blood advances

How donor age affects RBC deformability in storage

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In this issue of *Blood Advances*, Mykhailova et al[1] identified that donor age, rather than donor sex, predominantly affects stored red blood cell (RBC) deformability, a crucial property for transfusion success. Specifically, this study showed that red cell concentrates (RCCs) from younger donors, especially teenage males, undergo a more rapid decline in deformability during storage than those from older donors. This finding shifts the current focus from previously assumed determinants of RBC quality, such as donor sex and RBC biological aging, to how donor age affects RCC quality and post-transfusion efficacy. By analyzing the effects of donor age on the rheological properties of stored RBCs, this study highlights the potential of using age-based donor selection to improve transfusion outcomes.

RBC deformability or the ability of RBCs to alter shape and squeeze through the microvasculature is critical for oxygen delivery and overall RBC function. In transfusion medicine, improved deformability is linked to fewer posttransfusion complications and increased survival rates for transfused cells.[2] Factors affecting deformability include RBC membrane flexibility, cellular morphology, cytoplasmic viscosity, and mean corpuscular hemoglobin content (MCHC).[3] During cold storage, RBCs progressively lose deformability due to metabolic degradation and membrane remodeling. This study builds on existing evidence by examining how age and sex influence these degradative processes in stored RCCs from donors at opposite ends of the age spectrum.

The authors collected and stored RCCs from 4 distinct donor groups: male and female teenagers (aged 17-19 years), as well as male and female seniors (aged ≥75 years). Over a 42-day storage period, they separated RBCs into biologically "young" (Y-RBCs) or biologically "old" (O-RBCs) groups using density gradient centrifugation. The deformability of Y-RBCs, O-RBCs, and unseparated RBCs was evaluated using ektacytometry, which measures RBC elongation under varying osmotic conditions. Their findings consistently showed that donor age, rather than sex, dictated the rheological changes in RBCs during storage.

RCCs from teenage male donors exhibited the most significant reduction in the osmolality corresponding to half-maximal RBC elongation (O_{hyper}), indicating decreased cell flexibility. Additionally, teenage RBCs had a higher elongation index, suggesting lower deformability. Conversely, senior donor RBCs, regardless of sex, demonstrated greater deformability for both Y-RBCs and O-RBCs. The authors also found that older donor RBCs, particularly those in O-RBC subpopulations, showed strong negative correlations between O_{hyper} and MCHC values over storage.

Biological aging of RBCs is influenced by natural metabolic degradation and increased cellular fragility, which affects RBC deformability. As RBCs age, they undergo transformations such as membrane phosphatidylserine translocation, microvesiculation, and increased MCHC, resulting in reduced surface area and higher cellular density. This age-related decline, collectively referred to as "storage lesions," hinders the ability of RBCs to adapt to microvascular constraints, raising the risk of vascular blockages after transfusion.[3] Interestingly, the authors observed that although teen male RCCs had higher O_{hyper} values, senior female RBCs maintained better deformability despite age-induced alterations in membrane structure. This finding suggests that donor age-related differences in RBC properties could inform personalized transfusion strategies, potentially leading to age-matched donor-recipient pairings to improve clinical outcomes.

Mykhailova et al's findings partially align with previous studies that explored the relationship between donor factors and stored RBC quality. Specifically, Cloutier et al reported significant differences between teen and senior RCCs, noting male RBCs had greater susceptibility to lose their

deformability.[4] Similarly, Matthews et al and Islamzada et al demonstrated that RBC deformability was lower in male donors than female donors.[5,6] The study by van Cromvoirt et al, however, identified donor age, not sex, as the key determinant of O_{hyper} values,[7] supporting Mykhailova et al's findings that donor age affects deformability more substantially than sex.

These studies also explored the protective role of estradiol, which is known to increase nitric oxide production and boost RBC antioxidant capacity, particularly in female RBCs. Although estradiol may confer a deformability advantage to female RBCs as previously suggested,[5,6] Mykhailova et al observed that donor age alone was the overriding factor, suggesting that estradiol's protective effects might be limited by age-related biochemical changes in RBCs. This age-based difference reinforces the need for further studies examining how lifestyle and health status may influence RBC deformability.

The study's findings emphasize the potential need for age-specific donor selection to improve transfusion efficacy. The authors propose incorporating rheological parameters, such as O_{hyper} and MCHC into quality assessments to identify optimal RCCs for transfusion. By predicting RBC deformability through donor characteristics, clinicians may reduce transfusion-related complications and improve RBC survival in recipients. The ability to select RCCs based on deformability, particularly for patients at high risk of transfusion reactions, could transform current transfusion practices.

A notable limitation in this study is the exclusion of middle-aged donors, which leaves a knowledge gap on how deformability changes across the adult life span. Additionally, the methodology used to separate RBCs by biological age relies on density-based techniques, which may induce morphological changes in cells. Future research should explore alternative methods for profiling RBC age, minimizing any potential storage effects on deformability measurements.

Incorporating additional donor factors, such as genetic background and health status, could further enhance our understanding of donor-dependent differences in RCC quality.[8] Large-scale studies could verify whether these findings are applicable to broader populations, ultimately aiding in the development of comprehensive guidelines for age- and donor-matched transfusions.

In conclusion, the study by Mykhailova et al underscores the predominant role of donor age in determining RBC deformability, with RBCs from teen male donors showing greater rigidity and reduced quality over time compared with older donors. These findings highlight the complex interplay of donor factors in transfusion medicine, emphasizing the need for further research into age-based donor selection to improve clinical outcomes.

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