Red Blood Cell Concentrate Storage and Survival After Cardiac Surgery

Blood undergoes several physiological changes during storage. Observational studies have suggested that transfusion of stored red blood cell (RBC) concentrates may be harmful; however, the results are inconsistent. We performed a nationwide cohort study of RBC storage and adverse outcomes after cardiac surgery.

Methods | We identified all patients who underwent coronary artery bypass graft surgery, heart valve surgery, or both between 1997 and 2012 from the SWEDHEART register, which records information on patients who undergo heart surgery in Sweden. Transfusion data were obtained from the SCAN-DAT2 database, a nationwide register of blood transfusions. Linkage with national health data registers provided vital status and adverse outcomes.

Blood services in Sweden are part of the public health care system and follow national guidelines, whereby the oldest available blood unit of the appropriate blood type is allocated first. Storage of RBCs was classified as previously with discrete patient groups who had exclusively received blood stored less than 14 days, 14-27 days, or 28-42 days, and a mixed storage category for patients receiving blood of mixed age. Follow-up was completed on December 31, 2013.

We used multivariable Cox regression to estimate the 30-day, 2-year, and 10-year risk of death in relation to storage of transfused RBCs. We also considered the number of transfused units stored 28 days or longer and risk of death. Associations between RBC storage and the risk of complications within 30 days of surgery were assessed using multivariable logistic regression. Both regression models were adjusted for all the factors listed in the footnote for Table 1.

Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc). All statistical tests were 2-sided. P values <.05 were considered statistically significant. The study was approved by the local ethics committee, which also waived informed consent.

Results | Between 1997 and 2012, 47,071 patients were transfused in connection with cardiac surgery in 9 Swedish hospitals. Women constituted 39.2% and the mean (SD) age was 70.0 (9.7) years. Of these patients, 36.6% exclusively received RBCs stored less than 14 days; 26.8%, RBCs stored 14-27 days; 8.9%, RBCs stored 28-42 days; and 27.8%, RBCs of mixed age. Most clinical parameters were similar in the groups, although the less common blood groups (eg, AB and B) were more common with longer storage. Recipients of the freshest blood received more transfusions, 3.1 vs 2.7 (mean difference, 0.45; 95% CI, 0.37-0.52). No differences were observed for a range of comorbidities.

Table 1. Short-, Medium-, and Long-Term Survival of Patients Undergoing Cardiac Surgery in Relation to Duration of Storage of Transfused Red Blood Cell Concentrates (RBCs)

<table>
<thead>
<tr>
<th>Storage Age, d</th>
<th>Hazard Ratio (95% CI)</th>
<th>No. of Deaths/1000 Person-Years</th>
<th>Deaths/1000 Person-Years</th>
<th>Hazard Ratio (95% CI)</th>
<th>No. of Deaths/1000 Person-Years</th>
<th>Deaths/1000 Person-Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-13</td>
<td>1.31 (1.22-1.41)</td>
<td>1252 464.5</td>
<td>1201 450.4</td>
<td>0.73 (0.64-0.82)</td>
<td>253 454.4</td>
<td>253 454.4</td>
</tr>
<tr>
<td>14-27</td>
<td>1.27 (1.16-1.38)</td>
<td>1037 406.0</td>
<td>1036 406.0</td>
<td>1.05 (0.95-1.16)</td>
<td>213 412.7</td>
<td>213 412.7</td>
</tr>
<tr>
<td>28-42</td>
<td>1.23 (1.11-1.36)</td>
<td>983 382.6</td>
<td>982 382.6</td>
<td>1.14 (1.04-1.24)</td>
<td>205 392.5</td>
<td>205 392.5</td>
</tr>
<tr>
<td>Mixed Age</td>
<td>1.26 (1.16-1.36)</td>
<td>1026 414.2</td>
<td>1025 414.2</td>
<td>1.20 (1.10-1.31)</td>
<td>232 423.5</td>
<td>232 423.5</td>
</tr>
</tbody>
</table>

P values for trend <.001. Analyses were conducted using Cox regression adjusted for variables selected a priori that might affect allocation of units or model fit: sex, age, ABO blood group, hospital, calendar year, month, weekday, number of red cell transfusions, number of days each patient was transfused, whether the patient had received any plasma or platelet concentrates, and whether the patient had been transfused previously. Adding comorbidity did not alter the risk estimates. The assumption of proportionality was met. There was no evidence of effect heterogeneity between the different centers.
Table 2. Duration of Storage of Transfused Red Blood Cell Concentrates and Risk of Adverse Outcomes Within 30 Days of Surgery

<table>
<thead>
<tr>
<th>Type of Adverse Outcomea</th>
<th>Blood Stored 1-13 d</th>
<th>Blood Stored 14-27 d</th>
<th>Blood Stored 28-42 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Adverse Events</td>
<td>Unadjusted Odds Ratio (95% CI)</td>
<td>Adjusted Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>202</td>
<td>1 (Reference)</td>
<td>0.82 (0.65-1.02)</td>
</tr>
<tr>
<td>ARDS or respiratory failure</td>
<td>228</td>
<td>1 (Reference)</td>
<td>0.94 (0.77-1.15)</td>
</tr>
<tr>
<td>Serious infection</td>
<td>524</td>
<td>1 (Reference)</td>
<td>0.91 (0.80-1.05)</td>
</tr>
<tr>
<td>Stroke</td>
<td>403</td>
<td>1 (Reference)</td>
<td>1.00 (0.86-1.16)</td>
</tr>
<tr>
<td>Thrombosis or embolism</td>
<td>70</td>
<td>1 (Reference)</td>
<td>0.96 (0.66-1.38)</td>
</tr>
<tr>
<td>Composite adverse outcomeb</td>
<td>1670</td>
<td>1 (Reference)</td>
<td>0.94 (0.87-1.01)</td>
</tr>
</tbody>
</table>

Abbreviation: ARDS, acute respiratory distress syndrome.

a These were chosen because they have previously been associated with administration of stored blood and were recorded with high quality.

b The model was adjusted for the variables listed in the footnote for Table 1.

Compared with recipients of RBCs stored for less than 14 days (49.5 deaths/1000 person-years), there was no association between transfusion of RBCs stored 14-27 days (45.4 deaths/1000 person-years; adjusted hazard ratio, 1.02 [95% CI, 0.94-1.11]) or 28-42 days (41.1 deaths/1000 person-years; adjusted hazard ratio, 0.98 [95% CI, 0.86-1.11]) and 2-year mortality (Table 1). No associations were seen for 30-day and 10-year mortality. We also found no associations between the number of transfused units stored 28-42 days and risk of death (Table 1). There was no association with risk of selected serious complications (Table 2).

Discussion | In this cohort study of patients who underwent cardiovascular surgery in Sweden over a 16-year period, we found no association between RBC storage and adverse outcomes. The key strengths of this study include the large, detailed data set and complete follow-up, which was achievable by linking several high-quality nationwide registers.

The main weakness is the possibility that allocation of especially fresh RBC units was somehow related to patient prognosis. We do not believe this was the case because no such practice was in place, there were no major changes in blood storage during the study period, and blood storage was not associated with any important clinical parameters.

Results are consistent with data from 2 randomized trials that found no effect of RBC storage on change in multiple organ dysfunction score or risk of death. However, these trials relied on short-term surrogate endpoints or short-term mortality, which may have limited generalizability, and could not exclude small, yet clinically relevant effects. Therefore, these results complement recent randomized trials in providing further reassurance of the safety of current blood storage practices.

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Drafting of the manuscript: Sartipy, Holzmann, Edgren.

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Obtained funding: All authors.

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Study supervision: Hjalgrim.

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COMMENT & RESPONSE

Trends in Traumatic Spinal Cord Injury

To the Editor The use of the Nationwide Inpatient Sample (NIS) by Dr Jain and colleagues1 to estimate trends in the incidence of traumatic spinal cord injury in the United States raises several questions. Their finding of an incidence of 53 to 54 cases per 1 million inpatient hospitalizations appears only slightly lower than the cumulative incidence estimates from a study based on the Nationwide Emergency Department Sample (56.4 per 1 million), which used a more conservative approach to define acute traumatic spinal cord injury by including only persons with a principal diagnosis.2

To quantify traumatic spinal cord injury burden as accurately as possible would require a comprehensive nationwide survey similar to those used in prior regional, county-level studies, which is an arduous task involving significant costs and resources.3,4 Hence, identifying a proxy approach to estimating nationwide traumatic spinal cord injury burden is essential.

A primary concern with the use of data from inpatients only is the potential to substantially underestimate population-level incidence. Prior population-based regional studies suggest that up to 38% of individuals with traumatic spinal cord injury die before receiving definitive inpatient care.5,6 In addition, although the majority of patients presenting to the emergency department with such injuries are hospitalized at a short-term hospital, others are not. Nearly 15% of survivors are not admitted to short-term facilities that form the basis of the NIS, instead undergoing transfers to long-term facilities (including specialty rehabilitation centers), being discharged, leaving against medical advice, or having no discharge destination recorded.5

Although patients who are not admitted to short-term facilities after emergency department presentation may have relatively minor injuries,2 it is still important that they be accounted for when discussing traumatic spinal cord injury incidence. For example, a patient with an incomplete L4 injury resulting from a fall may not be admitted to a short-term hospital but may require rehabilitation services in the future.

Apart from injury severity, inpatient admission may also be influenced by insurance coverage, patient circumstances, family preferences, and physician recommendations. As such, using inpatient records to determine traumatic spinal cord injury incidence misses not only those who die prior to definitive inpatient care but also individuals with minor injuries and those who are unable to access inpatient care.

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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Schneider reported having a patent pending for a treatment and prevention of secondary injury after central nervous system trauma. No other disclosures were reported.


In Reply Dr Selvarajah and colleagues note that patients with traumatic spinal cord injury may die at the scene of the incident or be discharged from the emergency department without being admitted as inpatients. As discussed in our article, these patients were not included in our calculations because the NIS includes only those who were admitted as inpatients.

The 2 regional studies referenced by Selvarajah and colleagues in which 38% died before admission included 619 cases from California in 1970-1971 based in part on the identification of spinal cord injury using autopsy records1 and 154 cases from Olmsted County, Minnesota, from 1935-1981.2 In later studies based on state surveillance, 9% of patients in Utah in 1989-19911 died before hospital admission, as did approximately 23% in Mississippi in 1992-1994.4 These numbers suggest that older prehospital mortality data may not be able to be extrapolated to contemporary estimates of spinal cord injury given changes in seatbelt laws, traffic safety, motor vehicle designs, public awareness, drunk driving laws, changes in etiology with an aging population and increasing numbers of falls, and improvements in acute management of trauma.

A contemporary national study including autopsy reports of persons dying of traumatic causes would likely be needed to assess death from spinal cord injury prior to hospital admission. This study would also have to address the uncertainty of the diagnosis in patients who die at the scene because the definition of spinal cord injury includes both a structural lesion of neural elements in the spinal canal and resulting sensory and/or motor deficits.5 Patients who die at the scene do not contribute to the burden of disability or health care resource use after their death, but may inform policy decisions on preventable causes of death due to spinal cord injury.

In their previous report, Selvarajah et al6 used the Nationwide Emergency Department Sample from 2007-2009 and found that nearly 12% of patients were discharged home and 1.6% were admitted to a long-term care facility. We question