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Association between anaemia and hospital readmissions in patients undergoing major surgery requiring postoperative intensive care

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Summary

Anaemia is a common sequela of surgery, although its relationship with patient recovery is unclear. The goal of this investigation was to assess the associations between haemoglobin concentrations at the time of hospital discharge following major surgery and early post-hospitalisation outcomes, with a primary outcome of 30 day unanticipated hospital readmissions. This investigation includes data from two independent population-based observational cohorts of adult surgical patients (aged ≥ 18 years) requiring postoperative intensive care unit admission between 1 January 2010 and 31 December 2019 in hospitals in Olmsted County, Minnesota, and between 1 July 2010 and 30 June 2017 in the Kaiser Permanente Northern California integrated healthcare system, California. Cox proportional hazards models assessed the associations between discharge haemoglobin concentrations (per 10 $g.l^{-1}$) and outcomes, with prespecified multivariable adjustment. A total of 3260 patients were included from Olmsted County hospitals and 29,452 from Kaiser Permanente Northern California. In adjusted analyses, each 10 $g.l^{-1}$ decrease in haemoglobin at hospital discharge was associated with a 9% (hazard ratio 1.09, 95%CI 1.02–1.18; $p = 0.014$) and 8% increase (hazard ratio 1.08, 95%CI 1.06–1.11; $p < 0.001$) in the instantaneous hazard for readmission at 30 days in Olmsted County and Kaiser

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Permanente Northern California, respectively. In a sensitivity analysis exploring relationships across varying levels of pre-operative anaemia severity, these associations remained consistent, with lower discharge haemoglobin concentrations associated with higher readmissions irrespective of pre-operative anaemia severity. Anaemia at hospital discharge in surgical patients requiring postoperative intensive care is associated with increased rates of hospital readmission in two large independent cohorts. Future studies are necessary to evaluate strategies to prevent and/or treat anaemia in these patients for the improvement of post-hospitalisation outcomes.

Keywords

Anaemia; transfusion; preoperative anaemia; critical illness; intensive care; haemoglobin; readmission

Introduction

Approximately 10% of adults undergoing elective surgery globally are admitted to the intensive care unit (ICU) postoperatively [1]. Invariably, these patients are high risk for postoperative complications secondary to underlying comorbidities, surgical complexity or both. In an international cohort study of more than 44,000 patients, 50% of patients admitted to the ICU after elective surgery experienced a postoperative complication and 2.5% died during hospitalisation compared with 13% and 0.2%, respectively, for those not requiring postoperative ICU care [1]. Importantly, the development of a postoperative complication is the most important predictor of unanticipated hospital readmission [2], with approximately 1 in 5 surgical patients who survive their index hospitalisation with postoperative ICU admission requiring unanticipated readmission within 30 days [3].

In recognition of the substantial socio-economic costs of hospitalisation, critical illness and readmission, it is important to identify potential modifiable risk factors for improved peri-operative outcomes, of which anaemia may be one target. Anaemia is common in surgical patients; approximately one-third present for major surgery with anaemia and up to three-quarters are discharged with anaemia [4–7]. Pre-operative anaemia is associated with increased blood transfusion utilisation as well as postoperative complications, readmissions and mortality [8,9]. However, the impact of anaemia at the time of hospital discharge on patient outcomes is less clear. Immediate anaemia after major surgery is often a direct consequence of surgical blood loss and haemodilution. This postoperative anaemia may be further exacerbated by impaired nutritional status, phlebotomy and peri-operative inflammation, resulting in blunted postoperative erythropoiesis. Consequently, anaemia may persist long after resolution of the acute surgical episode [5,10,11], with potential effects on patient recovery and rehabilitation [12]. In survivors of critical illness, including both surgical and non-surgical patients, anaemia at discharge is associated with fewer days alive and at home in the first 90 days after hospitalisation [13]. Limited data specifically derived from surgical patients suggest that the presence of severe anaemia (i.e. haemoglobin (Hb) < 80 $g.l^{-1}$) at hospital discharge is associated with increased hospital readmission rates when compared with those with mild or no anaemia (i.e. Hb ≥ 100 $g.l^{-1}$) [14].

Fortunately, peri-operative anaemia presents an opportunity for therapeutic intervention. For example, intravenous iron may increase Hb levels in patients following critical illness and/or major surgery [15–18]. However, thresholds for treatment have not been established, and dedicated studies are necessary to identify hospital discharge Hb concentrations and patient and procedural factors which convey the greatest risk for adverse post-hospitalisation outcomes.

In this investigation, we aimed to assess the associations between Hb concentrations at the time of hospital discharge following major surgery and early post-hospitalisation outcomes, with a primary outcome of 30 day unanticipated hospital readmissions. We include data from two large population-based cohorts. These data will be used to inform future clinical trials aiming to optimise the treatment of postoperative anaemia in high-risk surgical patients.

Methods

We interrogated databases for two distinct patient cohorts of adults (aged ≥ 18 y) undergoing major surgery, defined as surgery associated with postoperative ICU admission. The first cohort was derived from the Rochester Epidemiology Project, a large epidemiological study and medical records linkage system with complete medical record data available for more than 95% of residents from Olmsted County, MN, USA [19], and included surgical patients admitted between 1 January 2010 and 31 December 2019 at hospitals within Olmsted County [5]. The second cohort, which serves as a validation cohort, was derived from the Kaiser Permanente Northern California integrated health care system (which includes 21 community hospitals in Northern California, USA) and includes surgical patients who underwent major surgery between 1 July 2010 and 30 June 2017. Of note, Olmsted County contains the Mayo Clinic, a large-volume referral centre characterised by high surgical complexity, while Kaiser Permanente Northern California is generally more representative of typical community-based surgical practices. This was an observational cohort study conducted under approvals from the appropriate institutional review boards with utilisation of the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines [20].

Inclusion criteria were: age ≥ 18 y; surgery with associated postoperative ICU admission including cardiac and non-cardiac surgeries; survival to hospital discharge; and availability of a hospital discharge Hb concentration (defined as the postoperative Hb concentration occurring nearest to the time of hospital discharge). The Olmsted County cohort was derived from a larger study of anaemia development and recovery in critically ill adults [5], which additionally excluded participants who did not have an admission Hb concentration (i.e. measured within the first 24 h of hospital admission). Patients in both cohorts were excluded if they died during index hospitalisation; patients with more than one hospitalisation with postoperative ICU admission during the study period were only included once.

The primary outcome was unanticipated hospital readmissions within 30 days of discharge. Planned readmissions for procedures, surgeries or inpatient treatments such as chemotherapy were not included. Secondary outcomes included 90 day unanticipated readmissions and allcause mortality at 30 and 90 days after initial hospitalisation. Covariates of interest included: age; gender; Charlson comorbidity index score; ICU and hospital length of stay; and the number of allogeneic red blood cell transfusions administered during index hospitalisation. Recognising that pre-operative anaemia may influence discharge Hb concentrations and post-discharge outcomes, the relationships between discharge Hb concentrations and the primary outcome was assessed across pre-operative Hb concentrations (i.e. those measured closest to surgery and occurring no more than 180 days before surgery). Pre-operative anaemia protocols or pathways were not routinely utilised at these centres during the study period. Additionally, red blood cell transfusion guidelines were consistent across centres (i.e. transfusion for Hb < 70–80 $g.l^{-1}$).

Clinical, hospitalisation and patient characteristics for each cohort are displayed as median (IQR [range]) and number (proportion) for continuous and categorical variables, respectively. Unadjusted outcomes were calculated by discharge anaemia severity: none, Hb ≥ 120 $g.l^{-1}$ for females or ≥ 130 $g.l^{-1}$ for males; mild, Hb ≥ 100 $g.l^{-1}$ and < 120 $g.l^{-1}$ for females or < 130 $g.l^{-1}$ for males; moderate, Hb ≥ 80 $g.l^{-1}$ and < 100 $g.l^{-1}$; severe, Hb < 80 $g.l^{-1}$[21]. Kaplan-Meier curves visually represent the relationships between anaemia severity at discharge and readmission or death. Cox proportional hazards models were used to assess the associations between discharge Hb concentrations (per 10 $g.l^{-1}$) and 30 day and 90 day unanticipated readmissions or death in each cohort, with pre-specified adjustment for the previously mentioned covariates. Given non-linear associations, log transformations were applied to the covariates of Charlson score, hospital length of stay and red blood cell transfusion volume. Interaction terms were explored between pre-operative and discharge Hb concentrations. Adjusted hazards for 30 day readmission for each 10 $g.l^{-1}$ decrease in discharge Hb concentration are provided as pre-operative Hb concentrations of 80 $g.l^{-1}$, 100 $g.l^{-1}$ and 140 $g.l^{-1}$. Pre-defined interaction analyses were also performed to assess if associations between discharge Hb concentrations and the primary outcome of 30 day readmissions differed based on ICU length of stay; cardiac vs. non-cardiac surgery; red blood cell transfusion during index hospitalisation (any vs. none); patient gender; and anaemia classification at hospital discharge (microcytic vs. normocytic or macrocytic).

In a secondary analysis, a flexible non-linear relationship between discharge Hb and 30 day readmission, including full covariate adjustment, was allowed by parameterising discharge Hb using natural cubic splines with knots at 70, 80, 100, 120, and 150 $g.l^{-1}$. Hazard ratios for selected values of discharge Hb compared with a reference value of 130 $g.l^{-1}$ were presented. As a post hoc analysis, patient characteristics and clinical features were compared between patients readmitted or not within the first 30 days. Analyses were done using R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria). No formal power analysis was performed. P-values < 0.05 were considered statistically significant.

Results

A total of 3260 surgical patients were included from Olmsted County and 29,452 from Kaiser Permanente Northern California (online Supporting Information Figure S1). Patients were generally older adults, with a median (IQR [range]) age of 67 (54–78 [18–104]) y in Olmsted County and 67 (57–75 [18–100]) y in Kaiser Permanente Northern California

(Table 1). Approximately 30% of patients in both cohorts underwent cardiac surgery. Overall, 822 (25.2%) patients in Olmsted County and 8745 (29.7%) in Kaiser Permanente Northern California had pre-operative anaemia (when defined as Hb < 130 $g.l^{-1}$ for men and < 120 $g.l^{-1}$ for women), with Hb concentrations measured a median (IQR [range]) of 18 (4–35 [0–180]) and 6 (2–14 [0–180]) days before admission in Olmsted County and Kaiser Permanente Northern California, respectively. Using an anaemia threshold of < 130 $g.l^{-1}$ for males and females, 1129 (34.6%) in Olmsted County and 11,728 (39.8%) in Kaiser Permanente Northern California had pre-operative anaemia. Haemoglobin concentrations fell by a median (IQR [range]) of 30 (16–43 [78–107]) $g.l^{-1}$ and 24 (13–36 [74–90]) $g.l^{-1}$ by hospital discharge in Olmsted County and Kaiser Permanente Northern California, respectively. This corresponded to an anaemia prevalence at hospital discharge of 89% in Olmsted County and 81% in Kaiser Permanente Northern California. Pre-operative and discharge Hb concentrations were generally consistent over the study period (online Supporting Information Table S1). Approximately one-third of Olmsted County patients and one-quarter of Kaiser Permanente Northern California patients were transfused with allogeneic red blood cells during hospitalisation. Median ICU and hospital durations were similar with 1 (1–2 [0–62]) and 6 (4–9 [0–131]) days in Olmsted County and 1 (1–3 [0–134]) and 5 (3–8 [0–316]) days in Kaiser Permanente Northern California, respectively.

In Olmsted County, 409 (12.5%) patients experienced readmission and 73 (2.2%) patients died in the first 30 days after hospital discharge (Table 2). In Kaiser Permanente Northern California, 3287 (11.2%) were readmitted and 412 (1.4%) died over this time period. In the first 90 days after discharge, readmission occurred in 601 (18.4%) and 4393 (14.9%) patients in Olmsted County and Kaiser Permanente Northern California, respectively. Readmission and mortality rates increased congruently with increasing severity of anaemia at discharge (Fig. 1). For example, in Olmsted County, 26.9% of patients with severe anaemia were readmitted or dead by 30 days compared with 9.5% without anaemia at the time of hospital discharge. In addition to having more severe anaemia at hospital discharge, patients readmitted within the first 30 days had modestly higher comorbid illness burden and longer ICU and hospital lengths of stay (online Supporting Information Table S2).

In adjusted analyses, each 10 $g.l^{-1}$ decrease in Hb concentration at the time of hospital discharge was associated with a 9% (hazard ratio 1.09, 95%CI 1.02–1.18; $p = 0.014$) and 8% increase (hazard ratio 1.08, 95%CI 1.06–1.11; $p < 0.001$) in the instantaneous hazard for readmission at 30 days in Olmsted County and Kaiser Permanente Northern California, respectively (Table 3). Similar relationships between Hb concentrations and readmissions were noted at 90 days but were only significant in Kaiser Permanente Northern California (hazard ratio 1.04, 95%CI 0.98–1.10; $p = 0.196$ for Olmsted County, hazard ratio 1.08, 95%CI 1.05–1.10, $p < 0.001$ for Kaiser Permanente Northern California). Discharge Hb concentrations were not associated with 30 or 90 day mortality in either cohort. In Olmsted County and Kaiser Permanente Northern California, lower discharge Hb concentrations were associated with an increased hazard ratio for readmission across all levels of pre-operative Hb, but the magnitude of hazard ratio increased as pre-operative Hb decreased (Table 4).

There were no significant interactions in either cohort with ICU duration, surgery type, red blood cell transfusion during index hospitalisation or discharge mean corpuscular volume group. Additionally, in Olmsted County there was no significant interaction with patient gender; however, this interaction was significant in Kaiser Permanente Northern California ($p = 0.012$), such that the increase in hazard ratio for readmission for each 10 g.l^{-1} decrease in discharge Hb was greater in women than in men (hazard ratio 1.14, 95%CI 1.09–1.18 for women and hazard ratio 1.06, 95%CI 1.04–1.10 for men).

Functional forms of the relationships between discharge Hb concentrations and 30 day readmissions are provided in online Supporting Information Figure S2, with the hazard ratios for 30 day readmissions in comparison with a reference Hb of 130 g.l^{-1} provided in online Supporting Information Table S3. In both cohorts, the hazard of readmission tended to remain constant across discharge Hb values above 110 g.l^{-1} however, below values of 110 g.l^{-1}, the hazard of readmission increased as Hb values decreased.

Discussion

In adult patients undergoing major surgery with postoperative ICU admission, greater severity of anaemia at hospital discharge was associated with increased hazard for unanticipated readmission in the first 30 days postoperatively. These results were confirmed in two large multicentre patient cohorts, and findings were generally consistent across pre-operative anaemia severity, surgery types, transfusion status and duration of postoperative ICU admission, which suggests that anaemia is an important risk factor for readmission irrespective of these features. Additionally, anaemia at hospital discharge was associated with readmissions in a dose-dependent manner.

These results build on previous work noting associations between discharge anaemia and readmission in surgical patients and the critically ill. In a study of nearly 2000 adult surgical patients requiring postoperative ICU admission, the presence of severe anaemia at the time of hospital discharge (i.e. Hb < 80 g.l^{-1}) was associated with a nearly two-fold increase in the rate of hospital readmission after multivariable adjustment compared with those discharged with Hb ≥ 100 g.l^{-1} [14]. More recently, in a study of more than 6000 critical illness survivors, including both medical and surgical patients, prevalent anaemia (i.e. Hb < 100 g.l^{-1}) at the time of hospital discharge was associated with fewer days alive and at home through 90 days post-hospitalisation, findings driven primarily by increased rates of hospital readmission [13]. These results are now validated through the present study, which includes data from more than 30,000 surgical patients that required postoperative ICU admission from two distinct geographic locations in the USA and with comprehensive capture of readmission events given the population-based design. In both cohorts, readmission rates increased as discharge Hb concentrations fell below 110 g.l^{-1} but remained stable at higher Hb concentrations. This suggests largely equivalent risk for readmission at discharge Hb concentrations above this threshold, which is consistent with the limited findings in existing literature [13,14]. Hence, patients able to preserve or recover to near physiologic Hb concentrations tend to have improved post-hospital outcomes, with a Hb concentration of 110 g.l^{-1} serving as a potential lower target in future clinical trials of anaemia optimisation after surgery.

With regards to pre-operative anaemia optimisation, there is debate regarding the Hb thresholds that may suggest the need for treatment in men and women, with some experts suggesting that a common Hb threshold irrespective of patient sex or gender identity [22]. In this study, we evaluated differences in discharge Hb concentrations and readmission relationships by self-identified patient gender. In Kaiser Permanente Northern California, females experienced greater reductions in readmission risk for any incremental increase in discharge Hb concentrations compared with males, with similar point estimates, though not meeting statistical significance, also observed in Olmsted County. While the exact mechanisms are unclear, it is possible that a 10 $g.l^{-1}$ increase in females, who experienced both lower discharge Hb concentrations and a narrower range of observed Hb concentrations, would represent a larger proportional change than that observed in their male counterparts. Further, there may be differences in iron status or underlying aetiologies of anaemia that may impact downstream outcomes including Hb recovery and readmission. It is important to note that males also experienced higher readmission rates with lower discharge Hb concentrations, suggesting that greater severity of anaemia is associated with adverse post-hospitalisation outcomes in both men and women.

Given these findings, the obvious question is how do we optimise Hb concentrations, which serve as a surrogate for red cell mass, after major surgery? There are several potential opportunities. First, there is evidence to support pre-operative anaemia therapy as an effective and safe method of optimising Hb concentrations, including multiple clinical trials, observational studies and consensus guidelines [18, 23–25]. However, it should be recognised that pre-operative optimisation is not uniformly possible and in isolation may be insufficient to prevent anaemia development after surgery. Importantly, greater severity of anaemia at discharge was associated with increased hazard for readmission across all levels of pre-operative Hb. However, this risk was highest in patients with greater severity of pre-operative anaemia, which highlights the importance of developing and evaluating strategies to address anaemia both before and after surgery. Second, prevention of iatrogenic anaemia development is critically important in maintaining Hb concentrations after surgery. This may be accomplished through dedicated patient blood management programmes, which employ various peri-operative techniques to minimise blood loss (i.e. anti-fibrinolytics, acute normovolaemic haemodilution, low volume phlebotomy), recapture shed blood (i.e. cell salvage) and prevent excessive haemodilution [26–30]. Third, treatment of anaemia after surgery with pharmacological drugs such as intravenous iron and/or erythropoiesis-stimulating agents is worthy of future study. Several recent trials in critical illness, though limited in scope, suggest that these therapies are associated with improved Hb recovery and post-hospitalisation outcomes such as lower readmission rates and decreased mortality [31,32]. Further, survivors of critical illness with improved Hb recovery in the first 30 days after hospitalisation experience fewer readmissions and lower mortality in the first year post-hospitalisation [33].

Whilst the ideal study population for clinical trials of postoperative anaemia management interventions remains undefined, surgical patients undergoing major surgery requiring postoperative intensive care, as defined in this study, with Hb concentrations $< 110\ g.l^{-1}$ would be a reasonable group to target. Given that tests commonly used to assess for iron deficiency (e.g. ferritin, transferrin saturation) may be of limited utility in the presence of peri-operative inflammation, dedicated studies are necessary to evaluate other laboratory assays which may be employed for this purpose (e.g. reticulocyte Hb content, soluble transferrin receptor, hepcidin).

There are several limitations to this work. First, the potential for residual confounding is present despite prespecified covariate adjustment for key variables that may influence Hb concentrations and readmission rates. Several variables such as surgical duration and estimated blood loss were unable to be incorporated due to incomplete data availability. Second, we were unable to ascertain aetiologies for anaemia, which may influence rates of recovery and subsequent outcomes. As previously mentioned, anaemia in postsurgical patients is frequently multifactorial, including contributions from peri-operative blood loss, organ dysfunction, inflammation and haemodilution amongst others. Assigning relative contributions to these various aetiologies at the patient-level would be a challenging task with no workable framework at present. Third, there is likely to be heterogeneity in patient tolerance of postoperative anaemia, and future studies are necessary to evaluate patient and procedural factors conveying increased risk in greater detail. Fourth, our analysis focused on surgical admissions with postoperative intensive care, which limits generalisability to patients with less acute illness severity after surgery. Moreover, we did not account for the presence or absence of hospitalisations preceding the index surgical admission, which may influence underlying severity of illness and downstream outcomes.

In addition, whilst our combined cohorts contain representation of many individuals in the USA, generalisability to specific patient populations or ethnic and racial groups may be limited. However, the consistency of results across two distinct multicentre cohorts strengthens the validity of findings, with Kaiser Permanente Northern California representative of typical community surgical practices while Olmsted County is additionally enriched for complex surgical care such as transplantation and high-risk cardiac surgery where peri-operative or discharge anaemia may be more closely aligned with longitudinal outcomes. Also, we did not account for the trajectories of Hb concentrations beyond hospital discharge, which may influence readmissions rates. Finally, we were unable to capture reasons for unanticipated readmissions, which will be essential in future investigations evaluating the impact of peri-operative anaemia interventions.

In summary, anaemia at hospital discharge in surgical patients requiring postoperative intensive care is associated with increased rates of hospital readmissions in the first 30 days after hospitalisation. Future studies are necessary to evaluate strategies to prevent and/or treat anaemia in these patients for the improvement of post-hospitalisation outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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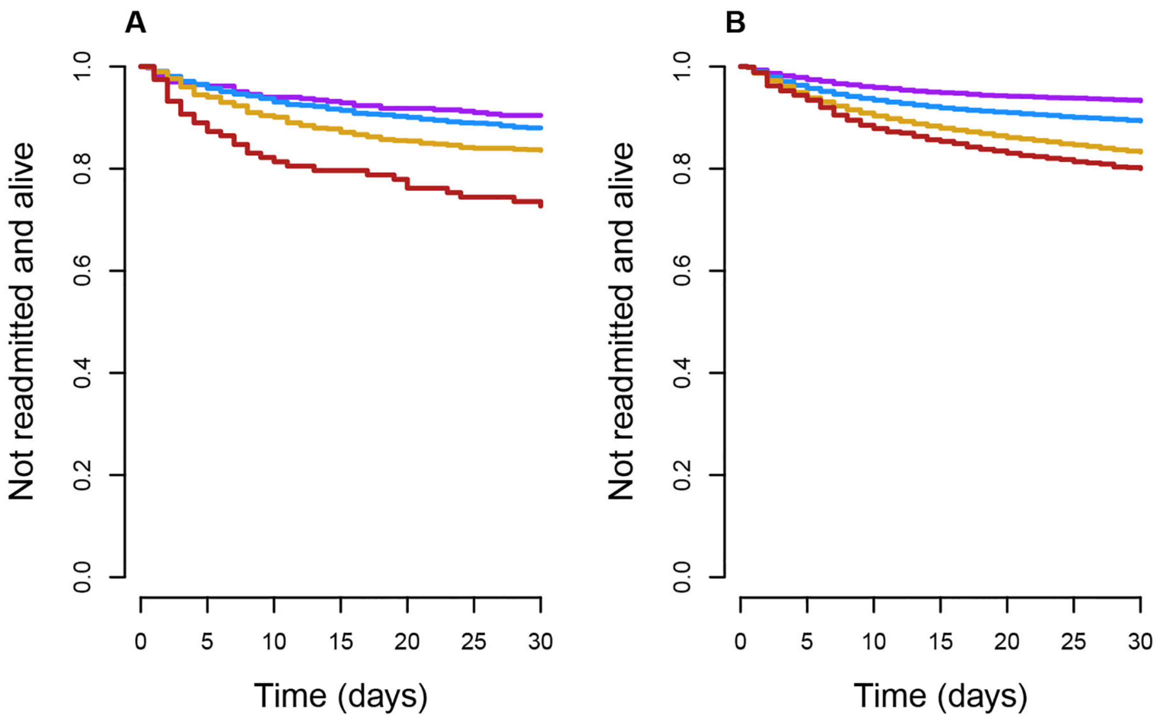

Figure 1.

Proportion of patients alive and not hospitalised over the first 30 days post-hospitalisation based on anaemia severity at hospital discharge at a) Olmsted County and b) Kaiser Permanent Northern California. Red, severe; orange, moderate; blue, mild; purple, none.

Table 1.

Patient and hospitalisation characteristics. Values are median (IQR [range]) or number (proportion).

	Olmsted County n = 3260	KPNC n = 29,452
Age; y	67 (54–78 [18–104])	67 (57–75 [18–100])
Male	1872 (57%)	17 335 (59%)
Race		
White	2969 (91%)	21,450 (73%)
Black	87 (3%)	2221 (7%)
Asian	65 (2%)	3483 (12%)
American Indian	5 (< 1%)	172 (1%)
Other	134 (4%)	2126 (7%)
Hispanic ethnicity *	-	3330 (12%)
Charlson comorbidity index	4 (2–6 [0–19])	2 (1–4 [0–18])
Congestive heart failure	392 (12%)	4820 (16%)
Cerebrovascular disease	408 (13%)	2287 (8%)
Chronic pulmonary disease	791 (24%)	5005 (17%)
Diabetes mellitus	827 (25%)	6586 (22%)
Myocardial infarction	271 (8%)	1541 (5%)
Peripheral vascular disease	700 (22%)	3740 (13%)
Admission APACHE 3 score **	56 (43–72 [4–166])	-
Type of surgery		
Cardiac	940 (29%)	8856 (30%)
Acute care	708 (22%)	3242 (11%)
General	461 (14%)	3890 (13%)
Orthopaedic	318 (10%)	2013 (7%)
Neurological	226 (7%)	2802 (10%)
Vascular	194 (6%)	4837 (16%)
Miscellaneous	134 (4%)	1181 (4%)
Transplant	84 (3%)	0
Obstetrics and gynaecology	74 (2%)	234 (1%)
Thoracic	51 (2%)	1154 (4%)
Urology	49 (2%)	761 (3%)
Head and neck	21 (1%)	482 (2%)
Pre-operative Hb; $g.l^{-1}$	134 (121–145 [22–214])	133 (121–145 [43–204])
Male	141 (127–151 [26–214])	139 (126–149 [43–204])
Female	127 (116–137 [22–181])	128 (117–137 [54–193])
Discharge Hb; $g.l^{-1}$	101 (92–114 [60–210])	106 (94–119 [51–199])
Male	103 (93–118 [60–210])	108 (95–123 [61–176])
Female	99 (90–109 [66–156])	103 (93–114 [51–199])
Anaemia at discharge	2894 (89%)	23,944 (81%)
Discharge MCV ***		

	Olmsted County n = 3260	**KPNC n = 29,452**
< 80	90 (3%)	904 (3%)
80–100	2643 (93%)	27 293 (93%)
> 100	102 (3%)	1226 (4%)
RBC transfusion during hospitalisation	1086 (33%)	7308 (25%)
RBC units	2 (1–4 [1–48])	2 (2, 4 [1–55])
ICU length of stay; d	1 (1–2 [0–62])	1 (1–3 [0–134])
Hospital length of stay; d	6 (4–9 [0–131])	5 (3–8 [0–316])

KPNC, Kaiser Permanente Northern California Health System; MCV, mean corpuscular volume; RBC, red blood cells.

Number of observations with complete data is listed when not all data were available.

[*] Hispanic ethnicity unavailable for Olmsted County

[**] APACHE scores unavailable for KPNC

[***] MCV values available for 2835 (86.9%) patients in Olmsted County and 29,423 (99.9%) in KPNC

Table 2.

Unanticipated readmissions and mortality rates by anaemia severity at hospital discharge. Values are number (proportion).

Olmsted County	**Non-anaemic n = 367**	**Mild n = 1413**	**Moderate n = 1361**	**Severe n = 119**	**Total n = 3260**
30 day readmissions	29 (7.9%)	153 (10.8%)	196 (14.4%)	31 (26.1%)	409 (12.5%)
90 day readmissions	48 (13.1%)	232 (16.4%)	284 (20.9%)	37 (31.1%)	601 (18.4%)
30 day mortality	10 (2.7%)	23 (1.6%)	35 (2.6%)	5 (4.2%)	73 (2.2%)
90 day mortality	12 (3.3%)	41 (2.9%)	63 (4.6%)	6 (5.0%)	122 (3.7%)
30 day readmission or death	35 (9.5%)	169 (12.0%)	222 (16.3%)	32 (26.9%)	458 (14.0%)
90 day readmission or death	56 (15.3%)	259 (18.3%)	321 (23.6%)	38 (31.9%)	674 (20.7%)
KPNC	**Non-anaemic n = 5508**	**Mild n = 13,509**	**Moderate n = 9508**	**Severe n = 927**	**Total n = 29,452**
30 day readmissions	330 (6.0%)	1315 (9.7%)	1476 (15.5%)	166 (17.9%)	3287 (11.2%)
90 day readmissions	493 (9.0%)	1793 (13.3%)	1892 (19.9%)	215 (23.2%)	4393 (14.9%)
30 day mortality	52 (0.9%)	165 (1.2%)	170 (1.8%)	25 (2.7%)	412 (1.4%)
90 day mortality	114 (2.1%)	361 (2.7%)	407 (4.3%)	49 (5.3%)	931(3.2%)
30 day readmission or death	366 (6.6%)	1,428 (10.6%)	1,578 (16.6%)	183 (19.7%)	3,555 (12.1%)
90 day readmission or death	571 (10.4%)	1,985 (14.7%)	2,075 (21.8%)	241 (26.0%)	4,872 (16.5%)

KPNC, Kaiser Permanente Northern California Health System.

Anaemia status defined as: non-anaemic, Hb ≥ 120 $g.l^{-1}$ for females or ≥ 130 $g.l^{-1}$ for males; mild, Hb ≥ 100 $g.l^{-1}$ and < 120 $g.l^{-1}$ for females or < 130 $g.l^{-1}$ for males; moderate, Hb ≥ 80 $g.l^{-1}$ and < 100 $g.l^{-1}$; severe, Hb < 80 $g.l^{-1}$.

Table 3.

Hazard ratio for readmission or death by each 10 $g.l^{-1}$ decrease in discharge haemoglobin

Olmsted County	Hazard ratio	95%CI	p
30 day readmission	1.09	1.02–1.18	0.014
90 day readmission	1.04	0.98–1.10	0.196
30 day mortality	0.99	0.84–1.17	0.900
90 day mortality	1.00	0.88–1.14	0.970
KPNC			
30 day readmission	1.08	1.06–1.11	< 0.001
90 day readmission	1.08	1.05–1.10	< 0.001
30 day mortality	0.94	0.88–1.01	0.075
90 day mortality	0.97	0.93–1.02	0.200

KPNC, Kaiser Permanente Northern California Health System.

Hazard ratio represents the hazard for hospitalisation or death, adjusted for age, sex, Charlson comorbidity index score, hospital length of stay and total red blood cell transfusion volume during hospitalisation.

Table 4.

Hazard ratio for 30 day readmission for each 10 $g.l^{-1}$ decrease in discharge haemoglobin concentration for varying levels of pre-operative haemoglobin

	Olmsted County			KPNC		
Pre-operative Hb	**Hazard ratio**	**95%CI**	**p**	**Hazard ratio**	**95%CI**	**p**
80 $g.l^{-1}$	1.23	1.04–1.45	0.016	1.12	1.05–1.19	< 0.001
100 $g.l^{-1}$	1.18	1.04–1.34	0.010	1.09	1.04–1.14	< 0.001
140 $g.l^{-1}$	1.08	1.00–1.16	0.039	1.04	1.01–1.06	0.009

KPNC, Kaiser Permanente Northern California

Hazard ratio represents the hazard for hospitalisation or death, adjusted for age, sex, pre-operative Hb concentration, Charlson comorbidity index score, hospital length of stay and total red blood cell transfusion volume during hospitalisation. Interaction p values for pre-operative Hb with discharge Hb and 30 day readmissions in Olmsted County and KPNC were 0.090 and 0.021, respectively.