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Preoperative anaemia and outcome after elective cardiac surgery: a Dutch national registry analysis

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Abstract

Background: Previous studies have shown that preoperative anaemia in patients undergoing cardiac surgery is associated with adverse outcomes. However, most of these studies were retrospective, had a relatively small sample size, and were from a single centre. The aim of this study was to analyse the relationship between the severity of preoperative anaemia and short- and long-term mortality and morbidity in a large multicentre national cohort of patients undergoing cardiac surgery.

Methods: A nationwide, prospective, multicentre registry (Netherlands Heart Registration) of patients undergoing elective cardiac surgery between January 2013 and January 2019 was used for this observational study. Anaemia was defined

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according to the WHO criteria, and the main study endpoint was 120-day mortality. The association was investigated using multivariable logistic regression analysis.
Results: In total, 35 484 patients were studied, of whom 6802 (19.2%) were anaemic. Preoperative anaemia was associated with an increased risk of 120-day mortality (adjusted odds ratio [aOR] 1.7; 95% confidence interval [CI]: 1.4–1.9; *P*<0.001). The risk of 120-day mortality increased with anaemia severity (mild anaemia aOR 1.6; 95% CI: 1.3–1.9; *P*<0.001; and moderate-to-severe anaemia aOR 1.8; 95% CI: 1.4–2.4; *P*<0.001). Preoperative anaemia was associated with red blood cell transfusion and postoperative morbidity, the causes of which included renal failure, pneumonia, and myocardial infarction.
Conclusions: Preoperative anaemia was associated with mortality and morbidity after cardiac surgery. The risk of adverse outcomes increased with anaemia severity. Preoperative anaemia is a potential target for treatment to improve postoperative outcomes.

Keywords: adverse event; anaemia; cardiac surgery; mortality; postoperative outcome; preoperative

Editor's key points

- Previous retrospective data indicate that preoperative anaemia is associated with perioperative morbidity and mortality in cardiac surgery.
- This study leveraged a large multicentre national cohort of patients undergoing cardiac surgery in the Netherlands to analyse the relationship between preoperative anaemia and short- and long-term mortality and morbidity.
- Of 35 484 patients analysed, 19.2% had preoperative anaemia, which was associated with an increase in 120-day mortality in proportion to anaemia severity, and increased red blood cell transfusion and postoperative morbidities.
- Whether this association between preoperative anaemia and mortality is causal and whether interventions to reduce anaemia preoperatively improve outcomes require further study.

Approximately 20–40% of patients undergoing cardiac surgery suffer from preoperative anaemia.[1] Several studies have shown that preoperative anaemia is associated with adverse outcomes after cardiac surgery, including organ failure, infections, and mortality.[1,2] The association between preoperative anaemia and poor outcome after cardiac surgery is important, as anaemia is a modifiable risk factor, and preoperative treatment may improve postoperative outcome. However, anaemia is not evaluated in ~25% of patients undergoing elective surgery.[3]

The level of evidence found in the available literature for the association between preoperative anaemia and adverse outcomes after cardiac surgery is limited. Most of the studies were performed in a single hospital, were retrospective in nature, and were limited by relatively small sample sizes.[4,5] Other studies focused on a single cardiac procedure (e.g. valve surgery) or short-term complications and were not designed to analyse the association between anaemia severity and postoperative outcomes.[1,6] Subsequently, current guidelines on the perioperative management of patients undergoing cardiac surgery do not make an explicit recommendation on the management of preoperative anaemia.[7] Finally, anaemia is quite often considered a consequence of underlying cardiac disease, and therefore is not routinely evaluated or treated by perioperative physicians.

The primary aim of this study was to investigate the association between preoperative anaemia severity and outcome after elective cardiac surgery in a large national cohort of patients undergoing elective cardiac surgery. The secondary aim was to investigate the prevalence of anaemia during the study period.

Methods

Study design and data collection

All data were extracted from the Netherlands Heart Registration (NHR).[8] The NHR is a Dutch nationwide, multicentre, prospective validated registry of patients undergoing cardiothoracic, cardiovascular, and catheter-based procedures designed to improve the outcomes of patients with cardiac disease. All heart surgical centres in the Netherlands participate in this registry. Data collection and registration were performed by the participating centres in a secured online environment. Yearly quality checks were performed, in which the data of a sample of patients were verified within the hospitals. Data included patient characteristics, patient comorbidities, medication use, laboratory values, operative and postoperative characteristics, and outcomes. The Medical Research Ethics Committee waived the need for informed consent (W19.269), and the local review board approved this study.

Study population

Patients eligible for inclusion underwent cardiac surgery (isolated coronary artery bypass graft [CABG], isolated heart valve surgery [i.e. aortic, mitral, tricuspid, or pulmonic valve replacement or repair], heart surgery for atrial fibrillation [i.e. maze procedure], aortic surgery [i.e. Bentall procedure or hemiarch replacement], or combined surgery) between January 2013 and January 2019, were aged 18 yr or older, and had a preoperative haemoglobin concentration available (defined as the last measured haemoglobin concentration before the start of surgery). Patients were excluded in cases of active infection, non-elective surgery (e.g. critical preoperative state or unstable angina), and heart transplantation. For patients who underwent two or more surgeries within the study period, only the first surgical procedure was included.

Preoperative anaemia

Anaemia was defined according to the WHO criteria.[9] First, anaemia was defined as a dichotomous variable (haemoglobin concentration ≤129 g L^{-1} for men and ≤119 g L^{-1} for women). Second, anaemia was defined according to severity (mild anaemia: haemoglobin concentration ≥111 and ≤129 g L^{-1} for men and ≥110 and ≤119 g L^{-1} for women; moderate-to-severe anaemia: haemoglobin concentration <111 g L^{-1} for men and <110 g L^{-1} for women).

Outcome parameters

Our main study endpoint was 120-day mortality. Secondary endpoints were 30-day mortality, 1-yr mortality, infection (pneumonia, urinary tract infection, postoperative arm or leg wound infections, or deep sternal wound infection), cardiac problems (arrythmia or perioperative myocardial infarction), neurological problems (cerebrovascular accident with and without sequalae), red blood cell (RBC) transfusion, prolonged tracheal intubation, ICU readmission, renal failure, re-thoracotomy, and any adverse event. We defined any adverse event as one or more of all the individual secondary endpoints, excluding mortality. Mortality was defined as all-cause mortality confirmed by the Personal Records Database (Basisregistratie Personen in Dutch). All endpoints were defined according to the definitions of the NHR (see Supplementary Appendix B).[10]

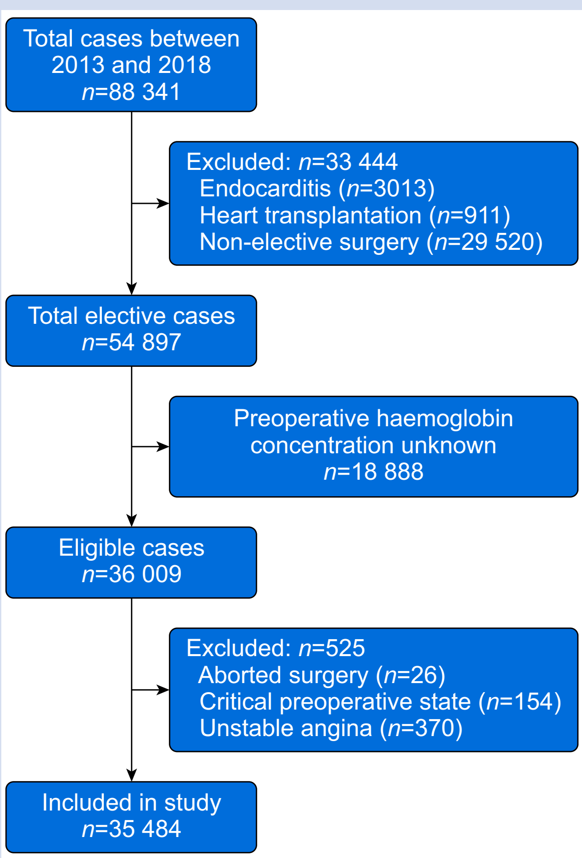

Fig 1. Flow chart of the study population.

Statistical analysis

Baseline and perioperative characteristics were compared for patients with anaemia *vs* no anaemia and for the different categories of severity of anaemia. Continuous data were described as mean (standard deviation) or median and inter-quartile range (IQR) depending on normality. Categorical variables were presented as numbers and percentages. Student's *t*-test or Mann–Whitney *U*-test was used to compare continuous variables when appropriate. One-way analysis of variance or Kruskal–Wallis test was used to compare continuous variables between the different categories of severity of anaemia. Fisher's exact test and Pearson's χ^2 test were used to compare categorical variables. Missing data were coded as missing. The prevalence and severity of anaemia were determined for each study year.

The primary study endpoint 120-day mortality and the secondary endpoints were analysed using separate univariable and multivariable logistic regression analyses. Anaemia was analysed as a dichotomous variable and as a categorical variable according to its severity. The following variables were considered potential confounders based on the literature and biological plausibility: age, sex, BMI, diabetes mellitus, chronic obstructive lung disease, extracardiac arteriopathy, haemodialysis, recent myocardial infarction, left ventricular ejection fraction, intervention weight (total number of interventions performed for the same procedure), and preoperative creatinine concentration. Multivariable models were created for each endpoint through stepwise model selection with all predefined confounders using a cut-off value of $P<0.1$, resulting in the final regression models. The final multivariable models used for analysis are listed in Supplementary Appendix C. We also analysed 120-day mortality separately for different strata: age ≤70 or >70 yr, sex, RBC transfusion, and type of intervention. Stratified analyses were performed for the other outcome variables and are shown in Supplementary Appendix D. Cox regression was used to analyse the effect of anaemia on 1-yr mortality. A *P*-value <0.05 was considered significant. For statistical analysis, SPSS version 26 (IBM, Armonk, NY, USA) was used.

Results

Baseline characteristics

In total, 35 484 patients undergoing elective cardiac surgery in 16 hospitals were included from January 2013 until January 2019 (Fig. 1). In total, 71.8% of patients were male, the median age was 67 (IQR: 61–74) yr, and the median BMI was 27.0 (IQR: 24.6–30.0) kg m^{-2}. The most common procedures performed were isolated CABG (47.1%) and isolated valve surgery (25.1%), and the median logistic euroSCORE I was 3.6% (IQR: 2.0–6.4%). Extracorporeal circulation (ECC) was used in 31 983 patients (90.1%), and the median length of cardiopulmonary bypass was 98 min (IQR: 75–136).

Compared with patients without anaemia, patients with anaemia were older ($P<0.001$); were more often female ($P<0.001$); suffered from more comorbidities, such as diabetes mellitus ($P<0.001$), chronic lung disease ($P<0.001$), and haemodialysis ($P<0.001$); and had a higher logistic euroSCORE I ($P<0.001$). Other baseline and operative characteristics are shown in Table 1.

Preoperative anaemia

The average preoperative haemoglobin concentration for men was 142 (16) g L^{-1} and 131 (15) g L^{-1} for women. Overall, 6802

Table 1 Baseline and perioperative characteristics according to the occurrence of anaemia. *P<0.05; **P<0.01; ***P<0.001. No anaemia was used as reference category for comparison between groups. Continuous variables are presented as mean (standard deviation) or median (inter-quartile range; Q1 [first quartile]–Q3 [third quartile]). Chronic lung disease is defined as the use of bronchodilators or steroids. Extracardiac arteriopathy is defined as either one of the following problems: intermittent claudication, carotid occlusion or >50% stenosis, and amputation caused by arterial disease or previous or planned surgery on abdominal aorta, arteries of the extremities, or carotids. Poor mobility is defined as extreme dysfunction of mobility caused by musculoskeletal or neurological dysfunction. Platelet aggregation inhibitor does not include acetylsalicylic acid. AoX, aortic clamping; CABG, coronary artery bypass graft; DOAC, direct oral anticoagulant; ECC, extracorporeal circulation; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

Variable	No anaemia (*n*=28 682)	Any anaemia (*n*=6802)	Mild anaemia (*n*=5032)	Moderate-to-severe anaemia (*n*=1770)	Missing (%)
Age (yr)	67 (60–73)	71 (65–77)***	71 (65–77)***	71 (63–77)***	0 (0.0)
Male sex, *n* (%)	20 817 (72.6)	4643 (68.3)***	3633 (72.2)***	1010 (57.1)***	0 (0.0)
BMI (kg m^{-2})	27.1 (24.7–30.1)	26.2 (24.1–29.7)***	26.8 (24.2–29.8)***	26.5 (23.8–29.7)***	142 (0.4)
Comorbidities					
Diabetes mellitus					19 (0.1)
No, *n* (%)	23 404 (81.6)	4565 (67.1)***	3403 (67.6)***	1162 (65.6)***	
Yes, not insulin dependent, *n* (%)	3753 (13.1)	1510 (22.2)***	1093 (21.7)***	417 (23.6)***	
Yes, insulin dependent, *n* (%)	1513 (5.3)	720 (10.6)***	532 (10.6)***	188 (10.6)***	
Chronic lung disease, *n* (%)	2864 (10.0)	896 (13.2)***	648 (12.9)***	248 (14.0)***	12 (0.0)
Atrial fibrillation, *n* (%)	3945 (13.8)	900 (13.2)***	718 (14.3)***	182 (10.2)	9321 (26.3)
Recent MI, *n* (%)	3436 (12.0)	1091 (16.0)***	789 (15.7)***	302 (17.1)***	17 (0.0)
LVEF (%)	54 (8.5)	52 (10)***	53 (9)***	52 (9)***	216 (0.6)
>50%, *n* (%)	22 364 (78.0)	4785 (70.3)***	3560 (70.7)***	1225 (69.2)***	
30–50%, *n* (%)	5549 (19.3)	1734 (25.5)***	1255 (24.9)***	479 (27.1)***	
<30%, *n* (%)	617 (2.2)	219 (3.2)***	166 (3.3)***	53 (3.0)***	
NYHA classification					8608 (24.3)
I, *n* (%)	7312 (25.5)	1641 (24.1)***	1232 (24.5)***	409 (23.1)***	
II, *n* (%)	8737 (30.5)	1999 (29.4)***	1447 (28.8)***	552 (31.2)***	
III, *n* (%)	5333 (18.6)	1531 (22.5)***	1095 (21.8)***	436 (24.6)***	
IV, *n* (%)	207 (0.7)	116 (1.7)***	75 (1.5)***	41 (2.3)***	
Extracardiac arteriopathy, *n* (%)	2432 (8.5)	1039 (15.3)***	728 (14.5)***	311 (17.6)***	14 (0.0)
Previous stroke, *n* (%)	1255 (4.4)	373 (5.5)***	277 (5.5)***	96 (5.4)**	4154 (11.7)
Neurological dysfunction, *n* (%)	527 (1.8)	208 (3.1)***	149 (3.0)***	59 (3.3)***	1449 (4.1)
Poor mobility, *n* (%)	641 (2.2)	710 (10.4)***	303 (6.0)***	407 (23.0)***	1455 (4.1)
Haemodialysis, *n* (%)	23 (0.1)	91 (1.3)***	55 (1.1)***	36 (2.0)***	24 (0.1)
Logistic euroSCORE I	3.28 (1.85–5.87)	5.08 (2.86–8.83)***	4.74 (2.76–8.07)***	5.69 (3.12–10.23)***	77 (0.2)
Previous cardiac surgery, *n* (%)	1362 (4.7)	545 (8.0)***	357 (7.1)***	188 (10.6)***	0 (0.0)
Previous PCI, *n* (%)	4242 (14.8)	1142 (16.8)**	865 (17.2)***	277 (15.6)	2572 (7.2)
Preoperative laboratory values					
Creatinine (μmol L^{-1})	88 (27)	106 (73)***	104 (67)***	111 (81)***	38 (0.1)
Haemoglobin (g L^{-1})	143 (11)	114 (11)***	121 (6)***	100 (8)***	0 (0.0)
Preoperative medication					
Acetylsalicylic acid, *n* (%)	11 694 (40.8)	2829 (41.6)*	2191 (43.5)	638 (36.0)***	8280 (23.3)
P2Y12 receptor blockers, *n* (%)	2567 (8.9)	799 (11.7)***	558 (11.1)***	231 (13.6)***	8270 (23.3)
DOAC, *n* (%)	485 (1.7)	66 (1.0)***	49 (1.0)***	17 (1.0)**	9515 (26.8)
Procedural characteristics					
Type of surgery					650 (1.8)
Isolated CABG, *n* (%)	13 648 (47.6)	3053 (44.9)***	2375 (47.2)	678 (38.3)***	
Isolated valve surgery, *n* (%)	7160 (25.0)	1752 (25.8)	1234 (24.5)	518 (29.3)***	
CABG and valve surgery, *n* (%)	3128 (10.9)	1069 (15.7)***	776 (15.4)***	293 (16.6)***	
Rhythm surgery, *n* (%)	774 (2.7)	51 (0.7)***	44 (0.9)***	7 (0.4)***	
Aortic surgery, *n* (%)	335 (1.2)	105 (1.5)*	69 (1.4)	36 (2.0)**	
Combined surgery, *n* (%)	3126 (10.9)	663 (9.3)***	446 (8.9)***	187 (10.6)	
ECC use, *n* (%)	25 749 (89.8)	6234 (91.6)***	4588 (91.2)**	1646 (93.0)***	3 (0.0)
ECC duration (min)	97 (74–133)	102 (77–145)***	101 (76–140)***	110 (81–159)***	207 (0.6)
AoX duration (min)	66 (49–93)	69 (50–98)***	67 (49–96)*	75 (54–106)***	181 (0.5)

patients were anaemic (19.2%), where 5032 had mild anaemia (14.1%) and 1770 had moderate-to-severe anaemia (5.0%). The prevalence of preoperative anaemia ranged from 16.6% to 23.1% between 2013 and 2019. The distribution of anaemia severity did not change substantially during the study period (Fig. 2).

Outcomes

The 30-day, 120-day, and 1-yr mortality rates were 1.4% (*n*=485), 1.9% (*n*=677), and 2.9% (*n*=836), respectively. Adverse outcomes occurred in 38.0% of patients (*n*=13 476). The most common complications were arrhythmia (35.3%; *n*=12 516), RBC transfusion (23.3%; *n*=8262), re-thoracotomy (4.3%; *n*=1512), and perioperative myocardial infarction (3.7%; *n*=1512).

Preoperative anaemia and outcome

In multivariable analysis, preoperative anaemia was independently associated with 120-day mortality (adjusted odds ratio

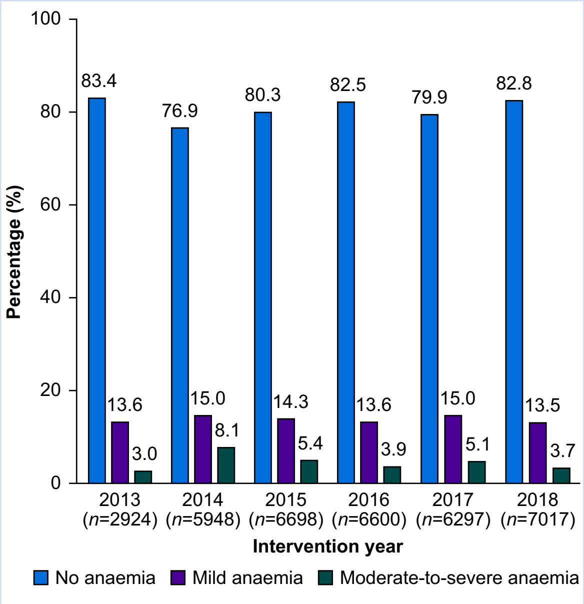

Fig 2. Prevalence of anaemia between 2013 and 2019.

[aOR] 1.7; 95% confidence interval [CI]: 1.4–2.0; $P<0.001$). The risk of 120-day mortality increased with anaemia severity (mild anaemia aOR 1.6; 95% CI: 1.3–1.9; $P<0.001$; and moderate-to-severe anaemia aOR 1.8; 95% CI: 1.4–2.4; $P<0.001$) (Table 2). The association between preoperative anaemia and 120-day mortality was consistent in the age and sex groups but not for RBC transfusion status and type of intervention (i.e. no association between anaemia and 120-day mortality in patients undergoing CABG or patients who received RBC transfusion).

Patients with anaemia had an increased risk of any adverse event (aOR 1.2; 95% CI: 1.1–1.3; $P<0.001$). Anaemia was associated with a higher chance of perioperative myocardial infarction (aOR 1.6; 95% CI: 1.4–1.8; $P<0.001$), re-thoracotomy (aOR 1.3; 95% CI: 1.1–1.4; $P<0.002$), prolonged tracheal intubation (aOR 1.4; 95% CI: 1.2–1.7; $P<0.001$), renal failure (aOR 2.4; 95% CI: 2.0–3.0; $P<0.001$), pneumonia (aOR 1.4; 95% CI: 1.2–1.6; $P<0.001$), ICU readmission (aOR 1.9; 95% CI: 1.6–2.2; $P<0.001$), and 30-day mortality (aOR 1.7; 95% CI: 1.4–2.1; $P<0.001$) (Fig. 3). There was also an association between preoperative anaemia and 1-yr mortality after cardiac surgery (hazard ratio [HR] 1.7; 95% CI: 1.5–2.0; $P<0.001$; Fig. 4).

Discussion

In this national cohort of 35 484 patients undergoing elective cardiac surgery in the Netherlands, preoperative anaemia was present in about one out of five patients and associated with 120-day mortality and adverse outcomes. The association of anaemia and 120-day mortality showed a dose–response relationship (i.e. more severe anaemia was associated with a greater risk of mortality). Preoperative anaemia was associated with an increased risk of death until 1 yr after cardiac surgery.

Our results confirm the findings of previous studies. In a multicentre retrospective study of 19 033 patients undergoing cardiac surgery,[1] preoperative anaemia was associated with an increased risk of RBC transfusion (aOR 1.4; 95% CI: 1.4–1.5) and 30-day mortality (aOR 1.4; 95% CI: 1.2–1.7). In another study of 2698 patients undergoing aortic valve surgery with or without a concomitant cardiac procedure, preoperative anaemia was associated with composite morbidity (aOR 1.4; 95% CI: 1.1–1.8) and in-hospital mortality (aOR 1.2; 95% CI: 1.0–1.3).[11]

Beyond the short-term effects of preoperative anaemia, patients with anaemia had worse 1-yr survival than patients without anaemia. This effect may last even longer, as the findings of a previous study of 3131 patients undergoing cardiac surgery, for whom a 3-yr follow-up was available, suggested.[12] They found that preoperative anaemia increased the risk of 3-yr mortality (HR 1.4; 95% CI: 1.2–1.7).

The negative impact of anaemia on outcome can be explained in several ways. As haemoglobin is a major determinant of tissue oxygen delivery, a decreased haemoglobin concentration may cause inadequate oxygen delivery and hypoxia at the cellular level. This results in a disturbed intracellular homeostasis, decreased concentrations of adenosine trisphosphate, and ultimately cell swelling and death.[13] This phenomenon may explain why we found a dose–response relationship between anaemia and mortality (i.e. risk of adverse outcome increased with anaemia severity). Another explanation for the increased risk of adverse outcomes in patients with anaemia may be that these patients have generally poorer health. Patients with anaemia may suffer from undiagnosed comorbidities or frailty, including malnutrition and sarcopenia. Ideally, statistical models, such as multivariable logistic regression analysis, should correct for these factors, but unmeasured confounding remains an issue in observational research, such as ours.[14]

The prevalence and severity of anaemia in patients undergoing cardiac surgery did not change between 2013 and 2019. On average, 20% of our patients suffered from preoperative anaemia. This prevalence is comparable with the results of a recent meta-analysis by Padmanabhan and colleagues[15] of preoperative anaemia in more than 100 000 patients undergoing urgent and elective cardiac surgery but less than the 31% reported by Klein and colleagues.[1] However, we limited our analysis to elective cases only. In this way, the sickest patients with a higher risk of anaemia were not studied, mitigating the prevalence of anaemia in our study cohort.

The clear impact of preoperative anaemia on postoperative outcomes in patients undergoing cardiac surgery calls for better preoperative management. The aetiology of anaemia should be assessed in all patients undergoing elective surgery. The evaluation of anaemia should include common causes, such as iron or vitamin deficiency (i.e. folic acid or B_{12}), chronic inflammation, and renal insufficiency.[16] However, whether treatment of preoperative anaemia actually improves patient outcomes is unclear.[17,18] In an RCT, treatment of patients undergoing cardiac surgery with a combination of iron, erythropoietin, vitamin B_{12}, and folic acid improved haemoglobin concentration and reduced the need for RBC transfusion without improving other patient outcomes.[19]

There are several limitations within this study. First, several variables had a relatively high rate of missing data, which may have resulted in bias. The variables collected within the NHR are partly voluntary and were not collected by some participating heart surgical centres. In addition, preoperative haemoglobin concentration was not available in every patient. We chose not to impute the missing data, as our database was large enough for high-powered analyses. Second, a substantial proportion of patients were excluded from

Table 2 Association between anaemia and mortality and adverse events. *P<0.05; **P<0.01; ***P<0.001. CABG, coronary artery bypass graft; CI, confidence interval; OR, odds ratio; RBC, red blood cell. Data are presented as OR (95% CI) unless reported as *n* (%).

	No anaemia (*n*=28 682)	Any anaemia (*n*=6802)	Mild anaemia (*n*=5032)	Moderate-to-severe anaemia (*n*=1770)
Mortality 120 days				
n (%)	425 (1.5)	252 (3.7)	167 (3.3)	85 (4.8)
OR unadjusted (95% CI)	Reference	2.51 (2.14–2.94)***	2.25 (1.87–2.69)***	3.43 (2.56–4.12)***
OR adjusted (95% CI)	Reference	1.65 (1.38–1.97)***	1.58 (1.29–1.94)***	1.83 (1.39–2.40)***
Strata OR adjusted				
Age				
≤70 yr	Reference	1.96 (1.46–2.64)***	1.75 (1.22–2.50)**	2.50 (1.63–3.83)***
>70 yr	Reference	1.43 (1.15–1.79)**	1.44 (1.12–1.84)***	1.40 (0.97–2.01)
Sex				
Male	Reference	1.54 (1.23–1.93)***	1.41 (1.10–1.81)**	1.88 (1.32–2.68)***
Female	Reference	1.73 (1.28–2.33)***	1.84 (1.31–2.61)**	1.62 (1.05–2.51)*
RBC transfusion				
Yes	Reference	0.96 (0.77–1.20)	0.96 (0.75–1.23)	0.95 (0.70–1.30)
No	Reference	1.38 (0.98–1.96)	1.41 (0.97–2.04)	1.40 (0.67–2.91)
Type of intervention				
CABG	Reference	1.18 (0.83–1.69)	1.09 (0.73–1.62)	1.43 (0.80–2.55)
Valve	Reference	1.91 (1.35–2.71)***	1.85 (1.24–2.75)**	2.28 (1.37–3.80)**
CABG and valve	Reference	1.37 (0.95–1.98)	1.54 (1.03–2.28)*	1.18 (0.65–2.13)
Other	Reference	1.86 (1.26–2.76)**	1.83 (1.15–2.89)**	2.03 (1.12–3.69)*
Mortality 30 days				
n (%)	301 (1.0)	184 (2.4)	120 (2.4)	64 (3.6)
OR unadjusted	Reference	2.62 (2.17–3.15)***	2.30 (1.86–2.85)***	3.53 (2.68–4.64)***
OR adjusted	Reference	1.69 (1.37–2.08)***	1.56 (1.22–1.98)***	2.03 (1.49–2.78)***
Any adverse event				
n (%)	10 540 (36.7)	2936 (43.2)	2150 (42.7)	786 (44.4)
OR unadjusted	Reference	1.34 (1.27–1.42)***	1.30 (1.22–1.38)***	1.47 (1.33–1.62)***
OR adjusted	Reference	1.18 (1.11–1.25)***	1.16 (1.08–1.24)***	1.21 (1.09–1.35)***
Other outcomes				
Infection				
n (%)	870 (3.0)	306 (4.5)	237 (4.7)	69 (3.9)
OR unadjusted	Reference	1.55 (1.36–1.77)***	1.63 (1.40–1.89)***	1.33 (1.03–1.71)*
OR adjusted	Reference	1.20 (1.03–1.39)*	1.32 (1.13–1.55)***	0.90 (0.68–1.19)
Neurological				
n (%)	294 (1.0)	91 (1.3)	71 (1.4)	20 (1.1)
OR unadjusted	Reference	1.29 (1.02–1.64)*	1.37 (1.06–1.78)*	1.07 (0.68–1.69)
OR adjusted	Reference	1.08 (0.84–1.38)	1.24 (0.95–1.62)	0.75 (0.46–1.22)
Cardiac				
n (%)	8733 (30.4)	2326 (34.2)	1715 (34.1)	611 (34.5)
OR unadjusted	Reference	1.16 (1.10–1.23)***	1.16 (1.09–1.24)***	1.16 (1.05–1.29)**
OR adjusted	Reference	1.03 (0.97–1.10)	1.05 (0.98–1.13)	0.97 (0.87–1.09)
RBC transfusion				
n (%)	4893 (17.1)	3369 (49.5)	2199 (43.7)	1170 (66.1)
OR unadjusted	Reference	4.86 (4.60–5.15)***	3.82 (3.58–4.07)***	10.01 (9.01–11.13)***
OR adjusted	Reference	4.51 (4.21–4.83)***	3.92 (3.63–4.23)***	7.91 (7.01–8.93)***
Renal failure				
n (%)	519 (1.5)	238 (3.5)	156 (3.1)	82 (4.6)
OR unadjusted	Reference	3.73 (3.14–4.45)***	3.27 (2.68–3.98)***	5.13 (3.99–6.59)***
OR adjusted	Reference	2.41 (1.97–2.95)***	2.20 (1.75–2.76)***	2.63 (1.96–3.54)***
Prolonged tracheal intubation				
n (%)	700 (2.4)	287 (4.2)	190 (3.8)	97 (5.5)
OR unadjusted	Reference	1.79 (1.56–2.06)***	1.59 (1.35–1.87)***	2.42 (1.95–3.01)***
OR adjusted	Reference	1.42 (1.21–1.67)***	1.32 (1.10–1.59)**	1.61 (1.25–2.06)***
ICU readmission				
n (%)	618 (2.2)	301 (4.4)	195 (3.9)	106 (6.0)
OR unadjusted	Reference	2.16 (1.88–2.49)***	1.86 (1.58–2.19)***	3.06 (2.48–3.79)***
OR adjusted	Reference	1.87 (1.59–2.19)***	1.67 (1.39–2.01)***	2.35 (1.85–2.99)***
Re-thoracotomy				
n (%)	1176 (4.1)	336 (4.9)	237 (4.7)	99 (5.7)
OR unadjusted	Reference	1.28 (1.13–1.45)***	1.20 (1.04–1.38)*	1.54 (1.24–1.90)***
OR adjusted	Reference	1.25 (1.09–1.43)**	1.16 (0.99–1.36)	1.40 (1.11–1.75)**

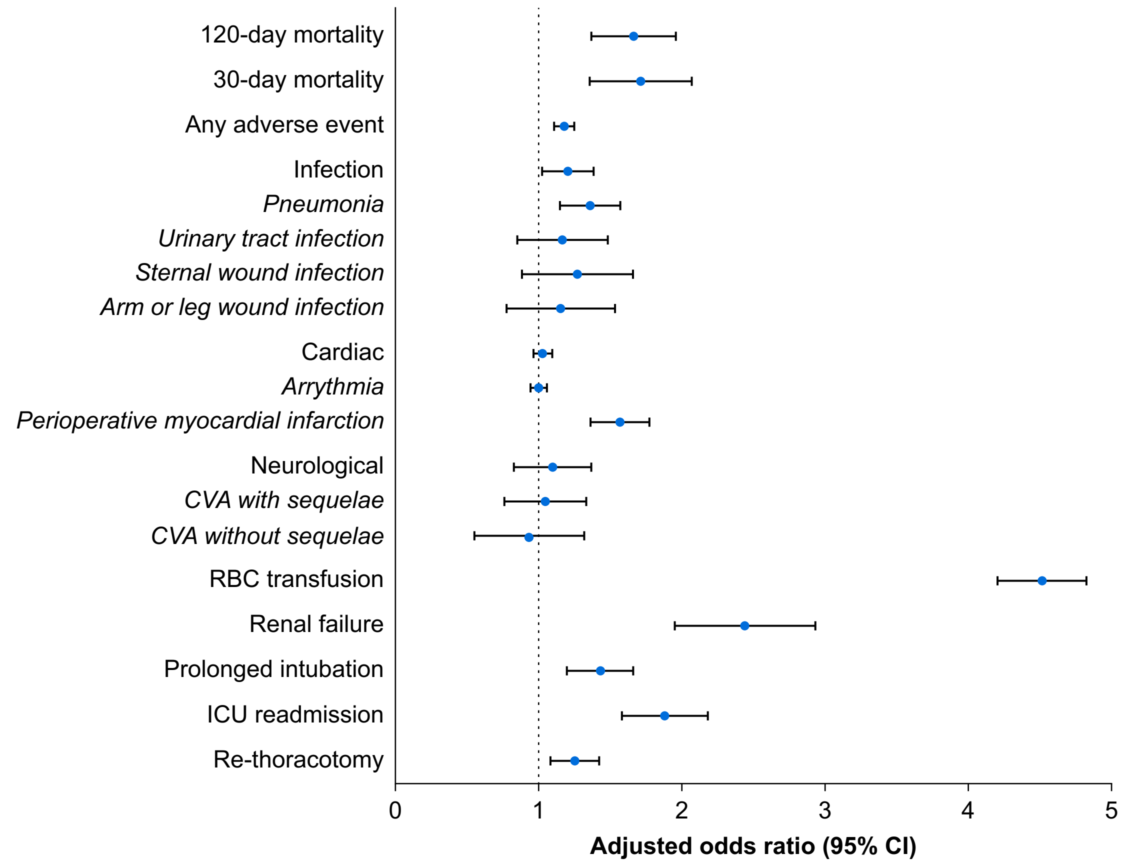

Fig 3. Association between anaemia and outcomes. CI, confidence interval; CVA, cerebrovascular accident; RBC, red blood cell.

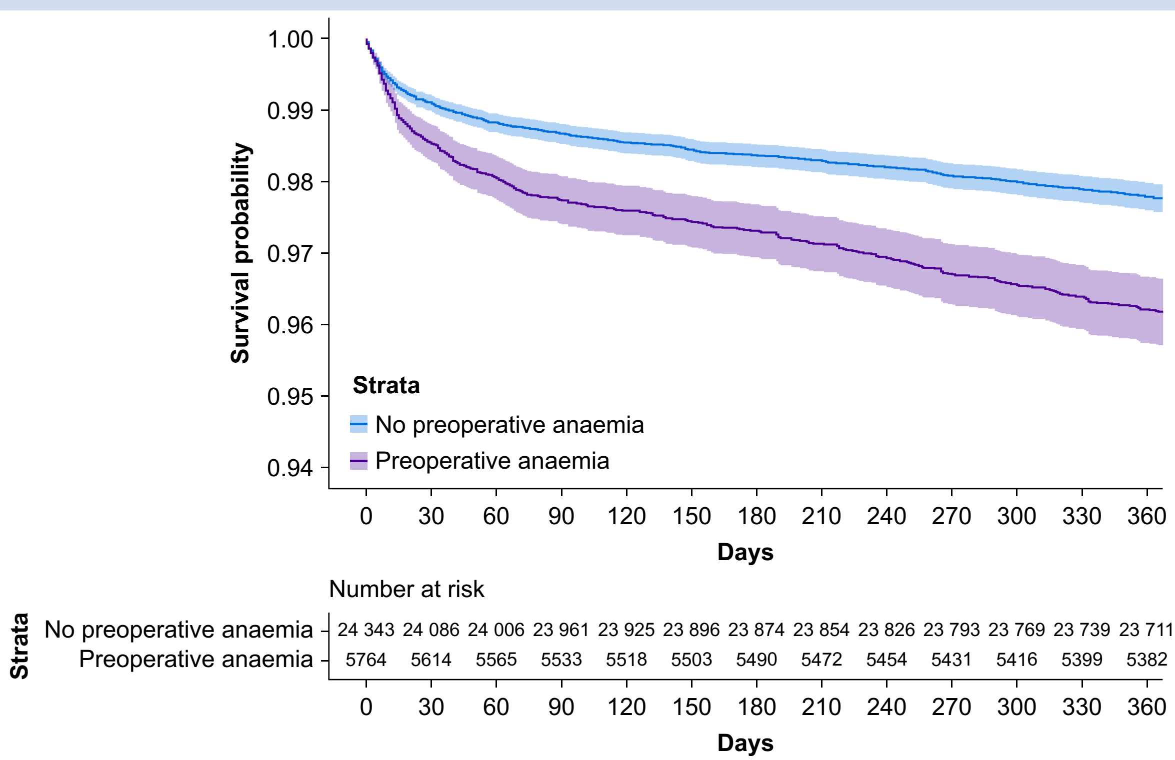

Fig 4. Association between anaemia and 1-yr mortality.

the analysis because they had emergency surgery. We chose to exclude these patients because it is unlikely that the prevalence of preoperative anaemia in this patient group changes over time. Additionally, the very short time interval between hospital admission and surgery limits the management of anaemia. Third, we did not have information on the causes of preoperative anaemia, as this was not part of the data registration of the NHR. Additional data on the causes of anaemia may aid perioperative clinicians in the diagnostic evaluation and treatment of preoperative anaemia.

The strengths of our study were the large number of patients studied and the fact that data were extracted from a prospective multicentre Dutch registry, which are suitable data for performing research. In this registry, all outcomes were clearly defined. In addition to mortality, many other adverse outcomes were available. Studies of this size with contemporary data on the association of preoperative anaemia and outcome after cardiac surgery have not yet been published.

In conclusion, preoperative anaemia is common in patients undergoing cardiac surgery and associated with short- and long-term adverse outcomes, including 1-yr mortality. Evaluation and treatment of preoperative anaemia might be an opportunity to improve postoperative outcomes in patients undergoing cardiac surgery.

Authors' contributions

Data collection: BMG, TVS, SB, RRB, RAB, SE, JSEH, JH, MTH, MFK, JVK, TK, MPJDK, JMAAVDM, AJS, NEW
Data analysis: YJJMH, PGN, SH, TCDR
Writing of paper: YJJMH, PGN, NJMM, TCDR
Revising of paper: all authors

Declarations of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2021.12.016.

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