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Risk prediction models for delirium in the intensive care unit after cardiac surgery: a systematic review and independent external validation

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Abstract

Numerous risk prediction models are available for predicting delirium after cardiac surgery, but few have been directly compared with one another or been validated in an independent data set. We conducted a systematic review to identify validated risk prediction models of delirium (using the Confusion Assessment Method-Intensive Care Unit tool) after cardiac surgery and assessed the transportability of the risk prediction models on a prospective cohort of 600 consecutive patients undergoing cardiac surgery at a university hospital in Hong Kong from July 2013 to July 2015. The discrimination (c-statistic), calibration (GiViTI calibration belt), and clinical usefulness (decision curve analysis) of the risk prediction models were examined in a stepwise manner. Three published high-quality intensive care unit delirium risk prediction models (n=5939) were identified: Katznelson, the original PRE-DELIRIC, and the international recalibrated PRE-DELIRIC model. Delirium occurred in 83 patients (13.8%, 95% CI: 11.2–16.9%). After updating the intercept and regression coefficients in the Katznelson model, there was fair discrimination (0.62, 95% CI: 0.58–0.66) and good calibration. As the original PRE-DELIRIC model was already validated externally and recalibrated in six countries, we performed a logistic calibration on the recalibrated model and found acceptable discrimination (0.75, 95% CI: 0.72–0.79) and good calibration. Decision curve analysis demonstrated that the recalibrated PRE-DELIRIC risk model was marginally more clinically useful than the Katznelson model. Current models predict delirium risk in the intensive care unit after cardiac surgery with only fair to moderate accuracy and are insufficient for routine clinical use.

Key words: cardiac surgical procedures; decision support techniques; delirium; postoperative complications; review, systematic; validation studies

Delirium is a serious clinical condition that is often underdetected and not treated promptly by health-care professionals.[1] The incidence of delirium after cardiac surgery ranges from 6 to 52%.[2] Although delirium is reversible, it is a precursor to poor patient outcomes. These include longer duration of mechanical ventilation [mean difference (MD) 1.79 days, 95% CI: 0.31–3.27],[3] a prolonged stay in the intensive care unit (ICU; MD 1.38 days, 95% CI: 0.99–1.77) and in hospital (MD 0.97 days, 95% CI: 0.61–1.33),[3] and persistent cognitive impairment after surgery.[4] Many studies have also supported an association between delirium and an increased risk of short-term mortality [relative risk (RR) 2.19, 95% CI: 1.78–2.70][3] and mortality up to 10 yr [hazard ratio (HR) 1.65, 95% CI: 1.38–1.97].[5] However, another study suggested that there was no association between delirium and mortality during ICU stay after adjusting for

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Editor's key points

- Delirium remains an important issue following cardiac surgery. Prediction of patients who will suffer delirium aids in providing appropriate post-surgical care and facilities, and has the potential to improve outcome.
- The authors examined the effectiveness of established risk-prediction models in a large multi-centre cohort of patients in Hong Kong.
- Moderate predictive accuracy was found, indicating potential future usefulness, but there was inadequate accuracy to allow current, routine, clinical use to be recommended.

a change in severity of disease before the onset of delirium (HR 1.19, 95% CI: 0.75–1.89).[6] Nevertheless, the health-care costs associated with ICU delirium are substantial, with both higher ICU (39%, 95% CI: 12–72%) and hospital costs (31%, 95% CI: 1–70%).[7]

Although the exact aetiology of delirium is unknown, its pathophysiology appears to be multifactorial.[8] Predisposing factors (e.g. elderly patients, medical co-morbidities, and cognitive, functional, visual, and hearing impairments) and precipitating factors (e.g. severity of illness, continuous infusion of benzodiazepine, blood product transfusion, and prolonged duration of mechanical ventilation) combine to trigger delirium.[2 8–10] Thus, risk prediction models incorporating strong risk factors are likely to be useful to support clinical decision-making. By targeting drug prophylaxis and other non-pharmacological interventions for patients at high risk of developing delirium, the incidence, severity, and duration of delirium may be reduced.

Numerous risk prediction models are available for predicting delirium after cardiac surgery,[11] but few have been directly compared with one another or been validated in an independent data set. Ideally, risk prediction models should undergo internal validation to ensure reproducibility and external validation to support generalizability before implementation into clinical practice.[12] After training our bedside ICU nurses on using the Confusion Assessment Method (CAM)-ICU screening tool for detecting delirium,[13] we searched for the most appropriate validated risk prediction model for early identification of patients at risk of developing delirium in the ICU after cardiac surgery.

The objective of this study was therefore to externally validate and assess the performance of all published validated risk prediction models of delirium, using the CAM-ICU assessment tool for detection of delirium. First, we performed a systematic review to identify all potential prediction models, and then critically appraised all validated risk prediction models using the CHARMS reporting guideline.[14] Then we updated the validated risk prediction models in a step-wise manner on a cohort of 600 consecutive patients undergoing cardiac surgery at a university hospital in Hong Kong from July 2013 to July 2015.

Methods

Systematic review

We searched electronic databases (Ovid MEDLINE and EMBASE) for validated clinical risk prediction models for ICU delirium, published from January 1990 onwards, which would be applicable on the first day after postoperative cardiac surgery. A systematic search was performed in October 2012 and repeated on April 15, 2016. We adopted the search filter for prognostic prediction studies described by Geersing and colleagues.[15] Further studies were identified from reviewing the reference lists of retrieved studies and review articles. We restricted the language of publication to English and Chinese.

Criteria for considering studies

The intended scope of the review was to identify published prognostic scores to help identify adults who will or will not develop ICU delirium after undergoing cardiac surgery. Studies were included if they met the following criteria: (i) prospective or retrospective cohort of adult patients admitted to an ICU after cardiac surgery; (ii) patients were assessed for delirium using CAM-ICU assessment tool (CAM-ICU has a higher discrimination performance than the Intensive Care Delirium Screening Checklist);[16] and (iii) prognostic models that reported internal validation of the development data set (random split of data or resampling methods, such as bootstrapping) or reported external validation (temporal, geographical, different setting, different investigators)[14] to predict the future occurrence of ICU delirium.

We excluded risk prediction models developed in children and risk prediction models where delirium was measured after the first day after cardiac surgery. Disagreements were resolved by discussion between the authors.

Data extraction and critical appraisal

After screening the titles and abstracts and selecting the potential eligible articles for full-text review (A.L.), a second author (V.K.W.L.) checked the selection. Two authors (A.L. and V.K.W.L.) independently extracted the following data: authors, year of publication, country where the study was conducted, study design, sample size, study population characteristics, risk predictors, model performance (calibration and discrimination measures), type of validation (internal or external), and incidence of delirium. Using the CHARMS checklist,[14] we rated the five risk domains (participant selection, predictor assessment, outcome assessment, attrition, and analysis for the development of the prediction model) as low, moderate, or high using criteria previously described.[17] Discrepancies in data extraction were resolved by discussion among the authors.

Validation cohort

Setting and participant characteristics

The reporting of this study was according to the TRIPOD checklist for prediction model development and validation.[18] The Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee approved the protocol for this prospective cohort study (CRE-2012.564). After written informed consent was given, we recruited 600 consecutive adult patients admitted to the ICU after undergoing emergency and elective cardiac surgery at The Prince of Wales Hospital in Hong Kong, a university teaching hospital. Patients were excluded if they had a sustained Richmond Agitation and Sedation Scale score[19] of −4 or −5 throughout the ICU admission, major auditory or visual disorders, were mentally incompetent, had no CAM-ICU assessment recorded, or were unable to understand Chinese or English. All patients received standardized surgical processes and perioperative care under existing protocols for postoperative ICU sedation, analgesia, and weaning from mechanical ventilation.

Two authors (J.L.M. and C.H.C.) collected patient characteristic data that included age, sex, ASA physical status, logistic EuroSCORE, urgency of ICU admission, details of surgical procedures, duration of anaesthesia, duration of mechanical ventilation, ICU length of stay, re-admission to the ICU, duration of the hospital stay, and the 30 day mortality status from the