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Original Article

Investigation of the current situation of massive blood transfusion in different surgical departments: a large multicenter study in China

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Abstract: Objective: This study aims to learn about the current situation of surgical massive blood transfusion of different surgical departments in China's Tertiary hospitals, which could provide the basis for the formulation of guidelines on massive blood transfusion. Method: A multicenter retrospective research on the application status of blood constituents during massive blood transfusion was conducted and a comparative analyses of survival and length of hospitalization in patients from different departments (trauma, cardiac surgery, obstetric conditions, or other common surgeries), were performed. Result: In China, during massive blood transfusion the ratio of the dosage of fresh frozen plasma to the dosage of red blood cell suspension reached 1:1-2, while the dosage of platelet and cryoprecipitate appeared to be very small. The risk of in-hospital death were associated with the primary disease in patients receiving massive blood transfusion (Log-Rank $P = 0.000$), cardiac surgery and trauma patients who received massive blood transfusion have a higher risk of death rate. Conclusions: Patients undergoing massive blood transfusion among different surgical departments have a certain difference in use of blood transfusion, mortality rate and the time of death. Our findings suggested that we should set up an independent transfusion program in cardiac surgery and trauma patients of massive blood transfusion.

Keywords: Massive transfusion, blood constituents, retrospective analysis, surgical department

Introduction

Massive blood transfusion is generally defined as the administration of ≥ 10 U of packed red blood cells (pRBC) to a patient [1, 2] or the transfusion of more than one blood volume in 24 h [1, 3-5]. Acute clinical situations that warrant the administration of massive transfusion include a 50% blood volume loss within 3 h or a blood loss rate of 150 ml/min [3]. Massive transfusion is generally necessary in severely injured military personnel or patients with multiple injuries. Such patients often require multiple, complex surgical procedures. A rational blood transfusion protocol can improve the outcome of surgery, whereas unreasonably excessive transfusion can lead to mortality, mainly due to coagulation disorders, acidosis, and hypothermia. Most of the studies published hitherto have been conducted in western countries and on trauma patients [5-10]. No multicenter data are currently available on the influence of massive transfusion on the application of blood constituents during the perioperative period in Chinese patients.

In this study, we in order to learn about the current situation of surgical massive transfusion in China's Class III general hospitals and provide the basis for the formulation of China's guidelines on massive transfusion (draft for recommendation), we undertook a retrospective in-

Table 1. The death situation in 1601 patients who received blood transfusion according to department and disease

Patients in different surgical departments			Control group§ (n = 553)	Research group§ (n = 1048)	*P**
Trauma (n = 268)	male	Death, n (%)	7 (14.89)	23 (16.67)	0.776
		Survival, n (%)	40 (85.11)	115 (83.33)	
	female	Death, n (%)	0	4 (8.16)	0.088
		survival, n (%)	34 (100)	45 (91.84)	
	Total	Mortality (%)	7/81 (8.64)	27/187 (14.44)	0.190
cardiac surgery (n = 383)	male	death, n (%)	1 (2.17)	34 (20.12)	0.003
		survival, n (%)	45 (97.83)	135 (79.88)	
	female	death, n (%)	3 (4.29)	15 (15.31)	0.023
		survival, n (%)	67 (95.71)	83 (84.69)	
	Total	Mortality (%)	4/116 (3.45)	49/267(18.35)	0.000
general surgery (n = 876)	male	death, n (%)	10 (6.25)	14 (4.13)	0.302
		survival, n (%)	150 (93.75)	325 (95.87)	
	female	death, n (%)	3 (1.71)	15 (7.43)	0.009
		survival, n (%)	172 (98.29)	187 (92.57)	
	Total	Mortality (%)	13/335 (3.88)	29/541(5.36)	0.319
Obstetrics (n = 74)	female	death, n (%)	0	3 (5.66)	0.266
		survival, n (%)	21 (100)	50 (94.34)	
	Total	Mortality (%)	0	3/53 (5.66)	0.266
Total (n = 1601)	male	death, n (%)	18 (7.11)	71 (10.99)	0.080
		survival, n (%)	235 (92.89)	575 (89.01)	
	female	death, n (%)	6 (2.00)	37 (9.20)	0.000
		survival, n (%)	294 (98.00)	365 (90.80)	
	Total	Mortality (%)	24/553 (4.34)	108/1048 (10.31)	0.000

§Patients who received transfusion of ≥ 10 U of pRBC over a period of ≤ 24 h were includedin the study as research group. Patients who received transfusions of < 10 U for ≤ 24 h were assigned to the control group.*Chi-square test was used to show the motility date difference between control group and research group according to the gender factor.

vestigation of 1601 cases of surgical inpatients from 20 large-scale, comprehensive hospitals in different regions of China and analyzed the the application of blood constituents in different surgical departments transfusion patients.

Methods

This study has been approved by the ethics committee of Shaanxi Provincial People's Hospital. The subject's informed consent was obtained from each of the participants.

Collecting data

In this study, the massive blood transfusion is defined as the administration of ≥10 U of packed red blood cells (pRBC) in 24 h. We collected data from the medical records of surgical inpatients who received massive transfusion at 20 large-scale hospitals (in the northwest, southwest, central south, north, and northeast parts of China) between January 2009 and December 2010, we distributed 2000 copies of the Massive Transfusion Survey Table (hereafter referred to as "Survey Table") to 20 Participate in the hospital. Members of the National Massive Transfusion Current Status Investigation Coordination Group (hereafter referred to as the "Coordination Group") were responsible for collecting the data from these hospitals using the Survey Table. The data analysis was conducted at Shaanxi Provincial People's Hospital, the Third Affiliated Hospital of the Medical College of Xi'an Jiaotong University. The center is a level-3 grade-A hospital and has 73 clinical departments, 7 research centers, 4500 well-trained staff members, and 2600 beds.

Study population

Patients who received transfusion of ≥ 10 U of pRBC over a period of ≤ 24 h for trauma, cardiac surgery, obstetric conditions, or other com-

Table 2. General blood-use of 1048 patients who received massive blood transfusion

	Trauma	Cardiac surgery	General surgery	Obstetrics	*P*
Number of patients, n (%)	187 (17.84)	267 (25.48)	541 (51.62)	53 (5.06)	0.000*
Males, n (%)	138 (21.4)	169 (26.2)	339 (52.5)	0 (0.0)	0.000*
female, n (%)	49 (12.2)	98 (24.4)	202 (50.2)	53 (13.2)	0.000*
Age (yr, mean ± SD)	40 (±15)	46 (±17)	47 (±17)	33 (±7)	0.000†
Weight (kg, mean ± SD)	60 (±10)	57 (±13)	59 (±11)	60 (±7)	0.000†
Length of hospital stay (d, mean ± SD)	31 (±28)	32 (±23)	30 (±24)	18 (±8)	0.353†
Length of ICU stay (d, mean ± SD)	9 (±12)	7 (±9)	13 (±43)	3 (±4)	0.917†
Operation time (h, mean ± SD)	3.47 (±4.38)	5.33 (±3.87)	3.18 (±3.70)	1.78 (±2.52)	0.000†
Clinical data (before transfusion)					
RBC×10^{12}/L, (mean ± SD)	3.3 (±1.0)	4.3 (±1.0)	3.8 (±1.0)	3.2 (±1.0)	0.000†
Hb in g/L, (mean ± SD)	108 (±76)	132 (±31)	115 (±31)	95 (±31)	0.000†
Hct as %, (mean ± SD)	16 (±17)	13 (±18)	19 (±17)	11 (±14)	0.000†
PLT ×10^{9}/L, (mean ± SD)	170 (±103)	145 (±67)	194 (±108)	161 (±77)	0.000†
PT in s, (mean ± SD)	16.9 (±11.1)	13.9 (±3.8)	13.5 (±4.1)	14.6 (±6.6)	0.000†
APTT in s, (mean ± SD)	41 (±29)	34 (±9)	35 (±18)	47 (±66)	0.009†
TT in s, (mean ± SD)	20.8 (±13)	17.1 (±4.5)	16.8 (±5)	17.6 (±6.9)	0.017†
INR, (mean ± SD)	1 (±1.0)	1	1 (±1.0)	2 (±3)	0.039†

RBC = red blood cell count; Hb = hemoglobin concentration; Hct = hematocrit; PLT = platelet count; PT = prothrombin time; APTT = activated partial thromboplastin time; TT = thrombin time; INR = international normalized ratio. *Chi-square test was used. †Analysis of variance was used.

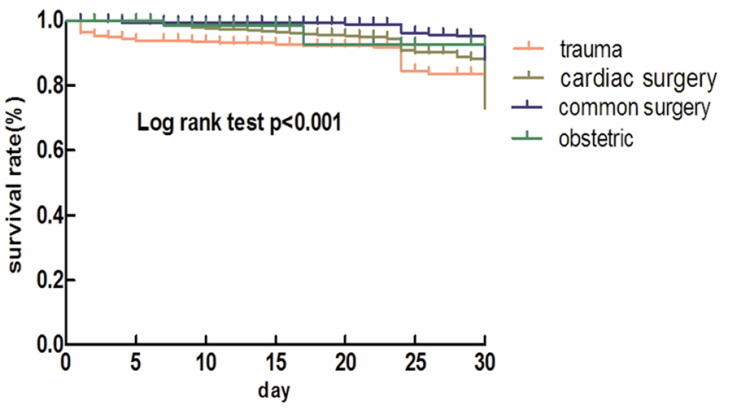

Figure 1. Kaplan- Meier survival chart of different surgical departments.

mon surgeries (e.g., orthopedic, thoracic, general, urinary, hepatobiliary, and neurological surgery) were included in the study as research group. Patients who received transfusions of < 10 U for ≤ 24 h were assigned to the control group. On the other hand, patients with coagulation disorders and/or hepatic failure due to medical causes were excluded from the analysis. The cases of death in this study refer to fatalities occurring during the period of hospitalization.

Design survey table

The directors of the transfusion departments of the 20 participating hospitals discussed the topic, consulted experts, and designed the Survey Table with reference to several international and domestic sources, in accordance with the principle of voluntary participation in this project. A meeting of the Coordination Group was then held (06-05-2010, Xi'an), where 35 experts of clinical transfusion, surgery, anesthesia, gynecology and obstetrics, hematology, and medical statistics discussed the study protocol and mode of data collection and also perfected and added supplements to the Survey Table. Suitable training was then offered to the investigating staff.

Components of the survey table

The survey table comprised 4 sections: 1, Clinical and demographic characteristics of the patient: including name, gender, age, body

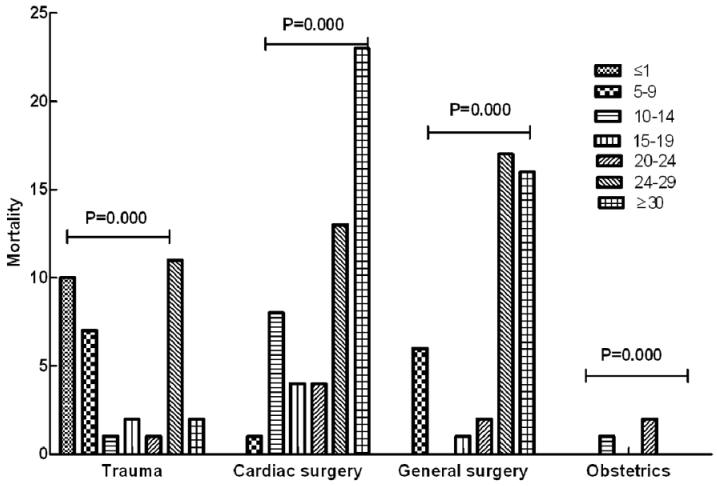

Figure 2. Comparison of hospitalization time in the deaths of massive transfusion among the four surgical groups.

weight, blood type, ethnicity, admission number, admission department, primary diagnosis, secondary diagnosis, pathologic diagnosis, nature of surgery, and vital signs on admission; 2, Details regarding the perioperative complications, clinical condition within 24 h and after 24 h of the transfusion, and the total amount of blood transfused; 3, The results of the following blood tests performed before, within 24 h, and after 24 h of transfusion: routine blood test, coagulation tests, liver function test, kidney function test, and arterial blood gas analysis;4, Adverse events due to massive transfusion.

Quality control

The Survey Table was first subjected to a small-scale preliminary test at Shaanxi Provincial People's Hospital so that revisions could be made on the basis of the results and comments by experts to further improve the table.

The protocol for massive transfusion, as per the Chinese standards, was as follows: one unit of pRBC derived from 200 ml of whole blood and with a volume of 140-172 ml; one unit of fresh frozen plasma (FFP) derived from 200 ml of whole blood and a volume of 100 ml; one bag of apheresis platelet of 10 U and a volume of 150-250 ml; and one unit of platelet concentrate derived from 200 ml of whole blood and with a volume of 20-30 ml. One bag of apheresis platelet is 10 U of platelet concentrate. The pRBC were stored at 2°C to 6°C. FFP was stored at ≤ -18°C and thawed in a 37°C water bath, for about 10 to 15 minutes. Platelets were stored at 20°C to 24°C in a platelet shaker.

The main test devices and reagents used were as follows: Sysmex XE-2100/XT-1800i hematology analyzer, Sysmex Corporation, Kobe, Japan; Beckman Coulter LH780 Coulter Hematology Analyzer, Beckman Coulter, CA, USA; Hitachi 7170A/7180 Biochemical Analyzer, Hitachi, Japan; Roche Modular DP Automatic Biochemical Analyzer, Roche, USA; Olympus AU640 Biochemical Analyzer, Olympus Corporation, Japan; Radiometer ABL-77 Blood Gas Analyzer, Radiometer, Copenhagen, Denmark; Roche Cobas-B123 Blood Gas Analyzer, Roche, US; Sysmex CA1500/CA7000 Automatic Blood Coagulation Analyzer, Japan. All test reagents used were device-supporting reagents.

Data on the blood tests were collected from the laboratory records: blood routine, coagulation tests, liver function test, kidney function, and blood gas analysis. The data were collected for the blood tests performed before transfusion and at 16 different time points during the 24-h transfusion (2 U, 4 U, 6 U, 40 U) and subjected to statistical analysis. The tests were conducted at the laboratory of each participating hospital, which undergoes internal quality control and an external quality assessment conducted by the National Center for Clinical Laboratories.

Statistical analysis

Statistical analysis was conducted using SPSS software (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago, IL: SPSS Inc.). Epidata (version 3.01; Epidata Association) was used for double data entry verification and database construction. The data on the demographic characteristics and clinical features were expressed as means with standard deviations or as absolute numbers. Chi-square test (x^2) was used to assess the group differences by considering patients who received massive transfusion within 24 h or not. ANOVA analysis was applied to indicate some demographic characteristics (e,g. weight, age) and clinical data (e, g. RBC, PLT) differences under the certain four surgical conditions. Survival analysis with log-rank test was

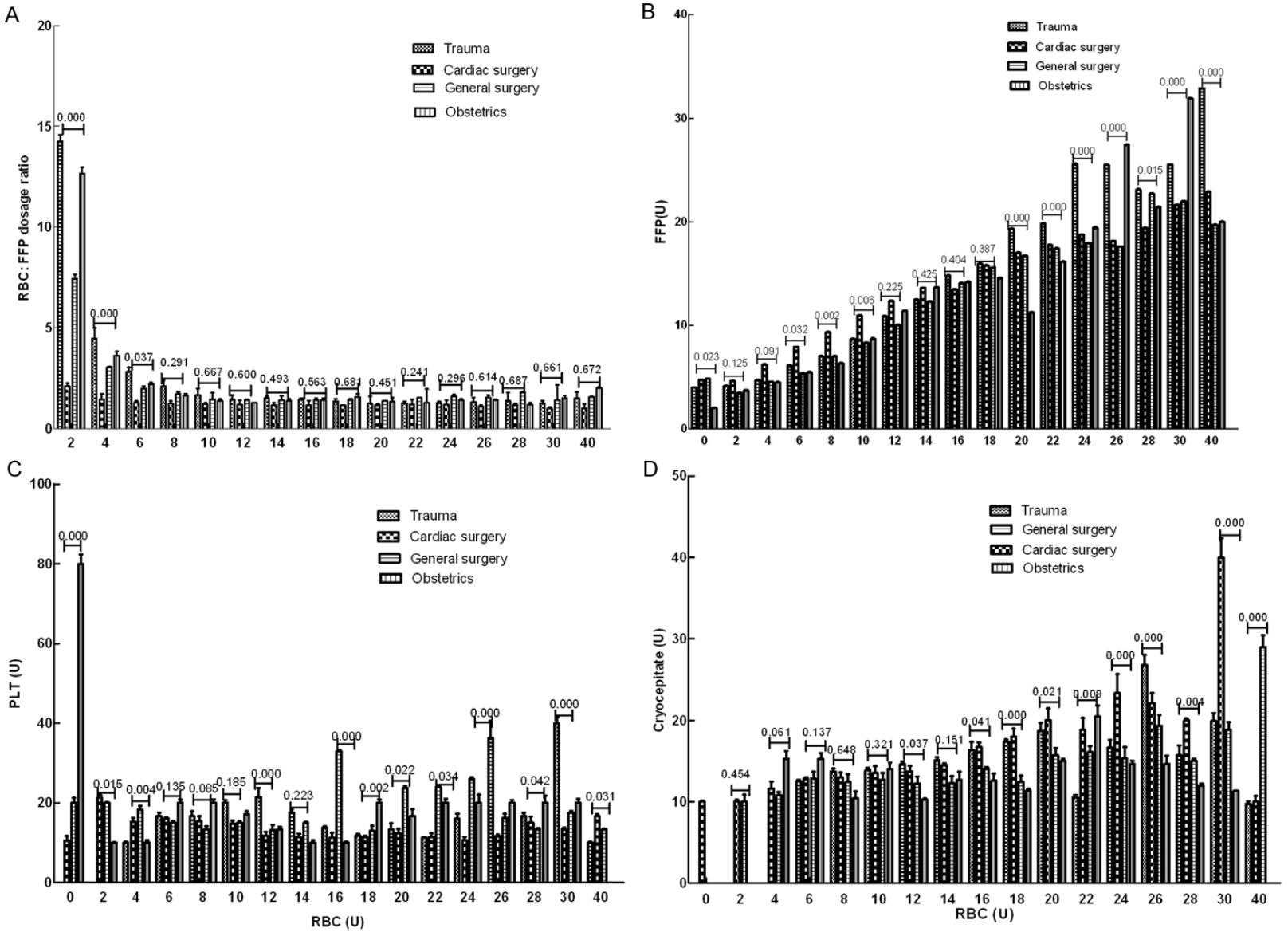

Figure 3. Dosage of RBC, plasma, Platelet and cryoprecipitate application in different surgical departments. A: RBC: FFP dosage's transfusion among among the four groups under different dosage of RBC. B: Plasma transfusion among the four groups under different dosage of RBC. C: The mean dosage of platelets infusion among the four groups under different dosage of RBC. D: The mean dosage of cryoprecipitate infusion among the four groups under different dosage of RBC.

showed the mortality differences among the four surgical departments. A two-sided *P*-value of < 0.05 was considered statistically significant.

Results

Patient characteristics

We were able to retrieve 1753 of the 2000 copies of the Survey Table from the 20 hospitals, at a recovery rate of 87.65%. After excluding tables with missing information, 1601 copies (91.33%; 889, male patients; 702, female patients) were used for the analysis. The age of the enrolled patients was 16-91 years (median: 46 years) and weight was 46-105 kg (median: 60 kg). The data regarding age and weight were tested by the Shapiro-Wilk test ($P < 0.01$) and showed abnormal distribution; therefore, they were described by median values. Among the 1601 patients who received blood transfusion, 1048 patients received ≥ 10 U of pRBC within 24 h (108 died, 940 survived; death rate: 10.31%), whereas 553 patients received < 10 U of pRBC within 24 h (24 died, 529 survived; death rate: 4.34%).

Comparing the clinical use of blood in different surgical departments

It was found that the mortality rate in patients treated with massive blood transfusion (≥ 10 U) was different from patients in the control group (< 10 U) between different clinical departments ($P < 0.001$), and there was no significance difference for mortality rate among trauma, general surgery and obstetrics groups ($P > 0.05$) excepting in the department of cardiac surgery ($P < 0.001$). The results indicated that if the transfusion of RBC ≥ 10 U within 24 h, the mortality rate of patients in four departments were, in order, cardiac surgery (18.4%), trauma (14.4%), obstetrics (5.7%) and general surgery (5.4%), however, when RBC transfusion < 10 U, the order of mortality rate were trauma (8.6%), general surgery (3.9%), cardiac surgery (3.4%) and obstetrics (0%), (**Table 1**).

General blood-use of 1048 patients who received massive blood transfusion

In the results of statistical analysis, we found that there were no significant difference in the length of hospitalization and ICU care with patients receiving massive blood transfusion among different surgery departments ($P > 0.05$), but significant difference in other indicators such as number of patients, gender, age, weight, operation time and preoperative hematologic parameters like blood routine as well as blood coagulation index were observed ($P < 0.05$) (**Table 2**).

Survival analysis of massive transfusion patients in different surgery departments

The survival analysis of massive transfusion patients in different surgery departments was preformed. The result showed that there was a certain degree of correlation between deaths of surgical patients in hospitalization and their primary disease (Log-Rank $P = 0.000$) when patients received a massive transfusion ≥ 10 units of RBC in 24 h. Meanwhile, after massive blood were transfused in patients who undergoing cardiac and trauma operation, their mortality rate in general surgery was higher than these in obstetrics during hospitalization, (**Figure 1**).

Comparing the time of in-hospital death in massive transfusion patients between different surgical departments

We found that there were differences in the time of in-hospital death in massive transfusion patients among different surgical departments. The patients in general surgery and cardiac surgery died 21 days after hospital admission and the time of death increased as time prolonged, patients in trauma had two peaks of death at first 5 days and 21-30 days after hospitalization, **Figure 2**.

Comparing the specific situation of clinical transfusion in different surgical departments

The application of blood components varied in different surgical departments, such as the number of RBC and plasma transfusion in different stage, as well as the plasma was often used in combination with RBC at earlier stage of cardiac surgery operation. The ratio of RBC application to plasma infusion is kept 1 to 1 at different stage of RBC transfusion. However, in any other departments, the plasma was rarely used when RBC infusion was less than 4 U. If reached to 10 U, the number of RBC application is same with plasma (**Figure 3A**). It was shown in **Figure 3B** that, the dosage of plasma is increase with RBC infusion at a ratio of 1 to 1

or 1.5 in different surgical departments. When it comes to the platelet application in patients with massive transfusion in surgery, the dosage of platelet was lesser and was not increased with RBC application. Only 3 patients in obstetric had been transfused with RBC in the earlier stage because of the reduction of it, and which is raise for trauma patients when RBC infusion is more than 40 U (**Figure 3C**). Cryoprecipitate is also less used in China, the dosage of which is not increase with RBC application. In cardiac surgical department, while RBC infusion was reach to 30 U, cryoprecipitate application was increased in equal proportion with it, but which is increased in trauma patients only the RBC infusion was up to 40 U (**Figure 3D**).

Discussion

Transfusion plays a significant role in first aid, dangerous and critically ill patients, which make an adequate blood supply timely for patients with massive blood loss. However, trauma patients remained a high mortality ranging from 19% to 70% after received massive blood infusion. This investigation suggested that transfusion patients of 1048 cases who received massive transfusion ≥ 10 units of RBC in 24 h have a mortality of 10.3% which lower than literatures reported (the mortality of trauma patients is 14.4%) [11-13]. It is wondered that we need a further study whether the 20 investigated health care organizations which belong to large general hospital in different eras of china have a better rescue condition, or this group of date contain relative fewer trauma cases comparing to the cases of general surgical patients, or have a sufficient preoperative preparation that contribute to this lower mortality. Our date classified by clinical department and the results indicated that when the massive transfusion ≥ 10 Unit of RBC within 24 h, the mortality rate of patients in four departments were, in order, cardiac surgery (18.4%), trauma (14.4%), obstetrics (5.7%)and general surgery (5.4%), however, when RBC transfusion < 10 Unit , the order of mortality rate were trauma (8.6%), general surgery (3.9%), cardiac surgery (3.4%) and obstetrics. the mortality in patients treated with massive blood transfusion (≥ 10 U) have a significant different from patients in the comparative group (< 10 U) among four clinical departments ($P < 0.001$), suggesting a relationship between mortality and the dosage of RBC infusion of hospitalization patients, and there was no significance in trauma, general surgery and obstetrics groups ($P > 0.05$) excepting in the department of cardiac surgery ($P < 0.001$). Therefore, transfusion at operation should be reduced as much as possible in order to lower the mortality.

This research surveyed general surgical patients with massive transfusion of 20 hospitals in china, the results shown that situation of blood application is different in different departments. The plasma was often used in combination with RBC at earlier stage of cardiac surgery operation. The ratio of RBC application to plasma infusion is kept 1 to 1 at different stage of RBC transfusion. However, in any other departments, the plasma was rarely used when RBC infusion was less than 4 U. If reached to 10 U, the number of RBC application is same with plasma. The dosage of plasma is increase with RBC infusion at a ratio of 1 to 1 or 1.5 in different surgical departments. When it comes to the platelet application in patients with massive transfusion in surgery, the dosage of platelet was lesser and was not increased with RBC application. Only 3 patients in obstetric had been transfused with platelet in the earlier stage because of the reduction of it, which maybe owing to the shortage of blood resources in our country or different habit of blood application. Platelet decrease dilutedly and the decreased haemostatic activity is the main reason of blood coaqulation disorders when massive blood loss, hence the guidelines of massive transfusion and research literature abroad advocated that the mortality of patients could be decreased when the ratio of plasma, RBC and platelet application was 1:1:1. This investigation also shown that cryoprecipitate application was not increased in equal proportion with it, but which is increased in trauma patients only the RBC infusion was up to 30 U.

Studied clinical situation before and after massive transfusion in varied departments, it was suggested that different departments hold different disease characteristics, and its baseline data have a significant difference ($P < 0.05$), such as number of patients, gender, age, weight, operation time and preoperative hematologic parameters like blood routine as well as blood coagulation index. Therefore, the death situation of patients with massive transfusion is different, and we could learn from survival analysis that there was a certain degree of correlation between deaths of surgical patients in

hospitalization and their primary disease (Log-Rank P = 0.000). Meanwhile, after massive blood transfusion in patients undergoing cardiac and trauma operation, mortality during hospitalization in general surgery was higher than which in obstetrics. Cardiac surgery and trauma patients who received massive blood transfusion have a higher risk of death rate, and there were difference in time of in-hospital death of four types of departments. Patients in general surgery and cardiac surgery died 21 days after hospital admission and Patients in trauma had two peak of death at first 5 days and about 21-30 days after hospitalization. It was suggested that we should set up an independent transfusion program in cardiac surgery and trauma patients of massive blood transfusion in order to reduce mortality.

Conclusion

The differences of blood application between different departments owe to there is no guideline currently. Most of them paid more attention to associated RBC transfusion with plasma application, but neglected the use of platelet and cryoprecipitate; characteristics of varies diseases were diverse in different surgical departments, which leads to a certain difference in mortality. We should consider disease characteristics of cardiac and trauma patients before guidelines for massive transfusion been constructed.

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Disclosure of conflict of interest

None.

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