EClinicalMedicine 36 (2021) 100894

Contents lists available at ScienceDirect

EClinicalMedicine

journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

Research Paper

Prevalence and intervention of preoperative anemia in Chinese adults: A retrospective cross-sectional study based on national preoperative anemia database

Jie Lin[a,#], Chao Wang[b,#], Junting Liu[a,#], Yang Yu[a], Shufang Wang[a], Aiqing Wen[c], Jufeng Wu[d], Long Zhang[e], Futing Sun[f], Xiaojun Guo[g], Fenghua Liu[h], Hailan Li[i], Na Li[j], Haibao Wang[k], Yi Lv[l], Zhonghua Jia[m], Xiaoyan Li[n], Jun Zhang[o], Zunyan Li[p], Shanshan Liu[q], Shuhuai Zhong[r], Jun Yang[s], Shuxuan Ma[t], Lingling Zhou[a], Xiaozhen Guan[a], Chunya Ma[a], Shijun Cheng[u], Shengxiong Chen[u], Zhenhua Xu[u,†,*], Gang Li[b,†,**], Deqing Wang[a,†,***]

[a] Department of Transfusion Medicine, The First Medical Center of PLA General Hospital, Beijing, China
[b] Institute of Statistics and Information, Beijing Center for Diseases Control and Prevention, Beijing, China
[c] Department of Blood Transfusion, Daping Hospital, Army Medical University, Chongqing, China
[d] Department of Blood Transfusion, Hainan Provincial People's Hospital, Haikou, Hainan, China
[e] Department of Blood Transfusion, Affiliated Hospital of Chifeng University, Inner Mongolia Autonomous Region, China
[f] Department of Blood Transfusion, Weifang People's Hospital, Shandong, China
[g] Department of Blood Transfusion, The First Hospital of Shanxi Medical University, Shanxi, China
[h] Department of Blood Transfusion, The First Affiliated Hospital of Harbin Medical University, Heilongjiang, China
[i] Department of Blood Transfusion, The People's Hospital of Guangxi Zhuang Autonomous Region, Guangxi Zhuang Autonomous Region, China
[j] Department of Blood Transfusion, General Hospital of Easter Theater Command, Jiangsu, China
[k] Department of Blood Transfusion, Hainan Hospital of PLA General Hospital, Hainan, China
[l] Clinical Laboratory Medicine Center, Zhengzhou Yihe Hospital Affiliated to Henan University, Henan, China
[m] Department of Blood Transfusion, Gaoan People's Hospital, Jiangxi, China
[n] Department of Blood Transfusion, Baoji Central Hospital, Shaanxi, China
[o] Department of Blood Transfusion, The First Affiliated Hospital of Bengbu Medical College, Anhui, China
[p] Department of Blood Transfusion, Affiliated Hospital of Beihua University, Jilin, China
[q] Department of Blood Transfusion, The First People's Hospital of GuiYang, Guizhou, China
[r] Department of Blood Transfusion, Guizhou Provincial People's Hospital, Guizhou, China
[s] Department of Blood Transfusion, Zigong Fourth People's Hospital, Sichuan, China
[t] Department of Blood Transfusion, Beijing Children's Hospital, Capital Medical University, Beijing, China
[u] HealSci Technology Co., Ltd, Beijing, China

ARTICLE INFO

Article History:
Received 18 December 2020
Revised 15 April 2021
Accepted 22 April 2021
Available online xxx

Keywords:
Preoperative anemia
Transfusion
Iron
Erythropoietin

ABSTRACT

Background: Preoperative anemia is an important pillar of perioperative patient blood management. However, there was no literature comprehensively described the current situation of preoperative anemia in China.

Methods: We conducted a national retrospective cross-sectional study to assess the prevalence and intervention of preoperative anemia in Chinese adults. Data were from the National Preoperative Anemia Database based on hospital administration data from January 1, 2013 to December 31, 2018.

Findings: A total of 797,002 patients were included for analysis. Overall, 27.57% (95% CI 27.47–27.67) of patients had preoperative anemia, which varied by gender, age, regions, and type of operation. Patients who were female, age over 60 years old, from South China, from provinces with lower per capita GDP, underwent operations on the lymphatic and hematopoietic system, with laboratory abnormalities were more likely to have a high risk of preoperative anemia. Among patients with preoperative anemia, 5.16% (95% CI 5.07–5.26) received red blood cell transfusion, 7.79% (95% CI 7.67–7.91) received anemia-related medications such as iron, erythropoietin, folic acid or vitamin B12, and 12.25% (95% CI 12.10–12.40) received

* Corresponding auhtor at: HealSci Technology Co., Ltd, 1606, Tower5, 2Rong Hua South Road, BDA, Beijing, 100176, China.
** Corresponding auhtor at: Institute of Statistics and Information, Beijing Center for Diseases Control and Prevention, Beijing, 100013, China.
*** Corresponding auhtor at: Department of Medicine Transfusion, The First Medical Center of PLA General Hospital, Beijing, 100853, China.
E-mail addresses: Xuzhenhua0@gmail.com (Z. Xu), ligang@bjcdc.org (G. Li), deqingw301@yeah.net (D. Wang).
# Contributed equally as first authors
† Contributed equally as corresponding authors

https://doi.org/10.1016/j.eclinm.2021.100894

anemia-related therapy (red blood cell transfusion or anemia-related medications) before operation. The probability of preoperative RBC transfusion decreased by 54.92% (OR 0.46, 95% CI 0.46−0.47) as each 10-g/L increase in preoperative hemoglobin. Patients with preoperative hemoglobin less than 130 g/L was associated with longer hospital stay and more hospital costs. Patients with severe preoperative anemia given iron preoperatively had lower intra/post-operative RBC transfusion rate, shorter length of stay and less hospitalization costs, but no similar correlation was found in patients with mild and moderate preoperative anemia and patients given erythropoietin preoperatively.

Interpretation: Our present study shows that preoperative anemia is currently a relatively prevalent problem that has not been fully appreciated in China. More researches will be required to optimize the treatment of preoperative anemia.

Funding: National Natural Science Foundation of China and the Logistics Support Department of the Central Military Commission.

Research in context

Evidence before this study

Most previous studies on preoperative anemia were limited to targeted specific procedures, and only few studies included more than 10,000 cases nationally or from multiple countries. There is no national preoperative anemia study about Chinese. The prevalence and intervention status of preoperative anemia in the Chinese population remain unclear.

Added value of this study

We found that the overall prevalence of preoperative anemia was 27.57% and the intervention rate for preoperative anemia was only 12.57% in China, with a lower proportion of patients being treated with medication. Most red blood cell (RBC) transfusions might have been avoided if restrictive transfusion strategy had been strictly followed because more than 70% of anemic patients who received RBC transfusions had hemoglobin levels above 70 g/l. Only patients with severe preoperative anemia given iron preoperatively had lower intra/post-operative RBC transfusion rate, shorter length of stay and less hospitalization costs, but no similar correlation was found in patients with mild and moderate preoperative anemia and patients given erythropoietin preoperatively.

Implications of all the available evidence

Our present study provides a useful addition to the existing medical literature that is limited to Caucasian data. Preoperative anemia is currently a relatively prevalent problem that has not been fully appreciated in Chinese patients. How to select the rational timing and medication regarding preoperative anemia should be further investigated.

1. Introduction

Anemia is defined as a common clinical symptom in which the number of red blood cells (RBCs) is insufficient to meet the body's physiologic needs. The 2010−2012 Survey of Nutritional and Health Status of Chinese Residents showed that the prevalence of anemia among urban residents in China was 9.7% [1]. However, the above data were based on the general Chinese population. Surgical patients are a special group who exhibit a variety of different diseases and pathophysiological characteristics. Anemia has been reported to be more common in preoperative patients, and the prevalence of preoperative anemia varies widely in different diseases [2]. Although there are some literatures about preoperative anemia, preoperative anemia in Chinese population has not been well documented in the English literature. Data from the Global Burden of Disease showed that there are great differences in the causes of anemia in different regions [3,4]. Ethnicity, economy, epidemic diseases, and dietary structure are all important influencing factors of anemia. Therefore, there is a need for a Chinese study to provide a useful addition to ensure that the medical literature is not limited to Caucasian data.

Previous studies have shown that preoperative anemia is associated with poor clinical outcomes and increased use of healthcare resources [5,6]. In addition, the probability of perioperative blood transfusion in patients with preoperative anemia is higher than that in patients without anemia, and transfusion itself is a risk factor for postoperative morbidity and mortality [7,8]. Over the last decade, there is a growing awareness of the need to integrate the pillars of patient blood management (PBM) into routine preoperative care. PBM is designed to improve patient outcomes through the safe and rational use of blood and blood products and by minimizing unnecessary exposure to blood products. Preoperative anemia management is an important pillar of PBM [9]. Although preoperative anemia is relatively easy to diagnose and treat, it seems that Chinese surgeons have not paid enough attention to preoperative anemia, and usually correct preoperative anemia via blood transfusion, or even without any intervention. Moreover, there have been few investigations on interventions for preoperative anemia in China. As such, the intervention status of preoperative anemia remains unclear.

Therefore, the present study conducted a multi-center survey of preoperative anemia in China, aiming to fully understand the overall prevalence and intervention of preoperative anemia and, thus, promote blood management for perioperative patients.

2. Methods

2.1. Study design and data collection

The data analyzed in the present study were obtained from the National Preoperative Anemia Database, which was established in August 2018 and is accessible to affiliated hospitals of the Chinese Clinical Blood Transfusion Alliance. The National Preoperative Anemia Database retrospectively gathered data, including patient basic information, operation-related information, transfusion-related information, laboratory-related information, and anemia-related drug records. The designated physician of each member hospital extracted the qualified data of inpatient surgical procedures from the Hospital Information System, and then uploaded the data to the platform annually after deidentification. Data quality is ensured through comprehensive training of the physicians, an audit of participating hospital, regular conference calls, and an annual training meeting. Contribution to the National Preoperative Anemia Database was

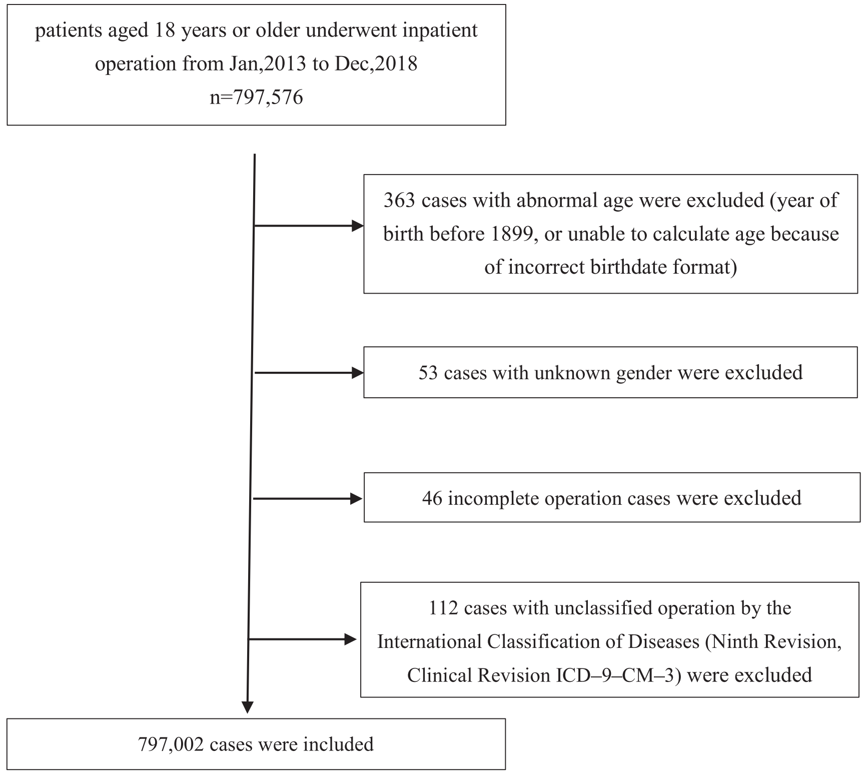

Fig. 1. Flow diagram for selection of the study cohort.

voluntary. Because our primary exposure variable was preoperative anemia, we only retained data without missing operation time, blood routine test time, preoperative hemoglobin, birth date, and gender in the database. In order to make laboratory results comparable between different hospitals, all of the laboratories providing data were required to pass internal quality control and external quality control evaluation organized by the National Health Commission of the People's Republic of China. Study cohort were included as shown in Fig. 1. Finally, 797,002 cases were included. Data were derived from 18 hospitals that were located among 15 provinces in China, including 17 tertiary general hospitals and one secondary general hospital. The present study was approved by the Medical Ethics Committee of the Chinese PLA General Hospital (approval number, S2018−245−01). This study followed RECORD guidelines for routinely collected health data.

2.2. Procedures

We defined preoperative hemoglobin concentration as the last hemoglobin measurement before operation. Anemia was diagnosed and graded according to the World Health Organization criteria [10]. Anemia was classified into microcytic anemia (mean corpuscular volume (MCV) $<$ 80 fl), normocytic anemia (80 fl $\leq$ MCV $<$ 100 fl) and macrocytic anemia (MCV $\geq$ 100 fl). According to age, patients were divided into 7 groups (18−29, 30−39,40−49,50−59, 60−69, 70−79, $\geq$80 years old). The geographical regions in China were divided into seven regions, namely, northeast, north, east, south, central, northwest, and southwest. Provincial per capita Gross Domestic Product (GDP) was divided into two levels ($<$ \$10,000/year, $\geq$ \$10,000/year) according to statistics provided by the National Bureau of Statistics in 2018. According to the top-two codes of the ICD−9−CM−3, procedures were classified into 16 categories, as listed below: operations on the nervous system (01−05); operations on the endocrine system (06−07); operations on the eye (08−16); operations on the ear (18−20); operations on the nose, mouth, and pharynx (21−29); operations on the respiratory system (30−34); operations on the cardiovascular system (35−39); operations on the hemic and lymphatic system (40−41); operations on the digestive system (42−54); operations on the urinary system (55−59); operations on male genital organs (60−64); operations on female genital organs (65−71); obstetrical procedures (72−75); operations on the musculoskeletal system (76−84); operations on the integumentary system (85−86); and other operations (00, 17, 87−99). Transfusion information included the amount and time of RBC transfusions (1 u packed RBCs were prepared from 200 ml whole blood by removing approximately 100 mL of plasma). We extracted information regarding the following prescribed anemia-related medications, including erythropoietin, intravenous iron (iron sucrose and iron dextran), oral iron (ferrous lactate, ferrous succinate, ferrous sulfate, ferrous gluconate, polysaccharide iron complex, ferrous fumarate, and iron dextran), folic acid, and vitamin B12.

2.3. Statistical analysis

We first described the demographic and relevant clinical characteristics of all of the patients and compared the characteristics of patients without preoperative anemia with those of patients with preoperative anemia. Categorical variables were described by numbers and rates, and data were analyzed by Pearson's chi-square tests. Continuous variables were described by means and 95% confidence intervals (CIs), and data were analyzed by independent-sample t-tests. We then characterized the prevalence and distribution of preoperative anemia. The standardized prevalence of preoperative anemia for age and sex was calculated using the national population data provided by the National Bureau of Statistics in 2009 as a standard population, which was then compared with the prevalence of anemia from the China Nutrition and Health Survey in 2010−2012. We performed multivariate logistic regression for preoperative anemia, which was also applied to determine the probability of receiving overall treatment, RBC transfusion, and medication for preoperative anemic patients. When the independent variable was an ordinal categorical variable, we additionally performed a trend test via logistic

Table 1
Characteristics of the study population by preoperative hemoglobin levels.

	Total	No anemia	Any anemia	Mild anemia	Moderare-severe anemia	p value
Overall	797,002	577,261 (72.43%)	219,741 (27.57%)	122,640 (55.81%)	97,101 (44.19%)	–
Sex						
Female	447,404 (56.14%)	306,453 (53.09%)	140,951 (64.14%)	71,703 (58.47%)	69,248 (71.31%)	<0.001
Male	349,598 (43.86%)	270,808 (46.91%)	78,790 (35.86%)	50,937 (41.54%)	27,853 (28.68%)	<0.001
Age groups, y						
18–29	108,440 (13.61%)	83,092 (14.39%)	25,348 (11.54%)	14,698 (11.98%)	10,650 (10.97%)	<0.001
30–39	129,516 (16.25%)	95,993 (16.63%)	33,523 (15.26%)	18,218 (14.85%)	15,305 (15.76%)	<0.001
40–49	161,972 (20.32%)	115,751 (20.05%)	46,221 (21.03%)	21,360 (17.42%)	24,861 (25.60%)	<0.001
50–59	168,908 (21.19%)	130,762 (22.65%)	38,146 (17.36%)	21,965 (17.91%)	16,181 (16.66%)	<0.001
60–69	142,043 (17.82%)	102,834 (17.81%)	39,209 (17.84%)	24,628 (20.08%)	14,581 (15.02%)	0.761
70–79	66,919 (8.40%)	40,557 (7.03%)	26,362 (12.00%)	15,974 (13.03%)	10,388 (10.70%)	<0.001
≥ 80	19,204 (2.41%)	8272 (1.43%)	10,932 (4.97%)	5797 (4.73%)	5135 (5.29%)	<0.001
Region of resident						
Northeast	144,234 (18.1%)	114,412 (19.82%)	29,822 (13.57%)	16,598 (13.53%)	13,224 (13.62%)	<0.001
East	157,424 (19.75%)	106,306 (18.42%)	51,118 (23.26%)	26,372 (21.5%)	24,746 (25.48%)	<0.001
Central	39,585 (4.97%)	27,852 (4.82%)	11,733 (5.34%)	7309 (5.96%)	4424 (4.56%)	<0.001
North	181,801 (22.81%)	141,300 (24.48%)	40,501 (18.43%)	24,175 (19.71%)	16,326 (16.81%)	<0.001
South	121,993 (15.31%)	77,963 (13.51%)	44,030 (20.04%)	23,784 (19.39%)	20,246 (20.85%)	<0.001
Northwest	24,925 (3.13%)	16,969 (2.94%)	7956 (3.62%)	4550 (3.71%)	3406 (3.51%)	<0.001
Southwest	127,040 (15.94%)	92,459 (16.02%)	34,581 (15.74%)	19,852 (16.19%)	14,729 (15.17%)	0.002
Per capita GDP (/year)						
≥ $10,000	358,503 (44.98%)	264,469 (45.81%)	94,304 (42.79%)	51,742 (42.19%)	42,292 (43.56%)	<0.001
< $10,000	438,499 (55.02%)	312,792 (54.19%)	125,707 (57.21%)	70,898 (57.81%)	54,809 (56.45%)	<0.001
Year of operation						
2013	89,434 (11.22%)	67,877 (11.76%)	21,557 (9.81%)	11,946 (9.74%)	9611 (9.90%)	<0.001
2014	115,856 (14.54%)	84,082 (14.57%)	31,774 (14.46%)	18,310 (14.93%)	13,464 (13.87%)	0.231
2015	136,759 (17.16%)	94,973 (16.45%)	41,786 (19.02%)	22,148 (18.06%)	19,638 (20.22%)	<0.001
2016	138,584 (17.39%)	100,386 (17.39%)	38,198 (17.38%)	22,109 (18.03%)	16,089 (16.57%)	0.942
2017	160,161 (20.10%)	117,618 (20.38%)	42,543 (19.36%)	24,489 (19.97%)	18,054 (18.59%)	<0.001
2018	156,208 (19.60%)	112,325 (19.46%)	43,883 (19.97%)	23,638 (19.27%)	20,245 (20.85%)	<0.001
Ethnic group						
Han	698,178 (87.60%)	514,115 (89.06%)	184,063 (83.76%)	103,702 (84.56%)	80,361 (82.76%)	<0.001
Non–Han	35,820 (4.49%)	26,032 (4.51%)	9788 (4.45%)	5374 (4.38%)	4414 (4.55%)	0.549
Unknown	63,004 (7.91%)	37,114 (6.43%)	25,890 (11.78%)	13,564 (11.06%)	12,326 (12.69%)	<0.001
Marital status						
Married	707,105 (88.72%)	510,358 (88.41%)	196,747 (89.54%)	110,178 (89.84%)	86,569 (89.15%)	<0.001
Not married	66,964 (8.40%)	51,191 (8.87%)	15,773 (7.18%)	8564 (6.98%)	7209 (7.42%)	<0.001
Unknown	22,933 (2.88%)	15,712 (2.72%)	7221 (3.29%)	3898 (3.18%)	3323 (3.42%)	<0.001
ABO blood group						
A type	180,436 (22.64%)	126,183 (21.86%)	54,253 (24.69%)	30,232 (24.65%)	24,021 (24.74%)	<0.001
AB type	66,746 (8.37%)	48,900 (8.47%)	17,846 (8.12%)	10,066 (8.21%)	7786 (8.02%)	<0.001
B type	190,939 (23.96%)	139,512 (24.17%)	51,427 (23.40%)	28,450 (23.20%)	22,977 (23.66%)	<0.001
O type	213,545 (26.79%)	150,199 (26.02%)	63,346 (28.83%)	34,700 (28.29%)	28,646 (29.50%)	<0.001
Unkonwn	145,336 (18.24%)	112,467 (19.48%)	32,869 (14.96%)	19,192 (15.65%)	13,677 (14.09%)	<0.001
RhD blood group						
RhD positive	662,465 (83.12%)	472,511 (81.85%)	189,954 (86.44%)	104,916 (85.55%)	85,038 (87.58%)	<0.001
RhD negative	6567 (0.82%)	4787 (0.83%)	1780 (0.81%)	998 (0.81%)	782 (0.81%)	0.253
Unkonwn	127,970 (16.06%)	99,963 (17.32%)	28,007 (12.75%)	16,726 (13.64%)	11,281 (11.62%)	<0.001
Operation type (ICD–9–CM–3)						
Operations on the nervous system	38,373 (4.81%)	29,228 (5.06%)	9145 (4.16%)	5681 (4.63%)	3464 (3.57%)	<0.001
Operations on the endocrine system	41,193 (5.17%)	33,998 (5.89%)	7195 (3.27%)	4406 (3.59%)	2789 (2.87%)	<0.001
Operations on the eye	33,727 (4.23%)	25,711 (4.45%)	8016 (3.65%)	5339 (4.35%)	2677 (2.76%)	<0.001
Operations on the ear	12,449 (1.56%)	10,686 (1.85%)	1763 (0.80%)	1257 (1.02%)	506 (0.52%)	<0.001

(*continued on next page*)

Table 1 (*Continued*)

	Total	No anemia	Any anemia	Mild anemia	Moderare-severe anemia	p value
Operations on the nose,mouth,and pharynx	43,048 (5.40%)	36,439 (6.31%)	6609 (3.01%)	4375 (3.57%)	2234 (2.30%)	<0.001
Operations on the respiratory system	38,851 (4.87%)	31,032 (5.38%)	7819 (3.56%)	5167 (4.21%)	2652 (2.73%)	<0.001
Operations on the cardiovascular system	44,925 (5.64%)	32,409 (5.61%)	12,516 (5.70%)	7048 (5.75%)	5468 (5.63%)	0.158
Operations on the hemic and lymphatic system	3849 (0.48%)	2240 (0.39%)	1609 (0.73%)	707 (0.58%)	902 (0.93%)	<0.001
Operations on the digestive system	145,079 (18.20%)	98,540 (17.07%)	46,539 (21.18%)	25,011 (20.39%)	21,528 (22.17%)	<0.001
Operations on the urinary system	49,118 (6.16%)	35,283 (6.11%)	13,835 (6.30%)	7858 (6.41%)	5977 (6.16%)	0.002
Operations on the male genital organs	21,303 (2.67%)	16,434 (2.85%)	4869 (2.22%)	3658 (2.98%)	1211 (1.25%)	<0.001
Operations on the female genital organs	84,824 (10.64%)	52,377 (9.07%)	32,447 (14.77%)	13,023 (10.62%)	19,424 (20.00%)	<0.001
Obstetrical procedures	65,067 (8.16%)	45,281 (7.84%)	19,786 (9.00%)	12,034 (9.81%)	7752 (7.98%)	<0.001
Operations on the musculoskeletal system	138,465 (17.37%)	99,631 (17.26%)	38,834 (17.67%)	22,229 (18.13%)	16,605 (17.10%)	<0.001
Operations on the integumentary system	36,438 (4.57%)	27,760 (4.81%)	8678 (3.95%)	4808 (3.92%)	3870 (3.99%)	<0.001
Others	293 (0.04%)	212 (0.04%)	81 (0.04%)	39 (0.03%)	42 (0.04%)	0.977
Serum creatine						
> 110 umol/L	20,005 (2.51%)	8356 (1.45%)	11,649 (5.30%)	4842 (3.95%)	6807 (7.01%)	<0.001
≤ 110 umol/L	570,757 (71.61%)	412,930 (71.53%)	157,827 (71.82%)	89,689 (73.13%)	68,138 (70.17%)	0.010
Unknown	206,240 (25.88%)	155,975 (27.02%)	50,265 (22.87%)	28,109 (22.92%)	22,156 (22.82%)	<0.001
Serum albumin						
< 35 g/L	57,754 (7.25%)	21,201 (3.67%)	36,553 (16.63%)	15,100 (12.31%)	21,453 (22.09%)	<0.001
≥ 35 g/L	564,771 (70.86%)	426,729 (73.92%)	138,042 (62.82%)	82,530 (67.29%)	55,512 (57.17%)	<0.001
Unknown	174,477 (21.89%)	129,331 (22.40%)	45,146 (20.55%)	25,010 (20.39%)	20,136 (20.74%)	<0.001
Total bilirubin						
> 17.1 umol/L	94,866 (11.90%)	70,323 (12.18%)	24,543 (11.17%)	13,427 (10.95%)	11,116 (11.45%)	<0.001
≤ 17.1 umol/L	481,064 (60.36%)	341,257 (59.12%)	139,807 (63.62%)	78,481 (63.99%)	61,326 (63.16%)	<0.001
Unknown	221,072 (27.74%)	165,681 (28.70%)	55,391 (25.21%)	30,732 (25.06%)	24,659 (25.40%)	<0.001
Alanine aminotransferase						
> 40 U/L	69,510 (8.72%)	49,879 (8.64%)	19,631 (8.93%)	10,634 (8.67%)	8997 (9.27%)	<0.001
≤ 40 U/L	553,461 (69.44%)	398,791 (69.08%)	154,670 (70.39%)	87,118 (71.04%)	67,552 (69.57%)	<0.001
Unknown	174,031 (21.84%)	128,591 (22.58%)	45,440 (20.68%)	24,888 (20.29%)	20,552 (21.17%)	<0.001
White blood cell count						
> 10 × 10^9/L	84,611 (10.62%)	56,025 (9.71%)	28,586 (13.01%)	14,240 (11.61%)	14,346 (14.77%)	<0.001
≤ 10 × 10^9/L	712,362 (89.38%)	521,220 (90.29%)	191,142 (86.99%)	108,395 (88.38%)	82,747 (85.22%)	<0.001
Unknown	29 (0.00%)	16 (0.00%)	13 (0.01%)	5 (0.00%)	8 (0.01%)	<0.001
Platelet count						
≤ 100 × 10^9/L	19,328 (2.43%)	9678 (1.68%)	9650 (4.39%)	4272 (3.48%)	5378 (5.54%)	<0.001
≥ 100 × 10^9/L	777,336 (97.53%)	567,474 (98.30%)	209,862 (95.50%)	118,267 (96.43%)	91,595 (94.33%)	<0.001
Unknown	338 (0.04%)	109 (0.02%)	229 (0.10%)	101 (0.08%)	128 (0.13%)	<0.001
Prothrombin time						
> 15 s	22,000 (2.76%)	11,505 (1.99%)	10,495 (4.78%)	4386 (3.58%)	6109 (6.29%)	<0.001
≤ 15 s	681,732 (85.54%)	497,690 (86.22%)	184,042 (83.75%)	104,709 (85.38%)	79,333 (81.70%)	<0.001
Unknown	93,270 (11.70%)	68,066 (11.79%)	25,204 (11.47%)	13,545 (11.04%)	11,659 (12.10%)	<0.001
Activated partial thromboplastin time						
> 45 s	15,157 (1.90%)	7862 (1.36%)	7295 (3.32%)	3283 (2.68%)	4012 (4.13%)	<0.001
≤ 45 s	676,987 (84.94%)	489,539 (84.80%)	187,448 (85.30%)	106,052 (86.47%)	81,396 (83.83%)	<0.001
Unknown	104,858 (13.16%)	79,860 (13.83%)	24,998 (11.38%)	13,305 (10.85%)	11,693 (12.04%)	<0.001
Length of operation,min (*n* = 736,346)	135.88 (135.60–136.16)	133.55 (133.22–133.88)	142.15 (141.61–142.69)	140.74 (140.01–141.47)	143.93 (143.12–144.74)	<0.001
Length of stay, d (*n* = 796,080)	12.21 (12.19–12.24)	11.36 (11.34–11.39)	14.45 (14.40–14.51)	13.78 (13.71–13.86)	15.30 (15.21–15.40)	<0.001
Mean hospitalization expenses, $ (*n* = 682,818)	5249.17 (5234.19–5264.15)	4743.38 (4728.50–4758.25)	6614.92 (6577.40–6652.43)	6191.47 (6149.72–6233.21)	7161.78 (7095.01–7228.56)	<0.001

Data are number (%) or mean (95% CI). Unknown means missing data for the variables ethnic group, RhD blood group, marital status and laboratory indicators, and for the variable ABO blood group unknown represents other subtypes except that listed above as well as missing data. P values were derived from comparing the any preoperative anemia group with the no preoperative anemia group.

regression using ordinal categorical variables as continuous variables. We then applied multivariate logistic regression to analyze the relationship between anemia and length of stay and hospitalization costs. When analyzing the relationship of treatment with intra/post-operative RBC transfusion rate, length of hospital stay and hospitalization costs in preoperative anemic patients, propensity score matching (PSM) analysis was applied to eliminate the difference in the treated and untreated group, and we further conducted a subgroup analysis according to anemia severity. The interaction of treatment and anemia severity was examined by Wald test. There were some missing data, and the reasons for data missing included: (1) The hospital information system of a few hospitals didn't support the extraction of these variables; (2) Doctors did not record these variables in hospital information system; (3) Some laboratory tests were not performed for the patient during the required time of the study. Further analysis showed there was a difference of missing data rates of certain variables including ABO blood group, Rh blood group ethnic group in different level of anemia, so these variables were not included in multivariate regression analysis.

In sensitivity analysis, we used hematocrit (HCT) as another diagnostic indicator to calculate the prevalence of anemia and analyzed whether the prevalence calculated from hematocrit was consistent with that calculated from hemoglobin. To eliminate the effect of RBC transfusion on hemoglobin, we described the characteristics of preoperative anemia in patients who had not been transfused preoperatively, as well as compared these characteristics with those of the overall study population.

A two-tailed P value less than 0.001 was considered statistically significant for all of the tests. Statistical analyses were performed using Stata version 15.1.

2.4. Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

3. Results

3.1. Baseline characteristics of study population

The included patients came from 34 provincial administrative regions (seven geographical regions) in China. The mean age of patients was 49.71 years (95% CI 49.90−50.00), of which 56.14% (447,404/797,002) were female. The characteristics of the study population were shown in Table 1.

3.2. Prevalence and distribution of preoperative anemia

Overall, the prevalence of preoperative anemia was 27.57% (219,741/797,002, 95% CI 27.47−27.67), which was higher in females (140,951/447,404, 31.50%, 95% CI 31.37−31.64) than that in males (78,790/349,598, 22.54%, 95% CI 22.40−22.68). Preoperative anemia

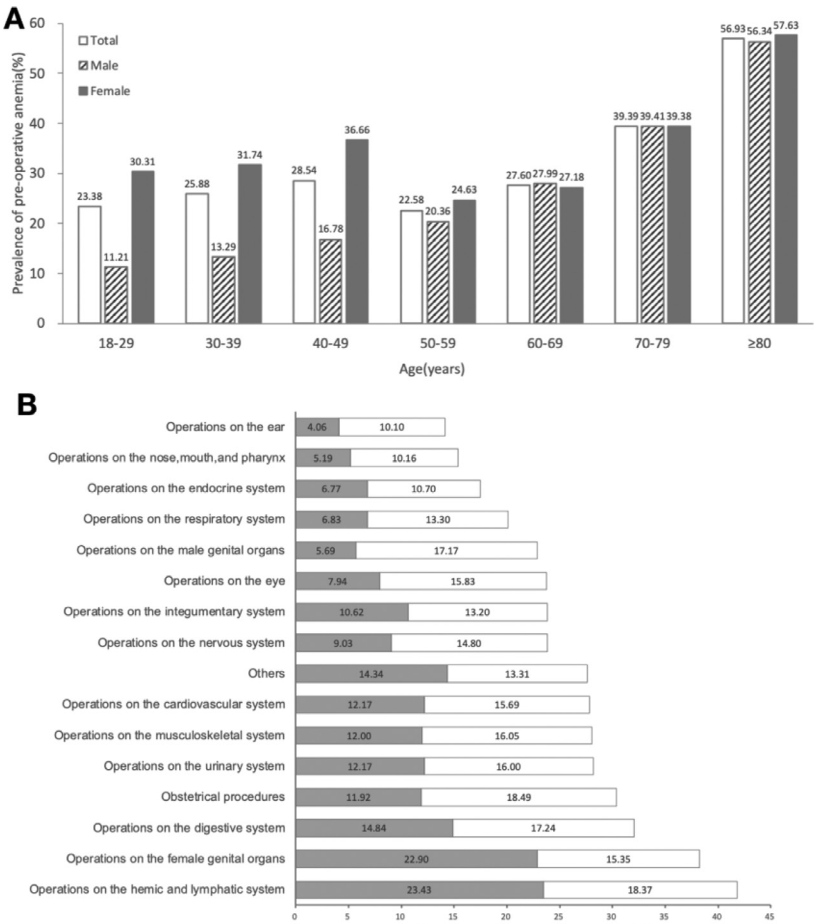

Fig. 2. Prevalence of preoperative anemia in different subgroup patients. A: Prevalence of preoperative anemia in adults aged 18 years or older. **B**: Prevalence of preoperative anemia in patients who underwent different operations (The dark color on the left part of each bar represents moderate to severe anemia. The light color on the right part of each bar represents mild anemia).

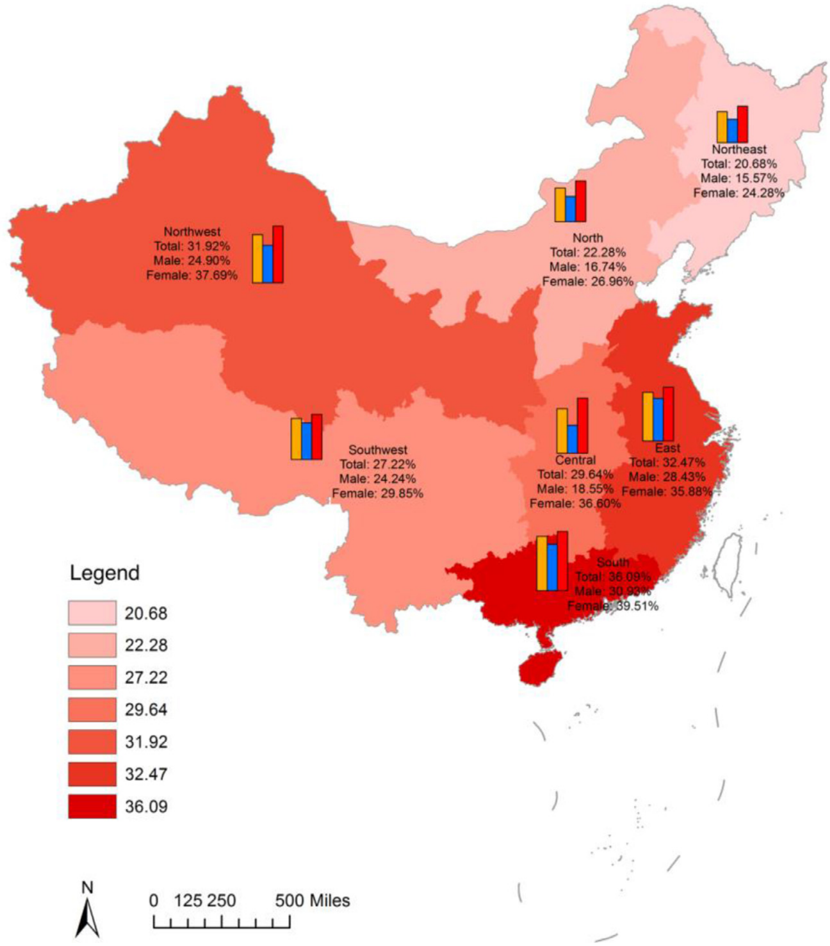

Fig. 3. Prevalence of preoperative anemia in different regions of China. The data used for the map did not include those from Hong Kong, Macao, and Taiwan, as data from these provinces were scarce.

was predominantly mild to moderate, with mild, moderate, and severe anemia accounting for 55.81% (122,640/219,741, 95% CI 55.60–56.02), 39.33% (86,435/219,741, 95% CI 39.13–39.54), and 4.85% (10,666/219,741, 95% CI 4.76–4.94), respectively. Normocytic anemia (167,368/219,741, 76.17%, 95% CI 75.99–76.34) was the most common type in patients with preoperative anemia, followed by microcytic anemia (44,789/219,741, 20.38%, 95% CI 20.21–20.55) and macrocytic anemia (7584/219,741, 3.45%, 95% CI 3.38–3.53). The proportion of microcytic anemia increased with the severity of anemia, which was 10.00% (12,270/122,640, 95% CI 9.84–10.17) in mild anemia, 32.58% (28,164/86,435, 95% CI 32.27–32.90) in moderate anemia, and 40.83% (4355/10,666, 95% CI 39.90–41.77) in severe anemia (trend test, coef. −0.98, 95% CI −1.00––0.96, $p < 0.001$).

The prevalence of preoperative anemia increased with age until the age of 50 years, with a slight decrease at the age of 50–60 years, and then increased with age again beyond the age of 60 years. After separate analysis by gender the prevalence of preoperative anemia increased completely with age in men. After the age of 60 years, the gap of prevalence between men and women narrowed. Notably, the prevalence of preoperative anemia in patients over 80 years was as high as 56.93% (Fig. 2). The prevalence and degree of preoperative anemia also varied in different operations. Moderate to severe anemia in operations on female genital organs and the lymphatic and hematopoietic system accounted for more than 50% of patients with preoperative anemia (Fig. 2). The prevalence of preoperative anemia varied in different regions in China, which is the highest in South China (36.09%44,030/121,993, 95% CI 35.82–36.36). and the lowest in Northeast China (20.68%, 29,822/144,234, 95% CI 20.47–20.89) (Fig. 3). The prevalence of preoperative anemia was 26.23% (94,034/358,503, 95% CI 26.09–26.37) in provinces with per capita GDP ≥ \$10,000/year, whereas it was 28.67% (125,707/438,499, 95% CI 28.53–28.80) in provinces with per capita GDP < \$10,000/year.

Multivariate logistic regression analysis identified several characteristics associated with the prevalence of preoperative anemia. Patients who were female, age over 60 years old, from South China, from provinces with lower per capita GDP, underwent operations on the lymphatic and hematopoietic system, with laboratory abnormalities (except total bilirubin and alanine aminotransferase) were more likely to have a high risk of preoperative anemia (Appendix 1).

The standardized prevalence of anemia in the three groups of 18–44 years old (22.3% vs 10.3%), 45–60 years old (24.03% vs 9.4%), and ≥ 60 years old (34.63% vs 12.5%) was significantly higher than the prevalence in the corresponding groups in the China Nutrition and Health Survey in 2010–2012.

3.3. Treatment of preoperative anemia

Among patients with preoperative anemia, 12.25% (23,171/189,134, 95% CI 12.10–12.40) received anemia-related therapy, 5.16% (10,903/211,168, 95% CI 5.07–5.26) received RBC transfusions, 7.79% (14,683/188,571, 95% CI 7.67–7.91) received anemia-related medications, and 1.28% (24,15/188,571, 95% CI 1.23–1.33) received both RBC transfusions and medications before surgery. In patients with severe anemia, 45.71% (36,91/8075, 95% CI 44.62–46.80) were treated (Appendix 2).

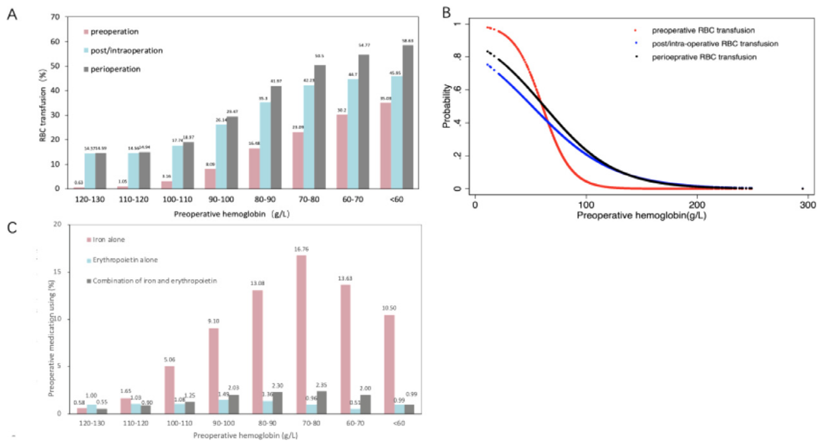

Fig. 4. Association of Treatment and preoperative hemoglobin. A: RBC transfusion rates as a function of preoperative hemoglobin levels. B: Predicted probability of RBC transfusion with change in preoperative hemoglobin. C: Preoperative iron and erythropoietin using rates as a function of preoperative hemoglobin levels.

A total of 22.26% (47,005/211,168, 95% CI 22.08–22.44) of patients with preoperative anemia received RBC transfusions perioperatively. The preoperative RBC transfusion rate, intraoperative and postoperative RBC transfusion rate, and perioperative RBC transfusion rate increased with the severity of anemia (Fig. 4). For each 10-g/L increase in preoperative hemoglobin, the preoperative RBC transfusion probability, intraoperative and postoperative RBC transfusion probability, and perioperative RBC transfusion probability decreased by 54.92% (OR 0.46, 95% CI 0.46–0.47), 24.07% (OR 0.76, 95% CI 0.76–0.76), and 27.98% (OR 0.73, 95% CI 0.73–0.73), respectively (Fig. 4). Among patients with preoperative anemia receiving preoperative RBC transfusion, 89.09% (9714/10,903, 95% CI 88.49–89.67) had hemoglobin levels above 70 g/l and 71.79% (7827/10,903, 95% CI 70.93–72.63) had hemoglobin levels above 80 g/l. The total amount of preoperative RBC transfusion in patients with preoperative anemia accounted for 89.62% (50,588/56,446, 95% CI 89.37–89.87) of the preoperative RBC consumption in all patients undergoing surgery, of which 89.29% (45,148/50,588, 95% CI 88.97–89.52) of RBC were used in anemic patients with hemoglobin higher than 70 g/L.

Intravenous iron was the more commonly used drug, with the percentage of preoperative anemic patients receiving intravenous iron being 3.82% (7202/188,571, 95% CI 3.73–3.91), followed by oral iron at 2.82% (5312/188,571, 95% CI 2.74–2.89), erythropoietin at 2.39% (4509/188,571, 95% CI 2.32–2.46), folic acid at 0.93% (1748/188,571, 95% CI 0.88–0.97), and vitamin B12 at 0.10% (190/188,571, 95% CI 0.08–0.11). Combination of iron and erythropoietin was administered in 1.27% (2399/188,571, 95% CI 1.22–1.32) patients with preoperative anemia. The rate of using preoperative iron alone or combination with erythropoietin increased with the decrease of hemoglobin when hemoglobin above 70 g/l, and decreased when hemoglobin less than 70 g/l. The rate of using preoperative erythropoietin alone increased with the decrease of hemoglobin when hemoglobin above 80 g/l and decreased when hemoglobin less than 80 g/l (Fig. 4).

Multivariate logistic regression analysis showed that patients who were male, with lower preoperative hemoglobin, not married, and with MCV < 80 fl had a higher likelihood of receiving any anemia-relate treatment, RBC transfusion, and medication. The likelihood of any anemia-related treatment and RBC transfusion increased with age. Doctors in South China and North China were more willing to carry out treatments including using medications. Patients from provinces with per capita GDP less than $10,000/year had higher overall treatment and RBC transfusion rates, but medication use rates were not significantly related to per capita GDP. Patients undergoing operations on female genital organs or those involving obstetric procedures were the most likely to be treated, including receiving medications. The rate of overall treatment and medication use increased from 2013 to 2018, while the rate of preoperative RBC transfusion gradually decreased (Table 2).

3.4. Relationship between preoperative anemia and length of stay and hospitalization costs

Compared with patients with preoperative hemoglobin higher than 130 g/l, patients whose preoperative hemoglobin was less than 130 g/l was associated with longer hospital stay and more hospitalization costs. Patients with more severe anemia had more hospitalization costs. Patients with mild or moderate anemia had longer length of hospital stay as preoperative anemia worsened (Fig. 5, Appendix 3). Among patients with severe preoperative anemia, those given iron preoperatively had lower intra/post-operative RBC transfusion rate, shorter length of stay and less hospitalization costs, but no similar correlation was found in patients with mild and moderate preoperative anemia and patients given erythropoietin preoperatively (Table 3).

3.5. Sensitivity analysis

The prevalence of preoperative anemia calculated by HCT was 26.92% (21,4574/796,995, 95% CI 26.83–27.02), and the distribution in each subgroup was consistent with that calculated by hemoglobin except when grouped by per capita GDP (Appendix 4). However, multivariate logistic regression analysis showed the relationship between per capita GDP and preoperative anemia was consistent between the two methods of calculation (Appendix 1). Then only patients without preoperative RBC transfusions were retained to analysis. The results showed that the preoperative anemia rate was 26.25% (200,265/762,840, 95% CI 26.15–26.35), which was lower than that of the total study population, but this distribution was also consistent with that of the total study population (Appendix 1 and Appendix 5).

4. Discussion

To the best of our knowledge, this is the largest and first nationwide study of the prevalence and treatment of preoperative anemia on Chinese patients. Our results showed that the overall prevalence of preoperative anemia was 27.57%, which varied by age, sex, region, and type of surgery. The intervention rate for preoperative anemia was only 12.57%, with a lower proportion of patients being treated with medication and irrational use of red blood cells. Patients with preoperative anemia was associated with longer hospital stay and more hospitalization costs, while patients given iron only in severe

Table 2
Characteristics associated with the rates of overall treatment, RBC transfusions, and medication use preoperatively.

	Any anemia–related treatment		Preoperative RBC transfusion		Medication use	
	Odds Ratio (95% CI)	p value	Odds Ratio (95% CI)	p value	Odds Ratio (95%CI)	p value
Age,y	1.05 (1.03–1.06)	<0.001	1.09 (1.08–1.11)	<0.001	1.02 (1.01–1.04)	0.005
Preoperative hemoglobin	0.93 (0.93–0.93)	<0.001	0.92 (0.92–0.93)	<0.001	0.95 (0.95–0.95)	<0.001
Year of operation	1.04 (1.03–1.05)	<0.001	0.93 (0.92–0.95)	<0.001	1.11 (1.10–1.13)	<0.001
Sex						
Male	1.00 (ref)	–	1.00 (ref)	–	1.00 (ref)	–
Female	0.60 (0.57–0.62)	<0.001	0.58 (0.55–0.61)	<0.001	0.73 (0.69–0.77)	<0.001
Marital status						
Married	1.00 (ref)	–	1.00 (ref)	–	1.00 (ref)	–
Not married	1.37 (1.30–1.45)	<0.001	1.32 (1.44–1.60)	<0.001	1.28 (1.20–1.37)	<0.001
Per capita GDP (/year)						
≥ $10,000	1.00 (ref)	–	1.00 (ref)	–	1.00 (ref)	–
< $10,000	1.15 (1.10–1.20)	<0.001	1.15 (1.08–1.22)	<0.001	1.04 (0.99–1.10)	0.128
Region of hospital						
Northeast	1.00 (ref)	–	1.00 (ref)	–	1.00 (ref)	–
East	0.67 (0.59–0.76)	<0.001	0.09 (0.07–0.10)	<0.001	2.66 (2.28–3.12)	<0.001
Central	0.42 (0.35–0.50)	<0.001	0.14 (0.10–0.20)	<0.001	1.67 (1.37–2.04)	<0.001
North	3.47 (3.16–3.80)	<0.001	0.62 (0.54–0.71)	<0.001	18.40 (16.26–20.81)	<0.001
South	5.53 (3.95–7.74)	<0.001	0.50 (0.41–0.62)	<0.001	3.61 (2.50–5.21)	<0.001
Northwest	0.92 (0.77–1.10)	0.35	0.76 (0.58–0.99)	0.041	2.25 (1.81–2.79)	<0.001
Southwest	0.42 (0.34–0.52)	<0.001	0.35 (0.26–0.48)	<0.001	0.58 (0.45–0.75)	<0.001
Region of resident						
Northeast	1.00 (ref)	–	1.00 (ref)	–	1.00 (ref)	–
East	1.05 (0.95–1.17)	0.325	1.22 (1.04–1.43)	0.014	0.92 (0.83–1.03)	0.163
Central	0.94 (0.84–1.06)	0.308	0.97 (0.80–1.17)	0.723	0.88 (0.78–1.00)	<0.001
North	0.82 (0.76–0.89)	<0.001	1.03 (0.91–1.17)	0.615	0.70 (0.64–0.76)	<0.001
South	0.17 (0.12–0.24)	<0.001	0.88 (0.72–1.09)	0.251	0.82 (0.58–1.16)	0.264
Northwest	1.20 (1.03–1.39)	0.019	1.13 (0.89–1.43)	0.325	1.15 (0.98–1.35)	<0.001
Southwest	1.11 (0.91–1.35)	0.319	1.07 (0.80–1.44)	0.636	1.04 (0.84–1.29)	0.74
Operation type (ICD–9–CM–3)						
Operations on the nervous system	0.79 (0.72–0.88)	<0.001	0.43 (0.37–0.50)	<0.001	1.42 (1.26–1.61)	<0.001
Operations on the endocrine system	0.27 (0.23–0.31)	<0.001	0.17 (0.13–0.21)	<0.001	0.49 (0.41–0.58)	<0.001
Operations on the eye	0.11 (0.09–0.15)	<0.001	0.01 (0.01–0.03)	<0.001	0.33 (0.25–0.42)	<0.001
Operations on the ear	0.15 (0.10–0.22)	<0.001	0.03 (0.01–0.10)	<0.001	0.30 (0.20–0.45)	<0.001
Operations on the nose,mouth,and pharynx	0.22 (0.18–0.27)	<0.001	0.19 (0.15–0.24)	<0.001	0.30 (0.23–0.38)	<0.001
Operations on the respiratory system	0.36 (0.31–0.42)	<0.001	0.31 (0.26–0.38)	<0.001	0.41 (0.33–0.51)	<0.001
Operations on the cardiovascular system	0.87 (0.81–0.94)	<0.001	0.39 (0.35–0.43)	<0.001	2.05 (1.89–2.24)	<0.001
Operations on the hemic and lymphatic system	1.06 (0.89–1.26)	0.516	0.98 (0.81–1.19)	0.867	0.80 (0.60–1.07)	0.132
Operations on the digestive system	1.00 (ref)	–	1.00 (ref)	–	1.00 (ref)	–
Operations on the urinary system	0.73 (0.67–0.79)	<0.001	0.57 (0.51–0.63)	<0.001	0.95 (0.84–1.08)	0.427
Operations on the male genital organs	0.38 (0.32–0.46)	<0.001	0.34 (0.27–0.42)	<0.001	0.47 (0.35–0.64)	<0.001
Operations on the female genital organs	2.90 (2.75–3.06)	<0.001	1.01 (0.95–1.09)	0.701	7.05 (6.57–7.56)	<0.001
Obstetrical procedures	1.52 (1.42–1.64)	<0.001	0.19 (0.17–0.22)	<0.001	4.81 (4.40–5.25)	<0.001
Operations on the musculoskeletal system	1.77 (1.69–1.86)	<0.001	0.99 (0.93–1.05)	0.678	3.05 (2.86–3.26)	<0.001
Operations on the integumentary system	0.63 (0.57–0.71)	<0.001	0.51 (0.44–0.58)	<0.001	0.97 (0.84–1.12)	0.658
Others	0.79 (0.36–1.72)	0.555	0.85 (0.34–2.10)	0.722	0.41 (0.10–1.76)	0.232
MCV						
MCV < 80fl	1.15 (1.11–1.19)	<0.001	1.52 (1.44–1.60)	<0.001	1.14 (1.09–1.20)	<0.001
80fl ≤ MCV < 100fl	1.00 (ref)	–	1.00 (ref)	–	1.00 (ref)	–
MCV ≥ 100fl	0.86 (0.78–0.94)	0.002	0.80 (0.70–0.91)	0.001	1.01 (0.90–1.14)	0.847

P values were derived from multivariate logistic regression for the probability of patients receiving any anemia-related treatment, preoperative RBC transfusion, and medication for preoperative anemia.

preoperative anemia had shorter hospital stay and less hospitalization costs than those not given iron.

Anemia is very common in preoperative patients. A previous systematic review showed that the prevalence of preoperative anemia was reported to be 5.0–75.8% in different studies [2]. The latest data reported by the *National Health and Family Planning Commission's Public Benefit Project: the Safety and Effect Assessment of Joint Arthroplasty* in 2016 showed that the prevalence of preoperative anemia in China was 29.5%, 26.4%, and 43.9% for total hip replacement, total knee replacement, and femoral head replacement, respectively [11]. Our findings were consistent with the prevalence of preoperative anemia reported previously but was much higher than the prevalence of anemia (9.7%) reported by the Survey of Nutritional and Health Status of Chinese residents in 2010–2012[1,5,6]. Additionally, the age-stratified standardized prevalence of anemia in our present study was significantly higher than that of the general population. This suggests that surgery-related diseases have been related to a significantly higher prevalence of anemia.

The gender and age distributions of preoperative anemia in China in our study were consistent with those reported in previous studies. It is noteworthy that China has entered an aging stage, with over 10% of the total population being over 65 years of age. Consequently, in the future, the burden of preoperative anemia in elder patients will also increase. Anemia in the elderly is associated with exposure to blood transfusions and higher perioperative morbidity and mortality because such individuals have a limited physiological compensatory capacity and a higher prevalence of underlying diseases [12,13]. Therefore, it is especially important to pay more attention to elderly patients with preoperative anemia.

We also found that the prevalence of preoperative anemia varied widely by region, economic factors and types of procedure. In general, preoperative anemia is more common among patients from low- and middle-income countries than it is in those from high-income countries, and patients in low- and middle-income countries more frequently suffer from severe anemia [14,15]. The prevalence of preoperative anemia for different types of surgeries has been

Table 3
The relationship of iron or erythropoietin with intra/post-operative RBC transfusion rate, length of stay and hospitalization costs in patients with preoperative anemia.

		Patients not given iron	Patients given iron	p	Patients not given erythropoietin	Patients given erythropoietin	p
Intra/post-operative RBC transfuison rate	**Mild anemia**	357/3828(9.33%)	1065/3109(34.26%)	<0.001	392/2158(18.16%)	1101/1785(61.86%)	<0.001
	Moderate anemia	1668/6482(25.73%)	2698/7268(37.12%)	<0.001	677/1986(34.09%)	1564/2455(63.71%)	<0.001
	Severe anemia	823/1609(51.15%)	610/1409(43.29%)	<0.001	186/368(50.54%)	112/253(44.27%)	.124
Length of stay, d	**Mild anemia**	10.73(10.44–11.02)	15.02(14.18–15.86)	<0.001	15.21(14.64–15.78)	18.53(17.46–19.60)	<0.001
	Moderate anemia	13.68(13.36–14.00)	14.85(14.55–15.16)	<0.001	18.52(17.67–19.36)	18.94(18.34–19.53)	.414
	Severe anemia	16.30(15.48–17.12)	14.20(13.26–14.89)	<0.001	17.40(15.87–18.94)	21.26(19.38–23.13)	.002
Hospitalization costs, $	**Mild anemia**	4307.82(4133.78–4481.85)	9267.15(8847.72–9686.57)	<0.001	6679.06(6376.09–6982.03)	15,032.55(14,345.41–15,719.68)	<0.001
	Moderate anemia	5689.86(5466.53–5913.19)	7069.69(6813.60–7325.79)	<0.001	8670.63(8166.19–9175.06)	13,725.89(13,104.27–14,347.51)	<0.001
	Severe anemia	8099.8(7434.66–8764.94)	5262.72(4672.88–5852.56)	<0.001	8812.41(7399.80–10,225.02)	13,044.44(10,502.46–15,586.42)	.003

Data are number (%) or mean (95% CI). Data in this table was after PSM.

reported in the literature as follows: 24–37% in cardiac surgery [16,17]· 24–51% in hip and knee surgery [18], 30–67% in colorectal cancer surgery [19], and 18–36% in gynecological surgery [20–22]. In our present study, the top-three rates of preoperative anemia were observed in patients who underwent lymphohematopoietic surgery, female genital surgery, and digestive surgery. The difference in the prevalence of preoperative anemia between different surgeries also reflects the impact of the disease itself on anemia.

Moreover, preoperative anemia increased transfusion requirements. An inverse relationship between preoperative hemoglobin concentrations and the incidence of transfusion in operations on elective hip and knee arthroplasty has been reported [23]. Our present study also demonstrated an increasing trend in the likelihood of preoperative and perioperative blood transfusions as preoperative hemoglobin levels declined. Of course, perioperative transfusions would be affected by many factors including how invasive the surgeries are, active medications as well as preoperative anemia. Furthermore, in our study, among patients with preoperative anemia receiving RBC transfusion, 89.09% had hemoglobin levels above 70 g/l, and 89.29% of RBCs were transfused to anemic patients with hemoglobin above 70 g/L. If the current restrictive transfusion strategy is exactly implemented, most patients do not require RBC transfusion although it is not accurate to use hemoglobin alone to determine whether patient need transfusion. On the other hand, we found that majority of patients with preoperative anemia didn't receive any anemia related treatment. It suggested most surgeons in China are not aware of the importance of preoperative anemia. Previously, no survey has ever reported the current incidence of treatments for preoperative anemia. Hence, our present study represents the first report of the current status of the incidence of treatments for preoperative anemia.

Furthermore, more severe anemia is associated with more severe adverse outcomes [24]. Although we did not directly analyze the relationship between preoperative anemia and surgical outcome, patients with preoperative anemia had longer length of stay and more hospitalization costs than patients without anemia. Although, National basic medical insurance includes basic medical insurance for employees, urban and rural residents, and new rural cooperative medical insurance, with reimbursement rates of 70%, 50%, and 70%, respectively, it still suggests that preoperative anemia is associated with higher overall medical burden not only for patient but also for government. Another interesting finding was that patients with severe anemia treated with iron had lower intra/post-operative RBC transfusion rate, shorter length of stay and less hospitalization costs, whereas there was no such link in patients with mild to moderate anemia and patients treated with rhEPO. This brings a challenge for the management protocol of preoperative anemia including selection of intervention timing and medication. 2018 Frankfurt Consensus on patient blood management recommended that use of iron supplementation in adult preoperative patients with iron deficiency anemia undergoing elective surgery to reduce rate of RBC transfusion and erythropoiesis stimulating agents should not be used routinely in general for adult preoperative patients with anemia undergoing elective surgery [25]. Some studies had shown iron or EPO can reduce RBC transfusion in certain causes of preoperative anemia, but the effect of iron and EPO on surgical outcomes has not been well established and administration EPO may not be cost-effective [26–28]. Our study found that only patients treated with iron in severe preoperative anemia have less medical burden, so it need better prospective randomized clinical studies to confirm the role of iron and EPO in preoperative anemia.

Currently, perioperative PBM has been implemented in more and more countries. In Australia, the implementation of PBM program was proved to be associated with significant reductions in hospital mortality, length of stay, blood transfusions, considerable product-acquisition and estimated activity-based transfusion cost saving [29].

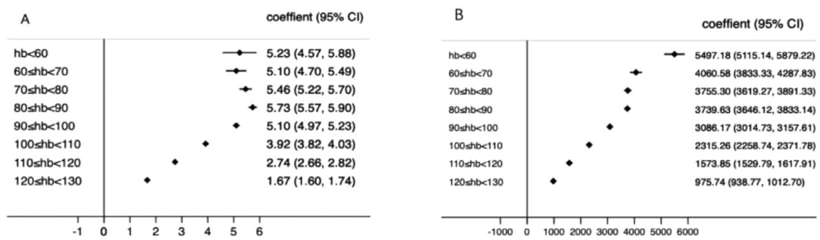

Fig. 5. Relationship of preoperative hemoglobin and length of stay and hospitalization costs. A: Relationship of preoperative hemoglobin and length of stay. B: Relationship of preoperative hemoglobin and hospitalization costs.

However, in China, there are a considerable number of surgeons lacking awareness of the risk of blood transfusion. The rationality of blood transfusion and anemia treatment needs to be further improved. On the other hand, the supply of blood donations in China is much lower than the corresponding demand, which may cause a blood shortage for clinical treatments at any given time. Therefore, it is urgent to widely implement the PBM strategy in China. It is promising that the rate of treatment (including medications) for preoperative anemia is increasing year by year, while the preoperative transfusion rate is gradually decreasing. Some consensus was published in china in recent years, such as expert consensus on diagnosis and treatment of preoperative anemia [30]. These suggested the concept of PBM was gradually beginning to be accepted in China. In addition, complete PBM should consist of 3 pillars: the optimization of red blood cell mass; reduction of blood loss and bleeding; and optimization of the patient's physiological tolerance toward anemia. Treating anemia and iron deficiency is only one small piece of PBM. We need to integrate these 3 pillars into the management of perioperative patients in order to better improve patient outcomes.

Our present study had several limitations. First, this study was a retrospective cross-sectional survey with big data, rather than a random, prospective survey. It may still have been subject to survey bias and it is indeed more likely to have a small P value. In this study, although $P < 0.001$ was used as the criterion for judging statistically significant difference, the use of smaller test level did not offset the effect of large sample size. Second, we may have underestimated the prevalence of preoperative anemia due to applying unadjusted anemia criteria for patients living more than 1000 m above sea level. Third, we did not consider any concomitant disease, complications and some unique characteristic of surgical specialty, which lead us not to properly build a valid predictive model. Finally, because some information related to the cause of anemia were not collected, we did not further explore the causes of anemia which may be very helpful for treatment, and we plan to investigate in future studies.

In conclusion, preoperative anemia is common in Chinese surgical patients. Despite its high prevalence, treatment of preoperative anemia has been inadequate. Our present findings support that preoperative anemia management should be strengthened in China, however, how to treat preoperative anemia needs further study. In the future, more data and clinical trials will be required to determine the effects of corrections of preoperative anemia on outcomes.

Contributors

Deqing Wang and Gang Li conceived and designed the study. Aiqing Wen, Jufeng Wu, Long Zhang, Futing Sun, Xiaojun Guo, Fenghua Liu, Hailan Li, Na Li, Haibao Wang, Yi Lv, Zhonghua Jia, Xiaoyan Li, Jun Zhang, Zunyan Li, Shanshan Liu, Shuhuai Zhong, Jun Yang, and Shuxuan Ma contributed to data collection. Zhenhua Xu, Chao Wang, Shijun Cheng, and Shengxiong Chen performed the aggregation, processing of the data, and contributed to the statistical analysis. Junting Liu, Yang Yu, Shufang Wang, Lingling Zhou, Xiaozhen Guan, and Chunya Ma contributed to data collection and analysis. Jie Lin performed statistical analysis, analyzed the data, interpreted the results, and drafted the manuscript. All of the authors revised the manuscript and approved the final version before submission.

Funding

This work was supported by the National Natural Science Foundation of China (grants 81,779,194 and 81,970,167) and the Logistics Support Department of the Central Military Commission (grants BWS16J006).

Data sharing statement

No additional unpublished data are available.

Declaration of Competing Interest

We declare no conflicts of interests.

Acknowledgments

We thank Accdon (www.accdon.com) for its assistance during the preparation of this manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2021.100894.

References

[1] Hu Y, Chen J, Li M, et al. Study on the anemia status of Chinese urban residents in 2010-2012. Chin J Prev Med 2016;50:213–6.
[2] Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence and outcomes of anemia in surgery: a systematic review of the literature. Am J Med 2004;116:58–69.
[3] Kassebaum NJ, Jasrasaria R, Naghavi M, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood 2014;123:615–24.
[4] Kassebaum NJ. The global burden of anemia. Hematol Oncol Clin North Am 2016;30:247–308.
[5] Baron DM, Hochrieser H, Posch M, et al. Preoperative anaemia is associated with poor clinical outcome in non-cardiac surgery patients. Br J Anaesth 2014;113:416–23.
[6] Musallam KM, Tamim HM, Richards T, et al. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. The Lancet 2011;378:1396–407.
[7] Keeler BD, Mishra A, Stavrou CL, Beeby S, Simpson JA, Acheson AG. A cohort investigation of anaemia, treatment and the use of allogeneic blood transfusion in colorectal cancer surgery. Ann Med Surg 2016;6:6–11.
[8] Gabriel RA, Clark AI, Nguyen AP, Waterman RS, Schmidt UH. The association of preoperative hematocrit and transfusion with mortality in patients undergoing elective non-cardiac surgery. World J Surg 2018;42:1939–48.
[9] WHO. WHO global forum for blood safety: patient blood management. 2011. https://www.who.int/bloodsafety/events/gfbs_01_pbm/en/ (accessed Feb 2, 2021).
[10] WHO. Nutritional anaemias. Report of a WHO Scientific Group. Geneva: World Health Organization; 1968.
[11] Zhou Z, Weng X, Sun T, et al. Expert consensus in enhanced recovery after orthopedic surgery in China: perioperative blood management. Chin J Bone Jt Surg 2017;10:1–7.

[12] Wu W-C, Schifftner TL, Henderson WG, et al. Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery. JAMA 2007;297:2481–8.
[13] Wu W-C, Smith TS, Henderson WG, et al. Operative blood loss, blood transfusion, and 30-day mortality in older patients after major noncardiac surgery. Ann Surg 2010;252:11–7.
[14] Stevens GA, Finucane MM, De-Regil LM, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. Lancet Glob Health 2013;1:e16–25.
[15] Fowler AJ, Ahmad T, Abbott TEF, et al. Association of preoperative anaemia with postoperative morbidity and mortality: an observational cohort study in low-, middle-, and high-income countries. Br J Anaesth 2018;121:1227–35.
[16] Kim C, Connell H, McGeorge A, Hu R. Prevalence of preoperative anaemia in patients having first-time cardiac surgery and its impact on clinical outcome. A retrospective observational study. Perfusion 2015;30:277–83.
[17] Miceli A, Romeo F, Glauber M, de Siena PM, Caputo M, Angelini GD. Preoperative anemia increases mortality and postoperative morbidity after cardiac surgery. J Cardiothorac Surg 2014;9:137.
[18] Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology 2010;113:482–95.
[19] Wilson MJ, van Haaren M, Harlaar JJ, et al. Long-term prognostic value of preoperative anemia in patients with colorectal cancer: a systematic review and meta-analysis. Surg Oncol 2017;26:96–104.
[20] Richards T, Musallam KM, Nassif J, et al. Impact of preoperative anaemia and blood transfusion on postoperative outcomes in gynaecological surgery. PLoS ONE 2015;10:e0130861.
[21] Lim S, Lee C-M, Park J-M, Jung S-Y, Lee K-B. An association between preoperative anemia and poor prognostic factors and decreased survival in early stage cervical cancer patients. Obstet Gynecol Sci 2014;57:471.
[22] Browning RM, Trentino K, Nathan EA, Hashemi N. The Western Australian patient blood management program. Preoperative anaemia is common in patients undergoing major gynaecological surgery and is associated with a fivefold increased risk of transfusion. Aust N Z J Obstet Gynaecol 2012;52:455–9.
[23] To J, Sinha R, Kim SW, et al. Predicting perioperative transfusion in elective hip and knee arthroplasty: a validated predictive model. Anesthesiology 2017;127:317–25.
[24] Seicean A, Seicean S, Alan N, et al. Preoperative anemia and perioperative outcomes in patients who undergo elective spine surgery. Spine 2013;38:1331–41.
[25] Mueller MM, Van Remoortel H, Meybohm P, et al. Patient blood management: recommendations from the 2018 Frankfurt consensus conference. JAMA 2019;321:983.
[26] Elhenawy AM, Meyer SR, Bagshaw SM, MacArthur RG, Carroll LJ. Role of preoperative intravenous iron therapy to correct anemia before major surgery: study protocol for systematic review and meta-analysis. Syst Rev 2015;4:29.
[27] Wilson MJ, Dekker JW, Bruns E, et al. Short-term effect of preoperative intravenous iron therapy in colorectal cancer patients with anemia: results of a cohort study. Transfusion (Paris) 2018;58:795–803.
[28] Bedair H, Yang J, Dwyer MK, McCarthy JC. Preoperative erythropoietin alpha reduces postoperative transfusions in THA and TKA but may not be cost-effective. Clin Orthop Relat Res 2015;473:590–6.
[29] Leahy MF, Hofmann A, Towler S, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals: patient blood management outcomes. Transfusion (Paris) 2017;57:1347–58.
[30] Transfusion medicine branch of Beijing medical association. Patient blood management—expert consensus on diagnosis and treatment of preoperative anemia. Natl Med J China 2018;98:2386–92.