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Preoperative thrombocytopenia and outcomes of hepatectomy for hepatocellular carcinoma

Raghunandan Venkat, MD, MPH,[a] *Jack R. Hannallah, MD, MPH, MBA,*[a] *Robert S. Krouse, MD, FACS,*[a,b] *and Felipe B. Maegawa, MD, FACS*[a,b,*]

[a] *Department of Surgery, University of Arizona, Tucson, Arizona*
[b] *Surgical Care Line, Southern Arizona VA Health Care System, Tucson, Arizona*

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ABSTRACT

Background: Platelet count is known to be an indirect indicator of portal hypertension but is not a part of the model for end-stage liver disease (MELD) score or the Child–Pugh score for risk stratification in hepatobiliary surgery.

Methods: Data from 2097 hepatic resections for hepatocellular carcinoma (HCC) were evaluated from 2005–2012 using the National Surgical Quality Improvement Program database. Patient demographics, morbidity, and mortality were evaluated.

Results: Median age and body mass index were 64 y and 26.5 kg/m^2, respectively. Majority of the patients had American Society of Anesthesiologists ≥3 (78.1%) and median MELD score was 7. On multivariate analysis, thrombocytopenia (platelet count <150/nL) and severe thrombocytopenia (platelet count <100/nL) were independently associated with an increased risk of mortality (odds ratio [OR], 1.79; $P = 0.024$ and OR, 4.19; $P < 0.001$), cardiopulmonary complications (OR, 1.61; $P = 0.009$ and OR, 1.96; $P = 0.018$), need for blood transfusion (OR, 1.35; $P = 0.05$ and OR, 1.60; $P = 0.05$), septic complications (OR, 1.53; $P = 0.025$ and OR, 1.96; $P = 0.016$), reintubation (OR, 1.91; $P = 0.004$ and OR, 2.64; $P = 0.003$), and renal insufficiency and/or failure (OR, 2.48; $P = 0.001$ and OR, 4.96; $P < 0.001$), respectively.

Conclusions: Thrombocytopenia, which is an indirect indicator for portal hypertension, is significantly associated with adverse outcomes after hepatectomy, independent of the MELD score. Platelet count should be integrated into the selection criteria for hepatic resections for HCC.

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1. Introduction

Hepatocellular carcinoma (HCC) with cirrhosis is the most common primary tumor of the liver and is the fifth most common malignancy worldwide [1,2]. In patients with cirrhosis, HCC has an annual incidence of 3%–5% [3]. In the United States, it is estimated that there will be 33,190 new cases diagnosed in 2014 and 23,000 deaths due to this disease [4]. The surgical treatment options for HCC, which offer the potential for cure, include liver transplantation, hepatic resection, and percutaneous ablation [5–7]. Limited organ availability for transplantation [8], better oncological outcomes than percutaneous ablation [9], and improvement in perioperative care over the recent years [10,11] have made

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* *Corresponding author*. Surgical Care Line 2-112, Southern Arizona VA Health Care System, 3601 South 6th Avenue, Tucson, AZ 85723. Tel.: +1 520 792 1450 (6156); fax: +1 520 629 4603.
E-mail addresses: Felipe.Maegawa@va.gov, fmaegawa@email.arizona.edu (F.B. Maegawa).

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hepatic resection the mainstay of treatment for HCC, especially for patients with normal liver function or well-compensated cirrhosis [12]. Furthermore, hepatectomy has been shown to be more cost-effective than liver transplantation [13].

Careful patient selection with assessment of the tumor burden and residual liver function are essential to optimize surgical outcomes after hepatic resection. However, the definition of selection criteria for hepatic resection is far from being established. Several tools can assess liver function. Traditionally, the Child–Pugh score has been widely used due to its ease of application [14]. However, because it uses subjective parameters such as ascites and encephalopathy, there are limitations to its discriminatory abilities [15]. The model for end-stage liver disease (MELD) score, which was first introduced to predict survival after transjugular intrahepatic portosystemic shunts, has been shown to be an efficient method to evaluate hepatic function and predict outcomes after liver resection [16–19]. Another method to evaluate liver function includes measurement of indocyanine green (ICG) clearance, which is more frequently used in Korea and Japan [20].

The presence of portal hypertension (PHT) is also indicative of poor liver function and may be associated with postoperative liver insufficiency and increased morbidity [21]. Significant PHT is usually considered a contraindication to liver resection, as recommended by the European Association for Study of Liver (EASL) [22] and American Associations for Study of Liver Diseases (AASLD) [23] guidelines for HCC treatment. PHT can be identified either instrumentally by hepatic venous pressure gradient (HVPG) measurement or clinically by the presence of esophageal and gastric varices, and a low platelet count associated with splenomegaly. Chronic PHT results in a vascular congestive splenomegaly that triggers a platelet sequestration causing thrombocytopenia. Preoperative platelet count may thus serve as an inexpensive and noninvasive laboratory indicator of PHT. PHT clinically manifested by ascites and encephalopathy is a clear contraindication for major liver resection in most centers. However, in some patients the only sign of PHT is low platelet count, lacking the other clinical signs described previously. In this setting, the Child–Pugh classification or MELD scores are within normal limits, misleading an adequate patient selection.

In this context, the focus of this study was to evaluate the association of preoperative platelet count, as a noninvasive marker for PHT, with postoperative outcomes in patients undergoing hepatic resection for HCC, independent of their MELD score. We hypothesized that preoperative thrombocytopenia was independently associated with increased postoperative morbidity and mortality, whereas accounting for patient comorbidities, MELD score, and the extent of liver resection.

2. Methods

2.1. Data source

We used the 2005–2012 American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database participant use file. The ACS-NSQIP obtains data on patients undergoing inpatient and outpatient surgical procedures from more than 250 university and private sector medical centers. Preoperative patient characteristics, intraoperative procedure characteristics, and 30-d postoperative mortality and complications, including more than 136 variables, are recorded in the data set and are well described elsewhere in the literature [24,25]. The University of Arizona Institutional Review Board determined that this study qualified for an exemption under the Department of Health and Human Studies regulations because of the use of deidentified administrative data.

We identified 2097 patients who underwent hepatic resection for HCC. The hepatic resections were classified into partial lobectomy (current procedural terminology [CPT] 47120), total left lobectomy (CPT 47125), total right lobectomy (CPT 47130), and trisegmentectomy (CPT 47122). HCC was defined by the International Classification of Diseases, Ninth Revision diagnosis code for primary liver cancer (155.0).

Patient characteristics were defined from reported NSQIP variables as follows: race and/or ethnicity was dichotomized to Caucasian, African–American, and other, American Society of Anesthesiologists (ASA) classification was dichotomized to 3 or higher or less than 3, and smoking status was dichotomized as current smoker within 1 y or not. Age and body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) were evaluated as continuous variables as well as classified in categories based on prior research examining the effect of age [26] and BMI [27] on postoperative complications. Age (in y) was classified in four categories: $\leq$49, 50–64, 65–79, and $\geq$80. BMI (in kg/m^2) was classified in five categories: $<$18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, and $\geq$35.0.

2.2. Assessment of preoperative liver function

The MELD score was calculated from preoperative laboratory variables using the standard equation: MELD = 9.57 $\times$ $\log_e$(creatinine mg/dL) + 3.78 $\times$ $\log_e$(bilirubin mg/dL) + 11.20 $\times$ $\log_e$(INR) + 6.43 [28]. Thrombocytopenia was defined as a platelet count $<$150/nL, and severe thrombocytopenia was defined as a platelet count of $<$100/nL. Child–Pugh score was not calculated because of the lack of the degree of ascites and encephalopathy in the ACS-NSQIP data set.

2.3. Definition of perioperative outcomes

Thirty-day outcomes were evaluated and included mortality, return to the operating room, postoperative complications, serious morbidity, and overall morbidity. Postoperative complications were categorized as previously described in the literature [29]: (1) wound complications (dehiscence, organ space surgical site infection [SSI], superficial SSI, and deep incisional SSI); (2) cardiopulmonary complications (cardiac arrest requiring cardiopulmonary resuscitation, myocardial infarction, ventilator dependence $>$48 h, pulmonary embolism (PE), unplanned intubation, and cerebrovascular accident); (3) postoperative transfusion; and (4) septic complications (septic shock and sepsis). The definition of serious morbidity was adapted from Ingraham *et al.* [30] as