Association of Storage Age of Transfused Red Blood Cells and Clinical Outcome of Cardiac Patients at Two Hospitals

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ABTRACT

Background: Studies indicate that transfusion of older red blood cell (RBC) units predicts a poorer outcome in cardiac surgery patients. The purpose of this study was to evaluate storage age of RBCs transfused in cardiac surgery and correlate with blood group and postoperative length of stay (POLOS).

Methods: Records for patients undergoing cardiac surgery at two hospitals were reviewed for a six-month period. Patient age, gender, ABO group, preoperative hemoglobin, blood units transfused, age of transfused RBCs, and POLOS were compiled.

Results: A total of 328 cardiac surgeries were performed, and 976 units of RBC were transfused. Numbers of RBCs transfused were correlated to female gender, increased patient age, lower preoperative hemoglobin, and POLOS. Age of the RBCs showed a weak inverse correlation to POLOS (trend for older RBCs to correlate with shorter POLOS). Blood group analysis showed a similar number of RBCs transfused, but a shorter age for the O units. Despite the fresher RBCs transfused, the POLOS tended to be longer in the O patients.

Conclusion: RBC units transfused in cardiac surgery increased with patient age, female gender, lower preoperative hemoglobin, and was important influence on the POLOS. The transfusion of older RBCs did not lengthen the POLOS.

INTRODUCTION

The transfusion of blood and its components may be associated with adverse events, some of which include transmission of infective agents, such as hepatitis and human immunodeficiency virus, acute and delayed transfusion reactions, transfusion associated acute lung injury, and graft versus host disease. All studies of red blood cell (RBC) transfusions in cardiac surgery show that transfused patients have worse clinical outcomes than non-transfused patients.[1-8] This is often interpreted to mean that red cell transfusions are a surrogate marker for disease severity and/or complexity of the cardiac procedure.

The duration of RBC storage before transfusion may alter RBC function and therefore, influence the incidence of complications. Observational studies indicate that storage age of the RBCs at the time of transfusion is an independent predictor of a worse outcome. Biochemical changes occur when RBCs are stored at 1-6 C. These changes contribute to storage lesions and to reduction in viability and levels of 2,3diphosphoglycerate (2,3-DPG). There is a decrease in pH and an increase in plasma potassium. ATP levels go down and there is a significant increase in plasma hemoglobin. As a result, RBCs undergo corpuscular changes, evolving into spherocytes which have increased osmotic fragility and loss of deformability. The concentration of 2,3DPG in the red cells affects the release of oxygen to the tissues. In stored RBCs, 2,3DPG levels fall at linear rate to zero after 2 weeks of storage and oxygen release is much less than in fresh RBCs.

The aim of this study was to determine whether a relationship between age of transfused RBCs and clinical outcome could be established in the light of data collected from the two hospitals.

STUDY DESIGN AND METHOD

Blood Bank records for patients who underwent cardiac surgery at 2 hospitals were reviewed for a six-month period from July-December 2008. Hospital #1 is a large community hospital with 719 licensed beds. Hospital #2, on the other hand, is a much smaller private hospital with 247 beds. For each patient, data were recorded on each patient's age, gender, ABO group, preoperative hemoglobin, number of RBC, fresh frozen plasma (FFP), and platelet units transfused, storage age of transfused RBC units and postoperative length of stay (POLOS). Student t-test, Chi-Square test, Kolmogorov-Smirnoff test, and multilinear regression analyses were performed as indicated. A p value of < 0.05 was deemed significant

Results

During the study period of 6 months, a total of 328 cardiac surgical procedures were identified; 180 at Hospital #1 and 148 at Hospital #2. The study population included only adult patients with an average age of 68 years (Table 1).

A total of 976 units of RBCs were transfused. The mean number of RBC units transfused was 3.3 units per patient with a median of 2 units, and the mean storage age of the transfused RBC units was 17.7 days with a median of 17 days (Figures 1 and 2). For POLOS, the mean was 8.4 days with a median of 6 days.

Storage age of red cells transfused is presented as a dot-plot in Figure 1 and a cumulative distribution in Figure 2. As can be seen, approximately 35% of the transfused cells are $\geq$ 20 days old at the time of transfusion.

Multilinear regression analysis with number of units of RBCS transfused as the outcome variable showed independent effects of gender (p=0.002), patient age (p=0.016) and preoperative hemoglobin (p=0.003). POLOS correlated with units of RBCS transfused (r=0.49, p<0.01).

In a multilinear regression analysis with POLOS as the outcome variable and number of units of RBC transfused, age of the first, second, third, fourth, or fifth units as predictor variables, only units of RBC transfused remained a strong predictor variable (p<0.01) (Figure 3). Storage age of the red cells showed nonsignificant weak correlation but in the opposite direction to that anticipated (i.e.: there was a weak trend for older RBCs to be correlated with shorter POLOS).

The dataset were subsequently divided into coronary artery bypass graft (CABG) procedures (n=232) and non-CABG procedures(n=94) (Table 2). No significant differences were evident between the subgroup populations.

Separation of the data into Group O (n=179) and non-Group O (n=150) patients showed a similar number of RBCs transfused (3.4 vs.3.2 units respectively, p=0.75), but a shorter mean red cell storage age for the Group O patients (13 vs. 21days respectively, p<0.01) (Table 3). Despite the fresher red cells transfused to the Group O patients, the POLOS showed a trend to be longer in the Group O patients (8.9 vs. 8.0 days, p=0.18).

Because of the observed gender effect, the data were divided by male and female (Table 4). Females clearly received more RBCs and (to a lesser extent) FFP than males. This is presumably partly related to the lower preoperative hemoglobin levels and lower body weights in females, both of which increase the likelihood of transfusion due to cardiac bypass pump hemodilution.

Transfusion data at the 2 hospitals were compared (Table 5 and Figure 4). On average, Hospital #2 transfused 1 unit less of RBCs per patient (2.7 vs. 3.8), but this appeared to be related to the 1 g/dL lower mean preoperative hemoglobin level at Hospital #1 (Table 5 and Figure 5). The average age of the transfused RBC units at both hospitals did not differ (Figure 6). Each hospital discharged a large proportion of patients with hemoglobin levels > 10 g/dL (Figure 7). In both hospitals, the number of units transfused correlates with POLOS (Hospital #1; r = 0.58, p<0.01 and Hospital #2: r = 0.35, p<0.01). There was a difference between the hospitals with regard to platelet and fresh frozen plasma (FFP) transfusions. At Hospital #1, 35% of the patients receive platelets compared to only 20% at Hospital #2 (Figure 8). This was reflected in the discharge platelet counts, which were higher at Hospital #1 than Hospital #2 (Figure 9). The reverse was the case for FFP where a higher proportion was transfused at Hospital #2 (Figure10).

CONCLUSION

A substantial number (60-70%) of cardiac surgery patients were transfused with RBCs. The mean number of transfused RBC units was correlated to lower preoperative hemoglobin levels, increased patient age, and the female gender. POLOS also correlated with the number of RBCs transfused which could either represent a transfusion effect or that RBC transfusions are a surrogate marker of cardiac disease severity.

The mean and median storage age of the transfused RBCs were ABO related; Group O patients received fresher units. Although POLOS was closely correlated with the number of RBCs transfused, the storage age of the RBC units did not negatively affect the POLOS. Paradoxically, a weak inverse relationship was demonstrated, but this may be related to an undefined ABO effect.

There was a difference in transfusion practices between the institutions. At Hospital #1, the preoperative hemoglobin was lower and associated with more RBC transfusions. At Hospital #2, the preoperative hemoglobin was higher and the RBC transfusions were less. Both hospitals discharged many patients with higher than expected hemoglobin levels, which indicated an educational opportunity to decrease RBC transfusions. The storage age of transfused RBCs were the same or very similar at both hospitals. Hospital #1 had a “platelet bias” and Hospital #2 appeared to have a “plasma bias” which indicated an inter-institutional variation or bias in the management of post cardiac bypass pump bleeding. A standard protocol between institutions could favorably influence these practices.

Lastly, RBC transfusions were an important predictor of POLOS, and therefore, a conservative approach to avoid RBC transfusions, within reason, merits consideration. Group O patients received “fresher” RBCs, but there was no evidence that this favorably affected the clinical outcome, at least as judged by POLOS, but 3 month mortality and 1 year mortality data were not presented. This study gave no support to a policy of selectively transfusing “fresher” red cells to cardiac surgery patients.

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Table 1 . Summary of 328 Cardiac Surgery Procedures

	Mean ± 1 SD	**Median**
Age (years)	68 ± 12	68.5
Preoperative (g/dL)	11.4 ± 2	11.4
Discharge Hb (g/dL)	9.6 ± 1	9.4
RBC Tf (units)	3.3 ± 4.3	2
Platelets Tf (units)	2.2 ± 5.6	0
Plasma Tf (units)	0.7 ± 2.2	0
Age of RBC (days)	17.7 ± 8.2	17
POLOS (days)	8.4 ± 6.5	6

Percent non-transfused = 28%; POLOS = Post operative length of stay (days); Tf = transfused.

Figure #1. Dot Plot of Storage Age of RBC (Days) at the Time of Transfusion

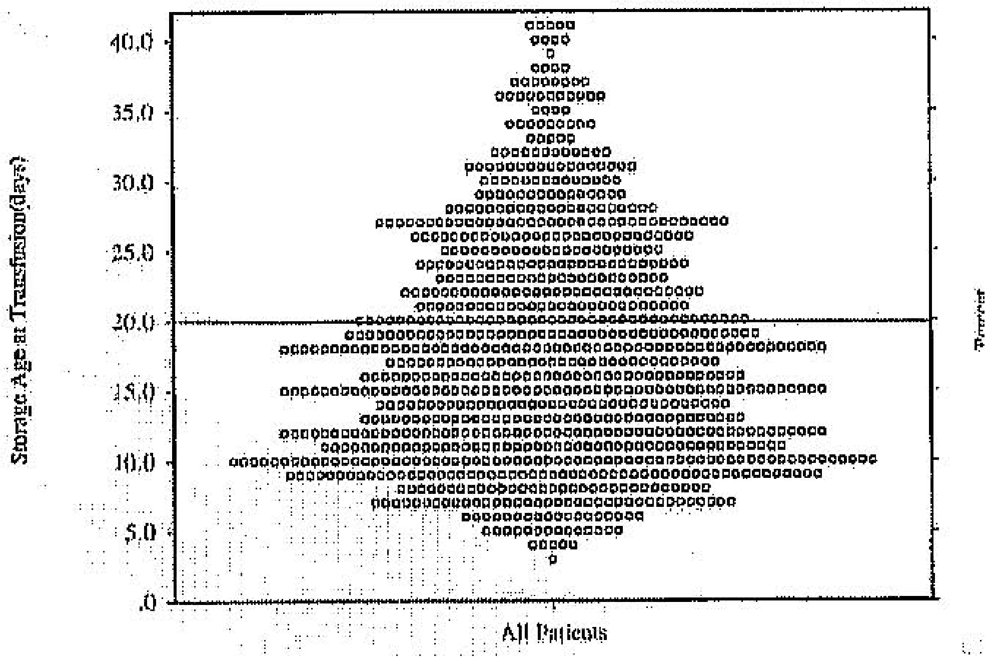


Figure #2. Cumulative Distribution Curve of Storage Age (Days) at Time of Transfusion

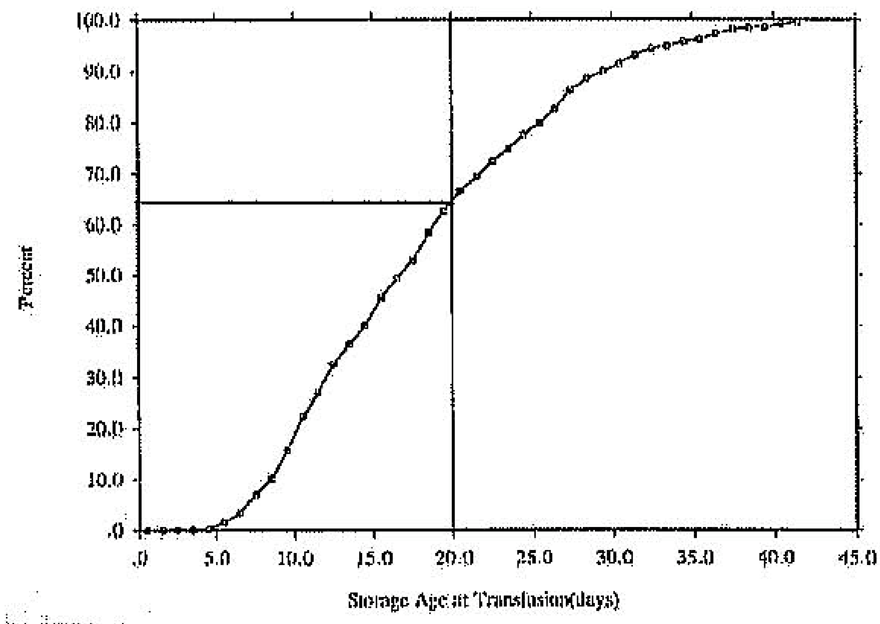
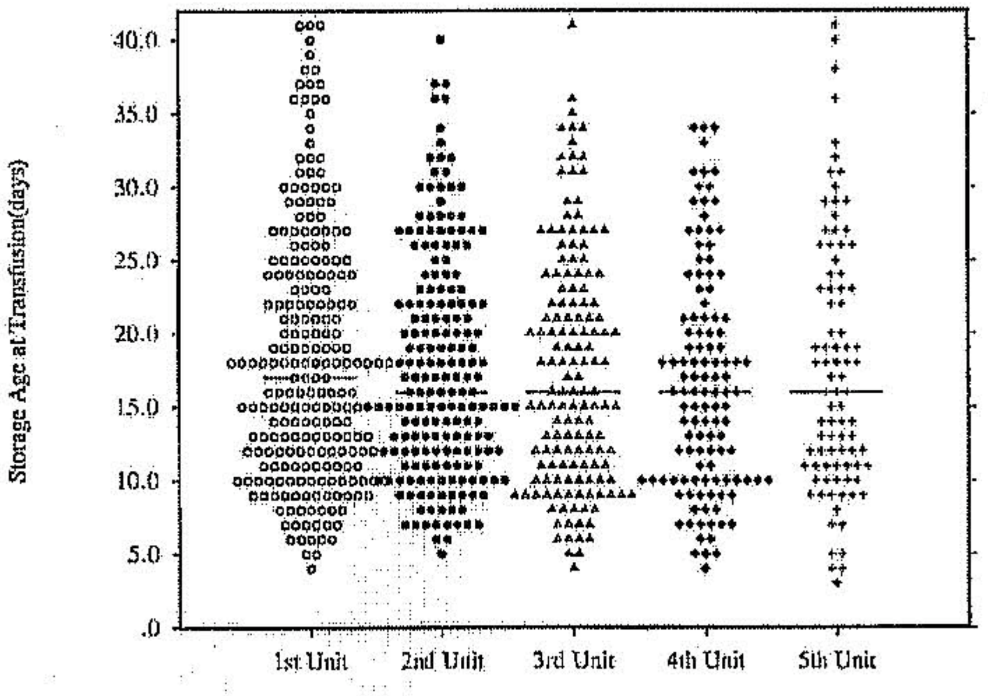


Figure 3. Storage Age at Transfusion vs. RBC Unit Order



Note: There was no difference in the median age of the first, second, third, fourth, or fifth RBC units transfused.

Table 2. Coronary Artery Bypass Graft (CABG) and Non-CABG Procedures

	CABG n = 232	non-CABG n = 94	p
Age (years)	68 ± 10	66 ± 13	0.29
Pre-op Hb (g/dL)	11.6 ± 2	11.1 ± 2	0.08
Discharge Hb (g/dL)	9.6 ± 1.1	9.5 ± 1.1	0.41
RBC Tf (units)	3.1 ± 3.5	3.4 ± 5.7	0.58
Plt Tf (units)	1.7 ± 3.3	2.5 ± 8.9	0.40
FFP Tf (units)	0.6 ± 1.5	0.9 ± 3.2	0.39
POLOS (days)	8.0 ± 5.5	8.6 ± 7.6	0.43

Table 3. Group O versus Non-Group O Patients

	Non-O n = 179	O n = 150	p
Age (years)	68 ± 12	67 ± 12	0.57
Pre-op Hb (g/dL)	11.2 ± 2	11.6 ± 2	0.07
Discharge Hb (g/dL)	9.6 ± 1.1	9.6 ± 1.0	0.74
RBC Tf (units)	3.2 ± 3.7	3.4 ± 5.0	0.75
Plt Tf (units)	2.0 ± 4.0	2.5 ± 7.2	0.41
FFP Tf (units)	0.7 ± 1.6	0.8 ± 2.7	0.53
POLOS (days)	**8.0 ± 5.4**	**8.9 ± 7.5**	**0.18**
Age 1st unit	**22 ± 8**	**14 ± 7**	**< 0.01**
Age 2nd unit	**21 ± 7**	**13 ± 6**	**< 0.01**
Age 3rd unit	**21 ± 7**	**13 ± 7**	**< 0.01**
Age 4th unit	**20 ± 7**	**13 ± 6**	**< 0.01**
Age 5th unit	**23 ± 8**	**13 ± 7**	**< 0.01**

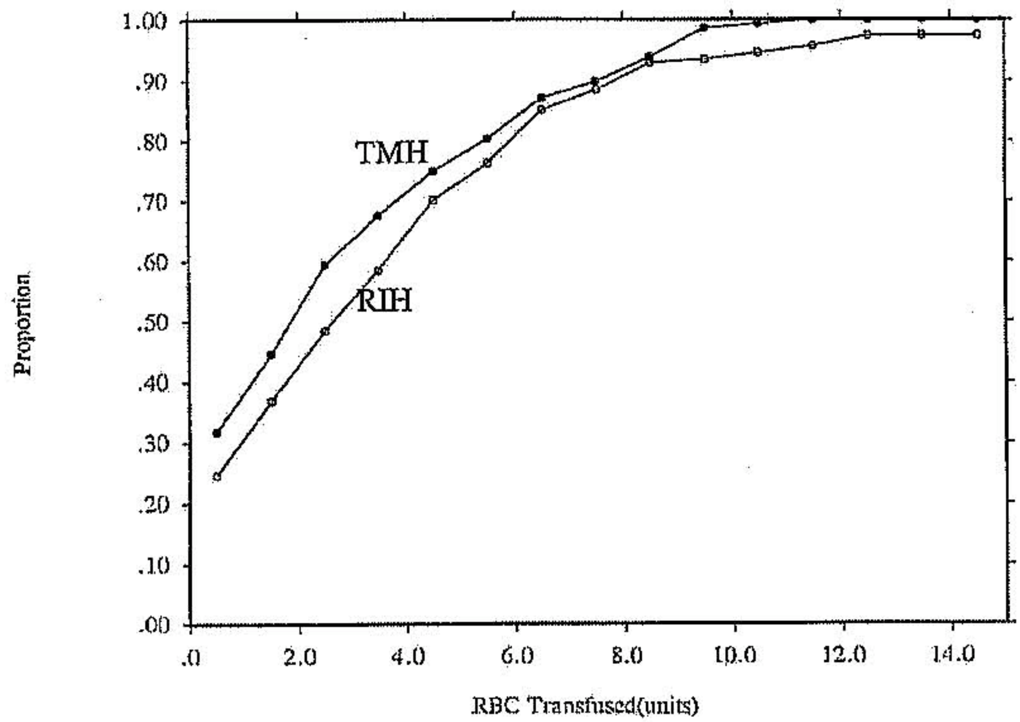
Table 4. Male versus Female Patients

	Males n = 241	Females n = 87	p
Age (years)	66 ± 11	72 ± 12	< 0.01
Weight (lbs)	**190 ± 36**	**160 ± 40**	**< 0.01**
Pre-op Hb (g/dL)	**11.5 ± 2.1**	**10.9 ± 1.8**	**0.006**
Discharge Hb (g/dL)	9.6 ± 1.1	9.7 ± 1.0	0.2
RBC Tf (units)	**2.7 ± 3.8**	**4.9 ± 5.3**	**< 0.01**
Plt Tf (units)	2.1 ± 6.1	2.4 ± 4.2	0.58
FFP Tf (units)	**0.6 ± 2.2**	**1.1 ± 2.3**	**0.02**
POLOS (days)	7.9 ± 5.5	9.8 ± 8.4	0.02

Table 5. Comparisons Between Hospitals #1 and #2

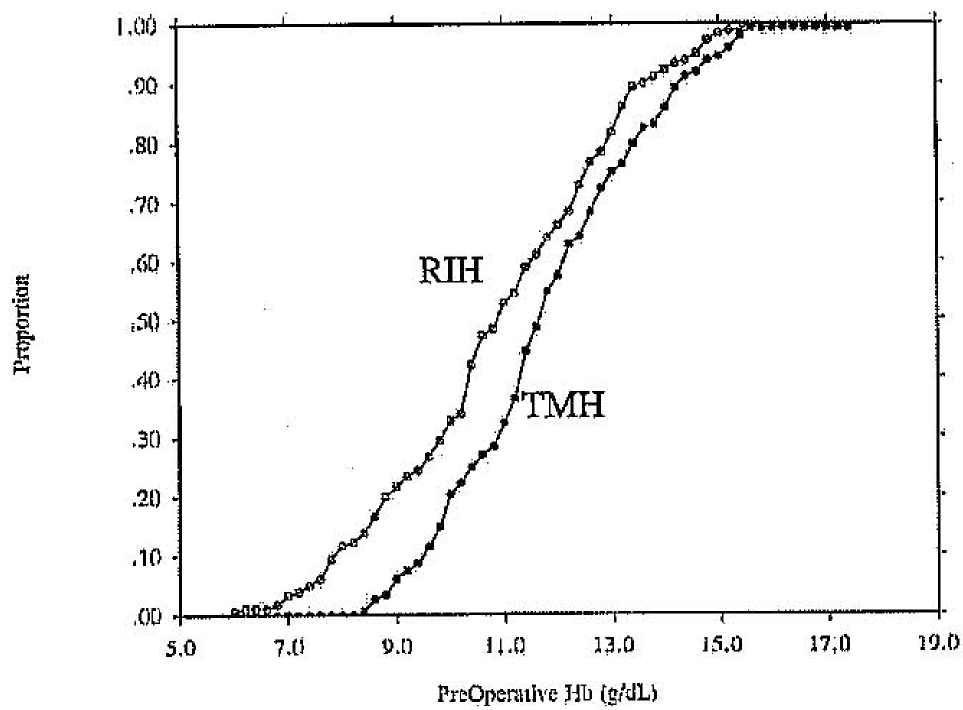
	Hospital #2	Hospital #1	p
Age (years)	68 ± 11	68 ± 12	0.86
Pre-op Hb (g/dL)	**11.8 ± 1.8**	**10.9 ± 2.1**	**< 0.01**
Discharge Hb (g/dL)	**9.4 ± 1.1**	**9.8 ± 1.1**	**0.006**
RBC Tf (units)	**2.7 ± 2.9**	**3.8 ± 5.2**	**0.02**
Plt Tf (units)	**1.4 ± 3.0**	**2.9 ± 7.1**	**0.01**
FFP Tf (units)	1.0 ± 1.8	0.5 ± 2.5	0.09
POLOS (days)	8.2 ± 6.2	8.5 ± 6.7	0.68
Age 1st unit	18 ± 8	19 ± 9	0.89
Age 2nd unit	18 ± 7	18 ± 8	0.83
Age 3rd unit	17 ± 7	18 ± 9	0.36
Age 4th unit	16 ± 8	17 ± 8	0.70
Age 5th unit	15 ± 7	19 ± 9	0.03
% untransfused	32%	24%	0.14

Figure 4. Cumulative Distribution Curve of RBC Transfusions at Hospitals #1 (RIH) and #2 (TMH)



Note: The one unit difference is more evident for Hospital #2 (TMH) when 6 or less units were transfused. The difference is significant by the t-test (p=0.02) but not by the Kolmogorov-Smirnoff test (p=0.28).

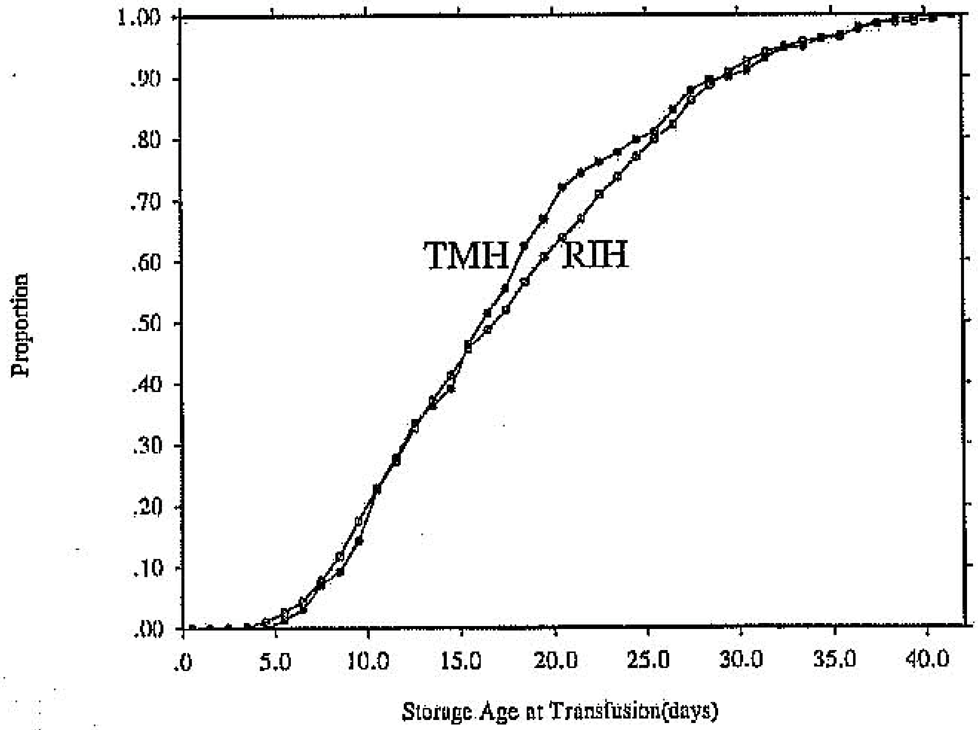
Figure 5. Cumulative Distribution Curve of Preoperative Hemoglobin at Hospitals #1 (RIH) and #2 (TMH)



Note: The 1 g/dL difference (lower) is clearly evident for Hospital #1 (RIH).

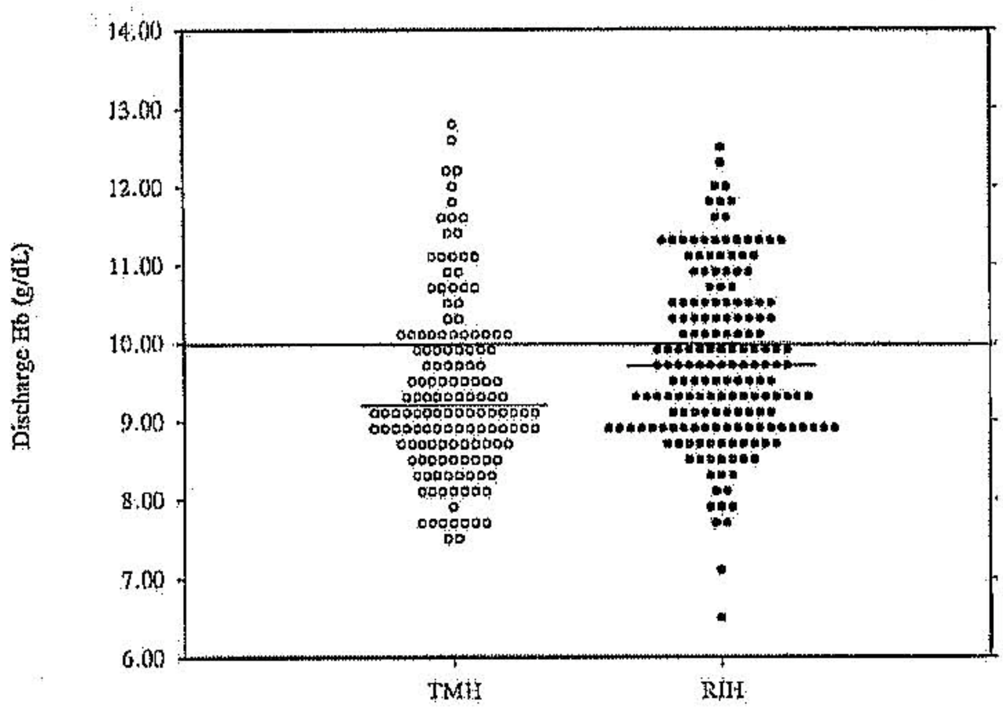
Kolmogorov-Smirnoff test, $p<0.01$.

Figure #6. Cumulative Distribution Curve of RBC Storage Age at Transfusion at Hospital #1 (RIH) and #2 (TMH)



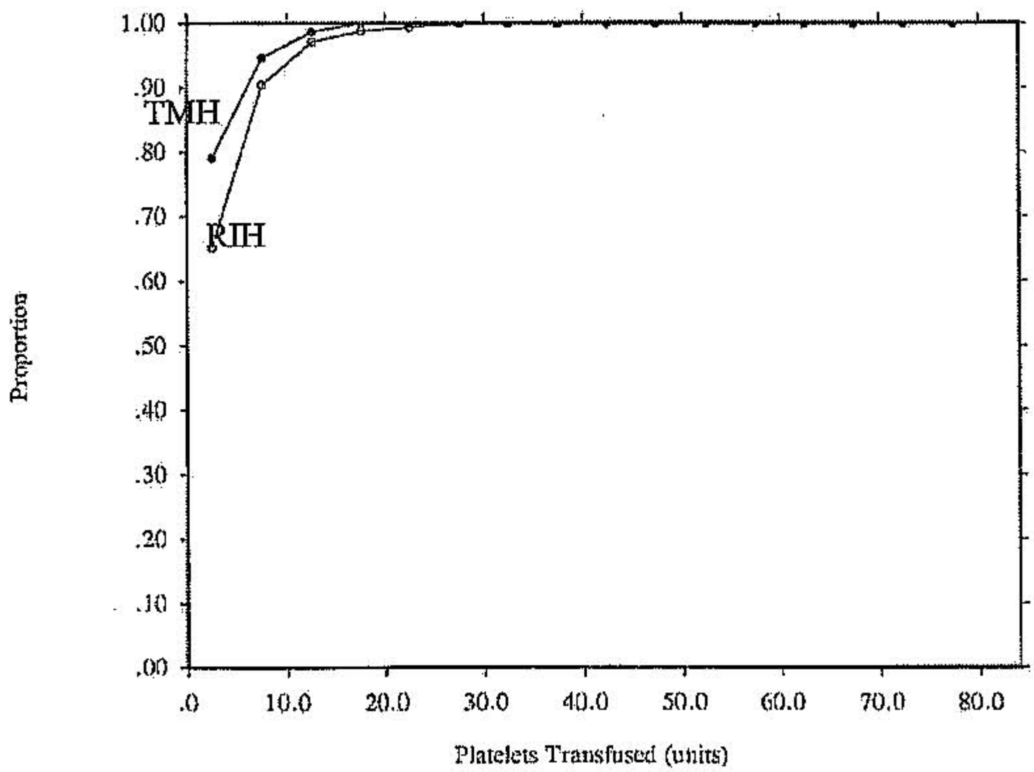
Note: The curves appear virtually identical but there may be a subtle difference. Kolmogorov-Smirnoff test, p=0.09.

Figure #7. Dot Plot of Discharge Hemoglobin Levels (G/dL) at Hospital #1 (RIH) and #2 (TMH)



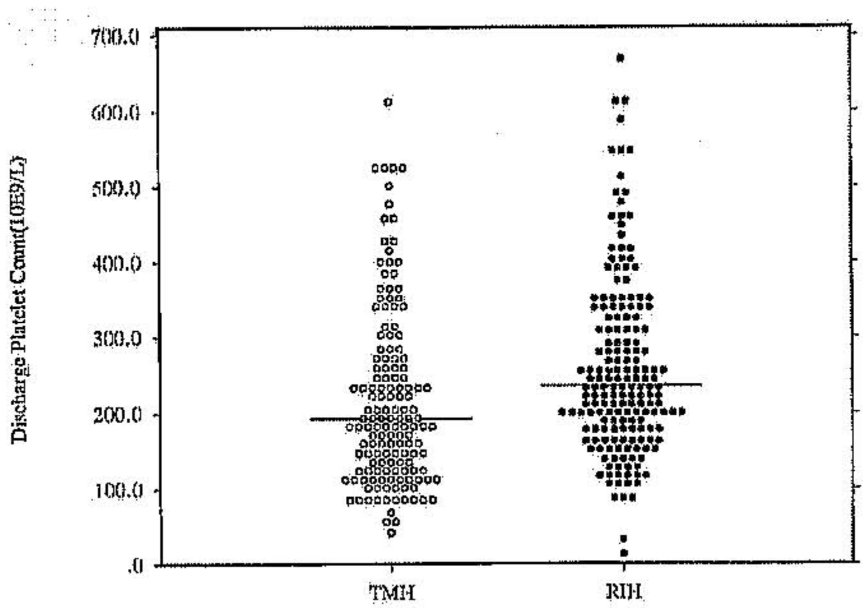
Note: A significant proportion of patients are discharged with hemoglobin >10g/dL. The discharge hemoglobin is slightly higher at Hospital #1 (RIH) - see Table #5 (p<0.01).

Figure 8. Cumulative Distribution Curve of Platelet Transfusions at Hospital #1 (RIH) and #2 (TMH)



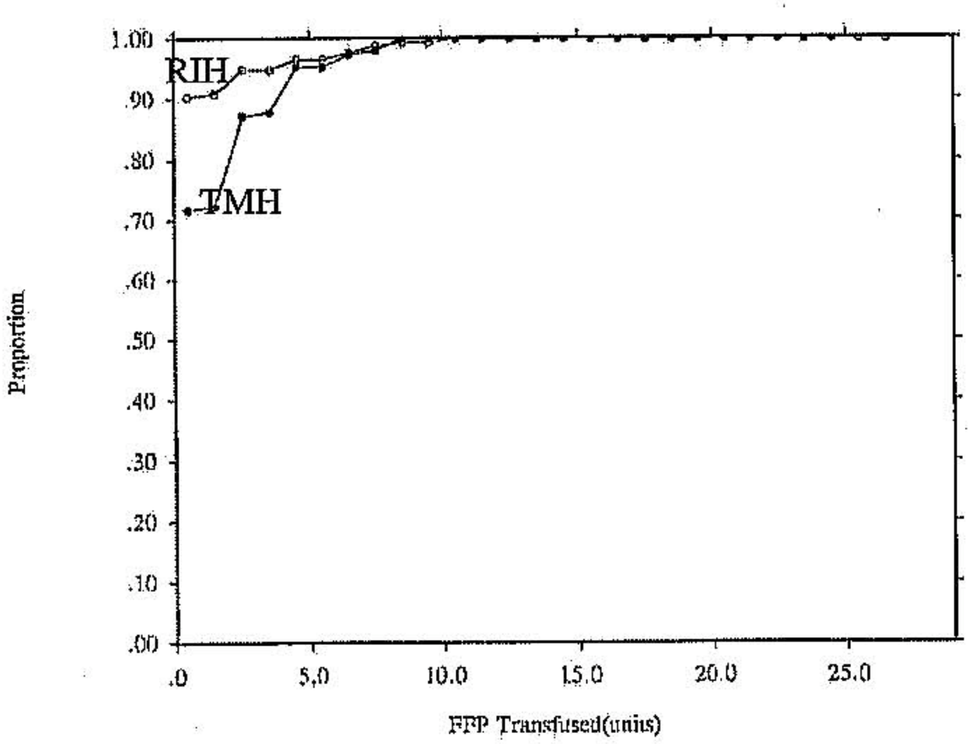
Note: Most patients did not receive platelets, but the fraction of non-transfused patients is lower at Hospital #2 (TMH) (20% vs. 35%; Chi-Square = 7.96, $p<0.01$).

Figure 9. Dot Plot of Platelet Counts at Discharge from Hospital #1 (RIH) and #2 (TMH)



Note: Notice higher platelet counts at Hospital #1 (RIH) and the tail of high discharge platelet counts at both hospitals ($p<0.01$ between hospitals).

Figure 10. Cumulative Distribution Curve of Plasma Transfusion at Hospital #1 (RIH) and #2 (TMH)



Note: Most patients did not receive plasma transfusion, but (unlike platelets) the fraction of non-transfused patients is lower at Hospital #1 (RIH) (10% vs. 30%, Chi-Square=20.5, p<0.01).