The impact of red blood cell transfusions on perioperative outcomes in the contemporary era of liver resection

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Background. *Perioperative red blood cell transfusions (RBCTs) are common in patients undergoing partial hepatectomy. We sought to explore the relationship between RBCTs and posthepatectomy perioperative outcomes in the contemporary surgical era.*
Methods. *We reviewed all patients undergoing partial hepatectomy from 2003 to 2012. Primary outcome was 30-day major morbidity (MM). We compared patients who did and received perioperative RBCT (defined as from time of operation until 30 days postoperatively. Multivariate analysis was performed to identify factors associated with MM and duration of stay, using logistic and negative binomial regression.*
Results. *Among 712 patients, 16.8% experienced MM, of whom 53.3% received RBCT. Patients who received RBCT experienced MM more commonly (30.8% vs 11.1%; P < .001). On multivariate analysis, the only factors associated with MM were age (relative risk [RR], 1.03; 95% CI, 1.00–1.06), greater operative time (RR, 1.29; 95% CI, 1.11–1.50), and RBCT (RR, 3.57; 95% CI, 1.81–7.04). RBCT was associated independently with a greater duration of stay (RR, 1.47; 95% CI, 1.13–1.91).*
Conclusion. *Receipt of RBCT is associated independently with perioperative MM and prolonged hospitalization after partial hepatectomy. These findings further the rationale supporting the need for a strategy of blood management to decrease the use of RBCT after hepatectomy. (Surgery 2016;159:1591-9.)*

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Advances in the perioperative and intraoperative management of patients undergoing partial hepatectomy have led to decreased postoperative morbidity and mortality.[1] Bleeding remains a substantial concern during liver resection. Despite the report of several anesthetic and surgical techniques to decrease blood loss during liver transection, including technical devices for parenchymal transection, hepatic inflow inclusion, pharmacologic interventions, and management of low central venous pressure,[2-6] ≤40% of patients undergoing partial hepatectomy still are given perioperative red blood cell transfusions (RBCTs).[7,8]

In addition to adverse transfusion reactions, such as transmission of infections, hemolytic reactions, acute lung injury, and volume overload, RBCTs have been associated with impaired postoperative recovery and even increased cancer recurrence from colorectal cancer surgery.[9-12] Transfusion-related immunomodulation is thought to be responsible for such negative impacts on postoperative outcomes.[13,14] In hepatic surgery, where RBCTs are common, the literature focuses mostly on

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identifying factors associated with the need for transfusion.[8,15] Studies examining the impact of RBCTs on postoperative outcomes are limited by either small sample sizes or noncontemporary cohorts.[16-18]

In this study, we sought to define the association between perioperative RBCTs and perioperative outcomes in a large set of patients (n = 712) undergoing liver resection.

METHODS

We conducted a retrospective review of the prospective liver resection database of the Odette Cancer Centre. This study was approved by the Sunnybrook Health Sciences Centre Research Ethics Board.

Selection of participants. Patients undergoing elective liver resection between 2003 and 2012 at a single tertiary care academic institution (Sunnybrook Health Sciences Centre–Odette Cancer Centre) specializing in hepatopancreatobiliary surgery were identified using the institutional liver resection database. Adult patients (≥18 years old) undergoing liver resection were included regardless of the indication or extent of resection. Patients for which morbidity could not be abstracted or classified were excluded.

Outcomes and data collection. The primary outcome was 30-day postoperative major morbidity (MM), defined as a Clavien-Dindo grade III, IV, or V complication.[19] Secondary outcomes were 30-day mortality, duration of stay, and 30-day readmission (unplanned >24-hour hospital stay). Perioperative RBCT was defined as transfusion of one or more units of allogeneic RBC during or 30 days postoperatively. The World Health Organization definition was used for anemia (hemoglobin ≤ 130 g/L), using the most recent hemoglobin value in the 30 days before hepatectomy.[20] The presence of underlying liver cirrhosis was captured from the description on the pathology report. Major liver resection was defined as resection of >3 liver segments. Intraoperative complications were captured based on the operative report dictated by the attending surgeon, including major bleeding, injury to surrounding structures, pneumothorax, hypotension, and clinically relevant cardiac events. Clinically relevant posthepatectomy liver failure (PHLF) was determined based as grades B and C of the International Study Group on Liver Surgery PHLF.[21] MM was broken down into system-specific complications, including cardiac events (atrial fibrillation, myocardial infarction, congestive heart failure, cardiac arrest), respiratory events (pulmonary edema, pleural effusion, pneumonia, respiratory failure), and venous thromboembolic events (deep vein thrombosis, pulmonary embolus, portal vein thrombosis).

Liver resections at our institution are performed at a low central venous pressure. Patients are monitored for ≥24 hours in an intensive care unit postoperatively. According to institutional guidelines, RBCTs were administered for a hemoglobin level of <70 g/L, in case of symptoms in the nonbleeding patient, and to maintain hemoglobin between 70 and 80 g/L in the bleeding patient.

Statistical analysis. Categorical data were reported as absolute number (n) and proportion (%), and continuous data as median with interquartile range. Comparisons were first made based on the presence or absence of MM to define specific characteristics of patients experiencing MM. The Pearson Chi-square test, Fisher exact test, or Mann–Whitney *U* test were used as appropriate. Primary and secondary outcomes were then compared based on transfusion status. A first multivariate model was constructed to examine factors associated with MM (logistic regression), and a second one for duration of stay (negative binomial regression). Variables identified as significantly associated with MM on univariate analysis ($P < .05$) were included in the model, in addition to covariates defined a priori as potential confounders (age, diagnosis, preoperative anemia, surgeon, number of liver lesions, size of the largest liver lesion, and major liver resection). In case of collinearity, the variable most relevant to the study question was included in the regression model. Results are reported as relative risks (RR) with 95% CIs. All analyses were conducted with SPSS 21.0 (IBM Corp., Armonk, NY).

RESULTS

During the study period, 712 liver resections were included in this analysis. Overall RBCT was administered to 29.2% of patients (n = 208/712). No difference was identified in the proportion of patients requiring RBCT over time (P = .368; Fig 1). The median number of RBCTs per patient was 3 (2–5), with 46.2% (n = 96/208) of transfused patients receiving ≥4 units. Baseline and clinical characteristics of the included patients based on RBCT status are presented in Table I. Patients receiving RBCT were more likely to be female and have preoperative anemia.

Overall rate of MM was 16.8% (n = 120/712). Patients experiencing MM were older with a median of 68.0 years old (60.5–74.0) compared with 63.0 years old (54.0–72.0; P = .01), and more likely to have underlying cirrhosis (7.5% vs 3.0%;