A meta-analysis of intraoperative factors associated with postoperative cardiac complications

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Keywords: meta-analysis, intraoperative factors, postoperative cardiac complications

Abstract

Background: Preoperative cardiac risk is commonly determined with the help of risk scores and risk stratification tools. This predetermined cardiac risk may be profoundly changed by intraoperative surgical events. This meta-analysis aimed to identify intraoperative factors that independently predict postoperative cardiac complications in the presence of preoperative cardiac risk factors.

Method: A PubMed Central search was conducted from January 1966 to June 2010, to identify independent intraoperative predictors of postoperative cardiac complications in observational perioperative studies and randomised controlled trials which controlled for preoperative cardiac risk factors.

Results: Eleven studies were identified for inclusion in this meta-analysis. Intraoperative blood transfusion [odds ratio (OR) 2.6, 95% confidence interval (CI) 1.8-3.4] was the only independent intraoperative risk predictor identified in more than one study. Other identified independent intraoperative factors included a > 20 mmHg fall in mean arterial blood pressure for > 60 minutes (OR 3.0, 95% CI 1.8-4.9), > 30% increase in baseline systolic pressure (OR 8.0, 95% CI 1.3-50), tachycardia in the recovery room (> 30 beats per minute from baseline for > 5 minutes) (OR 7, 95% 1.9-26), new onset atrial fibrillation (OR 6.6, 95% CI 2.5-20), hypothermia (OR 2.2, 95% CI 1.1-5) and remote ischaemic preconditioning (OR 0.22, 95% CI 0.07-0.67). None of these studies controlled for blood transfusion.

Conclusion: Both surgical and haemodynamic intraoperative events significantly increased the risk of postoperative cardiac complications. Intraoperative blood transfusion has the strongest evidence that supports this finding. It is possible that modification of these intraoperative risk factors by anaesthetists and surgeons might reduce postoperative cardiac events.

Ⓟ **Peer reviewed. (Submitted: 2012-01-23. Accepted: 2012-03-30.) © SASA** **South Afr J Anaesth Analg 2012;18(4):186-191**

Introduction

A recent study has shown that 5% of patients who undergo noncardiac surgery will suffer a perioperative myocardial infarction.[1] More than 11% of these patients will die within 30 days of the surgery. Preoperative cardiac risk is commonly determined with the help of risk scores and risk stratification tools, such as the Revised Cardiac Risk Index (RCRI).[2-5] These scores are of limited utility as intraoperative events that relate to the surgery itself profoundly alter this calculated cardiac risk.[6,7] If these events could be identified and their impact quantified, then surgeons and anaesthetists might be able to intervene to improve perioperative cardiac outcomes.

The aim of this meta-analysis was to identify intraoperative factors that changed a patient's preoperative cardiac risk of postoperative cardiac complications.

Method

A meta-analysis was conducted to identify modifiable independent intraoperative predictors of postoperative cardiac complications in studies that controlled for preoperative cardiac risk factors. The Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines were adhered to in conducting and reporting this meta-analysis.[8]

Study end-points

The intention was to extract data on postoperative cardiac complications from each study.

Study identification and selection

On 22 June 2011, a search of PubMed Central was conducted from January 1966 to June 2010. The terms that were used in the search strategy were "intraoperative risk stratification", "intraoperative risk prediction", "perioperative risk stratification" and "perioperative risk assessment". The limits that were activated on the search included "humans", "English" and "all adults 19+ years".

Observational perioperative studies and randomised controlled trials of noncardiac surgery were included. Studies published only in abstract form, non-human, cardiac surgical, and paediatric studies, those that considered preoperative risk factors only, those that did not report a postoperative cardiac complication, and studies of endovascular surgery only were excluded. Citations were independently screened, data abstracted and methodological quality assessed using a standardised data extraction sheet. Any disagreements were resolved by the reviewers who were not involved in the aforementioned processes. Full papers for all relevant citations were retrieved for detailed evaluation. Where potential intraoperative predictors of postoperative adverse outcomes were identified, but not reported, the authors of studies were contacted for the data.

Data analysis

The quality of each study was assessed for completeness of follow-up, method of patient follow-up, blinding of outcome adjudicators and factors entered into the multivariable analysis. Concordance of article extraction was determined using a kappa statistic. Comparability of the prevalence of preoperative cardiac risk factors between the cohorts from the included studies were analysed using a Kruskal-Wallis test [non-parametric analysis of variance (ANOVA) test] (GraphPad InStat version 3.06®, GraphPad Software, 2003).

The data from all the studies were converted to adjusted odds ratios (OR) for the meta-analysis. Additional data from two studies were received to enable this conversion to be performed.[7,9] Where the hazard ratio was presented, the relative risk (RR) was calculated using the following formula:[10,11]

$$RR = \frac{1-e^{HR\ln(1-P_0)}}{P_0}$$

, where P_0 is the proportion of patients without the intraoperative independent predictor who sustained an adverse cardiac outcome.

From the RR, the OR could be calculated as follows:[11]

$$OR = \frac{RR.(1-P_0)}{1-RR.P_0}$$

The meta-analysis was conducted using RevMan version 4.3® software (The Nordic Cochrane Centre, Kobehavn, Denmark). Heterogeneity between studies was assessed using univariate chi-square analysis. Random or fixed-effects models were used, based on the presence or absence of significant heterogeneity between studies, respectively. Pooled dichotomous outcomes were reported as the OR and the 95% CI.

Results

In the literature search from 1966-2010, 2 013 studies were identified. Forty-two studies were identified for full-paper analysis. The kappa statistic was 0.87 (95% CI 0.78-

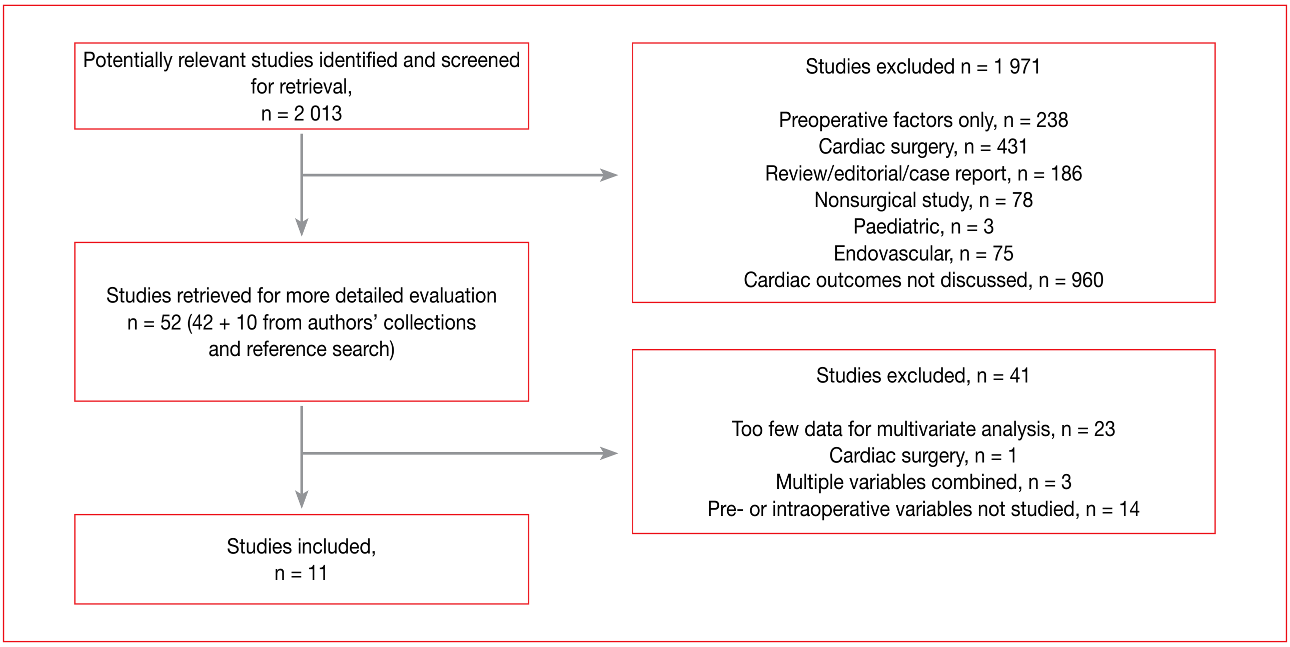

Figure 1: Flow chart showing the abstracts and articles identified and evaluated in the review process

Table I: Characteristics of included studies

Authors	Study period	Type of study	Number of patients	Types of surgery	Length of follow-up	Definition of adverse cardiac event
Charlson et al[12]	July 1982-September 1985	Prospective observational	278	Vascular surgery, cholecystectomy	7 days postoperatively, or death or discharge	Cardiac death, myocardial infarction, myocardial ischaemia
Frank et al[13]	November 1992-November 1995	Prospective randomised, single blinded	300	Abdominal, thoracic, vascular surgery	24 hours postoperatively	Cardiac arrest, myocardial infarction, unstable angina
Sprung et al[14]	January 1989-June 1997	Retrospective observational	6 948	Major or intermediate vascular surgery	Hospital discharge	Cardiac death, myocardial infarction
Ali et al[15]	February 2003-December 2005	Prospective randomised, single blinded	82	Elective AAA	7 days postoperatively	Myocardial infarction, myocardial injury
Davenport et al[6]	July 2002-June 2004	Retrospective observational	183 069	General surgery, vascular surgery	30 days postoperatively	Cardiac arrest, myocardial infarction
Bursi et al[16]	Not reported	Retrospective observational	359	Major vascular surgery	30 days postoperatively	Death, myocardial infarction
Kheterpal et al[7]	2002-2006	Retrospective observational	7 740	General surgery, vascular surgery, urology surgery	30 days postoperatively	Cardiac arrest, myocardial infarction, new dysrhythmia
Oscarsson et al[17]	April 2007-April 2008	Prospective observational	211	Emergent/urgent surgery in ASA 3 and 4 patients	12-48 hours post-operatively and 30 days-3 months postoperatively	Cardiac death, myocardial infarction
Winkel et al[18]	2004-2009	Retrospective observational	409	Elective AAA repair, peripheral bypass surgery	30 days postoperatively	Cardiac death, myocardial infarction, unstable angina
D'Ayala et al[9]	January 2004-January 2008	Retrospective observational	300	Lower limb amputations	Hospital discharge	Myocardial infarction, postoperative dysrhythmia
Devereaux et al[1]	October 2002-July 2007	Prospective randomised controlled	8 351	Noncardiac surgery	30 days postoperatively	Death, myocardial infarction

AAA: abdominal aortic aneurysmal surgery, ASA: American Society of Anesthesiologists

0.95). A further 10 studies were identified from the authors' records and by reviewing the references of papers identified for further analysis. From these 52 studies, 11 fulfilled the inclusion criteria (Figure 1).[1,6,7,9,12-18]

The characteristics of the included studies are shown in Table I. From the 11 included studies, five were prospective.[1,12,13,15,17] These studies recruited patients from a variety of surgical disciplines, and included both elective and emergency patients.

The study quality characteristics are shown in Table II.

The variation between the prevalence of the preoperative cardiac risk factors identified in the RCRI[5] did not differ significantly between the study cohorts (Table III).

Control for preoperative cardiac risk factors

Based on the five RCRI factors,[5] 10 studies (91%) controlled for a history of ischaemic heart disease,[1,7,9,12-18] eight studies (73%) controlled for congestive heart failure,[1,6,7,12,14,16-18] seven (64%) for renal dysfunction,[1,6,7,9,16-18] seven (64%) for diabetes,[6,7,9,12,13,16,18] and three (27%) for stroke.[6,7,18] One study controlled for the number of RCRI risk factors.[17] Two studies controlled for all five of the RCRI variables included in the European guidelines for cardiovascular assessment for noncardiac surgery,[7,18] two studies for four risk factors,[6,16] three studies for three of the risk factors,[1,9,12] two studies for two of the risk factors,[13,14] and one study for ischaemic heart disease only.[15]

Primary adverse cardiac outcome

The definition of a postoperative cardiac complication varied between the studies as shown in Table I. However, all the studies included myocardial infarction in the outcome definition.

Independent intraoperative factors predicting postoperative cardiac complications

Seven independent intraoperative factors were identified when controlling for preoperative cardiac risk factors. These included risk factors associated with surgical complexity (operative duration and blood transfusion), physiological

Table II: Study quality characteristics

Authors	Patients with completed follow-up (n/N)	Blinded outcome assessment	Method of patient follow-up	Preoperative cardiac risk factors adjusted for in the analysis
Charlson et al[12]	254/278 (91.4%)	Yes	Daily patient review	Coronary artery disease, cardiomegaly (only patients with hypertension and diabetes enrolled)
Frank et al[13]	270/300 (90%)	Yes	Holter monitoring	Age, ASA class, coronary artery disease, beta-blockade, diabetes, hypertension
Sprung et al[14]	6 948/6 948 (100%)	No	Patient charts	Coronary artery disease, cardiac failure, beta-blockade, valvular heart disease
Ali et al[15]	82/82 (100%)	Yes	Patient charts	Age, coronary artery disease, cholesterol, hypertension, NYHA functional capacity POSSUM score
Davenport et al[6]	182 900/183 069 (99.9%)	No	Chart review, morbidity and mortality meetings, letter or telephonic patient communication	Age, ASA class, cardiac failure, CVA, gender, renal dysfunction
Bursi et al[16]	359/359 (100%)	Yes	Chart review, telephonic interviews, death certificates, autopsy reports	Age, coronary artery disease, diabetes, gender, hypertension, renal dysfunction, smoking history
Winkel et al[18]	317/317 (100%)	No	Outpatient visits	Cardiac risk classification, gender, hypertension
D'Ayala et al[9]	300/300 (100%)	No	Chart review	Coronary artery disease, diabetes, hypertension, renal dysfunction
Devereaux et al[1]	8 331/8 351 (99.7%)	No	Telephonic interviews	Age, cardiac failure, heart rate, renal dysfunction, statin therapy

ASA: American Society of Anesthesiologists, CVA: cerebrovascular accident, NYHA: New York Heart Association, POSSUM: Physiologic and Operative Severity Score for the enUmeration of Mortality and Morbidity

Table III: Comparability of the preoperative Revised Cardiac Risk Index cardiac risk factors in included studies

Authors	Ischaemic heart disease	Cardiac failure	Diabetes	Renal dysfunction	Stroke
Charlson et al[12]	17%	12%	36%	8%	11%
Frank et al[13]	49%	Not reported	16%	2%	Not reported
Sprung et al[14]	2%	1%	1%	Not reported	1%
Ali et al[15]	26%	4%	5%	4%	Not reported
Davenport et al[6]	Not reported	23%	19%	22%	8%
Bursi et al[16]	27%	22%	38%	22%	Not reported
Kheterpal et al[7]	10%	1%	13%	2%	5%
Oscarsson et al[17]	53%	40%	20%	Not reported	28%
Winkel et al[18]	24%	6%	15%	8%	12%
D'Ayala et al[9]	47%	Not reported	70%	30%	Not reported
Devereaux et al[1]	43%	6%	29%	5%	15%
p-value	0.19	0.45	0.10	0.45	0.35

predictors (tachycardia, hypotension, hypertension and hypothermia), and an interventional predictor (remote ischaemic preconditioning).

In our study, a meta-analysis was conducted on the need for intraoperative blood transfusion only, as it was the only intraoperative risk predictor that was presented in more than one publication. Six studies reported on the association between blood transfusion and postoperative adverse cardiac events.[1,6,7,9,14,16] A single study[7] was excluded from the blood transfusion meta-analysis, as data from the same centre was included in a larger dataset.[6,19] The need for intraoperative blood transfusion was associated with significantly increased adverse cardiac events (OR 2.6, 95% CI 1.8-3.4) (Figure 2). However, there is significant heterogeneity in the estimate of risk for blood transfusion, probably due to different definitions of a postoperative cardiac complication between the studies (Table I) and different definitions for blood transfusion. These definitions

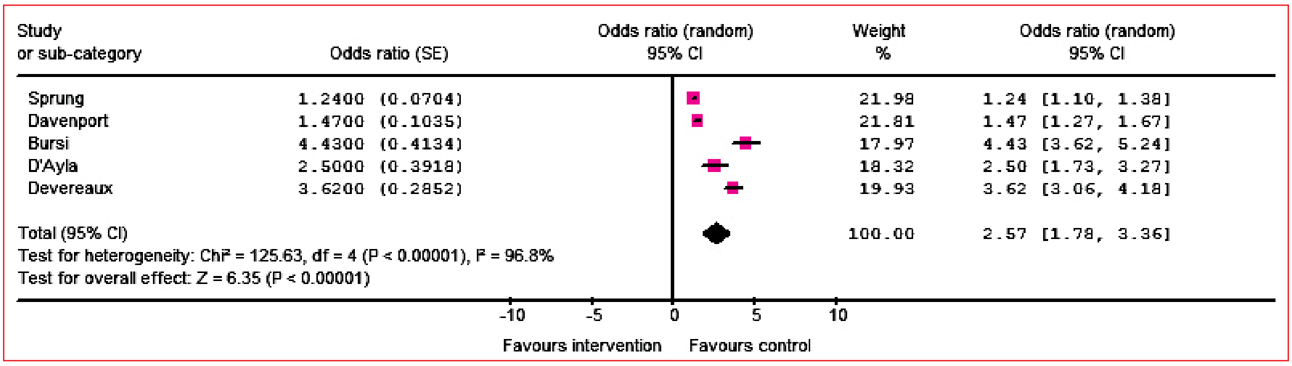

Figure 2: Meta-analysis of perioperative blood transfusion and associated adverse cardiac events

include bleeding disorder,[6] blood given,[7,9] units of blood given,[14] and serious bleeding (defined as disabling bleeding or two or more units given).[1] Only one of these studies controlled for hypotension and tachycardia, neither of which were independently predictive of adverse cardiac events in the presence of red blood cell transfusion and surgery exceeding 3.8 hours in duration (OR 2.2, 95% CI 1.3-3.7).[7]

Other identified independent intraoperative factors included > 20 mmHg fall in mean arterial blood pressure for > 60 minutes (OR 3.0, 95% CI 1.8-4.9),[12] > 30% increase in baseline systolic pressure (OR 8.0, 95% CI 1.3-50),[17] tachycardia in the recovery room (> 30 beats per minute from baseline for > 5 minutes) (OR 7, 95% 1.9-26),[17] new onset atrial fibrillation (OR 6.6, 95% CI 2.5-20),[18] hypothermia (OR 2.2, 95% CI 1.1-5),[13] and remote ischaemic preconditioning (OR 0.22, 95% CI 0.07-0.67).[15] None of these studies controlled for blood transfusion.

Discussion

Intraoperative events significantly increased the risk for postoperative cardiac complications. This meta-analysis has identified a number of intraoperative predictors, the majority of which fall into two broad groups, namely surgery-related predictors (e.g. intraoperative bleeding or operative time) and haemodynamic predictors (e.g. intraoperative tachycardia or hypotension). It is difficult to determine the relative importance of these two groups, as the majority of studies did not control for each other. Some controlled for surgical predictors only,[6,9,14,16] while others controlled only for physiological haemodynamic predictors.[12,17,18] Only two studies controlled for both groups.[1,7] However, the data from Devereaux et al[1] do not inform this discussion, as only haemodynamics are considered.

The data from Kheterpal et al[7] suggest that intraoperative surgical predictors may be stronger predictors of cardiac complications than perioperative haemodynamic changes. In this study, a number of haemodynamic variables for hypotension and tachycardia were examined in 10-minute epochs. None of these were shown to be independent predictors of adverse cardiac events after adjusting for operative duration and the number of packed red blood cell units given.[7] Although the heterogeneity associated with blood transfusion as a risk factor is large within this meta-analysis, the signal that perioperative blood transfusion is strongly associated with adverse perioperative cardiac outcomes is consistent. This is in keeping with other studies that suggest that surgery complexity[6 7] and the extent of the surgical insult[1,6,7,9,14,16,20] are strong modifiers of perioperative cardiac risk.

Adding independent intraoperative risk factors to preoperative risk prediction models reduces the significance of "traditional" preoperative risk factors. Arguably, the RCRI[5] is the most commonly used preoperative risk scoring system. Of the five risk factors in this model (a history of coronary artery disease, heart failure, stroke, diabetes and the presence of renal dysfunction), only a history of stroke[1,6,7] and renal dysfunction[1,6,9] were shown to remain as independent predictors once the intraoperative predictors were added to the models.

Not surprisingly, the strongest preoperative predictors of perioperative cardiac complications, known as "active cardiac conditions" (unstable coronary syndromes, decompensated cardiac failure, severe valvular disease and significant arrhythmias), also remain in the intraoperative models. These included active or recent congestive cardiac failure,[6,7,14] or recent coronary interventions.[7] Elective surgery should be postponed until these conditions are successfully managed.[2]

From these data, it would appear that anaesthetists and surgeons have the capacity to alter cardiac risk by management decisions taken prior to and during surgery. Preoperatively, this could include the decision to undertake a lesser procedure.[6 20] Intraoperatively, temporising measures could be undertaken in unexpectedly difficult or complicated cases. These management decisions might have a significant impact on patient cardiac morbidity.

This meta-analysis suggests that further work is necessary to accurately determine the relative importance of intraoperative risk factors on perioperative adverse cardiac events. Once these factors have been defined, interventional trials should be designed to test different intraoperative management plans.

Limitations

This meta-analysis is limited by a paucity of data specifically addressing intraoperative risk factors that modify preoperative cardiac risk prediction. Only a single risk factor, blood transfusion, provided enough data to conduct a meta-analysis. This analysis confirms that perioperative blood transfusion significantly and independently increases the risk of perioperative cardiovascular complications. Differences in baseline cardiac risk,[1] type of surgery performed (major noncardiac,[6] vascular surgery),[9,14,16] study quality (retrospective vs. prospective) and definitions used for blood transfusion and cardiac outcomes between the studies mean that this risk could not be accurately determined. Despite these limitations, perioperative physicians should keep in mind that perioperative blood transfusion significantly increases the risk of an adverse cardiac outcome in patients undergoing major noncardiac surgery. Other potential intraoperative predictors were identified in this review, although it is difficult to determine their impact on cardiac risk.

Sources of funding

Dr Rodseth is supported by a Canadian Institutes of Health Research (CIHR) Scholarship (Canada-HOPE Scholarship).

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