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Original Article

Association of anaemia, co-morbidities and red blood cell transfusion according to age groups: multicentre sub-analysis of the German Patient Blood Management Network Registry

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Abstract

Background: Blood transfusions are common medical procedures and every age group requires detailed insights and treatment bundles. The aim of this study was to examine the association of anaemia, co-morbidities, complications, in-hospital mortality, and transfusion according to age groups to identify patient groups who are particularly at risk when undergoing surgery.

Methods: Data from 21 Hospitals of the Patient Blood Management Network Registry were analysed. Patients were divided into age subgroups. The incidence of preoperative anaemia, co-morbidities, surgical disciplines, hospital length of stay, complications, in-hospital mortality rate, and transfusions were analysed by descriptive and multivariate regression analysis.

Results: A total of 1 117 919 patients aged 18–108 years were included. With increasing age, the number of co-morbidities and incidence of preoperative anaemia increased. Complications, hospital length of stay, and in-hospital mortality increased with age and were higher in patients with preoperative anaemia. The mean number of transfused red blood cells (RBCs) peaked, whereas the transfusion rate increased continuously. Multivariate regression analysis showed that increasing age, co-morbidities, and preoperative anaemia were independent risk factors for complications, longer hospital length of stay, in-hospital mortality, and the need for RBC transfusion.

Conclusion: Increasing age, co-morbidities, and preoperative anaemia are independent risk factors for complications, longer hospital length of stay, in-hospital mortality, and the need for RBC transfusion. Anaemia diagnosis and treatment should be established in all patients.

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Introduction

Despite recent advances in surgical techniques and medical procedures, major surgery is still commonly associated with subsequent anaemia, substantial blood loss, and the need for blood transfusion. As age is considered a risk factor for severe adverse events[1] and a predictor for poor outcome with significantly higher mortality rate and postoperative complications[2–5], patients at older age need higher care resources during and after the in-hospital stay. In addition, co-morbidities often lead to complications and prolonged cure.

Anaemia is one of the most common diseases worldwide. The major cause in more than 50 per cent is altered erythropoiesis due to iron deficiency, leading to iron deficiency anaemia[6]. The second most common is anaemia of chronic disease representing up to 45 per cent, also called anaemia of inflammation and caused by cancer, acute or chronic diseases, which is predominant in hospitalized patients. Less than 10 per cent of anaemia is caused by genetic inheritance, vitamin B12 or folate deficiency, or diseases of the bone marrow[6]. Among elderly patients, renal disease and chronic inflammation account for approximately one-third of all anaemia incidences[7]. Anaemia leads, independent of age, to increased use of allogenic blood products and is associated with an increased complication rate, hospitalization, and mortality rate[8–11].

The aim of this study was to examine the association of anaemia, co-morbidities, complications, in-hospital mortality, and transfusion according to age groups to identify patient groups who are particularly at risk when undergoing surgery in a large data set of more than 1 million patients.

Methods

A sub-analysis of an ongoing prospective multicentre observational trial[12] focusing on the implementation and establishment of patient blood management (PBM) in surgical patients (registration number: NCT02147795; http://www.clinicaltrials.gov) was performed. The study was approved by the ethics committee of the University Hospital Frankfurt (reference number 318/17) and the Hessian data protection office (reference number 43.60; 60.01.21-ga). The requirement for written informed consent by patients was waived. The data were extracted from the respective electronic hospital information systems by the local information technology staff and anonymized for further analysis.

Patients and procedures

All adult (18 years or more) in-house patients with defined sex undergoing surgery (German OPS code 5-01 to 5-99) were included in the analysis. The surgeries covered all surgical disciplines: visceral and endocrine surgery, cardiac surgery, thoracic surgery, otorhinolaryngology, gynaecology, neurosurgery, obstetrics, dermatology, and ophthalmology, oral and maxillofacial surgery, surgery of the haematopoietic and lymphatic system, trauma and orthopaedic surgery, urology, vascular surgery, and mixed surgery (OPS codes from at least two different surgical disciplines) (*Table S1*). All patients received standard German perioperative care. Patients were divided into subgroups according to their age: 18–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80–89, 90–99, and 100–109 years.

Anaemia was defined according to the WHO as haemoglobin (Hb) concentration of less than 12.0 g/dl in women and less than 13.0 g/dl in men. Anaemia was categorized into mild (Hb 11.0–11.9 g/dl for women and Hb 11.0–12.9 g/dl for men); moderate (Hb 8.0–10.9 g/dl); and severe (Hb less than 8.0 g/dl).

All allogeneic blood products (red blood cell (RBC) concentrates, platelet concentrates, fresh frozen plasma, fibrinogen, and prothrombin complex concentrate) were administered in accordance with the previous German transfusion guideline[13,14].

Existing co-morbidities (diabetes, hypertension, chronic kidney disease, chronic pulmonary disease, neurological disorder, heart insufficiency, and malignancy) were defined by their respective ICD codes (*Table S2*). Hospital-acquired complications indicated by new diagnoses during the in-hospital stay (pneumonia, sepsis, acute renal failure, myocardial infarction, and ischaemic stroke) were also defined by their respective ICD codes (*Table S2*). In-hospital mortality was analysed based on existing discharge codes and thereby defined as mortality during the in-hospital stay.

Statistical analysis

The aim of the analysis was to describe patient characteristics (for example co-morbidities, sex, surgery groups, and preoperative anaemia) and clinical outcomes (for example length of hospital stay (LOS), in-hospital mortality, complications, postoperative and hospital-acquired anaemia, and blood product consumption) for adult surgical patients divided into age groups of 10 years. In addition, multivariate regression analysis was performed to identify dependence of clinical outcomes on the chosen patients' characteristics and hence to give indications for risk factors in clinical routine that could be targeted for effective patient care.

Values for the descriptive analysis are reported as rates with 95 per cent confidence interval (c.i.) for categorical variables, and as mean(s.e.m.) or median and interquartile range for continuous variables. Patient characteristics (age, sex, co-morbidities, preoperative anaemia, and surgery type) and outcomes (postoperative and hospital-acquired anaemia rates and severity, postoperative complication rates, in-hospital mortality rates, LOS, blood product transfusion rates, and mean consumptions) within the different age groups are shown. A descriptive sub-analysis (regarding patient groups with and without preoperative anaemia) for chosen outcomes (composite endpoint of complications, LOS, and in-hospital mortality) was performed. Another descriptive sub-analysis was performed for patients with and without RBC transfusions for the outcome of in-hospital mortality.

The *P* values from the multivariate analysis were derived from mixed logistic regression models for categorical binary variables and from mixed linear regression models for continuous variables, including the hospitals as random variables and age group, sex, surgery discipline, preoperative anaemia, and sum of co-morbidities as fixed effects. The strength and direction of the included influence factors was estimated by the OR with 95 per cent c.i. for categorical binary variables and by the difference of the mean(s.e.m.) for continuous variables.

Analysis was performed using R version 3.6 for windows (R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org/).

Results

Age, sex, surgery disciplines, co-morbidities, and prevalence of preoperative anaemia

A total of 1 117 919 patients from 21 German hospitals underwent surgery between 1 January 2010 and 20 September 2019 and were included in the analysis. The minimum age was 18 years and the maximum age was 108 years. Overall, 51.3 per cent (573 816) of the

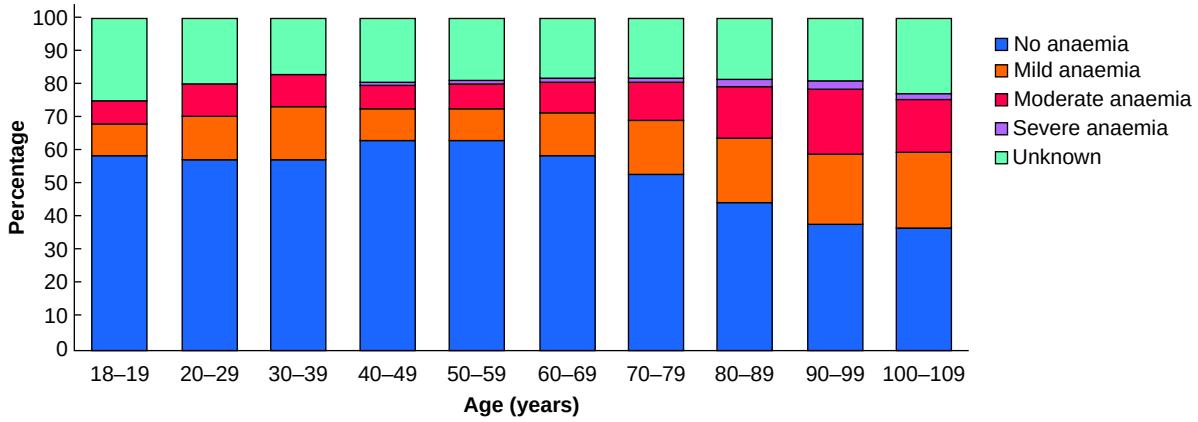

Fig. 1 Distribution of preoperative anaemia severities according to age groups

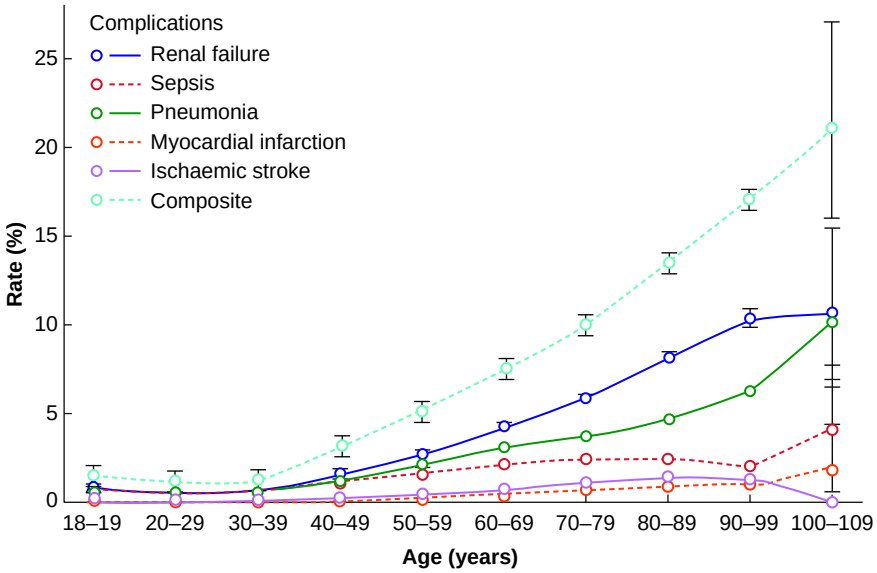

Fig. 2 Perioperative complication rates according to age groups: single and composite rate of complications with 95 per cent confidence interval per age group

patients were female. The proportion of female patients varied between the different age groups and was dominant at the ages of 20–49 years and 80–109 years (*Table S3*). Types of surgery performed varied between age groups: the majority of patients aged between 18–19 years underwent trauma and orthopaedic surgery (21.3 per cent); those aged between 20–29 and 30–39 years underwent obstetric surgery (34.0 per cent and 43.3 per cent); those aged between 40–49, 50–59, 60–69 years underwent visceral and endocrine surgery (18.7 per cent, 19.8 per cent and 18.4 per cent); those aged between 70–79 and 80–89 years underwent mostly dermatological and ophthalmological surgery (18.3 per cent and 22.5 per cent); and those aged between 90–109 years underwent trauma and orthopaedic surgery (28.1 per cent and 39.4 per cent) (*Table S3* and *Fig. S1*).

The total number of co-morbidities increased with age (*Table S4* and *Fig. S2*). The mean total number of co-morbidities increased from 0.1(0.0) at the age of 18–39 years up to 1.8(0.0) at the age of 90–99 years. The rate of patients with at least one co-morbidity rose from 9.1 per cent (8.6 to 9.6 per cent) for patients aged 18–19 years up to 83.7 per cent (83.1 to 84.2 per cent) for patients aged 90–99 years. The rate of each co-morbidity, except neurological diseases and chronical kidney diseases, increased only until a certain age and then stabilized or even decreased again (*Table S4* and *Fig. S3*).

Overall prevalence of preoperative anaemia increased from the age group of 18–19 years (22.3 per cent; 21.5 to 23.2 per cent) until a maximum at 90–99 years (53.3 per cent; 52.5 to 54.1 per cent) (*Table S3*). The prevalence of mild preoperative anaemia increased from 9.5 per cent (aged 40–49 years) up to 22.5 per cent (aged 100–109 years), of moderate preoperative anaemia from 7.3 per cent (aged 40–49 years) up to 19.5 per cent (aged 90–99 years), and of severe anaemia from 1.0 per cent (aged 40–49 years) up to 2.9 per cent (aged 90–99 years) (*Table S3* and *Fig. 1*).

Complications, in-hospital mortality, length of stay, and incidence of hospital-acquired anaemia

The mean total number of complications increased slightly from 0.1(0.0) at the age of 18–49 years up to 0.3(0.0) at the age of 100–109 years (*Table S5*). The rate of patients with at least one hospital-acquired complication rose from 1.0 per cent (1.0

Table 1 Complications, length of in-hospital stay, and mortality rate according to presence of preoperative anaemia by age groups. Postoperative and hospital-acquired anaemia rates according to age groups

Age (years)	18–19 n = 12 485	20–29 n = 100 762	30–39 n = 136 847	40–49 n = 112 220	50–59 n = 171 687	60–69 n = 198 869	70–79 n = 238 172	80–89 n = 128 631	90–99 n = 18 028	100–109 n = 218
Composite complication rate*‡	1.6 (1.4–1.8) n = 201	1.0 (1.0–1.1) n = 1028	1.2 (1.2–1.3) n = 1664	3.3 (3.2–3.4) n = 3728	5.1 (5.0–5.2) n = 8738	7.8 (7.6–7.9) n = 15 422	10.0 (9.9–10.2) n = 23 896	13.5 (13.3–13.6) n = 17 302	17.0 (16.4–17.5) n = 3060	21.1 (15.9–27.1) n = 46
With preoperative anaemia	5.8 (4.9–6.9) n = 123 of 2114	2.4 (2.2–2.6) n = 567 of 23 605	2.6 (2.4–2.8) n = 917 of 35 501	10.1 (9.7–10.5) n = 2023 of 20 043	14.7 (14.3–15.1) n = 4561 of 31 055	17.6 (17.2–17.9) n = 8225 of 46 818	18.5 (18.2–18.8) n = 12 978 of 70 298	19.9 (19.5–20.2) n = 9569 of 48 195	22.4 (21.5–23.4) n = 1760 of 7846	29.5 (20.3–40.2) n = 26 of 88
Without preoperative anaemia	0.9 (0.7–1.1) n = 66 of 7349	0.6 (0.6–0.7) n = 370 of 57 801	0.8 (0.7–0.9) n = 642 of 79 253	2.1 (2.0–2.2) n = 1457 of 70 814	3.3 (3.2–3.4) n = 3608 of 108 682	5.4 (5.3–5.5) n = 6303 of 117 035	7.6 (7.4–7.7) n = 9560 of 126 279	11.6 (11.4–11.9) n = 6631 of 56 972	15.8 (15.0–16.7) n = 1086 of 6870	18.5 (10.8–28.7) n = 15 of 81
Length of hospital stay (days)†	5.5 (±0.1)	5.0 (±0.0)	5.2 (±0.0)	6.6 (±0.0)	7.9 (±0.0)	9.2 (±0.0)	9.7 (±0.0)	10.1 (±0.0)	10.1 (±0.1)	8.8 (±0.5)
With preoperative anaemia	9.9 (±0.4)	6.8 (±0.1)	6.9 (±0.1)	11.7 (±0.1)	14.2 (±0.1)	14.9 (±0.1)	14.0 (±0.1)	12.9 (±0.1)	11.8 (±0.1)	9.6 (±0.9)
Without preoperative anaemia	5.1 (±0.1)	4.8 (±0.0)	4.9 (±0.0)	6.1 (±0.0)	7.2 (±0.0)	8.2 (±0.0)	9.0 (±0.0)	9.9 (±0.0)	10.5 (±0.1)	9.7 (±0.8)
Mortality rate*	0.3 (0.2–0.5) n = 42	0.2 (0.2–0.3) n = 234	0.3 (0.2–0.3) n = 374	0.8 (0.8–0.9) n = 932	1.4 (1.3–1.5) n = 2408	2.1 (2.0–2.1) n = 4140	2.7 (2.6–2.8) n = 6402	3.9 (3.7–4.0) n = 4955	6.3 (6.0–6.7) n = 1140	8.7 (5.3–13.3) n = 19
With preoperative anaemia	1.2 (0.8–1.7) n = 25 of 2114	0.6 (0.5–0.7) n = 139 of 23 605	0.6 (0.5–0.7) n = 222 of 35 501	2.9 (2.7–3.2) n = 586 of 20 043	4.8 (4.5–5.0) n = 1476 of 31 055	5.5 (5.3–5.7) n = 2564 of 46 818	5.6 (5.4–5.8) n = 3945 of 70 298	6.1 (5.9–6.3) n = 2922 of 48 195	8.1 (7.5–8.7) n = 633 of 7846	11.4 (5.6–19.9) n = 10 of 88
Without preoperative anaemia	0.1 (0.1–0.3) n = 11 of 7349	0.1 (0.1–0.1) n = 65 of 57 801	0.1 (0.1–0.2) n = 110 of 79 253	0.4 (0.3–0.4) n = 268 of 70 814	0.7 (0.6–0.7) n = 750 of 108 682	1.1 (1.0–1.2) n = 1287 of 117 035	1.6 (1.5–1.7) n = 2037 of 126 279	2.9 (2.7–3.0) n = 1628 of 56 972	6.0 (5.4–6.6) n = 412 of 6870	7.4 (2.8–15.4) n = 6 of 81
With RBC transfusion	9.0 (6.5–12.1) n = 40	8.0 (6.9–9.2) n = 184	8.3 (7.4–9.3) n = 284	12.4 (11.5–13.2) n = 712	13.3 (12.7–13.9) n = 1734	13.3 (12.8–13.7) n = 2917	13.6 (13.2–14.0) n = 4267	14.8 (14.3–15.3) n = 2754	14.2 (13.0–15.4) n = 477	24.4 (12.9–39.5) n = 11
Without RBC transfusion	0.0 (0.0–0.1) n = 2	0.1 (0.0–0.1) n = 50	0.1 (0.1–0.1) n = 90	0.2 (0.2–0.2) n = 220	0.4 (0.4–0.5) n = 674	0.7 (0.7–0.7) n = 1223	1.0 (1.0–1.1) n = 2135	2.0 (1.9–2.1) n = 2201	4.5 (4.2–4.9) n = 663	4.6 (2.0–8.9) n = 8
Postoperative anaemia rate	43.6 (42.5–44.6) n = 3519 of 8080	56.5 (56.1–56.9) n = 41 144 of 72 827	61.2 (60.9–61.5) n = 64 768 of 105 810	44.3 (44.0–44.7) n = 35 415 of 79 857	47.8 (47.5–48.1) n = 58 899 of 123 179	57.2 (56.9–57.4) n = 84 918 of 148 561	64.3 (64.1–64.5) n = 116 547 of 181 252	71.4 (71.1–71.7) n = 69 910 of 97 926	77.9 (77.2–78.6) n = 11 166 of 14 335	86.9 (80.9–91.5) n = 152 of 175
Hospital-acquired anaemia rate	26.6 (25.4–27.8) n = 1392 of 5241	39.1 (38.7–39.6) n = 17 152 of 43 848	45.1 (44.7–45.5) n = 28 683 of 63 630	29.2 (28.8–29.5) n = 16 102 of 55 219	33.6 (33.3–33.9) n = 28 708 of 85 443	41.1 (40.8–41.4) n = 39 347 of 95 739	46.1 (45.8–46.4) n = 48 994 of 106 278	49.9 (49.4–50.3) n = 23 987 of 48 087	56.3 (55.1–57.6) n = 3397 of 6030	75.0 (63.4–84.5) n = 54 of 72

The denominator is only shown for the subgroup analysis, otherwise it is equal to *n* of each age subgroup displayed in the first line of the table. *Values are % (95% c.i.). †Values are mean(±s.e.m.). ‡At least one complication present. RBC, red blood cell.

to 1.1 per cent) for patients aged 20–29 years up to 21.1 per cent (15.9 to 27.1 per cent) for patients aged 100–109 years (*Table S5* and *Fig. 2*).

The composite complication rate was higher in patients with preoperative anaemia than in patients without preoperative anaemia (*Table 1*).

The mean LOS raised from 5.0(±0.0) days in patients aged 20–29 years up to 10.1(0.0) in patients aged 80–89 years. With the additional diagnosis of preoperative anaemia, mean LOS was prolonged (*Table 1* and *Fig. S4*).

In-hospital mortality rate increased from 0.2 per cent (0.2 to 0.3 per cent) in patients aged 20–29 years to 8.7 per cent (5.3 to 13.3 per cent) in patients aged more than 100 years (*Table 1*). In-hospital mortality rate was higher in patients with preoperative anaemia (*Table 1* and *Fig. 3*).

Postoperative anaemia rate ranged from 43.6 per cent (42.5 to 44.6 per cent) in patients aged 18–19 years up to 86.9 per cent (80.9 to 91.5 per cent) in patients over 100 years (*Table 1* and *Table S5*). The rate of hospital-acquired anaemia ranged from 26.6 per cent (25.4 to 27.8 per cent) in patients aged 18–19 years up to 75.0 per cent (63.4–84.5 per cent) in patients more than 100 years (*Table 1*). The severity of hospital-acquired anaemia was categorized mostly as mild (dominant for patients aged 18–69 years) or moderate (dominant for patients aged 70–109 years) (*Table S5* and *Fig. S5*).

Blood product consumption with special focus on in-hospital mortality

The data indicate that receipt of RBC transfusion is more probable at an older age, whereas the number of RBCs per patient decreases at older age. The RBC transfusion rate increased continuously from 2.3 per cent (2.2 to 2.4 per cent) for patients aged 20–29 years until 20.6 per cent (15.5 to 26.6 per cent) (100–109 years) (*Table 2*). The mean number of RBCs per 1000 patients increased from 156 ± 6 units (20–29 years) until 678 ± 6 units (70–79 years). At all ages, the RBC transfusion rate and mean number of RBCs per 1000 patients were higher in patients with preoperative anaemia than in patients without preoperative anaemia (approximately 3.4- to 10.1-fold) (*Table 2*, *Fig. 4*). RBC transfusion is associated with higher in-hospital mortality in every age group, but causality cannot be proven (*Table 2* and *Fig. 4*). While in non-transfused patients, in-hospital mortality increased from 0.0 per cent (0.0 to 0.1 per cent) in patients aged 18–19 years continuously to 4.6 per cent (2.0 to 8.9 per cent) in patients aged 100–109 years; in-hospital mortality of transfused patients ranged from 8.0 per cent (6.9 to 9.2 per cent) at 20–29 years of age up to 24.4 per cent (12.9 to 39.5 per cent) at 100–109 years of age (*Table 1*).

Multivariate analysis of potential independent risk factors (age, preoperative anaemia, and co-morbidities) on transfusion outcomes, LOS, postoperative complications, and in-hospital mortality

To identify risk factors independently associated with postoperative outcome, linear and logistic multivariate regression models, including the hospitals as random variables

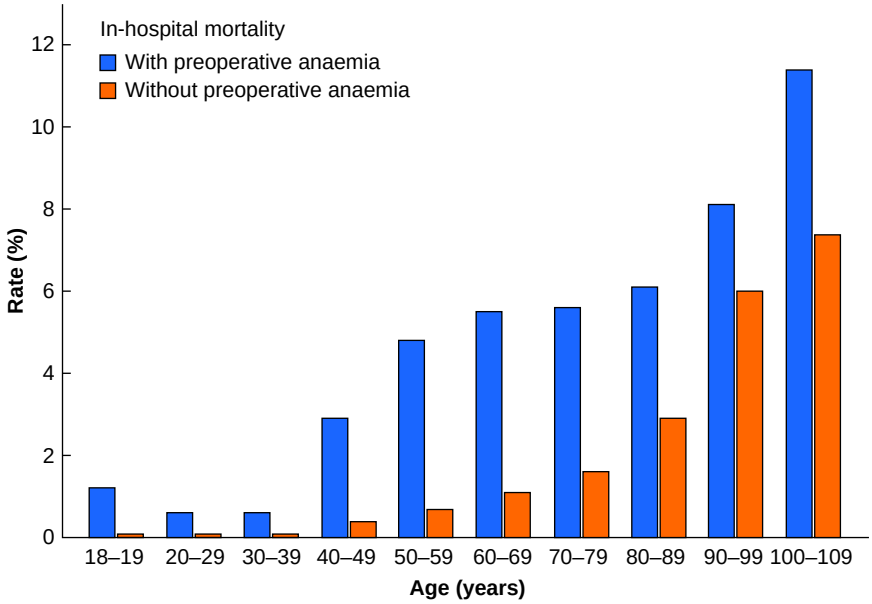

Fig. 3 In-hospital mortality rate with and without preoperative anaemia according to age groups

and all other variables such as age group, sex, surgery discipline, preoperative anaemia, and sum of co-morbidities as fixed effects, were performed. Age, preoperative anaemia, co-morbidities, surgery group, and sex were independent risk factors for the following outcomes: composite complications, single complications (renal failure, sepsis, pneumonia, ischaemic stroke, and myocardial infarction), postoperative anaemia, in-hospital mortality, LOS, RBC transfusion rate, RBC mean consumption, and hospital-acquired anaemia. In patients with preoperative anaemia, the mean difference in LOS and the OR of in-hospital mortality rate, composite complication rate, single complication rates, and RBC transfusion rate were significantly higher ($P < 0.001$). A higher sum of co-morbidities contributed significantly to a higher OR of all outcomes ($P < 0.001$). In women, mean LOS, in-hospital mortality, and event rates of complications were significantly lower, but RBC transfusion rate, RBC mean consumption, and hospital-acquired anaemia rate were significantly higher compared with men ($P < 0.001$) (*Table 3*, *Table S6* and *Table S7*).

Discussion

In the present multicentre analysis of more than 1 million surgical patients, anaemia, co-morbidities, and the need for allogeneic blood products was more common with rising age. Rates of perioperative complications, LOS, and in-hospital mortality also increased with age. Age, preoperative anaemia, and co-morbidities could be identified as independent risk factors for a longer LOS and higher in-hospital mortality, postoperative anaemia, and RBC transfusion rate as well as a higher mean consumption of RBCs. RBC transfusion was associated with a higher in-hospital mortality in every age group, but causality could not be proven. The data indicate that anaemia is associated with increased in-hospital mortality in all age groups, preoperative anaemia is an independent risk factor for postoperative complications, and patients with increasing age are more likely to receive an RBC unit.

In 2013, Loor *et al.* found that both anaemia and RBC transfusions may have an impact on patients' health[15]. The first conclusion could be that anaemia should be treated, even before a surgical

Table 2 Mean consumption and transfusion rates of allogeneic red blood cell (RBC) units with dependence on preoperative anaemia according to age groups

Age (years)	18–19 $n = 12\,485$	20–29 $n = 100\,762$	30–39 $n = 136\,847$	40–49 $n = 112\,220$	50–59 $n = 171\,687$	60–69 $n = 198\,869$	70–79 $n = 238\,172$	80–89 $n = 128\,631$	90–99 $n = 18\,028$	100–109 $n = 218$
RBC units mean per 1000 patients†	268(±22)	156(±6)	163(±6)	384(±10)	506(±8)	663(±8)	678(±6)	567(±6)	502(±11)	477(±92)
With preoperative anaemia	1126(±107)	448(±22)	436(±18)	1481(±43)	1857(±36)	1868(±26)	1518(±17)	1074(±14)	852(±21)	875(±208)
Without preoperative anaemia	111(±21)	68(±6)	70(±5)	152(±8)	227(±7)	328(±7)	380(±6)	305(±7)	253(±11)	198(±69)
RBC transfusion rate*	3.5 (3.2–3.9) $n = 442$	2.3 (2.2–2.4) $n = 2302$	2.5 (2.4–2.6) $n = 3403$	5.1 (5.0–5.3) $n = 5758$	7.6 (7.5–7.7) $n = 13\,063$	11.0 (10.9–11.2) $n = 21\,966$	13.2 (13.1–13.3) $n = 31\,413$	14.5 (14.3–14.7) $n = 18\,657$	18.6 (18.1–19.2) $n = 3359$	20.6 (15.5–26.6) $n = 45$
With preoperative anaemia	14.6 (13.1–16.1) $n = 308$	6.6 (6.3–6.9) $n = 1560$	6.4 (6.2–6.7) $n = 2278$	18.8 (18.3–19.4) $n = 3778$	25.9 (25.4–26.4) $n = 8052$	29.2 (28.7–29.6) $n = 13\,649$	28.3 (27.9–28.6) $n = 19\,880$	26.9 (26.5–27.3) $n = 12\,945$	30.6 (29.5–31.6) $n = 2397$	33.0 (23.3–43.8) $n = 29$
Without preoperative anaemia	1.3 (1.1–1.6) $n = 98$	0.9 (0.9–1.0) $n = 547$	1.2 (1.1–1.2) $n = 917$	2.4 (2.3–2.5) $n = 1678$	4.0 (3.9–4.1) $n = 4334$	6.2 (6.1–6.4) $n = 7303$	8.1 (7.9–8.2) $n = 10\,201$	8.2 (8.0–8.4) $n = 4670$	10.5 (9.8–11.2) $n = 719$	11.1 (5.2–20.0) $n = 9$

*Values are % (with 95% c.i.). †Values are mean(±s.e.m.). RBC, red blood cell.

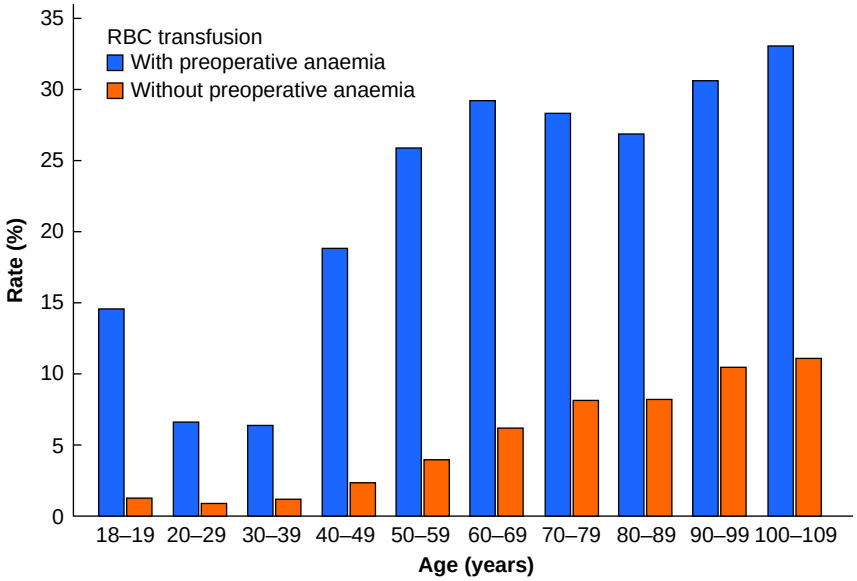

Fig. 4 RBC transfusion rate with and without preoperative anaemia according to age groups

RBC, red blood cell

intervention. But in Germany, anaemia screening and treatment is still not standard care in most hospitals and should therefore be supported. A second conclusion could lead to the aim to avoid unnecessary RBC transfusions during the entire stay in hospital. Therefore, rational transfusion regimens should be followed according to current guidelines, including in older patient cohorts[13].

The high percentage of visceral surgery in patients aged 40–60 years is explained by the high incidence of acute appendicitis and symptomatic gallstones or acute cholecystitis at the age of 40–60 years[16]. The number of co-morbidities increased continuously until the age of 80 years. In contrast, malignancies peaked at 60–69 years, and patients with malignancy have increased mortality. In addition, RBC consumption has been shown to be associated with increased mortality[17]. For colon cancer[18], gastric cancer[19], and bladder cancer[20] increased cancer recurrence rates have been reported in transfused compared with non-transfused patients. In addition, malignancy can lead to anaemia. The anaemia of chronic disease is highly prevalent in malignancy, but also in other chronic diseases such as heart failure and renal insufficiency[21]. As chronic diseases are more prevalent at higher age, anaemia is also more prevalent and the diagnosis of anaemia requires additional investigations to determine the underlying cause of anaemia[22].

Overall, the present data shows a higher incidence of the complications renal failure, sepsis, myocardial infarction, ischaemic stroke, and pneumonia in patients at increasing age. Age itself has been described as an independent risk factor in the development of acute kidney injury. Further explanations for the increase might be the decreasing glomerular filtration rate with increasing age, inflammation, and co-morbidities such as chronic kidney disease, congestive heart failure, and diabetes mellitus[23,24]. Likewise, these complications had an increasing incidence in the study population with increasing age.

In the present analysis, in-hospital mortality also increased significantly with increasing patient age, which is expected and in line with the results of recent studies. Caterino *et al.* explored

Table 3 Multivariate analysis of risk factors age, preoperative anaemia, sum of co-morbidities on outcomes LOS, mortality, composite complications, and red blood cell transfusion rate

		Length of hospital stay (days)*	Mortality rate†	Composite complication rate†	RBC transfusion rate†
Age (years)	20–29	−0.38(±0.12)*	NS	0.82 (0.72–0.92)*	0.74 (0.68–0.80)
	30–39	−0.41(±0.12)	NS	NS	0.73 (0.67–0.79)
	40–49	NS	1.71 (1.42–2.04)	1.41 (1.26–1.57)	NS
	50–59	0.66(±0.12)	2.29 (1.92–2.72)	1.52 (1.36–1.69)	1.27 (1.18–1.37)
	60–69	0.93(±0.12)	2.70 (2.78–3.21)	1.64 (1.47–1.82)	1.50 (1.40–1.62)
	70–79	0.85(±0.12)	3.22 (2.72–3.82)	1.71 (1.54–1.91)	1.57 (1.46–1.68)
	80–89	0.77(±0.12)	4.62 (3.90–5.49)	2.13 (1.91–2.37)	1.51 (1.50–1.73)
	90–99	0.48(±0.15)	9.14 (7.64–10.94)	3.10 (2.76–3.48)	2.40 (2.21–2.61)
	>99	NS	15.90 (10.11–25.01)	5.71 (4.09–7.99)	3.34 (2.72–4.09)
Preoperative anaemia		3.46(±0.03)	2.92 (2.82–3.01)	2.10 (2.07–2.14)	5.21 (5.12–5.29)
Sum of co-morbidities	Per increase of 1 co-morbidity	2.19(±0.01)	1.39 (1.38–1.41)	1.77 (1.76–1.78)	1.41 (1.40–1.42)

*Values are mean(±s.e.m.). †Values are OR (95% c.i.). For the age groups, all values are with respect to age group 18–19 years, for co-morbidities all values represent the values after augmentation by 1 unit (that means for 1 co-morbidity more) with respect to before the augmentation, and for preoperative anaemia with respect to without anaemia. All significant *P* values were $P < 0.001$, except for * ($P = 0.001$). RBC, red blood cell.

about 75 600 patients with traumatic injuries and found a significantly higher mortality rate in patients older than 70 years[25]. Milzman *et al.* analysed 7789 patients for pre-existing disease and showed that pre-existing diseases were an independent predictor of mortality. The median age of patients with pre-existing diseases was higher. The mortality rate for patients with two or more co-morbidities was higher[26]. Baron *et al.* analysed about 40 000 patients with moderate or severe anaemia and demonstrated higher in-hospital mortality and prolonged hospital LOS as well as a higher number of postoperative admissions to intensive care units in 27 European countries[8].

It should be mentioned that anaemia in women is still defined as Hb levels less than 12 g/dl, even though the classification of anaemia in non-pregnant women by WHO has been the subject of many discussions in recent years[27]. By accepting lower Hb levels in women, transfusions with all their possible side effects and complications are more likely in women[28,29], as shown in the present results, where RBC transfusion rate, RBC mean consumption, and hospital-acquired anaemia rate in women were significantly higher compared with men. In addition, women may be excluded from effective therapy of preoperative anaemia because of the 'accepted' Hb value[30].

Although this study presents a large patient cohort, including more than 1 million patients, some limitations need to be considered. Routine data were used, thus data amount and quality varied between the hospitals. The utilized ICD codes do not allow a clear distinction between an underlying disease as an indication for surgery and a new diagnosis made during the inpatient stay. For this reason, the complications of ischaemic stroke and acute myocardial infarction were not investigated in the group of neurosurgical and cardiac surgery respectively.

The group of 18–19-year-olds is special, as patients in this age group are often severely injured trauma patients or are suffering from malignant diseases[31] and are therefore only suitable for comparison to a limited extent. The group of patients aged 20–39 years includes a large number of healthy patients undergoing obstetric procedures. To some extent, LOS is certainly dependent on the days of the week, as more patients are usually discharged on weekdays rather than on weekends. Furthermore, the higher mortality rate in transfused patients compared with non-transfused patients is probably multifactorial. Patients who need transfusions may have a complicating surgical or medical condition, therefore, higher mortality cannot be directly attributed to RBC transfusion.

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Supplementary material

Supplementary material is available at *BJS Open* online.

Data availability

The data set generated during and/or analysed during the present study are available from the corresponding author on reasonable request.

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