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A multi-center study investigating vital sign changes occurring in complicated and uncomplicated transfusions

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Abstract

Background and Objectives—Many hospitals require transfusions to be discontinued when vital signs stray from predetermined ranges, regardless of clinical symptoms. Variations in vital signs may be unrelated to transfusion, however, and needlessly stopping a transfusion may delay medical care while increasing donor exposures and healthcare costs. We hypothesized that a detailed study of vital sign changes associated with transfusion of blood product by component, including those associated with potential reactions (complicated) and those deemed to be

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uncomplicated, would establish a useful framework of reference for treating clinicians and transfusion services alike.

Materials and Methods—A retrospective electronic record review of transfusion service and transfusion recipient data was completed on 3,852 inpatient transfusion episodes over a 6-month period at 4 academic tertiary care hospitals across the US. Vital signs pre- and post-transfusion were recorded by trained clinical research nurses. Serious reactions were adjudicated by a panel of transfusion medicine experts.

Results—In both uncomplicated transfusions (n=3765) and those including an adverse reaction (n=87), vital sign fluctuations were generally modest. Compared to uncomplicated transfusions, transfusions complicated by febrile reactions were associated with higher pre-transfusion temperature and higher pre-transfusion pulse rates. Episodes of transfusion circulatory overload were associated with higher pre-transfusion respiration rates compared to uncomplicated transfusions.

Conclusion—Most transfusions are associated with only modest changes in vital signs. Pre-transfusion vital signs may be an important yet previously understudied predictor of vital sign changes during transfusion. The optimal role of vital sign assessment during blood transfusion deserves further study.

Keywords

Transfusion reactions; Patient blood management; Blood safety

Introduction

In the developed world, blood transfusion is a routine, safe procedure. In the United States, over 10 million blood transfusions were performed in 2013 and over 2.5 million transfusions were performed in the United Kingdom in 2015 [1–2]. It is estimated that adverse events, including febrile non-hemolytic transfusion reactions and allergic reactions, complicate fewer than 1% of blood transfusions [3–4]. Serious adverse events are rare, but can include acute or delayed hemolysis, transfusion related acute lung injury (TRALI), transfusion associated circulatory overload (TACO), transfusion transmitted infection, transfusion associated graft-versus-host disease (TA-GVHD), and post-transfusion purpura (PTP) [5]. The study of serious, adverse transfusion related events is limited by their low incidence, lack of clinical recognition, inconsistent reporting to the blood bank, and variable case definitions.

A great deal of professional effort and public resources are committed to identifying ways to further enhance the safety of blood transfusion [3,5]. Recently, efforts have been directed at precisely defining the pertinent characteristics of common transfusion reactions. For the first time, the 30th edition of the AABB standards for blood banks and transfusion services requires the use of “standardized definitions” to categorize adverse reactions to blood transfusion [6]. Within the field of transfusion medicine, there is hope that specific, standardized definitions for transfusion-related adverse events could promote efforts to better understand and possibly even prevent their occurrence [7–8].

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Standardized definitions of some transfusion reactions (e.g., febrile non-hemolytic transfusion reactions, hypotensive transfusion reactions) are based in large part on changes to recipient peri-transfusion vital signs [5]. In addition, hospitals and transfusion services frequently adopt blood administration policies that encourage (or even require) discontinuing blood transfusions when vital signs stray outside of a pre-defined range [7]. However, multiple studies have shown that the majority of transfusions that meet vital sign criteria for transfusion reactions are never reported to the blood bank [3,7]. In addition, only a handful of studies that evaluate the expected effect of transfusion on vital signs have been published in the medical literature [7–11].

The purpose of the present study was to investigate vital sign changes associated with uncomplicated transfusions in addition to those associated with adverse events. Based on the widespread clinical practice of discontinuing transfusions when pre-determined vital sign thresholds are exceeded as well as standardized definitions of some transfusion reactions being based on vital sign changes, we hypothesized that transfusion episodes associated with documented adverse reactions would result in more vital sign variability compared to uncomplicated transfusions. Furthermore, we speculated that vital sign changes associated with adverse events would be great enough to be interpreted as representing a change in the clinical status of the patient. We also posited that the large dataset of vital signs associated with confirmed uncomplicated transfusions could as a reference set, for helping to define what a potentially deleterious response to transfusion (by component) may be.

Materials and Methods

Study approval

This study was approved by the Institutional Review Boards of all the participating hospitals and RTI, and was monitored by an NHLBI observational study monitoring board.

Study design

This retrospective chart review, recently described in greater detail [3], was funded by the National Heart, Lung and Blood Institute of the National Institutes of Health as part of the Recipient Epidemiology and Donor Evaluation Study–III (REDS-III). At each of 4 academic tertiary care hospitals in the US, active surveillance on adult inpatient transfusion episodes was completed. For the purposes of this study, a transfusion episode was defined as the series of all blood products released to a single patient with less than 6 hours elapsed between product release. De-identified information on all blood components transfused to inpatients over 18 years of age at each hospital during July-December 2014 was submitted to the REDS-III data coordinating center (RTI International; Rockville, MD). After an interval of approximately 3 months post-transfusion, research nurses at each site performed electronic chart reviews and data extraction on 200 randomly selected, confirmed transfusion episodes per month. The 200 episodes per month represented approximately 17% of all transfusion episodes. Prior to study initiation, nurse study coordinators at each of the 4 sites underwent centralized training by subject matter experts, focused on recognizing transfusion reactions.

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The nursing coordinators retrospectively reviewed the electronic medical records, focusing initially on blood components transfused, vital sign trends, chest x-ray (CXR) results, arterial blood gas (ABG) results, other laboratory results, and clinical notes (including nursing, resident/fellow/attending physician, respiratory therapy, and significant event notes) in temporal proximity to the transfusion(s). Data collection forms were developed to ensure accurate and systematic capture of information, and data were validated for accuracy. Screening data, capturing recipient age, gender, ethnicity, diagnosis, blood type, and components transfused, were gathered for all transfusion episodes. These data also included information regarding whether a transfusion reaction was reported to the transfusion service, whether the clinical team described the possibility of a transfusion reaction in their notes, and whether the nurse study coordinator determined that a transfusion reaction might have occurred.

Extended data forms were completed when the nurse coordinators or local study physicians felt that a serious transfusion reaction (pulmonary, hemolytic, septic, hypotensive, or anaphylactic) may have occurred based on the data captured by the screening form. Diagnostic criteria for severe cardiopulmonary reactions included, at a minimum, new onset hypoxemia (as evidenced by PaO2/FiO2 <300 mm Hg, SpO2/FiO2 <300 mm Hg or oxygen saturation <90%) and evidence of new or worsening pulmonary edema on CXR. The extended data form included detailed questions regarding clinical signs and symptoms, laboratory values, CXR, EKG, and echocardiogram results. All extended data forms and clinical synopses were reviewed independently by a panel of 3 transfusion medicine experts in a blinded fashion. The expert panel relied on their clinical expertise plus predefined criteria reported by a number of organizations including the Centers for Disease Control [12] as part of the US Biovigilance System [13] and the International Society of Blood Transfusion/International Society for Blood and Transplant [14].

Statistical Analyses

Transfusions were analyzed by reaction and product type/number of products transfused, with RBCs only, platelets only, plasma only, and “mixed products” (e.g. more than 1 component transfused) studied. Analyses were conducted using SAS/STAT software, Version 9.4, Cary, NC, USA.

Changes in five vital signs (pulse, respiration rate, temperature, and systolic and diastolic blood pressure) were compared for febrile, allergic, and TACO transfusion reactions vs. no reaction (uncomplicated transfusions). Descriptive statistics, frequencies and percentages for categorical variables, means, medians, minimums, maximums, standard deviations, and interquartile ranges for continuous variables were calculated to summarize the data. Unadjusted statistical significance of distribution and change in each vital signs and reaction type were tested using Wilcoxon rank-sum test and t-test, as appropriate.

Changes in each vital sign were computed as the difference between pre-transfusion and at completion measures. These changes in vital signs were normally distributed and were therefore appropriate to examine as outcome variables in general linear regression models. Using change in each vital sign as outcome variables in separate linear regression models, we examined the difference between each reaction group and the uncomplicated transfusion

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group after adjusting for pre-transfusion temperature, systolic BP, diastolic BP, respiration rate, pulse, and the total number of units transfused.

Vitals signs before transfusion and at the completion of transfusion were available for most (87% and 75%, respectively) of the subjects. Because the bulk of the data collected were at these time points, we performed most of our statistical analysis using vital sign values measured at these times. In some cases, data were available for subjects at other points during the transfusion, including 15-minutes into the transfusion (52% with data) and within 6 hours after the completion of transfusion (65% with data). To ensure that important changes in vital signs were not missed by the sampling, change in average vital signs at each time point was compared by transfusion reaction and no reaction groups using adjusted linear mixed modeling procedure for repeated measures. The four repeated measures of vital signs were unequally spaced. A spatial power low [SP (POW)] covariance structure was used to account for unequally spaced repeated measures of correlated data.

Separate repeated measures models were used for each vital sign and reaction group. Each model was adjusted for pre-transfusion temperature, pulse, respiration rate, systolic BP, diastolic BP, number of units transfused, and time of repeated measures. For each model, we examined the interaction between time and reaction type; the interaction was included in the final model if it was statistically significant. If the interaction was significant, we performed pairwise comparisons between time and the reaction group. We used adjusted p-values for multiple comparisons using Tukey-Kramer adjustment.

P-values less than 0.05 were considered statistically significant. All reported p-values are two-sided.

Results

Vital Sign Changes For Uncomplicated Transfusions

Uncomplicated RBC transfusions were associated with a mean change (from pre-transfusion to at completion measures) of 0 degrees in temperature, −1.6 beats per minute of pulse rate, 0 breaths per minute in respiration rate, +4.3 mmHg of systolic blood pressure, and +2.5 mmHg of diastolic blood pressure (Table 1). Transfusions of platelets and plasma were associated with smaller changes in pulse and blood pressure.

Vital Sign Changes for Transfusions Complicated by Reactions

Transfusion reaction incidence data (without vital sign analysis) of the 4857 studied transfusion episodes has recently been described [3]. In brief, 39 transfusion episodes (0.8%) were determined by the expert adjudication panel to be associated with definite or probable TACO, with 4 (0.08%) determined to be definite or probable TRALI. Thirty transfusion episodes (0.62%) were determined by the study nursing coordinators to meet criteria for a febrile reaction, and 14 (0.29%) met criteria for an allergic reaction.

On average, transfusion reactions were associated with only mild changes in vital signs, including essentially no change in temperature ((</=0.2ºC), </= 1 beat per minute of pulse rate, essentially no change in respiration rate (0), and changes of <10 mmHg of systolic

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blood pressure and <5 mmHg of diastolic blood pressure; Table 1 further details vital sign changes by reaction type and by component infused. Figure 1 graphically depicts vital sign changes for uncomplicated transfusions compared to those associated with reactions, organized by component infused.

We also evaluated each transfusion reaction type in aggregate, regardless of component infused (Table 2). Although there were only 2 total TRALI reactions with complete blood pressure data, these reactions had more extreme variations in systolic blood pressure (median change = 13 mmHg) and diastolic blood pressure (median change = 13 mmHg) compared to other transfusion episodes. Three TRALI reactions had temperature, pulse, and respiration data, which revealed only minor changes to temperature (median change = −0.4ºC), pulse rate (median change = −6 bpm), and respiration rate (median change = −3 rpm). TACO reactions were associated with an above average increase in pulse rate (median change = 2 bpm) and systolic blood pressure (median change = 8 mmHg). Febrile reactions were associated with above average increases in systolic blood pressure (median change = 5 mmHg) and temperature (median change = 0.5ºC). Allergic reactions were not associated with clinically significant vital sign changes.

Multivariable Analyses of Vital Sign Changes by Reaction Type

We performed statistical analyses to determine whether vital sign changes (pre-transfusion and at completion) associated with transfusion reaction type were statistically significant as compared to uncomplicated transfusions (Table 3). Febrile reactions were associated with a statistically significant increase in temperature (estimated increase of 0.62ºC, p<.0001 both adjusted and unadjusted) and in pulse rate (estimated increase of 6.68 bpm, p=0.0004 adjusted for pre-transfusion temperature, systolic blood pressure, diastolic blood pressure, respiratory rate, pulse and number of units transfused). Of note, in patients with febrile reactions, pre-transfusion temperature was higher (37.1ºC) compared to patients with uncomplicated transfusions (36.8ºC, p=0.0003), and pre-transfusion pulse was higher (98.5 bpm) compared to uncomplicated transfusions (86 bpm, p=.0002 unadjusted, see Tables 4 and 5). None of the changes in vital signs for TACO or allergic reactions, when assessed individually, were statistically significant. However, pre-transfusion respiratory rate was higher (20 rpm) for patients with TACO compared to patients with uncomplicated transfusions (18 rpm, p=.028 unadjusted). TRALI reactions could not be included in the individual analysis, due to the low sample size.

Repeated Measures Analysis

In order to determine whether changes in vital signs became apparent when evaluating time points other than pre-transfusion and at completion vital signs, a series of repeated measures analyses were performed. The repeated measures analyses confirmed that changes in temperature and pulse were significantly greater in the febrile reaction group compared to the uncomplicated transfusion group. Compared to pre-transfusion, temperature decreased slightly and non-significantly at 15 minutes, reached a maximum at completion and declined again post-transfusion. Otherwise, the repeated measures analysis revealed similar findings to those revealed by linear regression.

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Discussion

In sum, the majority of transfusion episodes in this study were associated with only minor changes in peri-transfusion vital signs, regardless of whether or not they were implicated in a transfusion reaction. These data, which were extracted from the electronic medical record at 4 hospitals over a 6-month period, are unique to the published literature because each transfusion episode – including vital sign changes, radiology, lab results, and clinical notes - was individually evaluated by a trained transfusion medicine nurse study coordinator. Therefore, we are confident that the "uncomplicated transfusions" were truly uneventful and that the transfusion reactions met consensus diagnostic criteria.

Based on our data, it is possible that pre-transfusion vital signs may be more important than previously thought in the prediction of intra-transfusion vital sign trends and transfusion-related adverse events. For example, patients with febrile reactions were noted to have elevated pre-transfusion temperature and pulse rates as well as greater variability in pulse rate as compared to patients who underwent uncomplicated transfusions. These observations raise the possibility that the transfusion was either incidental to the change in vital signs that triggered the reaction to be called, or that a patient with a borderline increased temperature or pulse rate may be more likely to be driven into the febrile range by a transfusion. Further, patients with TACO were observed to have an elevated pre-transfusion respiration rate as compared to patients who underwent uncomplicated transfusions.

The assumption that vital sign changes will be observed in complicated transfusions/ transfusion reactions has led to many institutions maintaining policies that require medical providers to stop transfusions and initiate a laboratory evaluation when certain preconceived thresholds in peri-transfusion vital signs are exceeded [7]. However, the fact that most transfusions – regardless of whether or not they are implicated in an adverse event - are generally associated with only mild changes in vital signs does not establish the optimum role of vital sign measurement in the recognition of adverse events and/or the assessment of transfusion safety. Indeed, the observation that uncomplicated transfusions are not routinely associated with vital sign changes does not establish: (1) that a lack of changes in vital signs indicates a safe transfusion; (2) that changes in vital signs indicate an unsafe transfusion; or (3) that changes in vital signs are actually a consequence of a concomitant transfusion. These considerations may at least partially explain why up to 75% of transfusions that exceed institution-specified peri-transfusion vital sign thresholds may not be reported to the blood bank, as a mild change in vital signs alone – in the absence of a recognizable clinical syndrome suggestive of an adverse event– may not persuade a provider to interrupt a medically necessary blood transfusion [7]. At present, there are also regional differences in the extent of vital sign changes that require stopping a transfusion. For example, guidelines in the United Kingdom allow for a transfusion to continue if the patient has a mild increase in temperature (1–2°C) to a maximum of <39°C [15]. Guidelines in the United States, however, generally dictate that transfusions associated with mild increases in temperature are discontinued immediately [5].

Previously, Andrzejewski et al. reported that many transfusion reactions were associated with only mild changes to vital signs [9]. However, his group also found that transfusions

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that contributed to circulatory overload (n=97) were associated with more substantial increases in pulse (mean change = 11.9 bpm), respiratory rate (mean change = 3.6 rpm), systolic blood pressure (mean change = 20 mmHg), and diastolic blood pressure (mean change = 7.9 mmHg) [9]. Similar changes have been reported by Lieberman et al, who examined 50 consecutive cases of TACO [16]. Parmar et al. recently reported that TACO was more frequently associated with fever compared to allergic reactions [17]. We did not find that cases of TACO were associated with statistically significant changes in fever, pulse, respiratory rate, or blood pressure in the present study, though we had a relatively small TACO sample size.

The impact of prematurely stopping transfusions and working up potential transfusion reactions is not trivial to patients or hospitals [18]. Mild changes in temperature or other vital signs are not necessarily pathological, nor are they inevitably attributable to the infusing blood product. While vital signs may play an important role in the evaluation of transfusion associated adverse events, it may be the case that current protocols are not adequately differentiating safe transfusions that are associated with mild, transient changes in vital signs from truly nefarious reactions that could result in substantial patient harm. Because stopping transfusions in the absence of any recognizable clinical syndrome is associated with delay in care, exposure to additional blood donors, and increased cost to the healthcare system, further study is needed to determine the role that vital sign analysis should play in the evaluation of transfused patient. Ideally, future studies would lead towards the development of patient-specific algorithms that may predict adverse reactions to transfusion in a timely manner. Interested parties may choose to use the detailed information in Table 1 as a “reference range” for changes in vital signs in response to blood component transfusion.

This study is limited by several factors. First, a relatively small number of transfusion reactions were studied in the 6-month period; larger studies of serious transfusion reactions would need to be undertaken to draw further conclusions regarding pre-transfusion and vital sign changes associated with transfusion reactions. Additional studies would also be needed to investigate the impact of underlying diagnosis, co-existent pharmaceutical, or supportive therapy on vital sign changes and transfusion outcomes. Further, vital sign changes distant to the completion of the transfusion (which may be observed with pulmonary reactions) would not have been captured by the vital sign measures described, although these changes would have been detected by the nursing coordinators during the chart review. Finally, the study design relied on the nursing coordinators/clinicians/expert panel members to correctly recognize transfusion reactions and on nurses to correctly measure vital signs.

In conclusion, this study provides one of the largest datasets ever generated of vital sign changes associated with blood transfusion by component. As expected, transfusions confirmed to be uncomplicated by trained clinical research nurses were associated with only marginal changes to peri-transfusion vital signs. Aside from the expected increase in temperature and pulse rate observed in febrile transfusion reactions, other notable findings include the observation that pre-transfusion vital sign abnormalities may predict vital sign changes temporally associated with transfusion or transfusion complications. Ultimately, the field of transfusion medicine would be enhanced by the development of an evidence-based

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algorithm – part of which may be based on vital signs -- that could use patient-specific factors to predict transfusion-related adverse events in advance of their occurrence.

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Appendix

The NHLBI Recipient Epidemiology Donor Evaluation Study - III (REDS-III), domestic component, is the responsibility of the following persons:

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National Heart, Lung, and Blood Institute, National Institutes of Health:

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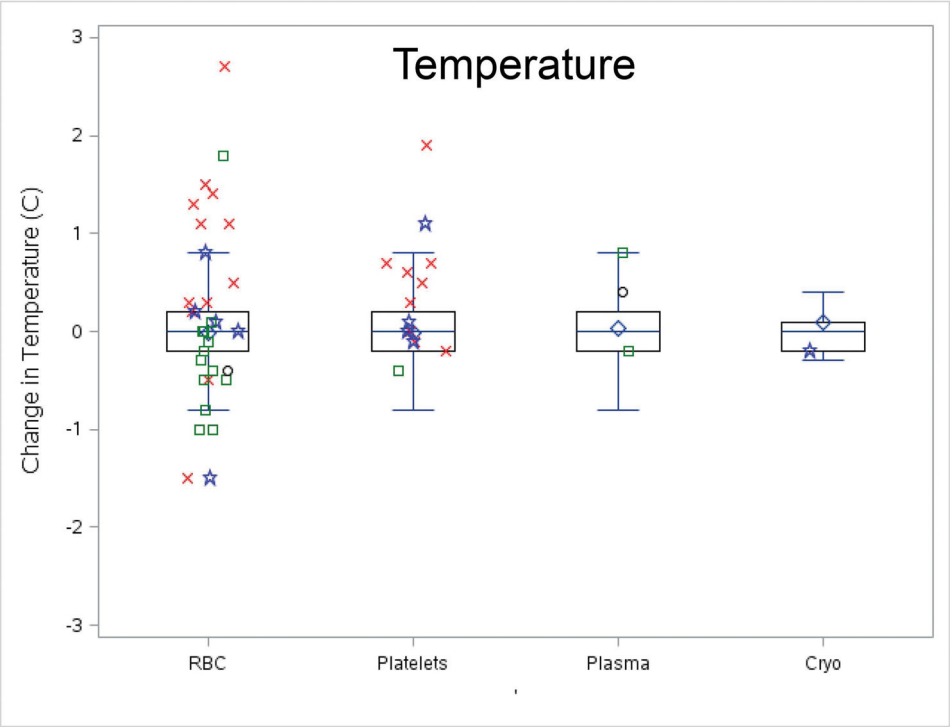

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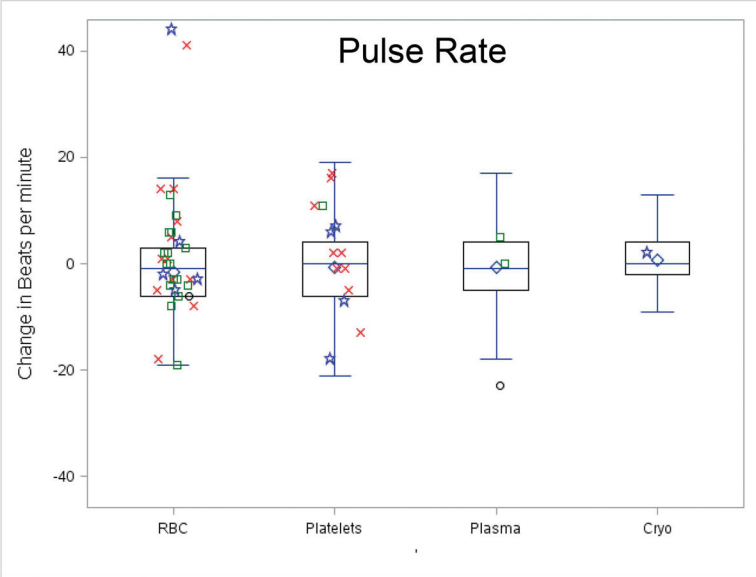

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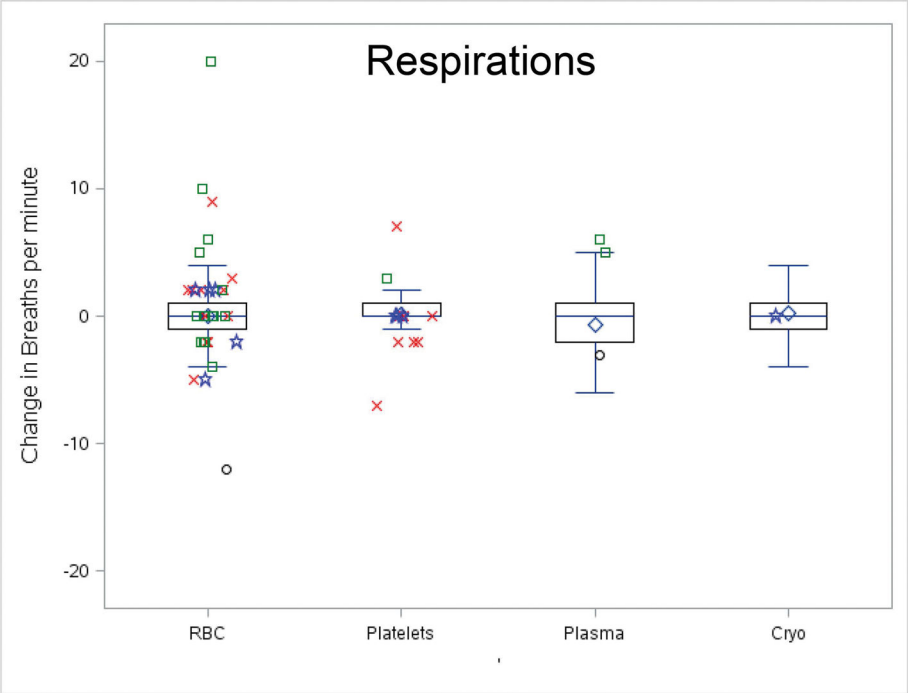

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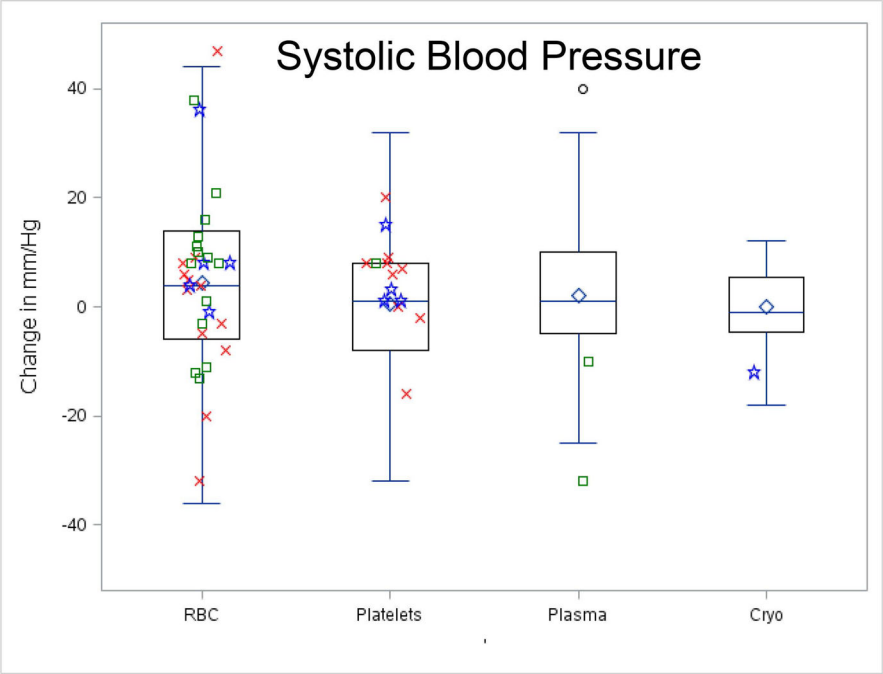

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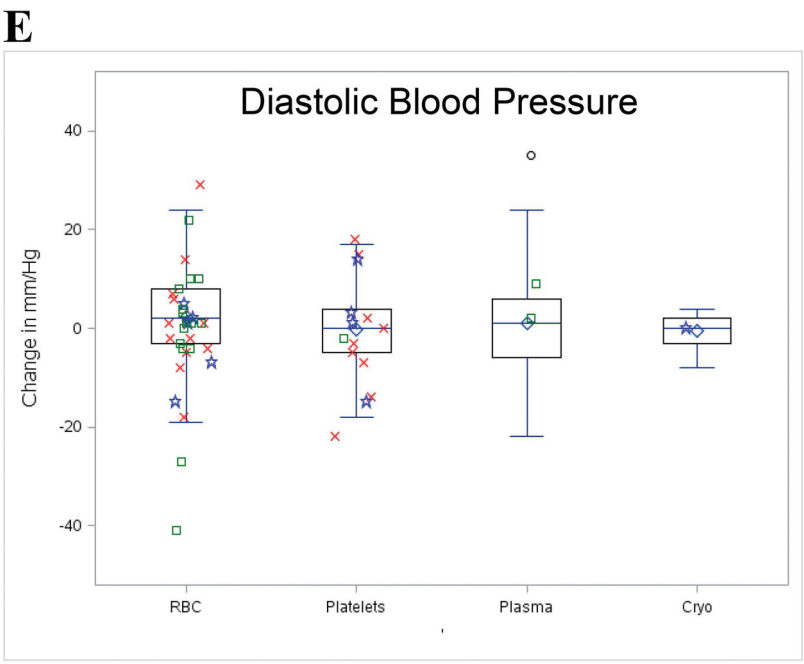

Figure 1.

Change in peri-transfusion vital signs, arranged by component transfused. **1A**: temperature; **1B**: pulse rate; **1C**: respiration rate; **1D**: systolic blood pressure; **1E**: diastolic blood pressure. Box and whisker plots - mean (diamond), median (horizontal line), 25^{th}-75^{th} percentiles (box) and 1.5 times the interquartile range above the 75^{th} percentile or below the 25^{th} percentile (whiskers, excluding extreme values) – represent data from clinically uncomplicated transfusions. Red Xs represent febrile reactions; blue stars represent allergic reactions; green squares represent TACO; black circles represent TRALI.

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Table 1

Changes in peri-transfuion vital signs, organize by component and reaction type.

		Δ Temperature					Δ Pulse					Δ Respirations					Δ Systolic Blood Pressure					Δ Diastolic Blood Pressure				
	Overall n	n	Mean	Median	25th %ile	75th %ile	n	Mean	Median	25th %ile	75th %ile	n	Mean	Median	25th %ile	75th %ile	n	Mean	Median	25th %ile	75th %ile	n	Mean	Median	25th %ile	75th %ile
Red Blood Cells																										
No Reaction	2464	1833	0.0	0.0	−0.2	0.2	2064	−1.6	−1.0	−6.0	3.0	1915	0.0	0.0	−1.0	1.0	1915	4.3	4.0	−6.0	14.0	1908	2.5	2.0	−3.0	8.0
TACO	19	13	−0.2	−0.3	−0.5	0.0	16	−0.4	0.0	−4.0	4.5	16	1.9	0.0	−2.0	3.5	15	7.1	9.0	−3.0	13.0	15	−1.3	1.0	−4.0	8.0
Mild Febrile	15	12	0.7	0.8	0.3	1.4	12	3.9	1.0	−4.0	11.0	11	1.0	2.0	−2.0	2.0	12	1.2	3.5	−6.5	7.0	12	1.6	−0.5	−4.5	6.5
Mild Allergic	5	5	−0.1	0.1	0.0	0.2	5	7.6	−2.0	−3.0	4.0	5	−0.2	2.0	−2.0	2.0	5	11.0	8.0	4.0	8.0	5	−2.8	1.0	−7.0	2.0
Plasma																										
No Reaction	302	181	0.0	0.0	−0.2	0.2	226	−0.7	−1.0	−5.0	4.0	210	−0.7	0.0	−2.0	1.0	205	2.0	1.0	−5.0	10.0	204	1.1	1.0	−6.0	6.0
TACO	2	2	0.3	0.3	−0.2	0.8	2	2.5	2.5	0.0	5.0	2	5.5	5.5	5.0	6.0	2	−21.0	−21.0	−32.0	−10.0	2	5.5	5.5	2.0	9.0
Platelets																										
No Reaction	817	614	0.0	0.0	−0.2	0.2	671	−0.6	0.0	−6.0	4.0	642	0.1	0.0	0.0	1.0	654	0.6	1.0	−8.0	8.0	654	−0.3	0.0	−5.0	4.0
TACO	1	1	−0.4	−0.4	−0.4	−0.4	1	11.0	11.0	11.0	11.0	1	3.0	3.0	3.0	3.0	1	8.0	8.0	8.0	8.0	1	−2.0	−2.0	−2.0	−2.0
Mild Febrile	9	9	0.5	0.5	0.0	0.7	9	3.1	2.0	−1.0	11.0	8	−0.8	−1.0	−2.0	0.0	9	4.4	7.0	0.0	8.0	9	−1.8	−3.0	−7.0	2.0
Mild Allergic	4	4	0.3	0.1	0.0	0.6	4	−3.0	−0.5	−12.5	6.5	3	0.0	0.0	0.0	0.0	4	5.0	2.0	1.0	9.0	4	0.8	2.0	−7.0	8.5
Mixed Products																										
No Reaction	550	353	0.0	0.0	−0.2	0.2	427	0.4	0.0	−4.0	5.0	382	−0.3	0.0	−2.0	2.0	392	3.1	3.0	−5.0	13.0	392	1.7	1.0	−4.0	7.0
TACO	9	6	0.2	0.1	0.0	0.4	8	0.5	2.0	0.0	4.5	6	0.5	0.0	−1.0	4.0	8	10.1	14.0	1.5	21.0	8	5.1	2.5	−4.5	14.0
Mild Febrile	4	4	−0.1	−0.2	−0.5	0.3	4	−2.5	−2.0	−9.0	4.0	4	1.8	1.0	0.0	3.5	4	14.3	10.0	1.5	27.0	4	11.5	10.5	8.0	15.0
Mild Allergic	3	3	0.6	0.3	0.0	1.5	3	1.7	−1.0	−8.0	14.0	2	−4.5	−4.5	−7.0	−2.0	3	−6.7	−3.0	−24.0	7.0	3	3.3	0.0	−8.0	18.0

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Table 2

Variation in vital signs by reaction type independent of blood component transfused

	Δ Temperature					Δ Pulse					Δ Respirations					Δ Systolic Blood Pressure					Δ Diastolic Blood Pressure				
Reaction Type	**n**	**Mean**	**Median**	**25th %ile**	**75th %ile**	**n**	**Mean**	**Median**	**25th %ile**	**75th %ile**	**n**	**Mean**	**Median**	**25th %ile**	**75th %ile**	**n**	**Mean**	**Median**	**25th %ile**	**75th %ile**	**n**	**Mean**	**Median**	**25th %ile**	**75th %ile**
Febrile	25	0.5	0.5	−0.1	1.1	25	2.6	1.0	−5.0	8.0	23	0.5	0.0	−2.0	2.0	25	4.4	5.0	−2.0	8.0	25	2.0	1.0	−5.0	10.0
Allergic	14	0.2	0.1	0.0	0.3	14	2.8	0.5	−5.0	6.0	12	−0.8	0.0	−2.0	1.0	14	3.0	2.0	−1.0	8.0	14	0.2	1.0	−7.0	4.0
TACO	28	0.0	−0.1	−0.3	0.1	35	1.3	2.0	−3.0	6.0	32	0.3	0.0	−2.0	3.5	34	4.4	8.0	−7.0	13.0	34	1.4	1.0	−4.0	10.0
TRALI	3	−0.1	−0.4	−0.4	0.4	3	−8.3	−6.0	−23.0	4.0	3	−3.7	−3.0	−12.0	4.0	2	13.0	13.0	−14.0	40.0	2	13.0	13.0	−9.0	35.0
Uncomplicated	3143	0.0	0.0	−0.2	0.2	3583	−1.1	−1.0	−6.0	4.0	3313	−0.1	0.0	−1.0	1.0	3348	3.2	2.0	−6.0	12.0	3337	1.7	1.0	−4.0	7.0

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Table 3

Variation in vital signs by reaction type, compared to uncomplicated transfusions

Comparison	Δ Temperature			Δ Pulse			Δ Respirations			Δ Blood Pressure					
										Systolic			Diastolic		
	Unadjusted p-value	Adjusted Linear Regression* Estimates (CI)	Adjusted* p-value	Unadjusted p-value	Adjusted Linear Regression* Estimates (CI)	Adjusted* p-value	Unadjusted p-value	Adjusted Linear Regression* Estimates (CI)	Adjusted* p-value	Unadjusted p-value	Adjusted Linear Regression* Estimates (CI)	Adjusted* p-value	Unadjusted p-value	Adjusted Linear Regression* Estimates (CI)	Adjusted* p-value
Febrile vs. Uncomplicated Transfusion	<.0001	0.62 (0.46, 0.77)	<.0001	0.072	6.68 (2.97, 10.39)	0.0004	0.527	0.25 (−1.29, 1.79)	0.747	0.703	4.63 (−1.25, 10.51)	0.122	0.890	1.17 (−2.67, 5.01)	0.550
Allergic vs. Uncomplicated Transfusion	0.125	0.10 (−0.12, 0.31)	0.377	0.157	2.18 (−2.93, 7.29)	0.403	0.537	−1.18 (−3.30, 0.94)	0.277	0.967	2.65 (−5.43, 10.73)	0.520	0.615	1.01 (−4.27, 6.30)	0.708
TACO vs. Uncomplicated Transfusion	0.619	−0.03 (−0.18, 0.13)	0.747	0.166	2.08 (−1.18, 5.34)	0.212	0.609	0.77 (−0.57, 2.10)	0.262	0.657	1.95 (−3.32, 7.22)	0.468	0.880	−0.15 (−3.60, 3.30)	0.934

*Adjusted for pre-transfusion temperature, systolic BP, diastolic BP, respiration rate, pulse rate, and number of units transfused.

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Table 4

Median pre-transfusion vital signs, by reaction type

	Group			
Median Pre-Transfusion Value	**Uncomplicated (n=4591)**	**Mild Allergic (n=14)**	**Mild Febrile (n=30)**	**TACO (n=39)**
Temperature (C)	36.8	36.7	37.1	36.85
Pulse rate (beats/min)	86	79.5	98.5	85
Respiration rate (breaths/min)	18	18	18	20
Systolic Blood Pressure (mmHg)	118	122	121	118
Diastolic Blood Pressure (mmHg)	65	72	64.5	64

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Table 5

Comparison of pre-transfusion vital signs for transfusion reactions vs. uneventful reactions

	P-values *		
	Allergic vs Uncomplicated	**Febrile vs. Uncomplicated**	**TACO vs. Uncomplicated**
Temperature	0.4580	0.0003	0.2102
Pulse	0.4432	0.0002	0.9837
Respiration	0.3690	0.5205	0.028
Systolic Blood Pressure	0.4017	0.2758	0.8388
Diastolic Blood Pressure	0.1252	0.2532	0.5203

* P-values using the Wilcoxon rank-sum test