Data mining: Digging for deeper understanding of blood components and transfusion outcomes

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What is this research about?

There is no question that blood transfusions save lives. Whether some blood products lead to better patient outcomes than others, however, has been up for much discussion. For the past 15 years, the biggest question has been: Does transfusing “older” red blood cells (i.e. those that have been stored longer before transfusion) lead to worse patient outcomes? The results of more than 50 observational studies investigating this question were contradictory, but recent clinical studies show no evidence of worse outcomes when older red blood cells are transfused.

Now other factors that could influence the quality of transfusion products are drawing attention. One of these is the method by which blood components are separated from whole blood donations. At Canadian Blood Services, whole blood is separated into components using one of two methods:

**Method 1.** The red cell filtration method (also known as the ‘buffy coat’ method), used when red blood cells, plasma and platelets are produced; and

**Method 2.** The whole blood filtration method, used when only red blood cells and plasma are produced.

The choice of method depends partly on the demand for platelet products, and overall about half of red blood cell units are produced using Method 1 and half are produced using Method 2. Red blood cells produced by each method are largely alike and are indistinguishable by physicians ordering transfusion components in the hospital. However, recent data from Canadian Blood Services’ scientists show subtle but possibly important differences between units produced by the two methods. For example, red blood cells produced by Method 1 tend to have lower levels of burst red blood cells (“hemolysis”) and those produced by Method 2 tend to have higher volumes. These differences suggest that the processing method may impact the quality of the product.

This raises the question of whether these product differences may have an impact on transfusion recipients. Any effects are likely to be subtle, so a thorough investigation required large amounts of data. In collaboration with Canadian Blood Services, researchers at McMaster University in Hamilton, Ontario gathered and analyzed vast blood processing and transfusion outcome datasets to answer the question: In adult patients who have received transfusions, is there an association between the processing method, the storage age of red blood cells, and in-hospital mortality (that is, the risk of dying while in hospital)?

What did the researchers do?

This was a retrospective study, which means the researchers ‘looked back’ at existing data. Records were reviewed from a database called the Transfusion Registry for Utilization, Surveillance and Tracking (or TRUST), which keeps records of patients who have received red blood cell transfusions. All adult patients who received a red blood cell transfusion in any of the three participating Hamilton-area hospitals between April 2008 and March 2014 were included in the study. These datasets were linked to blood processing (donation date, processing method) and donor information (sex and age; anonymously) from Canadian Blood Services. The researchers categorized red blood cell transfusions into seven distinct groups based on their processing method (Method 1 or 2) and storage age (fresh: 1–7 days; mid-age: 8–35 days; old: 36–42 days). Patients who were transfused with only “mid-age” red blood cells that were produced using Method 1 were considered the reference group, which means all other groups were compared to this group of patients.

In brief...

This study is the first to suggest a link between the way in which red blood cells are processed from whole blood donations and patient outcomes.
What did the researchers find?
The researchers examined data from 23,634 adults who received one or more red blood cell transfusion in-hospital. Data from 91,065 red blood cell transfusions revealed an association between in-hospital mortality and exposure to fresh red blood cells (stored for 1–7 days) produced using Method 2. This suggests that these red blood cells may be associated with a greater risk of harm compared with mid-age red blood cells produced by Method 1 (the reference group). No other significant associations were found.

How can you use this research?
This is the first study linking the method of processing blood components to patient outcomes. The results suggest that fresh red blood cells produced by the whole blood filtration method (Method 2) may lead to worse outcomes than older red blood cells produced the same way or red blood cells produced by the red cell filtration method (Method 1). This was a retrospective study and is hypothesis-generating — it was designed to find associations and stimulate further research questions but does not show any cause and effect. By their nature, retrospective studies can be confounded by uncontrolled or unrecognized factors. Thus, the results remain a suggestion at this point. Independent confirmation using other datasets and further evidence, preferably from prospective randomized controlled clinical trials, is needed before the finding can be validated. This association may not be applicable to all countries/blood centres, depending on how whole blood donations are processed. However, the finding is consistent with results emerging from recent randomized controlled trials examining whether the storage age of blood impacts transfusion outcomes. Surprisingly, these trials show trends towards fresh red blood cells leading to worse recipient outcomes.

If the results of the current study are validated, further studies to understand the biological mechanisms behind this effect would be valuable. Armed with this knowledge, changes to the whole blood processing method to improve the safety of transfusions could be considered. This Canadian study is at the forefront of what is potentially a new era in transfusion science; with these large datasets, that bring together information from the blood operator and from hospitals, and the tools to analyze them, transfusion medicine experts are well-placed to begin to dissect the factors that contribute to the optimal blood product. Gaining a deeper understanding of these life-saving products will help improve patient safety and outcomes in the future.

About the research team: This research was led by Prof. Nancy Heddle, a professor in the department of medicine at McMaster University, Hamilton, ON, and an adjunct scientist at Canadian Blood Services. The work was conducted with Canadian Blood Services colleagues: Dr. Jason Acker, Centre for Innovation senior development scientist and a professor in the department of laboratory medicine and pathology at the University of Alberta, Edmonton, AB; Dr. Sheila O’Brien, associate director, epidemiology and surveillance; Dr. Donald Arnold, medical officer and an associate professor in the department of medicine at McMaster University and Dr. Kathryn Webert, medical director and an associate professor in the department of pathology and molecular medicine at McMaster. Also on the team were colleagues from the department of medicine, McMaster University, and collaborators from the London Health Sciences Centre, London, ON, and the department of statistics and actuarial science, University of Waterloo, Waterloo, ON.

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