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Study Protocol

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Risk prediction strategies using intraoperative physiological data in adults undergoing surgery: a systematic review study protocol

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Abstract

Postoperative mortality accounts for 7.7% of all global deaths, while postoperative complications increase 1-year mortality by 60%. Risk prediction models for postoperative complications and mortality can facilitate tailored risk mitigation strategies. However, most models incorporate only preoperative patient-related factors as predictors and do not capture dynamic risks or intraoperative events. This systematic review seeks to evaluate the predictive capability of intraoperative physiology derived from routine anaesthetic monitoring and the feature extraction methods for these variables. This review will include both prospective and retrospective studies that incorporate intraoperative physiological measurements into the development, validation or updating of a statistical prediction model, to identify those at risk of major end-organ (cardiovascular, pulmonary, renal and neurological) complications and mortality up-to 90 days postoperatively. We will identify models developed in two settings: those undergoing cardiac surgery and heterogeneous adult patient cohorts undergoing non-cardiac surgery. The review will be reported according to the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. This review will evaluate the available literature on intraoperative physiology as predictor variables, to improve feature extraction methods for risk prediction models development while understanding how to capitalize on the vast routinely collected intraoperative physiological data sets that are increasingly available. This review is registered on PROSPERO, registration number CRD42023474384.

INTRODUCTION

More than 330 million major surgical procedures are estimated to take place every year and this number is increasing [1]. Postoperative complications are estimated to occur after one in every five surgical procedures [2, 3]. Such complications are associated with increased healthcare costs and a reduction of both life expectancy and quality [4–6]. Despite significant developments in perioperative medicine and healthcare systems, postoperative deaths account for 7.7% of global deaths, ranking only behind ischaemic heart disease and stroke as the greatest contributor to deaths [7].

Current strategies to identify high-risk situations for postoperative complications and death mainly focus on patient and procedure factors. A prognostic prediction model is a statistical tool that can be used to forecast an individual's risk of a particular outcome (such as a postoperative complication or mortality) [8]. Perioperatively such tools can facilitate informed consent, risk–benefit analysis, and perioperative risk reduction strategies. Among the well-validated and widely used risk prediction models for postoperative morbidity and mortality are Portsmouth- Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity score [9], EuroSCORE [10] and Acute Physiology and Chronic Health Evaluation [11].

The advent of electronic health records (EHR) has supported a growing body of predictive model development studies by providing a vast digital substrate. Despite compelling evidence that intraoperative physiological derangements are associated with postoperative morbidity and mortality [12–17], existing systematic reviews indicate that most current predictive models focus on preoperative patient-related data as predictor variables [10]. Additionally, models with intraoperative data as predictor variables (such as that used in the United Kingdom National emergency laparotomy audit) predominantly feature surgical events such as surgical urgency or peritoneal soiling [9, 18].

The only model incorporating intraoperative physiological data validated across multiple studies is the Surgical Apgar Score (SAS) [19, 20]. SAS was found to be consistently well in the discrimination for postoperative morbidity and mortality across multiple surgical disciplines even after pre-operative risk-adjustment [21]. This reflects the strong attribution of intraoperative management on the model's predictive performance [22]. However, even models such as SAS, which incorporates only 'minimum' or 'maximum'

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values for specific variables, do not fully draw on the vast quantity of physiological and pharmacological data stored within EHRs.

We aim to undertake the first systematic review to define the 'state of the art' in the use of intraoperative physiological data for the prediction of postoperative outcomes. We will provide a narrative synthesis review of risk prediction models using intraoperative physiological data to predict major end organ postoperative complications and mortality in adults undergoing surgery. Our main objectives are to critically examine the current state of risk prediction models that incorporate intraoperative physiological data, report on the methods used to model these variables, and report on model performance.

METHODS AND ANALYSIS

This systematic review has been registered with Prospective Register of Systematic Reviews (PROSPERO) (Registration number: CRD42023474384).

It will abide by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [23].

Defining intraoperative physiological measurements

We identified studies that developed risk prediction models incorporating core intraoperative physiological measurements defined based on routinely captured intraoperative parameters, as mandated by national guidelines, such as the UK Association of Anaesthetists [24]. These include heart rate, blood pressure, end tidal carbon dioxide tension, oxygen saturation, body temperature, electroencephalogram, capillary blood glucose and ketones, blood gas analysis and spirometry.

Outcomes

We will include any studies that aim to develop, validate, or update a predictive model for major end organ postoperative complications and within 90-day postoperative mortality. We define 'major end organs' as the cardiovascular, pulmonary, renal and neurological systems. Cardiovascular [25], pulmonary [26] and renal [27] complications are defined in accordance with the International Standardised Endpoints in Perioperative Medicine (StEP) initiative while the definition of neurological complications (not yet available from StEP) are taken from the postoperative morbidity survey [28]. We will include studies examining postoperative mortality up-to 90 days. Brief definitions of postoperative complications are described in Table 1.

Table 1. Definition of outcomes for which risk prediction models will be identified and included in this review. Cardiovascular, pulmonary, and renal complications are derived from the Standardised endpoint in perioperative medicine (SteP) inittiatives, neurological complications from the postoperative morbidity score (POMS)

Postoperative complication	Definition
Cardiovascular [25]	1) myocardial infarction 2) non-fatal cardiac arrest 3) coronary revascularisation within 30 days of surgery 4) cardiac death within 30 days of surgery
Pulmonary [26]	1) postoperative pulmonary complication 2) postoperative pneumonia 3) postoperative respiratory failure
Renal [27]	1) Acute kidney injury defined by the Kidney Disease: Improving Global Outcomes (KDIGO) consensus criteria 2) Acute kidney disease defined by ≥30% decline in estimated glomerular filtration rate from baseline at 30 days after operation in patients meeting the acute-kidney-injury criteria within 7 days of surgery 3) Composite of death or renal replacement therapy 4) Major Adverse Kidney Events (MAKE) composite
Neurological [28]	1) Presence of a *de novo* focal deficit, coma, or confusion/delirium
Mortality	1) Up-to 90 days postoperatively

Search strategy and article selection

A systematic search of the electronic bibliographic databases MEDLINE (Ovid) and EMBASE (Ovid), were performed for the timeframe of 1 January 2013 to 25 October 2023 and limited to English language. The search strategies for both databases are illustrated in Fig. 1 which uses cardiovascular complications as an example to demonstrate how this core searches structure is modified to identify all complications of interest. Full search details (including all specific complications and variables examined) which were developed in collaboration with a medical librarian are available in the supplementary material. The search used keywords to identify both general and specific post-operative complications.

Eligibility criteria

The inclusion and exclusion criteria are as summarized in Table 2. We will, *a priori*, consider studies in two groups: studies involving adult (aged 18 years or older) patients undergoing cardiac surgery or heterogeneous cohorts of individuals undergoing non-cardiac surgery. A 'heterogeneous patient cohort' is defined as a cohort of patients including at least two different surgical specialties. Cardiac surgery will be considered separately given the unique physiological state induced by cardiopulmonary bypass.

All procedures must take place in an operating theatre and be conducted by a surgeon with an anaesthetist in attendance. Participants should receive general or regional (spinal, epidural and nerve block) anaesthesia. Procedures that will not meet these criteria include endoscopic, angiographic, and interventional radiological procedures. To further improve generalizability, studies where participants are limited to those whose baseline characteristics and physiology are not transferable to the general adult population (e.g. patients with congenital heart disease) will be excluded.

Studies must have developed, validated or updated a predictive model as defined by the Prediction model Risk Of Bias ASsessment Tool (PROBAST) [29], to make individualized predictions for any one of the specified main outcomes as described. Predictor finding studies or prediction model impact studies that only assessed the relationship between variables and outcome but did not formally develop a prediction model as per PROBAST will similarly be excluded. The final prediction model present must incorporate intraoperative physiological data for core parameters defined by the UK association of anaesthetists [24]. Studies which reported insufficient data for appropriate analysis will be excluded.

Data extraction and analysis

Studies will be uploaded to Endnote X9 version 19.3.3.13966 and duplicates removed using inbuilt features. The title abstract

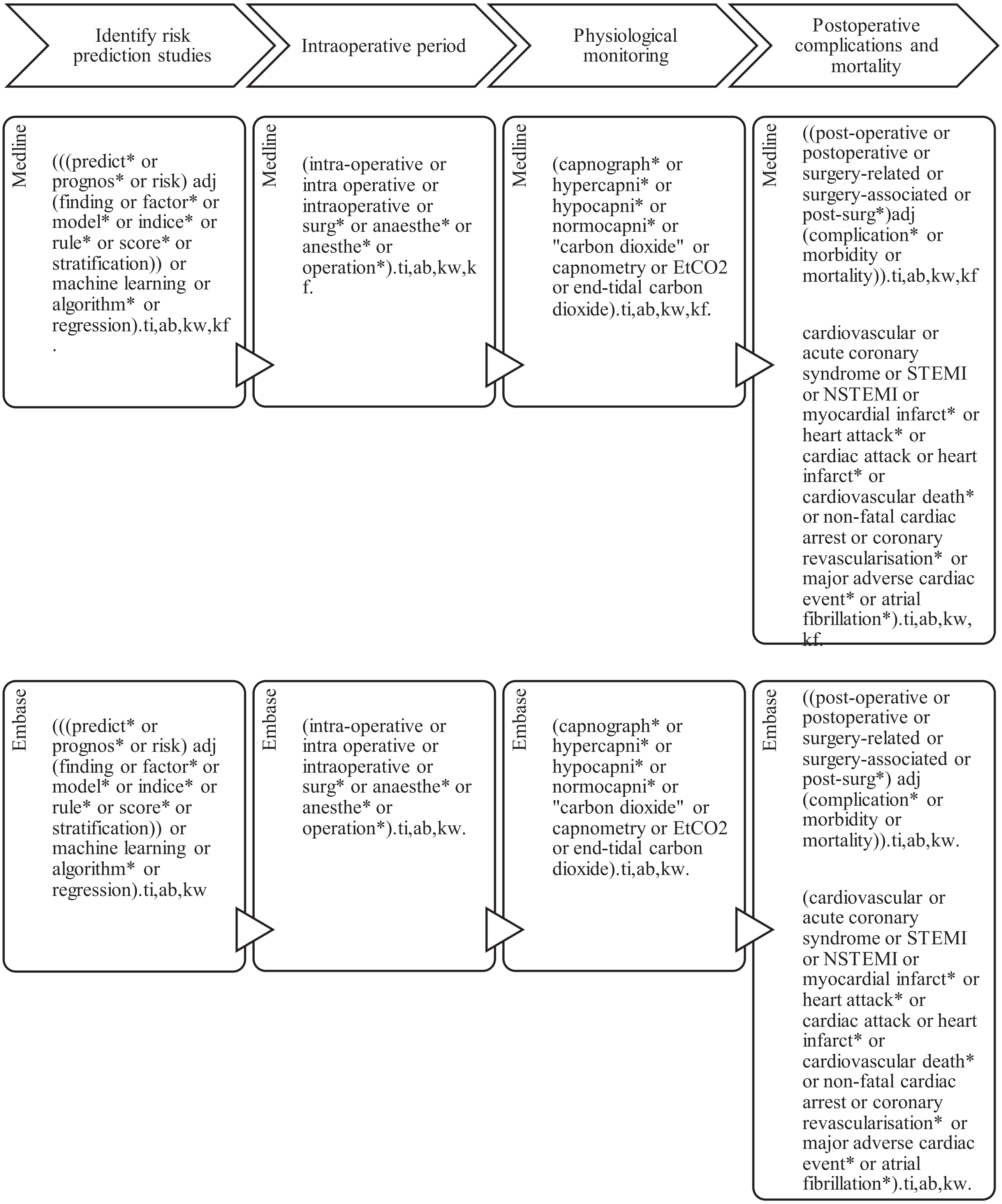

Figure 1: An example search strategy for the identification of cardiovascular complications in both MEDLINE and EMBASE.

screening and full text review will be carried out by two independent authors with reference to the inclusion and exclusion criteria using the systematic review software, Rayyan [30]. Any discrepancies are resolved by discussion and the involvement of the third author if consensus cannot be reached. Data extraction of the included articles will be conducted independently by two review authors using the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies where the extracted information are structured into 11 domains [31]. We will attempt to contact study investigators by email if data parameters of interest were stated to have been collected but were unavailable in the published article or supplementary material. The quality and utility of the prediction model studies will be assessed independently by two review authors against

Table 2. Inclusion and exclusion criteria

Criteria	Includes	Excludes
English language	English language	
Publication type	Peer-reviewed journal articles	Conferences abstracts Magazine articles Preprint articles Theses
Study type	Development, validation, and updates of prediction models	Review articles Systematic reviews Meta-analyses Editorials Case reports Case series
Population	Adult (age 18 years or older) patients Patients undergoing cardiac surgery or a heterogeneous patient cohort undergoing non-cardiac surgery Surgeries under general or regional anaesthesia with a surgeon and anaesthetist in attendance	Participants limited to those whose baseline characteristics and physiology are not transferable to the general adult population Surgical procedures performed not by a surgeon or performed under sedation alone
Method	Risk prediction, statistical model	Predictor finding studies Prediction model impact studies
Intervention	Intraoperative physiological data outlined in the standards of monitoring during anaesthesia and recovery 2021 as predictor variables in the final model	Limited to preoperative or postoperative physiological data Limited to intraoperative surgical or pharmacodynamic parameters
Outcome 1	Method of prediction specified	
Outcome 2	a) Reports the variables used in the model b) Reports any statistical method or processing of this variable (e.g. mean value, clustering)	
Outcome 3	Measures the performance of the model	

PROBAST [29]. The checklist reviews four domains to cover principal aspects of prediction model studies: participants, predictors, outcome and analysis.

Due to the heterogenous nature of the studies identified, we will present a descriptive summary of the data following extraction. The narrative synthesis of all the included studies will be conducted in accordance to the synthesis without meta-analysis guidelines for quantitative data [32]. Studies will be sub-grouped for analysis by postoperative complication and mortality as well as according to their use in cardiac or non-cardiac surgery. Studies where missing data cannot be obtained for the parameter of interest will be excluded from the analysis of the parameter.

CONCLUSION

We present a protocol for a systematic review on the use of intraoperative physiological data in risk prediction modelling for postoperative major end-organ complications and mortality up-to 90 days postoperatively. The results of the review will be valuable synthesis of the current use of routinely collected intraoperative physiological data as predictors and will serve as the key reference for emerging studies in this field.

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SUPPLEMENTARY MATERIAL

Supplementary material is available at *Journal of Surgical Protocols and Research Methodologies* online.

CONFLICT OF INTEREST STATEMENT

All authors declare no competing interests.

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ETHICS AND DISSEMINATION

This systematic review will be disseminated in a peer-reviewed journal article with contributions from individuals in the study conceptualization, literature search, data extraction, data-analysis and write-up recognized accordingly via authorship.

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