Supplementary information

Factors associated with red blood cell transfusion among hospitalized patients: a cross-sectional study

Peiwen ZHANG[1], Dandan XU[1], Xinhan ZHANG[2], Mengyin WU[2], Xuecheng YAO[2], Dawei CUI[1], Jue XIE[1]

[1]*Department of Blood Transfusion, the First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310003, China*

[2]*Department of Epidemiology and Biostatistics, Zhejiang University School of Public Health, Hangzhou 310058, China*

Materials and methods

Data acquisition and preprocessing

All data was collected from The First-Affiliated Hospital, School of Medicine, Zhejiang University (FAHZU), a large-size general hospital with six campuses in Hangzhou, Zhejiang Province. Hangzhou, located in the southeast of China, boasts a resident population of 10.36 million and achieving an urbanization of 78.5%. The studied hospital Qingchun Campus is equipped with 2500 beds and lie on the center of Hangzhou bearing a huge medical pressure of Hangzhou. The Department of Blood Transfusion in Qingchun Campus is responsible for formulating the plan for the use of blood in the clinic as well as strict monitoring of the blood reserves according to national laws and regulations.

The daily total applied units of red blood cell were cumulative from all requirements of patients from 1st January 2013 to 31st December 2020. In addition, we collected the information about patients receiving RBC including apply units, age (years old), sex, body mass index (BMI, kg/m^2), the result of blood test (hemoglobin, platelet, prothrombin time, red blood cell-specific volume, andalanine aminotransferase), ABO type, usage classification, history of blood transfusion and departments. Repeated application of RBC from a patient were summed up into one record during a hospital stay. Furthermore, subjects with the following characteristics were excluded: (1) lack of accurate identity information; (2) without complete blood test results and blood type; (3) lack of the applied units of RBC; (4) age <18 years old; (5) missing records of sex, anthropometric data, or blood transfusion and disease histories.

The apply units were estimated by the clinical doctors caring for the patients based on the health condition. Age was calculated using the application date and birthday of each patient. The blood test results were chosen as the test nearest to the date of the RBC application. The study was approved by the Medical Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine, Zhejiang, China.

Hospital Inventory perspective

We conducted the time-series analysis using the triple exponential smoothing method to decompose the factors from the hospital inventory which affect the amount of given RBC. The basic principle of the exponential smoothing method is to give different weights to observed values of the time-series sequence. Compared with the earlier data, the more recent data will be given greater weights, by which it can better eliminate the influence of noise and get more reasonable and reliable models. Triple exponential smoothing method, which applies exponential smoothing three times,could incorporate seasonal effects into the model.

In our study, we have run the statistics weekly to facilitate the analysis and reduce the influence of extreme values on fitting the models. Furthermore, due to the impact of the coronavirus-19 epidemic in early 2020, there is a large gap in the total number of applications. Thus, we did not include the data of that period for analysis.

We use simple seasonal, Winters' Additive, and Winters' Multiplicative procedures to implement the construction of the models. The simple seasonal exponential smoothing method is suitable for sequences with seasonal trends which remain constant over time. Winters' Additive exponential smoothing method is suitable for the time-series with line trends which does not depend on the seasonal effects of the sequences which is the opposite of Winters' Multiplicative exponential smoothing method.

Due to years of practice, the studied hospital, FAHZU, can maintain a balance between blood supply and demand under the circumstance of blood limitation, and the change in total instant application of RBC can reflect the pressure of blood inventory to some extent.Thus, we considering the trend of blood inventory in the association with the transfusing units to patients.

Patient perspective

Along with the risk factors from hospital inventory, the basic characteristics and health condition of patients can cause varied red blood cell demand, leading to the insufficiency between demands and supplies as well. We conducted a binarylogistic regression model to estimate the odds ratios (OR) and 95% confidence intervals (CIs) for the effects of selected individual and seasonal variables on transfusion units. The giving units of red blood cells were categorized into a binary variable by the median of transfusing RBC, which was 0 (stood for <2 units) and 1 (stood for ≥2 units). The season variable was classified by the application date for each patient. Winter included December, January, and February and spring was from March to May while summer including June, July, and August and autumn including October, November, and September in this southeastern city of China.

BMI was calculated as weight (kilograms) divided by the square of height (meters squared) and categorized into <18.5 kg/m^2, 18.5 kg/m^2–23.9 kg/m^2, 24 kg/m^2–27.9 kg/m^2 and ≥28 kg/m^2 according to BMI standard for Chinese populations. Usage classification included surgical use, ward use, and emergency use and ward use pooled ward preparation and ward given. The departments standard for where the patients were hospitalized in and we recategorized the departments into several kinds which were surgical department, internal medicine department, obstetrics& gynecology department, urgency department, and others.

We adjusted for full selected factors in the first model including age (years old), sex (male, female), BMI (<18.5 kg/m^2, 18.5 kg/m^2–23.9 kg/m^2, 24 kg/m^2–27.9 kg/m^2 and ≥28 kg/m^2), HGB (g/L), platelet (PLT, 10^9/L), prothrombin time (PT, second), red blood cell specific volume (HCT, %), alanine aminotransferase (ALT, U/L), ABO blood type (A, AB, B and O), usage classification (surgical use, ward use, and emergency use), history of blood transfusion (Yes, No), department (surgical department, internal medicine department, obstetrics& gynecology department, urgency department, and others) and seasons (Spring, Summer, Autumn and Winter). We further conducted the second model using the backward step in binary logistic regression based on the first model. And to assist the translation of the generated statistical model, we further made a risk assessment nomogram as a graphic model representation. Subgroup analysis was performed to identify potential modifications by different seasons.

Statistical analyses

Categorical variables were presented as frequency (percentage) and continuous variables were shown as mean±standard deviation (SD). The difference in seasons was tested using the student t-test for continuous variables and chi-square tests for categorical variables. All analyses were carried out using R software (version, 4.0.0). Two-tailed $P<0.05$ was considered statistically significant.

Table S1 The characteristics of the total patients accepting the RBC transfusion and patients by seasons of apply dates

Variables		Total (*n*=20,041)	Spring (*n*=4526)	Summer (*n*=5240)	Autumn (*n*=5132)	Winter (*n*=5143)	*P*
Apply unit [median (IQR)]		53.00 (207.7)	51.71 (196.1)	56.06 (233.5)	51.47 (191.9)	52.55 (205.0)	0.657
Age [mean (SD), years]		55.91 (16.2)	55.16 (16.6)	56.72 (15.8)	55.99 (16.3)	55.65 (16.1)	<0.001
Sex [*n* (%)]							
	Male	11248 (56.1)	2610 (57.7)	2881 (55.0)	2763 (53.8)	2994 (58.2)	<0.001
	Female	8793 (43.9)	1916 (42.3)	2359 (45.0)	2369 (46.2)	2149 (41.8)	
BMI [*n* (%), kg/m^2]							
	<18.5	2993 (23.1)	798 (24.8)	692 (21.2)	748 (23.3)	755 (22.9)	0.01
	18.5–24	6661 (51.3)	1577 (49.1)	1688 (51.7)	1684 (52.5)	1712 (52.0)	
	24–28	2662 (20.5)	682 (21.2)	702 (21.5)	627 (19.6)	651 (19.8)	
	≥28	658 (5.1)	157 (4.9)	180 (5.5)	147 (4.6)	174 (5.3)	
HGB [mean (SD), g/L]		85.11 (32.2)	81.27 (31.5)	87.04 (32.6)	87.43 (32.3)	84.21 (31.9)	<0.001
PLT [mean (SD), 10^9/L]		152.08 (120.8)	147.31 (122.1)	158.75 (122.3)	152.37 (115.9)	149.21 (122.6)	<0.001
PT [mean (SD), s]		13.15 (3.8)	13.26 (3.5)	13.41 (4.6)	12.95 (3.6)	13.00 (3.4)	<0.001
HCT [mean (SD), %]		26.01 (9.8)	24.77 (9.6)	26.70 (9.9)	26.79 (10.0)	25.63 (9.7)	<0.001
ALT [mean (SD), U/L]		43.53 (161.4)	44.66 (131.8)	41.77 (157.8)	45.42 (211.1)	42.41 (127.9)	0.632
ABO type [*n* (%)]							
	A	6738 (33.6)	1514 (33.5)	1719 (32.8)	1750 (34.1)	1755 (34.1)	0.057
	AB	1500 (7.5)	317 (7.0)	431 (8.2)	383 (7.5)	369 (7.2)	
	B	4519 (22.5)	981 (21.7)	1238 (23.6)	1146 (22.3)	1154 (22.4)	
	O	7284 (36.3)	1714 (37.9)	1852 (35.3)	1853 (36.1)	1865 (36.3)	
Usage classification [*n* (%)]							
	Emergency	7405 (36.9)	1942 (42.9)	1775 (33.9)	1743 (34.0)	1945 (37.8)	<0.001
	Surgery	9640 (48.1)	1877 (41.5)	2757 (52.6)	2640 (51.4)	2366 (46.0)	
	Ward	2996 (14.9)	707 (15.6)	708 (13.5)	749 (14.6)	832 (16.2)	
History of blood transfusion [*n* (%)]							
	No	11988 (59.8)	2477 (54.7)	3295 (62.9)	3180 (62.0)	3036 (59.0)	<0.001
	Yes	8053 (40.2)	2049 (45.3)	1945 (37.1)	1952 (38.0)	2107 (41.0)	
Department [*n* (%)]							
	Surgical	2066 (46.8)	2829 (55.6)	2692 (53.4)	2551 (50.4)	2066 (46.8)	<0.001
	Internal Medicine	1452 (32.9)	1350 (26.5)	1352 (26.8)	1563 (30.9)	1452 (32.9)	
	Obstetrics & Gynecology	91 (2.1)	132 (2.6)	118 (2.3)	120 (2.4)	91 (2.1)	
	Urgency	647 (14.7)	601 (11.8)	694 (13.8)	663 (13.1)	647 (14.7)	
	Others	155 (3.5)	176 (3.5)	186 (3.7)	166 (3.3)	155 (3.5)	

BMI, body mass index; HGB, hemoglobin; PLT, platelet; PT, prothrombin time; HCT, red blood cell specific volume; ALT, alanine aminotransferase.

Table S2 The OR [95% CI] of the factors affecting the quantity of RBC transfusion

Variables		Model1[a]	Model2[b]
Apply unit		1.00 [1.00, 1.00]	-
Age		**0.99 [0.99, 0.99]**	**0.99 [0.99, 0.99]**
Sex			
	Female	Ref.	-
	Male	0.94 [0.86, 1.04]	-
BMI			
	<18.5	Ref.	-
	18.5–24	1.01 [0.90, 1.13]	-
	24–28	1.10 [0.96, 1.27]	-
	≥28	0.99 [0.79, 1.23]	-
HGB		1.00 [0.99, 1.00]	-
PLT		**1.00 [1.00, 1.00]**	**1.00 [1.00, 1.00]**
PT		0.99 [0.97, 1.00]	**0.99 [0.98, 1.00]**
HCT		1.00 [0.99, 1.02]	-
ALT		1.00 [1.00, 1.00]	-
ABO type			
	A	Ref.	Ref.
	AB	**1.26 [1.04, 1.54]**	**1.26 [1.04, 1.53]**
	B	**1.38 [1.21, 1.57]**	**1.38 [1.21, 1.57]**
	O	**0.87 [0.79, 0.97]**	**0.87 [0.79, 0.97]**
Usage classification			
	Emergency	Ref.	Ref.
	Surgery	**2.70 [2.24, 3.27]**	**2.66 [2.26, 3.13]**
	Ward	**1.23 [1.07, 1.41]**	**1.22 [1.07, 1.40]**
History of blood transfusion			
	No	Ref.	Ref.
	Yes	**1.25 [1.10, 1.43]**	**1.26 [1.10, 1.43]**
Department			
	Internal Medicine	Ref.	Ref.
	Surgical	0.87 [0.67, 1.14]	**0.84 [0.72, 0.98]**
	Obstetrics & Gynecology	**0.83 [0.70, 0.97]**	1.01 [0.69, 1.52]
	Urgency	**0.75 [0.64, 0.88]**	**0.77 [0.66, 0.89]**
	Others	0.96 [0.65, 1.45]	0.87 [0.67, 1.13]
Season			
	Winter	Ref.	Ref.
	Spring	0.98 [0.90, 1.07]	0.98 [0.90, 1.07]
	Summer	**0.72 [0.66, 0.79]**	**0.72 [0.66, 0.79]**
	Autumn	**1.11 [1.01, 1.22]**	**1.11 [1.01, 1.22]**

BMI, body mass index; HGB, hemoglobin; PLT, platelet; PT, prothrombin time; HCT, red blood cell specific volume; ALT, alanine aminotransferase.

a. We used logistic regression to conduct model1 which was adjusted for full risk factors.

b. Model2 was based on model1 and further used backwards step; the factors with "-" means that they were removed when fitting the model.

Table S3 Stratified analyses of the risk factors for the quantity of RBC transfusion in four seasons

Variables		Spring	Summer	Autumn	Winter
Apply unit		1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Age		1.00 [0.99, 1.00]	**0.98 [0.98, 0.99]**	**0.99 [0.98, 0.99]**	**0.99 [0.99, 1.00]**
Sex					
	Female	Ref.	Ref.	Ref.	Ref.
	Male	**0.79 [0.65, 0.97]**	0.90 [0.74, 1.09]	1.00 [0.84, 1.20]	1.05 [0.88, 1.25]
BMI					
	<18.5	Ref.	Ref.	Ref.	Ref.
	18.5–24	1.05 [0.81, 1.35]	1.08 [0.85, 1.37]	1.11 [0.90, 1.38]	0.87 [0.70, 1.08]
	24–28	1.18 [0.87, 1.60]	1.03 [0.77, 1.37]	**1.41 [1.08, 1.86]**	0.90 [0.70, 1.17]
	≥28	1.38 [0.86, 2.31]	0.99 [0.62, 1.64]	1.10 [0.74, 1.67]	0.68 [0.45, 1.04]
HGB		1.01 [0.99, 1.02]	**0.99 [0.97, 1.00]**	1.00 [0.99, 1.01]	1.01 [1.00, 1.02]
PLT		1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
PT		0.99 [0.96, 1.01]	0.99 [0.97, 1.02]	0.98 [0.96, 1.01]	0.99 [0.96, 1.02]
HCT		0.98 [0.93, 1.02]	**1.04 [1.00, 1.09]**	1.01 [0.98, 1.04]	0.98 [0.94, 1.02]
ALT		1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
ABO type					
	A	Ref.	Ref.	Ref.	Ref.
	AB	1.00 [0.66, 1.53]	1.42 [0.95, 2.17]	**1.50 [1.02, 2.26]**	1.17 [0.83, 1.69]
	B	1.10 [0.84, 1.45]	**1.33 [1.01, 1.76]**	**1.54 [1.20, 1.99]**	**1.47 [1.15, 1.89]**
	O	**0.68 [0.54, 0.86]**	0.81 [0.65, 1.00]	0.97 [0.80, 1.18]	0.99 [0.81, 1.20]
Usage classification					
	Emergency	Ref.	Ref.	Ref.	Ref.
	Surgery	**2.86 [1.90, 4.31]**	**3.06 [2.06, 4.57]**	**2.72 [1.91, 3.91]**	**2.40 [1.66, 3.48]**
	Ward	**1.59 [1.15, 2.22]**	1.32 [0.99, 1.78]	1.10 [0.85, 1.42]	1.14 [0.88, 1.47]
History of blood transfusion					
	No	Ref.	Ref.	Ref.	Ref.
	Yes	1.24 [0.92, 1.66]	**1.48 [1.10, 1.98]**	1.25 [0.97, 1.60]	1.11 [0.87, 1.41]
Department					
	Internal Medicine	Ref.	Ref.	Ref.	Ref.
	Surgical	0.75 [0.52, 1.07]	0.90 [0.62, 1.29]	0.80 [0.59, 1.09]	0.81 [0.60, 1.10]
	Obstetrics & Gynecology	0.76 [0.34, 1.86]	0.70 [0.33, 1.63]	0.94 [0.47, 2.01]	1.56 [0.70, 4.00]
	Urgency	0.76 [0.54, 1.08]	0.77 [0.55, 1.09]	**0.67 [0.49, 0.91]**	0.80 [0.60, 1.06]
	Others	1.00 [0.55, 1.89]	0.79 [0.47, 1.36]	0.87 [0.53, 1.46]	0.90 [0.53, 1.55]

BMI, body mass index; HGB, hemoglobin; PLT, platelet; PT, prothrombin time; HCT, red blood cell specific volume; ALT, alanine aminotransferase.

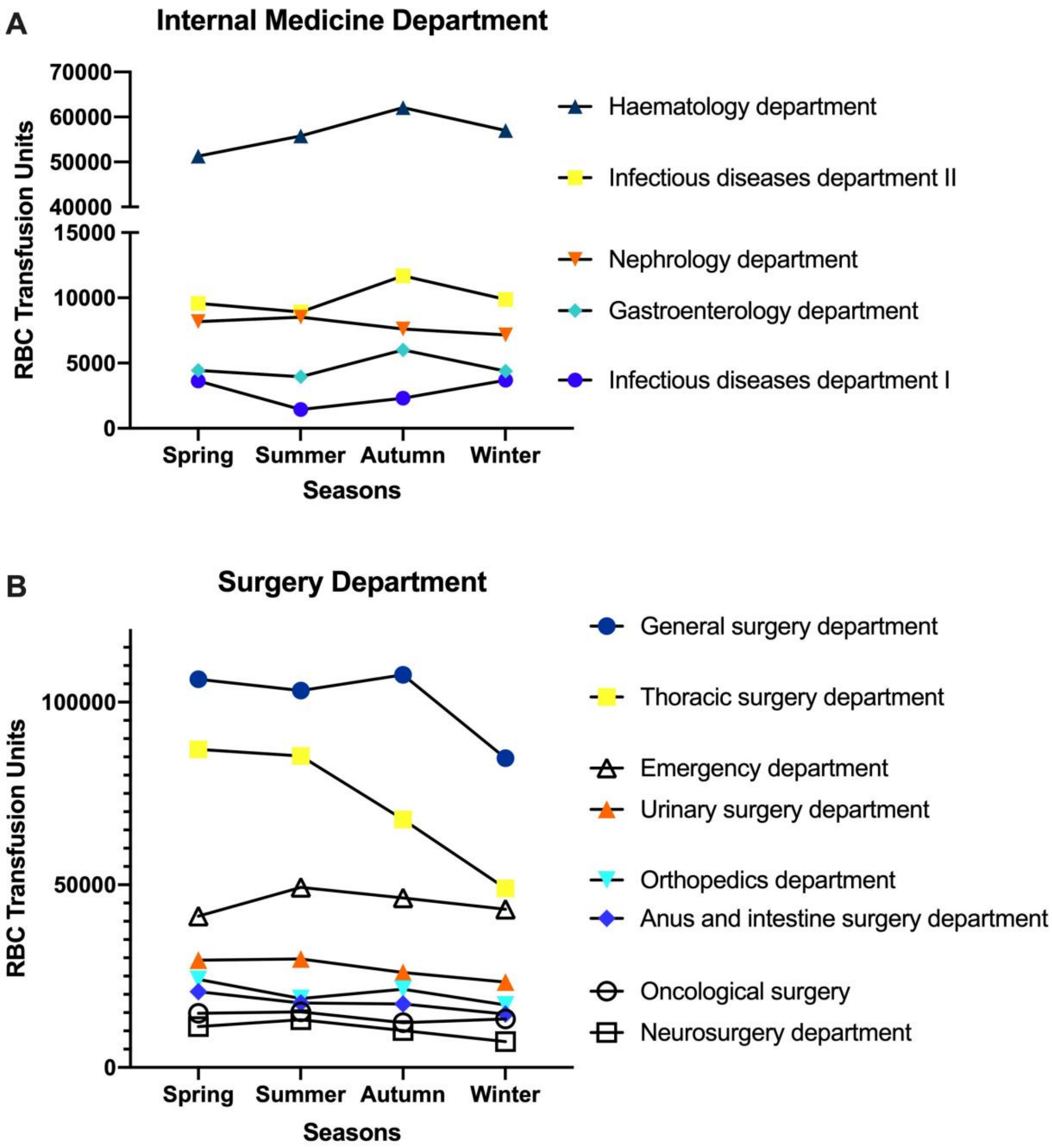

Fig. 1S The seasonal trend associated with blood transfusion in different diseases. A, The seasonal trend in Internal Medicine Department; B, The seasonal trend in Surgery Department.