BJA

British Journal of Anaesthesia, 0 (0): 1–9 (2017)

doi: 10.1093/bja/aex090
Clinical Investigation

CLINICAL INVESTIGATION

Influence of anaemia and red blood cell transfusion on mortality in high cardiac risk patients undergoing major non-cardiac surgery: a retrospective cohort study

S. Feng*, M. Machina and W. S. Beattie

Department of Anesthesia and Pain Management, Toronto General Hospital, University Health Network, 200 Elizabeth Street, Toronto ON, M5G 2C4 Canada

*Corresponding author. E-mail: simon.feng@mail.utoronto.ca

Abstract

Background. Perioperative anaemia is common. Physicians believe that patients at increased cardiac risk do not tolerate anaemia and, consequently, these patients receive transfusions earlier and more often. This practice runs counter to a growing body of evidence that perioperative red blood cell (RBC) transfusion is harmful. The aims of this study were as follows: (i) to assess the effects of transfusion at moderate to severely low ranges of postoperative haemoglobin concentrations; and (ii) to assess whether transfusion was beneficial in patients at high cardiac risk within these haemoglobin ranges.
Methods. A single-centre retrospective cohort study enrolled 75 719 consecutive major, non-cardiac surgery patients. Multivariable logistic regressions with 98.4% confidence intervals looking at specific nadir postoperative haemoglobin groups were compared to examine the effects of anaemia, RBC transfusion, and cardiac risk on postoperative 30 day in-hospital mortality.
Results. Patients at moderate to high cardiac risk had a two-fold greater prevalence of preoperative anaemia. In unadjusted analysis, RBC transfusion was associated with increased mortality at all transfusion thresholds in all patients. After adjustment, RBC transfusion in patients with high cardiac risk was associated with decreased mortality when the postoperative haemoglobin concentration was <80 g litre^{-1} [odds ratio 0.37 (98.4% confidence interval 0.17–0.77)].
Conclusions. High cardiac risk was associated with increased incidence of anaemia, transfusion, and mortality. Red blood cell transfusion is associated with reduced mortality only in high cardiac risk patients with nadir postoperative haemoglobin concentration <80 g litre^{-1}. Transfusion, the main treatment for postoperative anaemia, does not appear to be associated with reduced postoperative mortality at higher nadir haemoglobin ranges.

Key words: anaemia; blood component transfusion; erythrocyte transfusion; haematological diseases; perioperative care; surgical procedures, operative

Anaemia affects nearly one-third of surgical patients and is known to be associated with postoperative mortality and morbidity.[1 2] In addition, red blood cell (RBC) transfusion occurs more frequently in patients with perioperative anaemia.[3] However, it is also known that RBC therapy carries risks and has also been associated with morbidity and mortality.[4 5]

Patients with chronic cardiac disease are more likely to be anaemic.[6] Surveys of acute care physicians show that they tend

Editorial decision: February 28, 2017; **Accepted:** March 8, 2017

Editor's key points

- Patients with high cardiac risk undergoing non-cardiac surgery are more likely to receive red blood cell transfusions at higher haemoglobin concentrations compared with patients who have low cardiac risk.
- In a retrospective single-centre cohort study of >75 000 consecutive patients, the association of postoperative anaemia, red blood cell transfusion, and cardiac risk with 30 day in-hospital mortality was studied.
- Patients with high cardiac risk had more anaemia, transfusions, and mortality.
- Red blood cell transfusion was associated with reduced 30 day mortality only for anaemic patients with high cardiac risk with postoperative haemoglobin <80 g litre^{-1}.

towards using RBC transfusions in cardiac patients at haemoglobin concentrations that are higher than for anaemic patients without cardiac disease.[7] The current American Association of Blood Banks (AABB) guidelines for perioperative RBC transfusions state that asymptomatic cardiac patients should receive blood products when haemoglobin concentration reduces below 80 g litre^{-1}.[8] The current perioperative transfusion guidelines in patients at elevated cardiac risk having non-cardiac surgery are largely based on the Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS) trial, which predominately enrolled elderly women having emergency hip fracture surgery. The primary outcome measure in FOCUS was a measure of functional recovery and, consequently, this study was underpowered to examine myocardial infarction or death.[8 9] Thus, the FOCUS trial results cannot be extrapolated directly to the overall major non-cardiac surgery population.

Current transfusion guidelines are a source of continued discussion that has recently intensified. A 2016 meta-analysis comparing transfusion thresholds across the cardiac risk spectrum suggests that a restrictive strategy in patients with elevated cardiac risk results in more ischaemic outcomes and death.[10]

Thus, there is a need to re-examine the risks of transfusion across a range of postoperative haemoglobin concentrations (transfusion thresholds) in a population that reflects the diverse characteristics of patients who undergo different types of major non-cardiac surgery. Our *a priori* hypothesis is that in patients at elevated cardiac risk undergoing non-cardiac surgery, a restrictive transfusion strategy is associated with increased mortality. We therefore conducted a retrospective cohort study to examine whether RBC transfusions administered at decreasing postoperative haemoglobin thresholds in patients at increased cardiac risk were beneficial. The primary outcome measure was death within 30 days of surgery.

Methods

This study was conducted with University Health Network Research Ethics Board approval. Owing to the retrospective nature of the study and anonymity of the data, individual patient consent was waived.

Study population

This single-centre retrospective cohort study was conducted at University Health Network, a tertiary referral centre in Toronto, ON, Canada, affiliated with the University of Toronto. The study population was a consecutive cohort of all major, non-cardiac surgery patients between January 1, 2003 and December 31, 2015. Major non-cardiac surgery was determined *a priori* as surgeries representing >1% of patients, with >0.5% 30 day mortality, and with patients staying at least one night in hospital. The study excluded all cardiac, solid organ transplant, and day surgeries. The study population and exclusion criteria are outlined in Fig. 1.

Exposure and outcomes

The study examined the risks of 30 day mortality associated with a range of postoperative haemoglobin concentrations, postoperative transfusion, and high cardiac risk (HCR). Postoperative haemoglobin concentration used in the analysis was defined as the lowest recorded haemoglobin concentration from postoperative days 1–5. Preoperative anaemia was defined by the World Health Organization (WHO) guidelines.[11] The nadir postoperative haemoglobin concentrations examined were <80, 80–89, and ≥90 g litre^{-1}. These cut-offs were based on the ranges previously used by Hébert and colleagues[7] in assessing Canadian physician transfusion thresholds. A category for haemoglobin <70 g litre^{-1} could not be specified because there were only 322 patients with HCR and haemoglobin concentration in that range. As suggested by the results of the FOCUS trial with 2016 patients were recruited into the trial, the analysis would have been underpowered to determine significance. Instead, these patients were included in the haemoglobin <80 g litre^{-1} group.

Red blood cell transfusion was defined as the number of RBC transfusions from postoperative days 1–7, inclusive. High cardiac risk was defined as a preoperative revised cardiac risk index (RCRI) of ≥2, based on a previous meta-analysis suggesting that this risk score effectively differentiates a high risk of perioperative cardiac complications after non-cardiac surgery.[12]

Data sources

Patient data were collected from linked institutional electronic databases. Data (including patient characteristics, surgical and anaesthetic variables, laboratory tests, ICD-10 codes, and date of death) were retrieved from the University Health Network electronic data warehouse, specifically from the following four sources: the surgical bookings database (Operating Room Scheduling Office System, ORSOS^{TM}; McKesson Corporation, San Francisco, CA, USA); the electronic patient record (QuadraMed CPR; QuadraMed Corporation, Reston, VA, USA); the blood transfusion database (Hemocare; Mediware Information Systems, Alton, IL, USA); and the electronic preoperative anaesthesia assessment (CAIS PreOp Clinic; Adjuvant Informatics, Flamborough, ON, Canada). All data were linked using the patient's unique hospital identifier and date of surgery. After data linking, data were de-identified, and ICD-10 codes for preoperative co-morbidities were analysed according to the method previously outlined by Quan and colleagues.[13] The accuracy of this data set has been previously verified.[14]

Data analysis

We calculated summary statistics (count and percentage; mean and SD) for population characteristics, exposure covariates, and outcome of interest.

Multivariable logistic regression models with 98.4% confidence intervals (CI; determined using Bonferroni correction to account for multiple testing) were performed for each of the