ORIGINAL ARTICLE

Preoperative anemia and postoperative outcomes after hepatectomy

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Abstract

Background: Preoperative anaemia is associated with adverse outcomes after surgery but outcomes after liver surgery specifically are not well established. We aimed to analyze the incidence of and effects of preoperative anemia on morbidity and mortality in patients undergoing liver resection.

Methods: All elective hepatectomies performed for the period 2005–2012 recorded in the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) database were evaluated. We obtained anonymized data for 30-day mortality and major morbidity (one or more major complication), demographics, and preoperative and perioperative risk factors. We used multivariable logistic regression models to assess the adjusted effect of anemia, which was defined as (hematocrit <39% in men, <36% in women), on postoperative outcomes.

Results: We obtained data for 12,987 patients, of whom 4260 (32.8%) had preoperative anemia. Patients with preoperative anemia experienced higher postoperative major morbidity and mortality rates compared to those without anemia. After adjustment for predefined variables, preoperative anemia was an independent risk factor for postoperative major morbidity (adjusted OR 1.21, 1.09–1.33). After adjustment, there was no significant difference in postoperative mortality for patients with or without preoperative anemia (adjusted OR 0.88, 0.66–1.16).

Conclusion: Preoperative anemia is independently associated with an increased risk of major morbidity in patients undergoing hepatectomy. Therefore, it is crucial to readdress preoperative blood management in anemic patients prior to hepatectomy.

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Introduction

Anemia is commonly encountered in the preoperative setting when patients are being evaluated for surgery. Preoperative anemia has been shown to be an independent risk factor for increased morbidity and mortality in patients undergoing cardiac surgery.[1–3] In non-cardiac surgery, the prevalence of anemia in the preoperative setting varies widely from as low as 5% in geriatric women having hip surgery to as high as 76% in patients with advanced colorectal cancer undergoing colectomy.[4,5] However, the effect of preoperative anemia on outcomes in non-cardiac surgery has not been firmly established since previous studies had limited sample sizes and lacked a uniform definition of anemia.[6] In addition, preoperative anemia is generally viewed as a surrogate marker for overall poorer health of the patient or as a risk factor for postoperative outcomes only due to its association with the higher need for perioperative transfusions.

With the development and increased utilization of large national databases such as the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) database, the role of preoperative anemia could be better delineated using a large sample of patients with a unified definition of anemia and ability to adjust for several confounders. Indeed, Musallam *et al.* studied the role of preoperative anemia in 227,425 patients from the ACS-NSQIP database undergoing major non-cardiac surgery in 2008, of whom 30.4% had preoperative anemia. In their analysis, they showed that preoperative anemia

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was associated with increased morbidity and mortality at 30 days after adjustment of several known risk factors including transfusions.[7] However, the same results may not be valid for the subgroup of patients undergoing liver surgery as they constituted <1% of the total sample. In addition, liver surgery is a more complex procedure with more anticipated blood loss when compared to laparoscopic appendectomy or cholecystectomy which were the top procedures in the above analysis.

Only a few studies have explored the implications of preoperative anemia and post-operative outcomes specifically in the post-liver resection patients. However, such studies have been only undertaken in specific subgroups of patients such as the elderly and have not adjusted for the major known confounders, especially the use of perioperative transfusions.[8,9] Therefore, in this study, we aimed to identify the prevalence of preoperative anemia in a cohort of patients from the ACS-NSQIP database who underwent liver resection. In addition, we examined whether preoperative anemia is independently associated with higher rates of 30 days morbidity and mortality as this information may trigger changes in the preoperative blood management of patients undergoing liver resection.

Methods

Data acquisition and patients

We analyzed data from the American College of Surgeons' National Surgical Quality Improvement program (ACS NSQIP) participant use files for the years 2005–2012. We queried hepatectomy procedures by CPT codes and included partial (CPT 47120), right (47130), left (47125) and extended (47122) hepatectomies performed as a primary procedure. Patients undergoing emergency procedures were excluded (n = 143). We also excluded patients with missing data regarding height, weight and gender (n = 90) or preoperative hematocrit (n = 346).

Variables

Our main independent variable of interest was preoperative anemia, defined as a hematocrit concentration of less than 36% for women and less than 39% for men according to the WHO's criteria.[10] Postoperative outcomes included mortality and morbidity at 30 days. We defined major morbidity as the occurrence of one or more of these serious complications affecting the heart (acute myocardial infarction or cardiac arrest necessitating cardiopulmonary resuscitation), respiratory system (unplanned intubation, ventilator support for >48 h, or pneumonia), central nervous system (cerebrovascular accident with deficits or coma lasting >24 h), kidneys (progressive renal insufficiency requiring replacement therapy), wound (deep incisional surgical site infection, organ or space surgical site infection or wound dehiscence), sepsis or septic shock, pulmonary embolism, or postoperative bleeding as defined by the ACS-NSQIP variable "bleeding transfusion," which included any postoperative transfusion given on postoperative day (POD) 1 and beyond.[11] Of note, we defined perioperative transfusion as any transfusion given intraoperatively, in the postoperative recovery room, blood finishing from the operating room, or any blood given on POD 0.

Missing data

Missing data was almost exclusively limited to preoperative laboratory data, and the proportion of missing data for each variable is listed in Table 1 and Supplementary Table 2. Multiple imputation was performed using predictive mean matching and 5 imputation sets to address this deficiency.[12,13] Summary statistics for the complete cases as well as each imputation set are presented in Supplementary Table 1.

Statistical analysis

We analyzed several preoperative and perioperative variables between patients with or without anemia with the chi-squared test for categorical variables and the independent samples t-test or Mann–Whitney U-test for normal and non-normal continuous variables. The primary outcomes were death or major morbidity at 30 days from the index surgery in the preoperative anemia group compared with the no anemia group.

We created separate univariable and multivariable logistic regression models for 30-day mortality and major morbidity. To accommodate model selection within the multiple imputation framework automated stepwise selection procedures (entry threshold ≤ 0.15, removal threshold > 0.25) were applied individually to the complete case data as well as each imputation set to generate candidate models. The final multivariable models were constructed by including any predictor exhibiting significant association with the outcome ($p < 0.05$) in any of the candidate models. Final model estimates were then generated by estimating the final multivariable model in the imputed dataset. We completed all statistical analyses using Stata 13.1 (StataCorp, College Station, TX), and considered two-sided p-values < 0.05 to be statistically significant.

Results

Of the 13,562 patients who underwent the hepatic procedures of interest, 575 patients met exclusion criteria and 12,987 were included in the analysis. The mean patient age was 59 and 48.4% were male. A total of 4260 (32.8%) patients met criteria for anemia. Of these, 3868 (29.8%) experienced mild anemia (hematocrit >29–<36% for women and >29–<39% in men), while 392 (2%) experienced moderate-severe anemia (hematocrit ≤29% for both women and men). Both the mild and moderate-severe anemia groups had increased rates of major morbidity and mortality compared to patients without anemia, but since there were relatively few patients with moderate-severe anemia we have decided to combine both groups as one group of patients having anemia in all further analyses.