

Identified metabolic signature for assessing red blood cell unit quality is associated with endothelial damage markers and clinical outcomes - DTU Orbit (08/11/2017)

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BACKGROUND: There has been interest in determining whether older red blood cell (RBC) units have negative clinical effects. Numerous observational studies have shown that older RBC units are an independent factor for patient mortality. However, recently published randomized clinical trials have shown no difference of clinical outcome for patients receiving old or fresh RBCs. An overlooked but essential issue in assessing RBC unit quality and ultimately designing the necessary clinical trials is a metric for what constitutes an old or fresh RBC unit. **STUDY DESIGN AND METHODS:** Twenty RBC units were profiled using quantitative metabolomics over 42 days of storage in SAGM with 3- to 4-day time intervals. Metabolic pathway usage during storage was assessed using systems biology methods. The detected time intervals of the metabolic states were compared to clinical outcomes. **RESULTS:** Using multivariate statistics, we identified a nonlinear decay process exhibiting three distinct metabolic states (Days 0-10, 10-17, and 17-42). Hematologic variables traditionally measured in the transfusion setting (e.g., pH, hemolysis, RBC indices) did not distinguish these three states. Systemic changes in pathway usage occurred between the three states, with key pathways changing in both magnitude and direction. Finally, an association was found between the time periods of the metabolic states with the clinical outcomes of more than 280,000 patients in the country of Denmark transfused over the past 15 years and endothelial damage markers in healthy volunteers undergoing autologous transfusions. **CONCLUSION:** The state of RBC metabolism may be a better indicator of cellular quality than traditional hematologic variables.

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