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# 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

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### 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

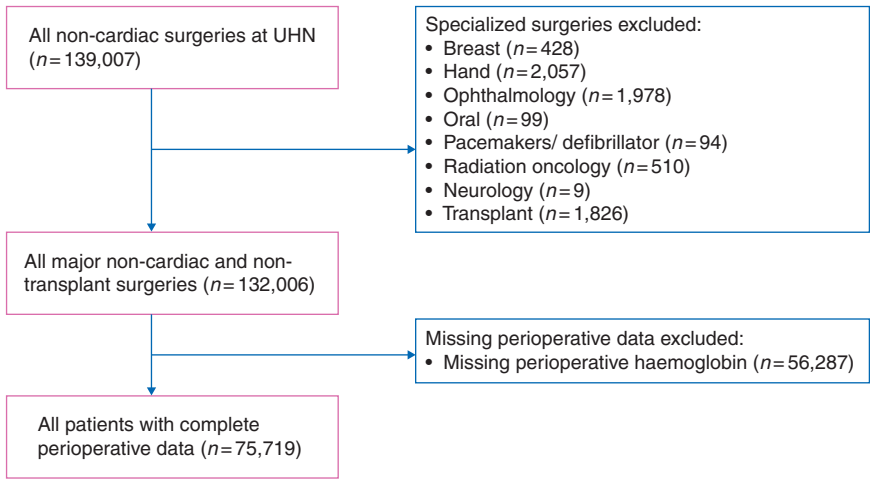


Fig 1 Inclusion and exclusion criteria. UHN, University Health Network.

three postoperative haemoglobin ranges assessed (<80, 80–89, and ≥90 g litre$^{-1}$). The association between HCR, postoperative RBC transfusion, and the interaction term, on 30 day in-hospital mortality was then assessed. The model incorporated clinically sensible patient-level and surgical risk factors including age, gender, ASA physical status, inpatient > 5 days before surgery, urgent or emergency status, oncology-related surgery, regional anaesthesia use, and surgical service (Table 1).

Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test.[15] Model performance was assessed using a receiver operating characteristic curve and the associated c-statistic.

### Sensitivity analysis

A follow-up sensitivity analysis included patients with missing perioperative haemoglobin concentrations. In this analysis, we assumed these patients did not have haemoglobin concentration measured because they were not believed to be at risk of anaemia. In our opinion, these assumptions bias the results towards the null hypothesis.

A second sensitivity analysis was conducted where HCR was defined as RCRI of ≥3. Previous studies have shown a significant increase in the incidence of major cardiac complications in patients with RCRI of ≥3 compared with RCRI of 2.[16]

Statistical analyses were performed using STATA MP 11.2 (StataCorp LP, College Station, TX, USA). Significance was assumed at $P<0.005$ to account for multiple testing bias.

## Results

### Study population and surgical characteristics

A total of 139 007 patients underwent major non-cardiac surgeries during the study period. After applying all exclusion criteria, 75 719 patients were included in the final analysis. The mean age of the study patients was 60.2 (SD 15.7) yr old. Of these patients, 20 009 (26.4%) were >70 yr old and 37 133 (49.0%) were female (Table 1). The HCR patients were more likely to be male, be an inpatient >5 days before surgery, undergo an urgent or emergency procedure, and have a higher ASA score. High cardiac risk patients were less likely to undergo oncology-related procedures.

### Perioperative anaemia

The overall prevalence of preoperative anaemia was 28% (21 173 of 75 719), with a higher rate in HCR patients (58.4%, 2664 of 4562). Comparing year with year, patients with HCR were consistently about twice as likely to have preoperative anaemia, ranging from 51.7 to 65.6%. The yearly prevalence of preoperative anaemia in low cardiac risk (LCR) patients ranged from 21.2 to 34.0%. However, the overall prevalence of preoperative anaemia in LCR patients decreased throughout the 13 yr in this study (Fig. 2).

The overall prevalence of postoperative anaemia was 63.4% (48 012), with a greater prevalence of 80% (3651 of 4562) in the HCR patient population. High cardiac risk patients were more likely to be both anaemic and more severely anaemic, with 30% (1090 of 3651) having postoperative haemoglobin concentration <80 g litre$^{-1}$, compared with 12.8% (9077 of 44 361) of LCR patients.

### Red blood cell transfusion and high cardiac risk

Of the 75 719 patients, 9823 (13.0%) received RBC transfusions and 4562 (6.0%) had HCR. The annual transfusion rate in patients with HCR (annual prevalence 16.2–31.7%) was also consistently about twice that of LCR patients (annual prevalence 7.9–15.7%) throughout the 13 yr (Fig. 2). The HCR patients were transfused more frequently at all thresholds of postoperative haemoglobin (Table 1 and Fig. 3).

### Thirty day mortality

The multivariable logistic regressions showed that preoperative anaemia, urgent or emergency surgery, age >70 yr, oncology procedures, inpatient >5 days before surgery, and increasing ASA score were independently associated with increased mortality. Conversely, female gender was associated with lower mortality.

Table 1 Patient characteristics and perioperative variables. P-values refer to the comparison between low- and high-cardiac risk groups. The percentage refers to the percentage of the population at the top of the column, unless otherwise specified. RBC, red blood cell

| Variables | Total population (75 719) | Low cardiac risk (71 157, 94.0% of total population) | High cardiac risk (4562, 6.0% of total population) | P-value |
|---|---|---|---|---|
| Female [*n* (%)] | 37 133 (49.0) | 35 535 (49.9) | 1578 (34.6) | <0.001 |
| Age >70 yr [*n* (%)] | 20 900 (27.6) | 18 706 (26.3) | 2194 (48.1) | <0.001 |
| Year of surgery | | | | <0.001 |
| 2003 | 4700 (6.2) | 4507 (6.3) | 193 (4.2) | |
| 2004 | 5092 (6.7) | 4879 (6.9) | 213 (4.7) | |
| 2005 | 5360 (7.1) | 5122 (7.2) | 238 (5.2) | |
| 2006 | 5252 (6.9) | 4941 (6.9) | 311 (6.8) | |
| 2007 | 5862 (7.7) | 5458 (7.7) | 404 (8.9) | |
| 2008 | 5765 (7.6) | 5382 (7.6) | 383 (8.4) | |
| 2009 | 5591 (7.4) | 5232 (7.4) | 359 (7.9) | |
| 2010 | 5851 (7.7) | 5458 (7.7) | 393 (8.6) | |
| 2011 | 6155 (8.1) | 5779 (8.1) | 376 (8.2) | |
| 2012 | 6452 (8.5) | 5990 (8.4) | 462 (10.1) | |
| 2013 | 6655 (8.8) | 6264 (8.8) | 391 (8.6) | |
| 2014 | 6475 (8.6) | 6061 (8.5) | 414 (9.1) | |
| 2015 | 6509 (8.6) | 6084 (8.6) | 425 (9.3) | |
| Inpatient >5 days [*n* (%)] | 4041 (5.3) | 3335 (4.7) | 706 (15.5) | <0.001 |
| Urgent or emergency [*n* (%)] | 17 174 (22.7) | 15 351 (21.6) | 1823 (40.0) | <0.001 |
| Oncology [*n* (%)] | 33 590 (44.4) | 32 553 (45.7) | 1037 (22.7) | <0.001 |
| Regional [*n* (%)] | 15 015 (19.8) | 14 144 (19.9) | 871 (19.1) | 0.198 |
| ASA [*n* (%)] | | | | <0.001 |
| I–II | 23 549 (31.1) | 23 420 (32.9) | 129 (2.8) | |
| III | 39 517 (52.2) | 38 431 (52.6) | 2347 (51.4) | |
| IV–V | 12 653 (16.7) | 10 306 (14.5) | 2347 (51.4) | |
| Surgery service [*n* (%)] | | | | |
| General | 15 132 (20.0) | 14 206 (20.0) | 926 (20.3) | 0.585 |
| Neurological | 8343 (11.0) | 7994 (11.2) | 349 (7.7) | <0.001 |
| Orthopaedic | 14 652 (19.4) | 13 824 (19.4) | 828 (18.1) | 0.034 |
| Ear, nose, and throat | 3737 (4.9) | 3562 (5.0) | 175 (3.8) | <0.001 |
| Plastic | 1257 (1.7) | 1173 (1.6) | 84 (1.8) | 0.323 |
| Spinal | 5646 (7.5) | 5493 (7.7) | 153 (3.4) | <0.001 |
| Thoracic | 7765 (10.3) | 7564 (10.6) | 201 (4.4) | <0.001 |
| Gynaecology | 5351 (7.1) | 5247 (7.4) | 104 (2.3) | <0.001 |
| Urology | 9202 (12.2) | 8640 (12.1) | 562 (12.3) | <0.001 |
| Preoperative anaemia [*n* (%)] | 21 173 (28.0) | 18 509 (26.0) | 2664 (58.4) | <0.001 |
| Postoperative anaemia [*n* (%)] | 48 012 (63.4) | 44 361 (62.3) | 3651 (80.0) | <0.001 |
| Nadir postoperative haemoglobin [*n* (%)] | | | | <0.001 |
| ≥90 g litre$^{-1}$ | 55 234 (72.9) | 52 825 (74.1) | 2509 (55.0) | |
| 80–89 g litre$^{-1}$ | 10 318 (13.6) | 9355 (13.1) | 962 (21.1) | |
| <80 g litre$^{-1}$ | 10 167 (13.4) | 9077 (12.8) | 1090 (23.9) | |
| RBC transfusion [*n* (%)] | 9823 (13.0) | 8616 (12.1) | 1207 (26.5) | <0.001 |
| Transfusion by nadir postoperative haemoglobin [*n* (% of nadir haemoglobin range] | | | | <0.001 |
| ≥90 g litre$^{-1}$ | 819 (1.5) | 741 (1.4) | 78 (3.1) | |
| 80–89 g litre$^{-1}$ | 1913 (18.5) | 1637 (17.5) | 276 (28.7) | |
| <80 g litre$^{-1}$ | 7091 (69.7) | 6238 (68.7) | 853 (78.3) | |
| 30 day in-hospital all-cause mortality [*n* (%)] | 1293 (1.7) | 1018 (1.4) | 275 (6.0) | <0.001 |

Both RBC transfusion and HCR were independently associated with increased mortality in all patients at each nadir haemoglobin range (Table 2 and Fig. 4). The interaction term between RBC transfusion and HCR suggested that RBC transfusion only provided a protective effect in HCR patients when postoperative nadir haemoglobin was below 80 g litre$^{-1}$ [OR 0.37 (CI 0.17–0.77), $P<0.001$; Table 2 and Fig. 4].

The Hosmer–Lemeshow test suggested that all three models fitted the data well, while the receiver operating characteristic curve suggested good statistical model performance.

## Sensitivity analysis

Sensitivity analysis, which included the 56 287 patients with missing perioperative haemoglobin data, found associations

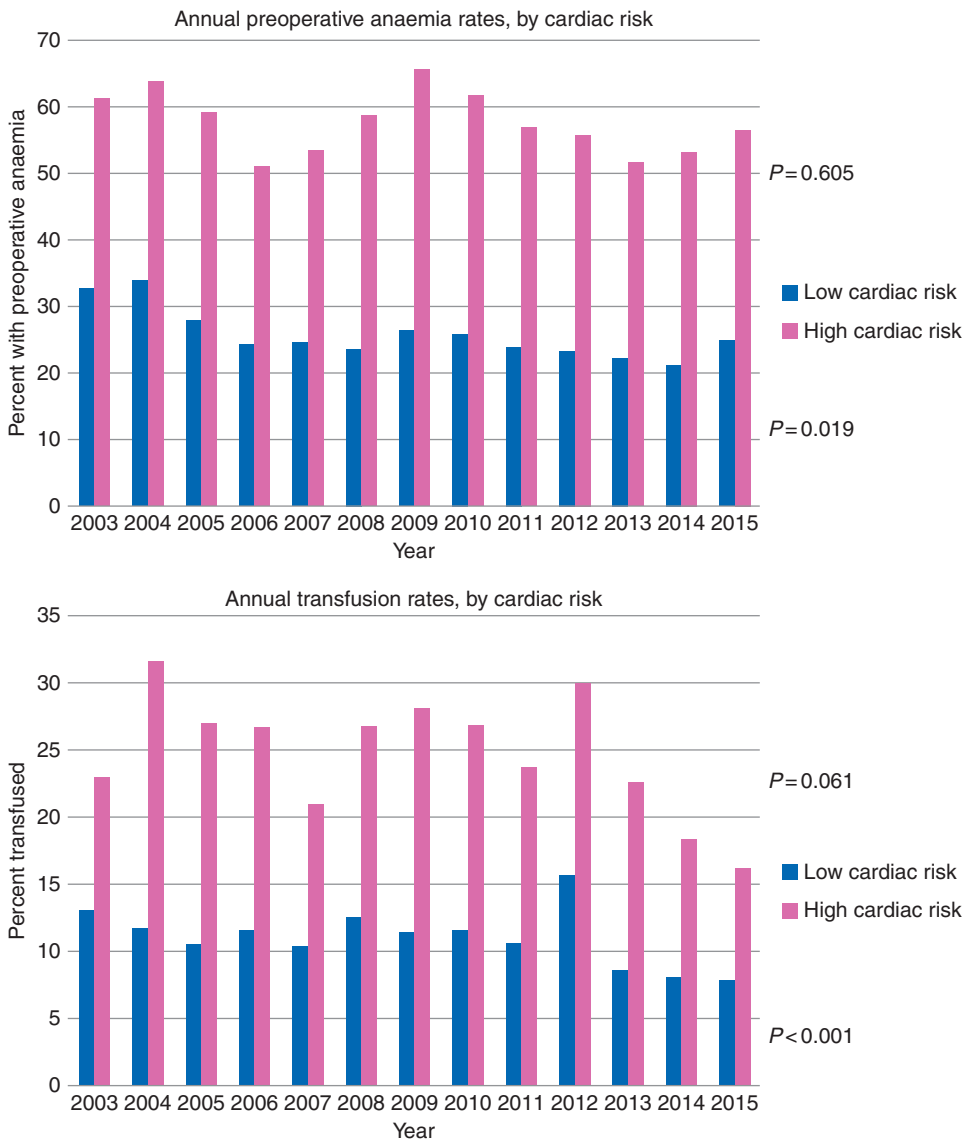


**Fig 2** P-values represent significance of the difference between rates of transfusion in each group across the years of the study. Top panel is a histogram of preoperative anaemia rates by cardiac risk across years. Bottom panel is a histogram of transfusion rates by cardiac risk across years.

consistent with the original analysis. Transfusion at postoperative haemoglobin concentration <80 g litre$^{-1}$ continued to show benefit in the HCR population [OR 0.39 (CI 0.20–0.77), $P$<0.001].

The second *post hoc* sensitivity analysis, with HCR defined as RCRI of ≥3, had 906 (1.2%) patients with HCR. The analysis showed that RCRI of ≥3 was independently associated with increased 30 day in-hospital mortality when the postoperative nadir haemoglobin threshold was <80 g litre$^{-1}$ [OR 3.84 (CI 1.49–9.93)] and ≥90 g litre$^{-1}$ [OR 3.76 (CI 2.25–6.17)]. An RCRI of ≥3 trended towards increased mortality when postoperative nadir haemoglobin was 80–89 g litre$^{-1}$ [OR 1.65 (CI 0.64–4.27)]. Red blood cell transfusion in patients with a RCRI of ≥3 was associated with decreased mortality when postoperative haemoglobin concentration was <80 g litre$^{-1}$ [OR 0.28 (CI 0.09–0.85)].

## Discussion

In this single-centre retrospective cohort study that included 75 719 patients who underwent major non-cardiac surgery, we explored the relationship between perioperative anaemia, cardiac risk, and RBC transfusion in the 30 days after surgery. Red blood cell transfusion was associated with a two- to four-fold increase in mortality, decreasing as postoperative anaemia increased in severity. We found that 80% of patients with HCR also experienced postoperative anaemia. These HCR patients were also more likely to be transfused than their low-risk counterparts, but RBC transfusion was not associated with decreased mortality unless postoperative nadir haemoglobin was <80 g litre$^{-1}$.

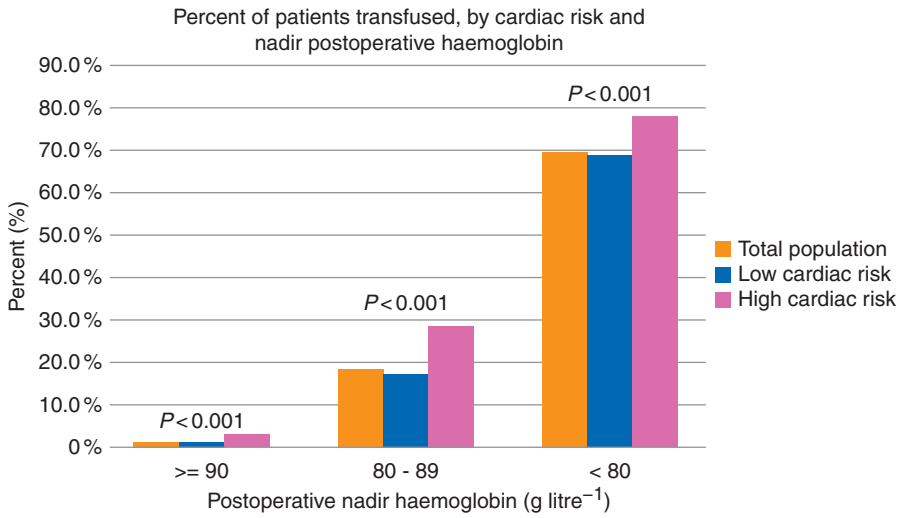


Fig 3 Histogram of the percentage of patients transfused in each postoperative nadir haemoglobin range distinguished by total population, low cardiac risk, and high cardiac risk. *P*-values represent the significance of the difference between low and high cardiac risk groups.

Table 2 Multivariable modelling for the three variables of interest and the significant interaction term. CI, confidence interval; OR, odds ratio; RBC, red blood cell

| Variables | Haemoglobin ≥90 g litre$^{-1}$ | | Haemoglobin 80–89 g litre$^{-1}$ | | Haemoglobin <80 g litre$^{-1}$ | |
|---|---|---|---|---|---|---|
| | OR (99.4% CI) | *P*-value | OR (99.4% CI) | *P*-value | OR (99.4% CI) | *P*-value |
| Preoperative anaemia | 1.87 (1.45–2.40) | <0.001 | 1.23 (0.84–1.81) | 0.190 | 1.03 (0.77–1.36) | 0.818 |
| RBC transfusion | 3.97 (2.49–6.33) | <0.001 | 2.97 (2.07–4.25) | <0.001 | 1.98 (1.42–2.76) | <0.001 |
| High cardiac risk | 1.83 (1.30–2.56) | <0.001 | 1.68 (1.01–2.79) | 0.013 | 3.51 (1.95–6.31) | <0.001 |
| RBC transfusion and high cardiac risk | 0.29 (0.08–1.08) | 0.023 | 0.67 (0.31–1.43) | 0.202 | 0.37 (0.19–0.70) | <0.001 |

Similar to previous reports, this single-centre retrospective cohort study showed that perioperative anaemia is associated with increased postoperative 30 day in-hospital mortality in major non-cardiac surgery patients.[12 17–19] The HCR patients were more likely to have severe perioperative anaemia. The components of the RCRI (coronary artery disease, congestive heart failure, chronic kidney disease, and diabetes mellitus) have all been shown to be associated with increased rates of anaemia.[20–23] A high RCRI score is an independent predictor of mortality in all ranges of postoperative anaemia, but especially when haemoglobin is <80 g litre$^{-1}$.[12]

Similar to previous studies, we also found that RBC transfusion was independently associated with increased 30 day in-hospital mortality at all postoperative nadir haemoglobin concentration ranges.[24] Current perioperative guidelines for perioperative transfusion in patients at risk of cardiac complications are based on the FOCUS trial's restrictive arm haemoglobin transfusion threshold of 80 g litre$^{-1}$.[8 9] However, the FOCUS study population was skewed towards elderly female patients with hip fractures. Recent meta-analyses suggest that cardiac surgery and HCR patients may be distinct surgical populations that need a different set of perioperative transfusion guidelines.[10 25] The results presented here show that transfusion at postoperative concentration <80 g litre$^{-1}$ is associated with decreased mortality in the subgroup of patients with RCRI ≥2.

Our study has reproduced the findings that intensive care and anaesthesia specialists have a propensity to transfuse patients with HCR at higher haemoglobin concentrations.[7] However, the interaction term between RBC transfusion and HCR suggests that RBC transfusion was beneficial only at haemoglobin concentrations <80 g litre$^{-1}$ in this HCR population.

Our study has several strengths. The large sample size that reports >1200 deaths allows a robust assessment of mortality. The large sample size also allowed the inclusion of a variety of operative procedures with numerous co-morbidities and covariates, making this population widely generalizable. Additionally, it adjusted for many confounders that other studies did not have the power to account for. The results demonstrate multiple significant associations between covariates and mortality that align with current literature.[1 2 14 17 19 24] Our results also align with current transfusion guidelines by suggesting that a restrictive transfusion strategy in patients with HCR is superior

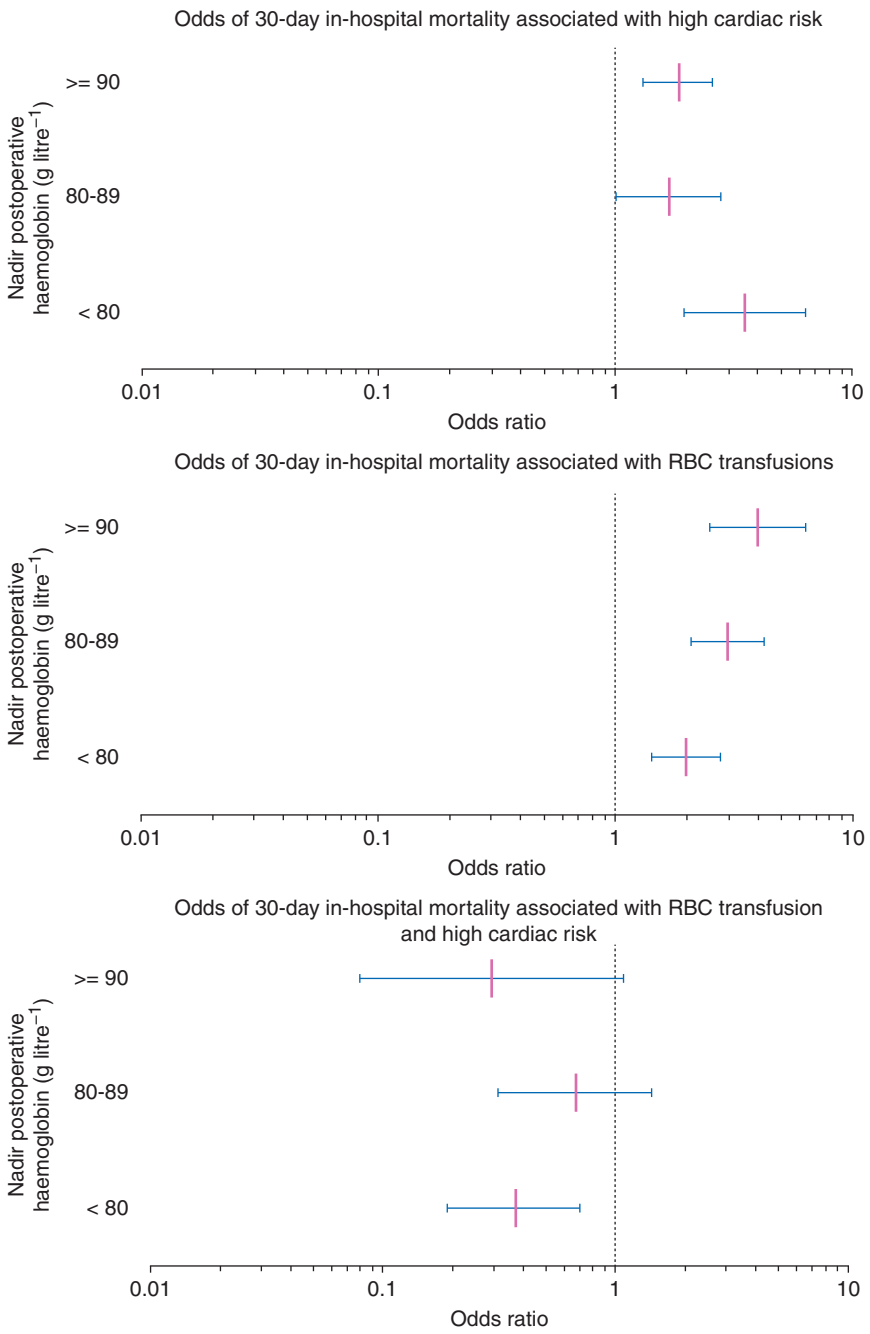


**Fig 4** Forest plots displaying the odds ratio associated with 30 day in-hospital all-cause mortality in the three different nadir haemoglobin thresholds. From top to bottom: (i) high cardiac risk; (ii) RBC transfusion; and (iii) high cardiac risk and RBC transfusion interaction term. RBC, red blood cell.

to a liberal transfusion strategy in terms of 30 day in-hospital mortality.[8] Collectively, these findings lend support to the external validity of our study.

Conversely, this was a retrospective observational study, and the effects of unknown or unmeasured confounders cannot be ruled out. The major unmeasured variable that we cannot adjust for is factors that lead to a decision to transfuse, and this could potentially influence our results. In addition, we did not assess preoperative, intraoperative, or per unit of RBC transfusion, which might also have affected mortality and morbidity outcomes. For these reasons, the so-called 'transfusion threshold trial' is considered the 'gold standard'. Although our results are in line with current recommendations, a randomized clinical trial of a restrictive *vs* a liberal transfusion strategy in a wide

non-cardiac surgical population is necessary to provide definitive evidence. Mortality was the only outcome considered in this analysis, but other outcomes, including acute coronary syndrome, pulmonary oedema, and acute kidney injury, could have been included as other sensible outcome measures.[26] Postoperative myocardial infarction or injury cannot be assessed accurately because we did not routinely order postoperative cardiac biomarkers.[27] We also based our conclusion on three separate logistic regressions, which exposes the study to multiple comparison bias. However, increasing the confidence intervals to 98.4% using the Bonferroni correction should help to mitigate that possible bias. Our database was also underpowered to determine whether transfusion with a postoperative haemoglobin concentration $<70\,g\,litre^{-1}$ would have yielded different results.

Although not the primary objective of this analysis, the detrimental effects of perioperative anaemia are prominent. Acute perioperative treatment of anaemia is hindered by the reproducible findings that the risks of RBC transfusion outweigh its benefits until the patient is severely anaemic. Sixty per cent of surgical patients are exposed to the mortality risk associated with severe perioperative anaemia, without an apparent effective treatment. This risk is accentuated in patients with HCR because they are exposed to RBC transfusion more often than LCR patients. Studies aimed at developing strategies to prevent perioperative anaemia and at finding effective alternatives to transfusion for correcting anaemia in patients with moderate anaemia are urgently required.

### Conclusions

Our results support the current postoperative transfusion threshold of $<80\,g\,litre^{-1}$ in asymptomatic HCR patients undergoing major non-cardiac surgery. Furthermore, our study provides evidence that the transfusion thresholds from the FOCUS trial are translatable to a general major non-cardiac surgery population.[8 9] Our findings also support the idea that our propensity for liberal transfusions (haemoglobin of $>80\,g\,litre^{-1}$) in HCR patients is only exposing these patients to increased risk of mortality. It is noteworthy that in the FOCUS trial, the restrictive arm (transfusion threshold of haemoglobin $<80\,g\,litre^{-1}$) experienced more anaemia symptoms, hypotension, and heart failure than patients in the liberal arm.[8] This led to more protocol violations, with increased use of RBC transfusions for symptomatic treatment of anaemia. It is thus reassuring to know that these deviations, transfusion of symptomatic anaemia above the specified threshold, did not result in increased mortality either at 30 days or at 3 yr. Our results, combined with the outcomes of the FOCUS trial with its protocol deviations in the restrictive arm, lead us to believe that HCR patients should be transfused when haemoglobin decreases $<80\,g\,litre^{-1}$ if they are otherwise asymptomatic or at a more liberal threshold if they experience symptoms associated with anaemia. However, prospective trials in a diverse, major non-cardiac surgery population are needed to evaluate the hypothesis that patients at increased cardiac risk require a higher transfusion threshold and what that specific transfusion threshold should be.

## Authors' contributions

Full access to all data in the study and responsibility for the integrity of the data and the accuracy of the data analysis: S.F., M.M.

Advice on the statistical analysis and interpretation of the results: W.S.B.

Preparation, review, and approval of the final manuscript: S.F., M.M., W.S.B.

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## Declaration of interest

None declared.

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