediction models should probably also reflect the multifactorial nature of outcome prediction.[9] Therefore, in this review, we focus on the multivariate models which have been used for this purpose. In a descriptive review of some models, Shende and colleagues[10] reported poor validation and performance, and Dutta and colleagues reported overestimation of mortality in a quantitative data synthesis of POSSUM (Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity)[11] models in a mixed gastric and oesophageal cancer cohort.[12] To our knowledge, there are no current systematic reviews of methodology and performance of available prediction models of perioperative mortality after oesophagectomy.

The methods for studying and reporting multivariate prediction models have been well described,[7 13–15] as have

causes of poor performance.[15] In this systematic review, we aim to report the performance of currently available clinical multivariate prediction models and to report recognized sources of methodological bias, which could contribute to impaired performance.

Methods

This systematic review was carried out in accordance with guidelines published in the PRISMA statement.[16]

Inclusion criteria for primary studies

Studies of development, validation in new patient groups, or clinical impact of multivariate prediction models of perioperative mortality were included. The study population included adult patients, who underwent elective open surgical resection of oesophageal cancer. Studies of laparoscopic, thoracoscopic, minimally invasive, and endoscopic techniques were excluded. Perioperative mortality was defined as 'all cause' mortality associated with the hospital admission for oesophagectomy ('in-hospital' mortality), or 30 day 'all cause' mortality.

Selection filters

Reported perioperative mortality from oesophagectomy has decreased from 72% in 1941[17] to 2.9% currently.[18] This trend has been observed across European, American, and Far Eastern centres.[19–24] This review was intended for contemporary practice; therefore, we only included studies that were published after 1990.

Improved outcome has also been associated with 'higher volume' centres;[19 22 25–28] therefore, we included only studies from 'high volume single centres' or results from large databases. 'High volume' was defined as 10 or more cases annually, based on approximating Killeen and colleagues'[25] definition of eight or nine cases required annually to reduce mortality by one case per year. Annual volume was estimated by dividing the reported total operating load by the duration of the study period. Studies were confined to English language reports.

Search strategy

Medline and Embase were searched from 1990 to 2012, and hand searches were made of reference lists from primary research studies, review articles,[10 29] and standard texts.[30] The search strategy used the 'AND' logical operator to combine population definition (e.g. oesophagectomy), study type (e.g. cohort study), and a combination of outcome (e.g. mortality) 'OR' prognostic testing (e.g. prediction). The full search strategy is available in Supplementary material.

Study selection and data extraction

Two reviewers (I.W. and M.C.) screened titles and abstracts from potentially relevant studies and examined full-text versions of selected articles for inclusion criteria. The selection process is summarized in Figure 1. Data items were extracted into an Excel spreadsheet by one reviewer (I.W.) and validated by the second (M.C.); 'potential for bias' items were extracted and compared independently by both reviewers. Disagreements were resolved by consensus.

The following study characteristics were extracted: study period, geographical location, data source (e.g. population database, clinical centre), modelling and validation methods, sample size, case mix descriptors (e.g. surgical procedure,

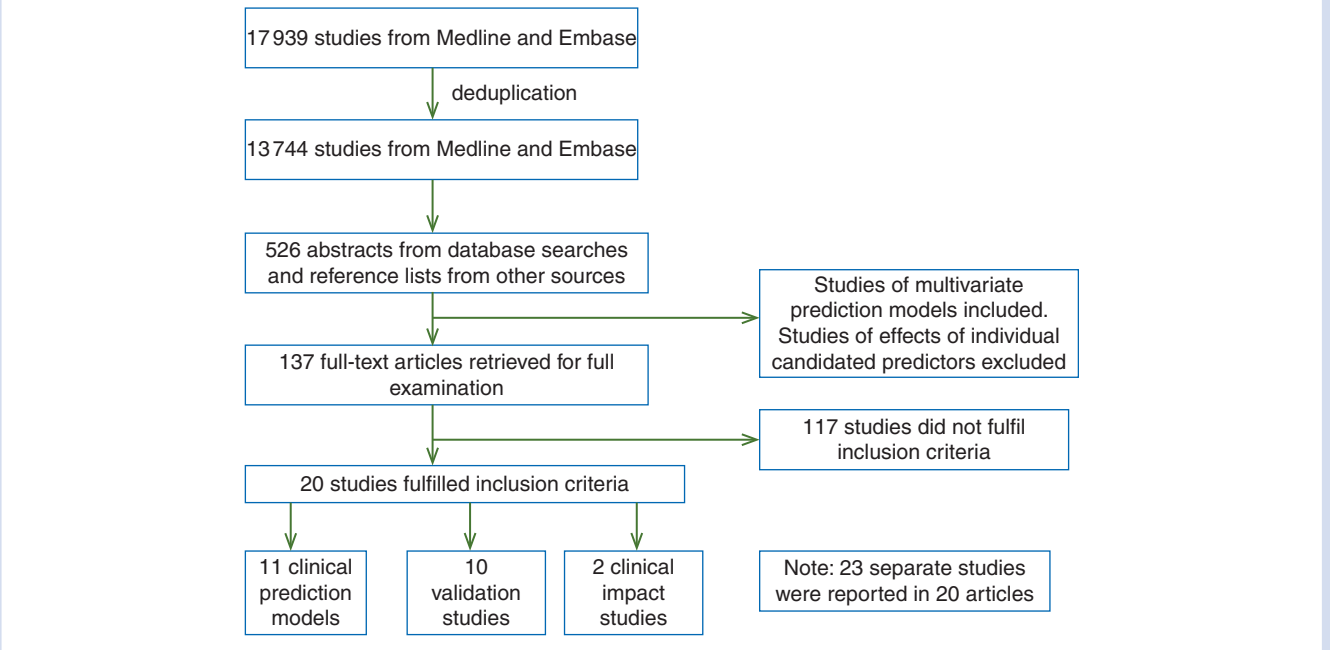

Fig 1 Flow chart of selection process for included studies.