The impact of red blood cell storage duration on tissue oxygenation in cardiac surgery

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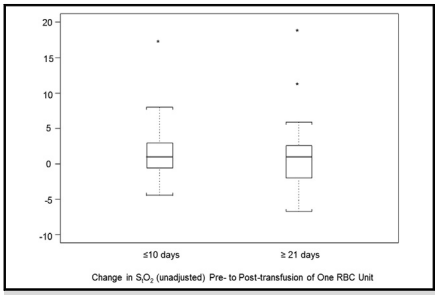
ABSTRACT

Objective: Although storage alters red blood cells, several recent, randomized trials found no differences in clinical outcomes between patients transfused with red blood cells stored for shorter versus longer periods of time. The objective of this study was to see whether storage impairs the in vivo ability of erythrocytes to traverse the microcirculation and deliver oxygen at the tissue level.

Methods: A subset of subjects from a clinical trial of cardiac surgery patients randomized to receive transfusions of red blood cells stored ≤10 days or ≥21 days were assessed for thenar eminence and cerebral tissue hemoglobin oxygen saturation (S_tO_2) via the use of near-infrared spectroscopy and sublingual microvascular blood flow via side-stream darkfield videomicroscopy.

Results: Among 55 subjects, there was little change in the primary endpoint (thenar eminence S_tO_2 from before to after transfusion of one unit) and the change was similar in the 2 groups: +1.7% (95% confidence interval, −0.3, 3.8) for shorter-storage and +0.8% (95% confidence interval, −1.1, 2.9) for longer-storage; $P = .61$). Similarly, no significant differences were observed for cerebral S_tO_2 or sublingual microvascular blood flow. These parameters also were not different from preoperatively to 1 day postoperatively, reflecting the absence of a cumulative effect of all red blood cell units transfused during this period.

Conclusions: There were no differences in thenar eminence or cerebral S_tO_2, or sublingual microcirculatory blood flow, in cardiac surgery patients transfused with red blood cells stored ≤10 days or ≥21 days. These results are consistent with the clinical outcomes in the parent study, which also did not differ, indicating that storage may not impair oxygen delivery by red blood cells in this setting. (J Thorac Cardiovasc Surg 2017;153:610-9)



Change in thenar eminence tissue hemoglobin oxygen saturation Pre- to Posttransfusion of red blood cells stored ≤10 days or ≥21 days.

Central Message

Red cell storage did not impair tissue oxygenation or microcirculation in cardiac surgery patients, consistent with lack of difference in clinical outcomes.

Perspective

The impact of red cell storage on clinical outcomes has been controversial, but recent randomized trials have demonstrated no differences between patients receiving red cells stored for shorter versus longer periods. In a subset of cardiac surgery patients in one of these trials, we found no differences in tissue oxygenation and microcirculatory blood flow, consistent with the clinical outcomes.

See Editorial Commentary page 620.

The changes occurring in red blood cells (RBCs) under conventional storage conditions have been well described[1] and have led to the hypothesis that they might impair RBC function in the transfusion recipient.[2] A number of observational, usually retrospective, studies comparing clinical outcomes in patients receiving RBCs stored for different

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Abbreviations and Acronyms

CI = confidence interval
ICU = intensive care unit
MFI = microcirculatory flow index for small vessels
⊿MFI = change in MFI
NIRS = near-infrared spectroscopy
OR = operating room
PVD = perfused small vessel density
⊿PVD = change in PVD
PPV = proportion of perfused small vessels
⊿PPV = change in PPV
RBC = red blood cells
RECAP = Red Cell Storage Duration Study Ancillary Physiologic Study
RECESS = Red Cell Storage Duration Study
SDF = sidestream darkfield
S_tO_2 = tissue hemoglobin oxygen saturation
TVD = total small vessel density
⊿TVD = change in TVD
TRUST = Transfusion Risk Understanding Score Tool

Scanning this QR code will take you to supplemental tables, video, and appendix for this article.

periods of time have yielded conflicting results,[3,4] including studies that were conducted in patients undergoing cardiac surgery.[5,6] The Red Cell Storage Duration Study (RECESS), the parent trial for the study reported here, compared clinical outcomes among patients undergoing complex cardiac surgery who were randomized to receive RBC stored ≤10 days or ≥21 days.[7] Other randomized clinical trials addressed the clinical impact of RBC storage duration in neonates[8] and critically ill adults,[9] but none of these 3 trials demonstrated any differences in clinical outcome measures. A large, randomized study in children with severe anemia measured lactate clearance as well as clinical endpoints and also found no differences between the patients receiving RBCs stored 1 to 10 days versus 25 to 35 days.[10]

Relatively few studies in humans have addressed the effect of RBC storage at the tissue level via the use of physiologic endpoints such as tissue oxygen saturation of hemoglobin[11-14] or microcirculatory blood flow,[15,16] and none of them were designed to correlate such physiologic measurements with clinical outcomes. The primary objective of the National Institutes of Health–funded Red Cell Storage Duration Study Ancillary Physiologic Study (RECAP) was to determine whether the storage duration of RBCs affects tissue oxygen saturation of hemoglobin, as measured by near-infrared spectroscopy (NIRS), and microcirculatory blood flow, as measured using sidestream darkfield (SDF) videomicroscopy, in patients who had undergone complex cardiac surgery, and whether these measurements would be consistent with the clinical outcomes observed in the parent trial. The intention of this study was to examine events at the tissue level that might provide insight into the apparent paradox between the well-documented changes that occur to RBCs during storage and the lack of measurable clinical impact.

MATERIALS AND METHODS

Oversight

RECAP (NCT01274390) was a multicenter, prospective, clinical trial that enrolled patients at 4 sites belonging to the Transfusion Medicine and Hemostasis Clinical Trials Network. RECAP was conducted as an ancillary trial to a parent study carried out by the network, RECESS (NCT00991341) and was funded independently by National Heart, Lung, and Blood Institute/National Institutes of Health with no commercial support. The 4 enrolling sites for RECAP were Duke University, the Johns Hopkins University, Massachusetts General Hospital, and the University of Pittsburgh. The Data Statistical Coordinating Center was New England Research Institutes. The study was designed by the authors and approved by the institutional review boards at each participating hospital. Study subjects provided written informed consent. The same data and safety monitoring board oversaw the parent study and RECAP. This study received the following institutional review board approvals: Duke University Medical Center, 12/07/2009 21198; Johns Hopkins Hospital, 10/25/2012 NA_00075888; Massachusetts General Hospital, 04/07/2010 2009 P002612/1; University of Pittsburgh, 09/12/2012 PRO12060386; and New England Research Institutes, 03/18/2010 #788.10.

Study Patients

The patients participating in this study were a subset of subjects who were enrolled in the RECESS study at 4 of the participating sites. Patients were eligible for the parent study[11] if they were scheduled for complex cardiac surgery via median sternotomy and were likely to require RBC transfusion as determined by a Transfusion Risk Understanding Score Tool (TRUST) of 3 or greater.[17] Additional eligibility criteria for RECAP were age at least 18 years and scheduled coronary artery bypass grafting, valve repair or replacement, or a combination. Patients were approached and consented for RECAP at the same time they were consented for the parent study. Randomization could not be done any earlier than the day before surgery. Subjects who could not be randomized were no longer eligible for RECAP.

Study Design and Treatment Protocols

For the parent study, subjects were assigned randomly, in a 1:1 ratio, to receive units of RBCs stored for ≤10 days or ≥21 days for all transfusions from the time of randomization through the earliest of day 28, death, or discharge from the hospital. Randomization was balanced by site[18] with the use of a centralized computer system. All units were prestorage leukoreduced RBCs collected in standard, licensed additive solution systems and were not irradiated or washed. The expiration dates of the units were not obscured, but the central laboratory (Shapiro Laboratory, Center for Vascular Biology Research, Beth Israel Deaconess Medical Center, Boston, Mass), which analyzed the primary raw electronic data files for the oxygenation and microcirculatory flow measurements, was blinded to study arm assignment.