Selecting Patients for Acute Normovolemic Hemodilution during Hepatic Resection: A Prospective Randomized Evaluation of Nomogram-Based Allocation

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BACKGROUND: Acute normovolemic hemodilution (ANH) decreases transfusion rates but adds to the complexity of anesthetic management during hepatectomy. A randomized controlled trial was conducted to determine if selecting patients for ANH using a transfusion nomogram improves management and resource use compared with selection using extent of resection.

STUDY DESIGN: One hundred fourteen patients undergoing partial hepatectomy were randomized to a clinical arm (ANH used for resection of $\geq$3 liver segments) or a nomogram arm (ANH used for predicted probability of transfusion $\geq$50% based on a previously validated nomogram). The primary end point was appropriate management, defined as avoidance of ANH in patients at low risk or use of ANH in patients at high risk for allogeneic red blood cell transfusions.

RESULTS: Between September 2009 and May 2011, 58 patients were randomized to the clinical arm and 56 to the nomogram arm. Demographics, diagnoses, extent of resection, blood loss, and incidence and grade of complications did not differ between the 2 groups. There were no differences in perioperative transfusions or laboratory values. Nomogram-based allocation did not change appropriate management overall (80% vs 76% in the clinical arm; $p = 0.65$), but did result in comparable perioperative outcomes and a trend toward decreased ANH use (30% vs 47%; $p = 0.09$), particularly in low blood loss (estimated blood loss $\leq$400 mL) cases (12% vs 25%; $p = 0.04$).

CONCLUSIONS: Although allocation of intraoperative management using a transfusion nomogram did not improve appropriate management overall, it more effectively identified low blood loss cases and reduced ANH use in patients least likely to benefit. (J Am Coll Surg 2013;217: 210–220. © 2013 by the American College of Surgeons)

During the past 3 decades, hepatic resection has been widely used to treat primary and metastatic liver tumors. Recent advances in anesthetic management and operative technique have allowed for large hepatic resections to be performed with fewer complications and reduced hemorrhage.[1,2] Despite improvements, the need for perioperative allogeneic packed red blood cell (PRBC) or fresh frozen plasma (FFP) transfusion remains high, with 30% to 40% of patients requiring perioperative transfusion, even at large-volume centers.[3,4] The risks associated with allogeneic transfusions are well known and include transmission of blood-borne infections,[5,6] immune-related transfusion reactions,[7] and complications related to immunosuppression, such as increased perioperative morbidity[8] and worse long-term oncologic outcomes.[9-12]

Driven by the realization of increased cost and adverse outcomes associated with blood transfusions, strategies

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Abbreviations and Acronyms
ANH = acute normovolemic hemodilution
EBL = estimated blood loss
FFP = fresh frozen plasma
INR = international normalized ratio
PBRC = packed red blood cell

have been sought to reduce their use. These have been extensively reported in the orthopaedic and cardiac surgical literature and include reinfusion of washed shed blood (Cell Saver),[13,14] preoperative autologous blood donation,[15,16] and acute normovolemic hemodilution (ANH).[17,18] The benefits of ANH over autologous preoperative transfusion include decreased risk of administration error, reduced cost, and elimination of the need to cool and store blood. Acute normovolemic hemodilution does have limitations, including need for specialized equipment and training, increased operating room time, and theoretical dilution of coagulation factors during volume expansion.

The authors previously conducted a randomized controlled trial of ANH vs standard perioperative management in patients undergoing major hepatic resections (>3 liver segments).[19] Patients in the ANH arm had higher postoperative Hgb levels and required fewer intraoperative allogeneic transfusions. For patients with greater blood loss, the effect was more dramatic, with reductions in both intra- and postoperative RBC and FFP requirements. Criticisms of this study include the relatively high proportion of patients treated with ANH with no benefit and the unpredictability of blood loss and transfusion requirements related solely to the amount of liver resected. It is clear that a better means of identifying patients at high risk for transfusion is required, especially as hepatic resection continues to evolve and major hepatectomy is performed less frequently.

Recent efforts have been made to improve prognostication of transfusion requirement to better allocate the resources needed for ANH. Sima and colleagues[4] proposed a nomogram that used preoperative variables to predict the likelihood of perioperative red blood cell transfusion in patients undergoing liver resection. Allotting points based on preoperative Hgb and platelet level as well as details about the operation, including planned number of segments to be resected, primary vs metastatic disease, and need for extrahepatic resection, a score was created that predicted the percent probability of transfusion.

The aim of the current study was to determine if nomogram-based allocation of ANH was superior to allocation using extent of resection alone in patients undergoing partial hepatectomy. A trial was designed in which patients were randomized to different management strategies: a clinical arm (patients assigned to ANH or standard intraoperative management based on extent of resection) or a nomogram arm (patients assigned to ANH or standard intraoperative management based on the nomogram-predicted transfusion risk). The primary aim was to assess the impact of the nomogram on appropriate management by assessing its ability to target ANH to patients most likely to benefit.

METHODS

Patients scheduled for partial hepatectomy for any liver lesion, with or without a concomitant procedure, were approached for enrollment in an Institutional Review Board–approved prospective randomized controlled trial. Preoperative assessment, operation, and perioperative care all took place at Memorial Sloan-Kettering Cancer Center.

Patient eligibility

Inclusion criteria were all adult (older than 18 years) patients undergoing hepatectomy with a preoperative Hgb concentration ≥11 mg/dL in male and ≥10 mg/dL in female patients, as recorded within 14 days of registration. Exclusion criteria are listed in Table 1. In addition, patients participating in preoperative autologous donation or those receiving erythropoietin were excluded from the study.

Study design

We predicted that a nomogram-based allocation would more appropriately select patients for ANH when compared with selection based on extent of resection alone for patients undergoing partial hepatectomy. Patients were randomized to the clinical arm, where the decision to use ANH was based solely on the hepatic resection extent (≥3 segments),[19] or a nomogram arm, in which ANH was performed only when the probability of requiring a transfusion was

Table 1. Patient Exclusion Criteria

Active coronary artery disease, unless a cardiac stress study shows no reversible ischemia and normal left ventricular function within 30 days of operation
History of cerebrovascular disease
Congestive heart failure
Uncontrolled hypertension
COPD
Renal dysfunction (creatinine > 1.8)
Abnormal coagulation parameters (international normalized ratio >1.5 not on warfarin, or platelet count <100,000 K/mL)
Presence of active infection
Evidence of hepatic metabolic disorder (bilirubin >2 mg/dL, ALT >75 U/L in the absence of biliary tract obstruction)
Preoperative autologous blood donation
Erythropoietin use

ALT, alanine aminotransferase.