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Associations between ABO Non-identical Platelet Transfusions and Patient Outcomes-A Multicenter Retrospective Analysis

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Abstract

BACKGROUND: Due to platelet availability limitations, platelet units ABO mismatched to recipients are often transfused. However, since platelets express ABO antigens and are collected in

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plasma which may contain ABO isohemagglutinins, it remains controversial as to whether ABO non-identical platelet transfusions could potentially pose harm and/or have reduced efficacy.

STUDY DESIGN AND METHODS: The large four-year publicly available Recipient Epidemiology and Donor Evaluation Study -III (REDS-III) database was used to investigate patient outcomes associated with ABO non-identical platelet transfusions. Outcomes included mortality, sepsis, and subsequent platelet transfusion requirements.

RESULTS: Following adjustment for possible confounding factors, no statistically significant association between ABO non-identical platelet transfusion and increased risk of mortality was observed in the overall cohort of 21,176 recipients. However, when analyzed by diagnostic category and recipient ABO group, associations with increased mortality for major mismatched transfusions were noted in two of eight subpopulations. Hematology/Oncology blood group A and B recipients (but not group O) showed a Hazard Ratio (HR) of 1.29 (95% CI: 1.03-1.62) and intracerebral hemorrhage group O recipients (but not groups A and B) showed a HR of 1.75 (95% CI: 1.10-2.80). Major mismatched transfusions were associated with increased odds of receiving additional platelet transfusion each post-transfusion day (through day 5) regardless of the recipient blood group.

DISCUSSION: We suggest that prospective studies are needed to determine if specific patient populations would benefit from receiving ABO identical platelet units. Our findings indicate that ABO-identical platelet products minimize patient exposure to additional platelet doses.

Keywords

Platelet transfusion; ABO

Introduction

Approximately 40% of platelet transfusions in the United States are ABO mismatched to the recipient^{1,2}, a practice that remains controversial and requires a balance between demand and availability constraints due to the short shelf life of platelet products. In the US, platelet products are mostly obtained by apheresis, but platelet units are also derived from whole blood^{1,2}. A recent international survey on platelet transfusion policies and practices² indicated mixed policies among respondents for the priority of major vs minor compatibility for platelet transfusion if identical products were not available.

Several retrospective studies have examined the impact of ABO non-identical platelet transfusions on various clinical outcomes in select populations. Trends toward increased mortality were associated with ABO non-identical platelet transfusions in cardiac surgery patients³ and acute promyelocytic leukemia (APL) patients⁴ and ABO incompatible (major mismatched) platelet transfusions in intracerebral hemorrhage (ICH) patients⁵. ABO major mismatched platelets are associated with decreased patient peripheral blood platelet count increment⁶⁻¹⁰. Additionally, though reactions are rare, minor mismatched platelet transfusions are the most common cause of acute hemolytic reactions¹¹ and have been associated with fatal outcomes¹¹⁻¹⁴.

The Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) public use donor-recipient linked database contains information about blood donors, components, and recipients of transfused blood products at 12 hospitals served by four blood centers in the United States¹⁵. In the current report, we utilized this database to identify associations between ABO non-identical platelet transfusions and the clinical outcomes of mortality, sepsis, thrombosis, and subsequent platelet transfusion requirements.

Materials and Methods

Patient Population

This analysis utilized the NHLBI RED-III public use database available through BioLINCC¹⁶ to include inpatients at least 16 years old at hospitals participating in REDS-III from January 2013 through December 2016 who received a platelet transfusion during their hospital stay.

Blood group O recipients who, by definition, could not receive minor mismatched platelet transfusions were analyzed separately from blood group A and B recipients, who were combined for these analyses (Figure 1). There were low numbers of blood group AB recipients rendering analysis of their transfusions non-informative. Hence, they were excluded as were patients who had previously received an allogeneic stem cell transplant or who had received an ABO non-identical plasma transfusion (Figure 1). Patients with multiple hospitalizations that each required platelet transfusion contributed multiple encounters to the analysis.

Platelet transfusion events were defined (Supplemental Table 1) as ABO identical (platelet donor and recipient were the same ABO type), major mismatched (donor platelets carry A/B antigen that is not compatible with recipient ABO type, i.e. platelets from a type A donor transfused into a type O recipient), minor mismatched (donor platelets contained in plasma that is not compatible with recipient ABO type, i.e. platelets from a type O donor into a type A recipient), or bidirectional mismatched (donor platelets and plasma are not compatible with the recipient, i.e. platelets from a type A donor into a type B recipient or transfusion of multiple platelet products that included at least one major and one minor mismatched unit).

Encounters

Evaluable encounters started when an inpatient received a platelet transfusion and ended when the patient was discharged, received a platelet transfusion of an unknown ABO type, or 25 days after the first platelet transfusion within an encounter, whichever came first. Person-time within an encounter was categorized according to exposure to identical only, major, minor, or bidirectional mismatched platelets (Supplemental Table 1). For inpatients receiving multiple platelet transfusions within an encounter, ABO compatibility status upon receipt of a subsequent platelet transfusion was updated in a time-varying manner in an escalating classification from identical to major or minor to bidirectional (Figure 2, Supplemental Table 2). Because encounters may have included multiple platelet transfusions of differing ABO compatibility status, the sum of encounters by ABO identical/non-identical category exceeds the total number of encounters in Figure 1.

Outcomes

The primary outcome was inpatient mortality during the same encounter as the platelet transfusion event. Secondary outcomes were sepsis, thrombotic complication events, and subsequent platelet units transfused.

Sepsis was identified by a blood culture positive for bacteria or fungus excluding usual bacterial contaminants. The start of sepsis was defined as the time of obtaining the first blood culture specimen that tested positive for bacteria or fungus. All platelet transfusions completed within the encounter prior to the diagnosis of sepsis were included in the analysis.

Thrombosis events were identified, and their onset determined as previously reported¹⁷. Briefly, this approach identified in-hospital thrombotic events as patients who were admitted without evidence of thrombosis and who had a discharge diagnosis of thrombosis with the administration of therapeutic doses of an anticoagulant or anti-platelet agent. The timing of the thrombotic event was identified as the time of administration of therapeutic anticoagulation or anti-platelet therapy.

Platelet Transfusions

At each platelet transfusion, the time, in hours, until the next platelet transfusion and the transfusion category were determined. All transfusions occurring within 4 hours of one another were considered a single transfusion episode. This time window was chosen because all transfusions within four hours are typically based on the desired result while transfusions after four hours often occur in response to the laboratory results from post-transfusion monitoring such as corrected count increment (CCI)^{8,18} followed by a request for subsequent platelet transfusion.

Statistical Analysis—Except where noted, analyses were based on evaluable encounters with each evaluable encounter being independently analyzed. All variables included in the multivariable models were selected a priori for their expected association with the outcomes. Summary statistics were reported as frequencies (N and percentage), means with standard deviations, or medians with interquartile ranges (IQR) and maximums, as appropriate. The level of significance was alpha equal to 0.05. All analyses were performed in R version 4.1.2 (R Core Team, 2021) or SAS software, version 9.4 (SAS Institute Inc., Cary, NC).

To examine mortality and sepsis risk in relation to time-dependent exposure to ABO non-identical platelet transfusions, compared with exposure only to ABO identical transfusions, Cox proportional hazards regression models^{19,20} were used to estimate hazard ratios and 95% confidence intervals with robust standard errors to account for multiple encounters per patient. The Cox models used time since the first transfusion as the time scale and were stratified by the hospital and, for the combined A and B group, on recipient blood type. Analyses were also adjusted for recipient age (natural cubic spline), sex, weighted Elixhauser comorbidity index using the AHRQ algorithm²¹, time-dependent cumulative sum of platelet transfusions (natural cubic spline), and time-dependent cumulative sum of ABO identical plasma transfusions (continuous).

Additional sub-analyses were performed within disease subsets defined by ICD9/10 codes associated with the encounter. These diagnostic categories were selected based on the frequency with which patients received platelet transfusions and/or prior studies suggesting a possible impact of platelet transfusions on patient outcomes. The four diagnostic categories included were Hematology/Oncology (Hem/Onc)⁴, Trauma^{22,23}, Cardiac Surgery²⁴⁻²⁶, and Intracerebral Hemorrhage (ICH)^{5,27}. For the dose-dependent analysis, bidirectional mismatches were tabulated as both major and minor mismatches.

A potential confounding variable for the analyses included the transfusion of other blood products. Encounters with ABO non-identical plasma transfusions were excluded to reduce the possibility of unanticipated confounding bias. In contrast, encounters with any RBC transfusion and/or ABO identical plasma transfusions were included under the assumption that these transfusions have a minimal physiologic influence on the patient outcomes and that any small effects could be adjusted for. We performed a sensitivity analysis that excluded encounters with any concomitant plasma transfusion (Supplemental Table 3, Supplemental Figure 1).

Subsequent platelet transfusions during the same encounter were assessed using a multivariable logistic regression model to examine the association between major, minor, and bidirectional mismatched ABO platelet transfusions and the odds of receiving a subsequent platelet transfusion within a given number of days (1–7). Results are presented as odds ratios and 95% confidence intervals.

Results

Study Population

The included patient demographics and encounter characteristics are shown in Tables 1 and 2. There were 26,902 encounters among 21,176 patients who received 79,473 platelet transfusions. These platelet units were collected by apheresis (59%) or were whole blood-derived (41%); 93% were leukoreduced, 69% irradiated and less than 1% stored in platelet additive solution (PAS) or pathogen reduced. The average age of platelet transfusion recipients was 63 years and 60% were male. The median encounter duration was 6 days. At least one non-identical platelet product was transfused in 58% of the encounters. Identical plasma was transfused in approximately 20% of the encounters whereas red blood cells were transfused in over 60% of the encounters. The majority (85%) of the encounters were in the Hem/Onc diagnostic category with some encounters included in more than one diagnostic group. The distribution of A, B and O blood type among platelet transfusion recipients was as expected overall and within diagnostic groups. Unlike blood group A recipients, there were more mismatched encounters than identical encounters for blood group O and B recipients (Figure 1).

Platelet Transfusion and Mortality

The all-cause in-hospital mortality was 2,432 deaths (Table 1) across encounters (9.0%). The hazard ratios (HR) for mortality following ABO non-identical platelet transfusion for all the encounters and in each of the diagnostic groups are presented in Figure 3. No statistically

significant association between ABO non-identical platelet transfusion and mortality was observed in the overall cohort of 21,176 recipients. Among blood group O recipients, the multivariable-adjusted HR for any major mismatch was 1.03 (95% CI: 0.89, 1.20). Among combined blood groups A and B recipients, the multivariable-adjusted HR for any major mismatch, any minor mismatch, and any bidirectional mismatch was 1.22 (95% CI: 0.99, 1.50), 1.13 (95% CI: 0.97, 1.31), and 0.97 (95% CI: 0.83, 1.14), respectively.

In the Hem/Onc diagnostic subgroup, which included most of the recipients, mortality risk was significantly higher among blood groups A and B recipients of major mismatch platelet transfusions (HR: 1.29; 95% CI: 1.03, 1.62) and trended higher among A and B recipients receiving minor mismatched platelet transfusions (HR: 1.17, 95% CI: 1.00, 1.38). Of note, the HR for mortality for major mismatch platelet transfusion among blood group O recipients with ICH was significantly elevated at 1.75 (95% CI: 1.10, 2.80). No association of mortality with ABO non-identical platelet transfusions was observed in the other diagnostic categories. A sensitivity analysis, excluding all encounters with plasma transfusions (Supplemental Table 3, Supplemental Figure 1), again showed an association with increased risk of mortality for group A and B Hem/Onc (HR 1.34; 95% CI: 1.02, 1.77) and group O ICH recipients of major mismatched platelet transfusions (HR: 1.85; 95% CI: 1.15, 2.98) but also showed a significant association with increased risk of mortality for group A and B Hem/Onc recipients of minor mismatched platelet transfusions (HR: 1.26; 95% CI: 1.02, 1.55) and group O cardiac surgery recipients of major mismatched platelet transfusions (HR: 1.73; 95% CI: 1.02, 2.94). However, these results were accompanied by larger confidence intervals, likely due to a decrease in evaluable encounters by approximately 20%. In analyses evaluating a dose-response, receipt of more than one ABO non-identical platelet product was not associated with an enhancement of increased overall mortality even in the two subgroups that showed increased HRs (Figure 4).

Sepsis and Thrombosis

The same approach was used to determine whether exposure to ABO non-identical platelet products was associated with an increased risk of sepsis (Figure 5). There were no statistically significant associations of ABO non-identical platelet transfusions with sepsis overall or within the diagnostic categories of Hem/Onc or cardiac surgery. Sepsis associated with ABO non-identical platelet transfusions could not be evaluated within the trauma or ICH groups because of the limited number of events in those groups. Thrombotic events occurred in only a small number of encounters, and the thrombosis risk associated with ABO non-identical platelet transfusions could not be reliably analyzed. Therefore, no conclusions about the altered risk for thrombosis can be made.

Subsequent Platelet Transfusions

Recipients of ABO major incompatible platelet transfusions had increased odds of receipt of a subsequent platelet transfusion. Blood group O and blood groups A and B recipients each had increased risk, with an odds ratio (OR) of at least 1.2 for receiving an additional platelet transfusion within the first 2 days (Figure 6, Supplemental Table 4). A similar trend was noted for blood groups A and B recipients within 24 hours following bidirectional platelet

transfusions (OR 1.09, 95%CI: 1.00-1.18). No increase for a subsequent platelet transfusion was observed for blood groups A and B following minor platelet transfusions.

Discussion

Understanding the interaction of ABO antigens and anti-A and anti-B immunoglobulins is a foundational goal of transfusion medicine. For RBC transfusion, type O units are transfused as “universal” because the RBCs do not express A or B antigens and the units contain only a small amount of plasma. However, controversy remains regarding acceptable policies for the transfusion of other ABO non-identical blood products. Platelets carry ABO antigens²⁸ and are suspended in plasma (potentially containing soluble ABO isohemagglutinins) leading to inconsistencies as to what is considered “compatible” for non-identical platelet products^{1,2}.

This retrospective multi-center analysis investigated the association of ABO non-identical platelet transfusions with mortality, sepsis, thrombosis, and subsequent platelet transfusion requirements. Of the 26,902 encounters analyzed, 58% involved transfusion of at least one ABO non-identical platelet product with type O and B recipients more likely to have a mismatched than an identical encounter. This may reflect donor recruitment strategies, for example group O donors may be recruited for whole blood donations over platelet apheresis collections.

The overall outcomes of this study indicated that ABO non-identical platelet transfusions were not associated with increased mortality or sepsis in the comprehensive patient cohort. However, when analyzed by recipient diagnostic category and ABO group, associations with increased mortality for major mismatched transfusions were noted in two of eight subpopulations. The Hem/Onc diagnostic cohort, comprising the majority of the encounters, demonstrated a significant association between ABO major mismatched platelet transfusions and increased mortality among blood groups A and B recipients but not group O recipients. In addition, an association with increased risk of mortality was observed with blood group O recipients (but not group A or B recipients) receiving major mismatched platelet transfusions in the ICH diagnostic group.

Our findings support some published small studies but not others. For example, in contrast to studies that showed a trend of increased mortality with ABO non-identical platelet transfusion in cardiac surgery³, we found no such association. The two associations with increased risk of mortality we did find (ICH, Heme/Onc patients) have previously been reported in separate small studies^{4,5} of fewer than 50 mismatched platelet transfusions; however, these previous studies did not stratify their data by the blood group of the recipients.

It is difficult to explain why the associations we found were present in recipients of one blood group but not in recipients of the other blood group (group O versus groups A and B combined). Furthermore, in an additional dose-response analysis, these associations did not show an escalating risk with increasing numbers of mismatched platelet transfusions. One notable fact is that major mismatched transfusions for blood group O recipients are from donors who are group A, B, or AB whereas major mismatched transfusions

involving blood group A or B recipients are from group AB donors. Our study was not designed to investigate this or other characteristics of platelet donors that could have differed between our group O and combined groups A or B recipients and thereby influenced patient outcomes.

Possible mechanisms that could contribute to an explanation for detrimental outcomes following ABO non-identical platelet transfusions involve transfusion of non-compatible ABO antigens on cells/plasma proteins or anti-A/-B antibodies directly promoting clearance of platelets and other cells or leading to the formation of immune complexes (ICs) which may alter platelet²⁹⁻³¹ or endothelial cell³² function. However, we are unaware of any data that suggest such mechanisms differ in group O versus other blood group recipients.

Transfusion of compatible non-identical plasma is associated with increased rates of sepsis²³ and in animal studies, ICs have been shown to increase the risk of sepsis^{33,34}. We hypothesized that ABO non-identical platelet transfusions could increase sepsis risk through ICs formed between circulating ABO substances and corresponding antibodies. However, this study did not observe an association between ABO non-identical platelet transfusions and sepsis. Further, newly diagnosed thrombotic events following platelet transfusions were rare and appropriate analyses of risk for thrombosis following non-identical platelet transfusions could not be performed.

Major mismatched platelet transfusions promote clearance of transfused platelets, lowering the CCI⁷⁻⁹, decreasing the efficacy of the transfusion, and shortening the time for a subsequent platelet transfusion, thus increasing the demand for platelet transfusions. Two previous studies^{7,8} found a 4-5 hour decrease in the platelet transfusion interval for those who received an ABO major mismatched platelet transfusion. Similarly, we found an increased requirement for a subsequent platelet transfusion for recipients of a major mismatched platelet transfusion with 20% increased odds of receiving another platelet transfusion within 2 days.

Apheresis and whole blood-derived platelet units contain large amounts of plasma, and minor mismatched platelet transfusions are common¹. Our analysis found a weak association with mortality and minor mismatched platelet transfusions in the group A and B Hem/Onc cohort but not with any of the remaining evaluated clinical outcomes. Minor mismatched platelet transfusions in our study were defined as type A or B recipients transfused with platelet units from type O donors, who, in general, tend to have higher anti-A/-B antibody titers than either type A or B donors^{35,36} and, while not evaluated in this study, hemolysis has been documented after minor mismatched platelet transfusions¹¹. Non-identical plasma transfusions, which are often transfused emergently to trauma patients, are also controversial and have been the subject of several recent studies. Two retrospective analyses found no statistical difference in mortality risk between compatible (identical plus major mismatched) and minor mismatched plasma transfusions in trauma patients^{37,38}. In contrast, an analysis using the SCANDAT database found an association between major mismatched plasma transfusions and increased mortality risk in recipients receiving 5 or more units compared to recipients of identical only plasma products³⁹. The authors

hypothesized the pathophysiologic cause for the increased mortality risk involves ICs formed between anti-A/B antibodies and soluble A/B substances³¹.

The analysis overall and within the diagnostic categories included the assumption that identical plasma transfusions would not, after adjustment, confound the outcomes. To account for the possibility that ABO identical plasma transfusions could be a confounder, a sensitivity analysis was performed with the exclusion of all encounters with a concomitant plasma transfusion. Results were similar to the primary analysis, however, with larger CIs most likely due to the reduction in the number of evaluable encounters. A sensitivity analysis with the elimination of RBC transfusion was not performed because over 60% of the evaluable encounters would have been excluded. Major mismatched RBC transfusions do not occur and minor mismatched RBC transfusions (13% of all encounters in this study) contain a minimal amount of plasma compared to platelet and plasma products.

A major strength of our study is the large number of platelet transfusions; 21,176 transfused patients who received 79,743 platelet units during 26,902 hospitalizations. Other strengths include the involvement of multiple hospitals and blood centers participating in the REDS-III program and the detailed information on component characteristics, timing of transfusion, and recipient information in the database. In addition, adjustments for several potential confounders, such as Elixhauser co-morbidity score, hospital, the number of transfused platelet units, and demographic factors, were incorporated into the calculations.

Limitations of this study involve transfusion of blood components other than platelets. No special consideration was given for minor ABO mismatched RBC transfusions. However, encounters in which the patient received an ABO non-identical plasma transfusion were excluded from the analysis. These criteria maximized the study population while minimizing confounding factors. Also, almost all platelet units in our study were suspended in plasma; this may limit generalization of our minor mismatched findings to platelet units suspended in PAS. Other potential limitations of this study include the utilization of ICD9/10 codes; while these are universally used, they lack granularity and do not allow full evaluation of disease severity. Also, this is a retrospective analysis of practice rather than a prospective randomized trial so causation cannot be established. While the analyses were adjusted for several potential confounders, the possibility of residual confounders in our subgroup analysis cannot be ruled out despite our attempts to control for factors known to affect recipient mortality.

In summary, this multicenter, retrospective study showed no association of ABO non-identical platelet transfusions with mortality or sepsis overall but showed significant associations between major mismatched platelet transfusions and mortality in group A and B recipients in the Hem/Onc cohort and with group O recipients in the ICH cohort. We also found that major mismatched platelet transfusions were associated with an increase in the likelihood of a subsequent platelet transfusion resulting in increased donor exposure for the recipient and increased demand for platelet products. Therefore, when possible, ABO-identical platelet products should be transfused to maximize efficacy and minimize patient exposure to additional platelet doses. However, there are certain populations (e.g. trauma patients) in which prompt transfusions may be required and platelet availability should take

priority over ABO matching if ABO identical units are not readily available⁴⁰. Additional prospective studies are warranted to determine if Hematology/Oncology, Intracerebral Hemorrhage, and Cardiac Surgery patients, in particular, may benefit from receiving only ABO identical platelet products.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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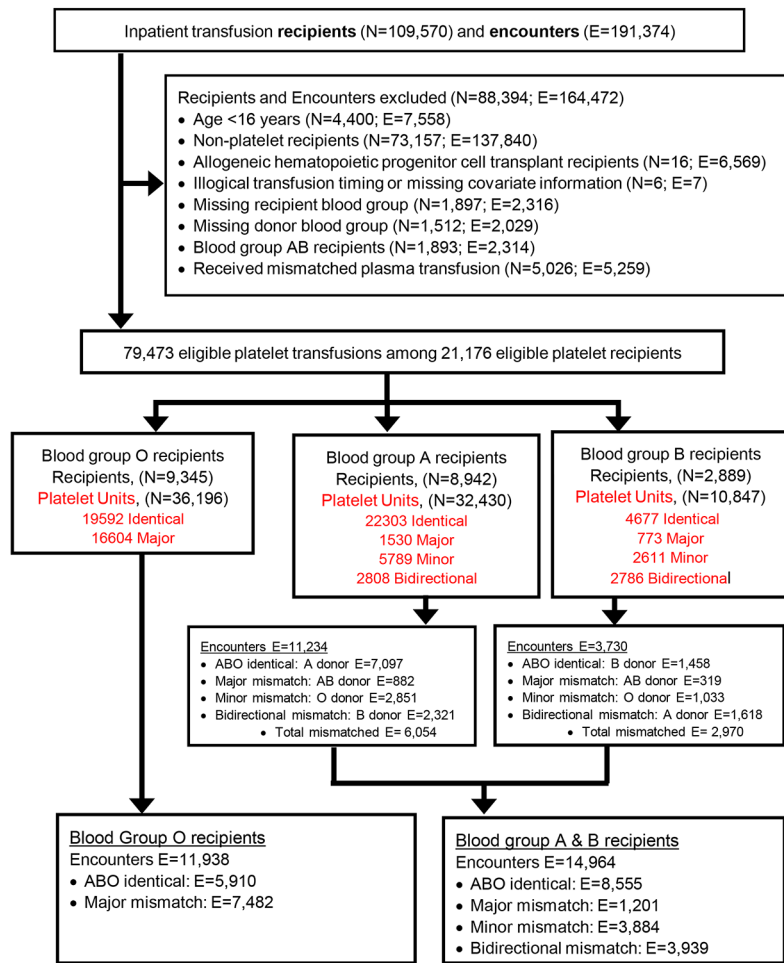


Figure 1:
Study Flow Chart depicting subject and encounter inclusion and exclusion criteria.

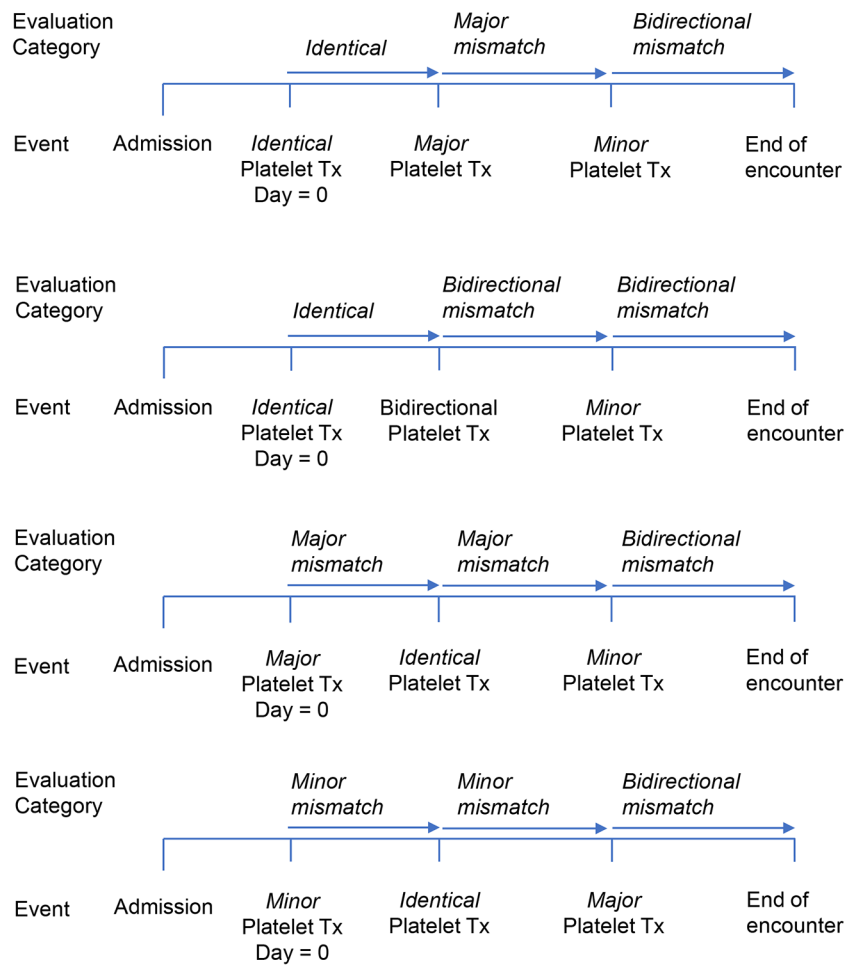


Figure 2:
Example Encounter Schematic Encounters initiate with a platelet transfusion defined as shown in Supplemental Table 1. Upon subsequent platelet transfusion, encounters were reclassified in an escalating manner of identical to major or minor to bidirectional. Examples are not all-inclusive.

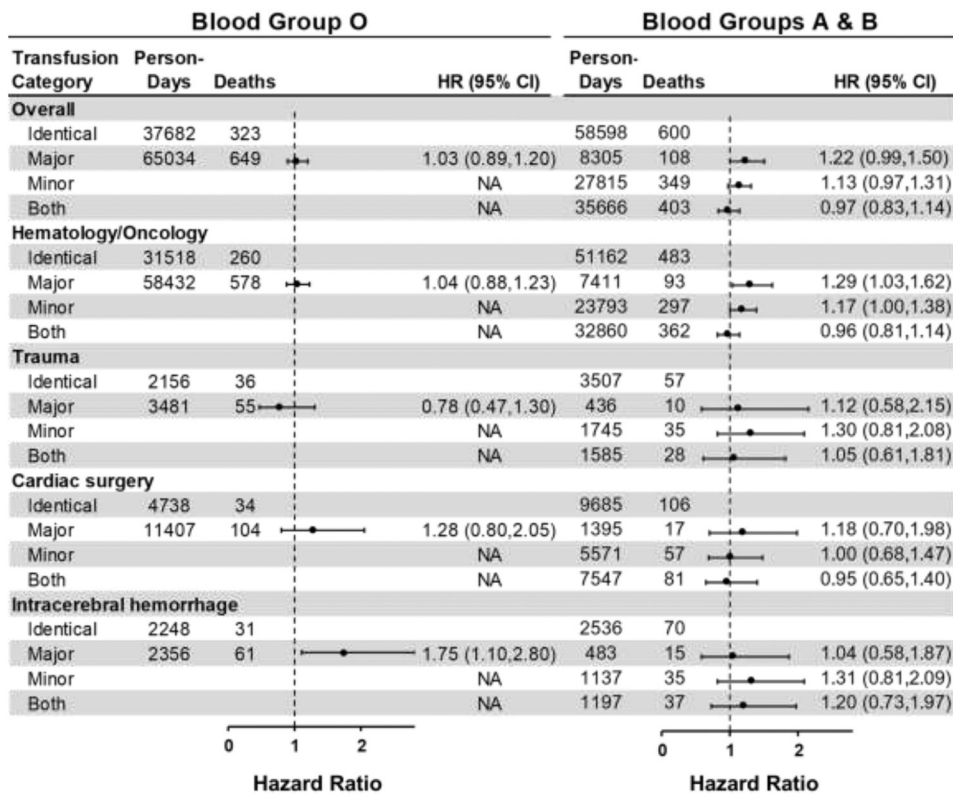


Figure 3:
Risk of mortality associated with exposure to ABO non-identical platelet transfusions
 by recipient blood group and diagnosis category: Forest plots of Hazard ratio (HR) and 95% Confidence Intervals (95% CI) from Cox proportional hazards model relative to identical only platelet transfusions, see Methods. Left panel: blood group O recipients. Right panel: blood groups A and B recipients. Diagnostic categories were assigned based on ICD9/10 codes. An encounter may fall into more than one diagnostic category.

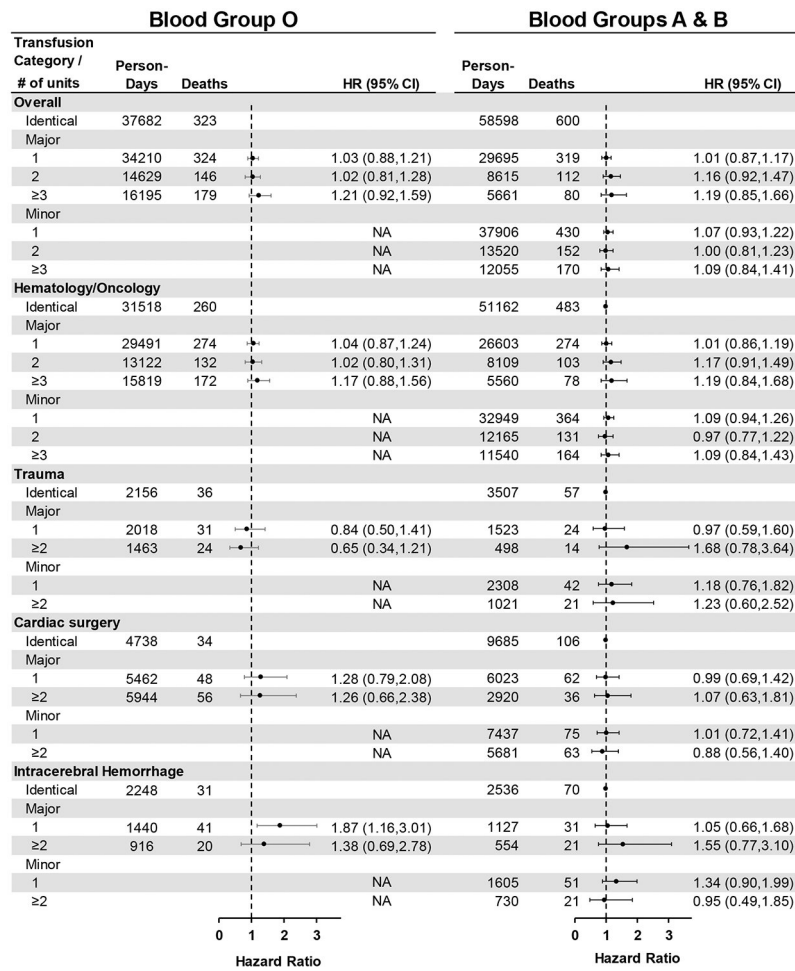


Figure 4:
Risk of mortality associated with exposure to an increasing number of ABO non-identical platelet transfusions by recipient blood group and diagnosis category: Forest plots as described in Figure 3 in a dose-dependent response. For blood groups A and B, bidirectional exposures are included in both the major and minor categories.

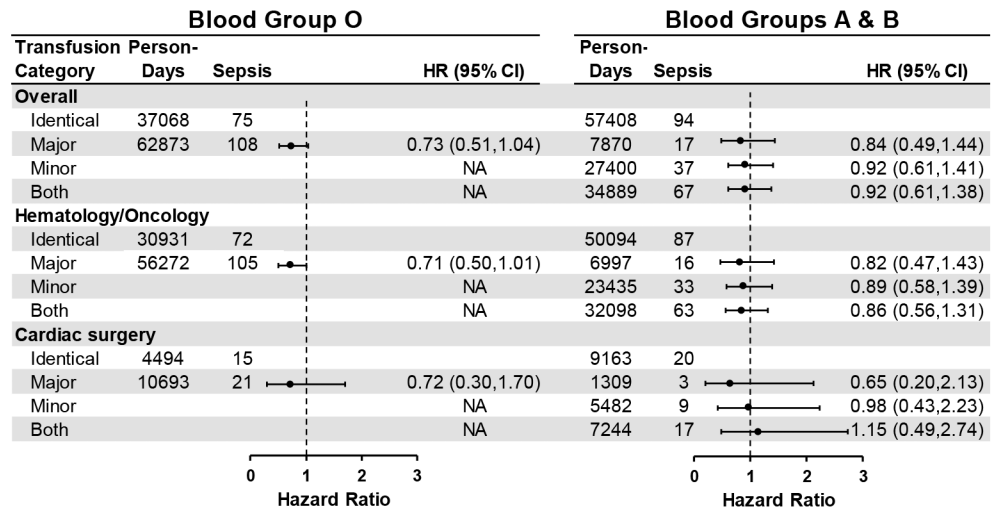


Figure 5:
Risk of sepsis associated with exposure to ABO non-identical platelet transfusions by recipient blood group and diagnosis category: Forest plots as described in Figure 3 except with an endpoint of sepsis. Trauma and Intracerebral Hemorrhage were not analyzed due to an insufficient number of events.

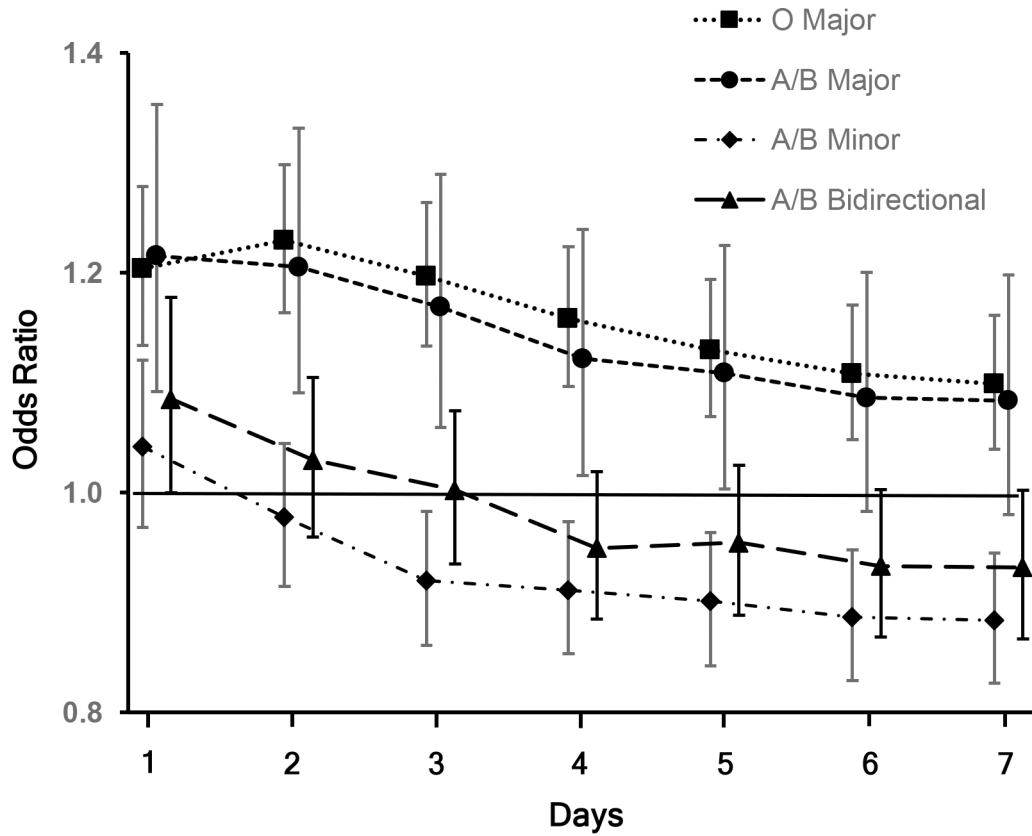


Figure 6: Odds Ratio for receiving a subsequent platelet transfusion following a non-identical platelet transfusion: Odds Ratio and 95% Confidence Intervals from a multivariable logistic model for a subsequent platelet transfusion following a non-identical platelet transfusion relative to identical only platelet transfusions for each 24-hour period after receipt of a platelet transfusion. Blood group O following a major mismatch platelet transfusion is represented by the filled square, dotted line. Blood groups A and B following a major mismatch is the filled circle, dashed line, minor mismatch is the filled diamond, long dashed line and bidirectional is the filled triangle, dot/dashed line. Values are offset for clarity.

Table 1:**Study Recipient Demographics^a**

	Encounter	Subject
Total N	26902	21176
Deaths [†]	2432 (9.0)	2432 (11.5)
Sex [†]		
Female	10956 (40.7)	8483 (40.1)
Male	15946 (59.3)	12693 (59.9)
Age [‡]	61.6 (15.9)	63.1 (15.6)
Blood Type [†]		
Type O	11938 (44.4)	9345 (44.1)
Type A	11234 (41.8)	8942 (42.2)
Type B	3730 (13.9)	2889 (13.6)
Race [†]		
White	20845 (77.5)	16402 (77.5)
Black or African American	2661 (9.9)	2110 (10.0)
Asian	633 (2.4)	491 (2.3)
Other	248 (0.9)	206 (1.0)
Missing	2515 (9.3)	1967 (9.3)
Ethnicity [†]		
Not Hispanic or Latino	23864 (88.7)	18862 (89.1)
Hispanic or Latino	1914 (7.1)	1338 (6.3)
Missing	1124 (4.2)	976 (4.6)
Body mass index (kg/m²) [†]		
Normal/Healthy Weight (18.5-24.9)	7843 (29.2)	5835 (27.6)
Underweight (<18.5)	712 (2.6)	481 (2.3)
Overweight (25.0-29.9)	8674 (32.2)	6847 (32.3)
Obese (≥ 30)	8876 (33.0)	7228 (34.1)
Missing	797 (3.0)	785 (3.7)

^aData are reported as [†] N (%) or [‡] mean (SD).

Table 2:**Study Encounter Characteristics^a**

Encounter days	6.0 (3.0, 12.0)
Platelet transfusions	2 (1, 3)
Non-identical platelet transfusions	1 (0, 1) [44]
Encounters with 1 non-identical platelet unit [†]	15609 (58.0)
Plasma transfusions	0 (0, 0)
Encounters with 1 plasma transfusion [†]	5349 (19.9)
RBC transfusions	1 (0, 4)
Non-identical RBC transfusions	0 (0, 0) [32]
Encounters with 1 RBC transfusion [†]	16350 (60.8)
Encounters with 1 mismatched RBCs [†]	3611 (13.4)
Diagnosis category^{b †}	
Hematology/Oncology	22786 (84.7)
Type O	10075 (44.2)
Type A	9508 (41.7)
Type B	3203 (14.1)
Trauma	1782 (6.6)
Type O	777 (43.6)
Type A	764 (42.9)
Type B	241 (13.5)
Cardiac surgery	3783 (14.1)
Type O	1530 (40.4)
Type A	1782 (47.1)
Type B	471 (12.4)
Intracerebral hemorrhage	1061 (3.9)
Type O	470 (44.3)
Type A	433 (40.8)
Type B	158 (14.9)
Comorbidity index[†]	
<0	2517 (9.4)
0-4	3762 (14.0)
5-14	7530 (28.0)
15-25	6501 (24.2)
26	6592 (24.5)

^aData are reported as [†] N(%) or ^{||} median (IQR) [Max],

^bEncounters may fall into more than one diagnosis category.