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Malignancy does not dictate the hypercoagulable state following liver resection

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Abstract

BACKGROUND: A hypercoagulable state following intra-abdominal malignant resections has been reported. Whether this is because of the operation or the malignancy, a known cause of hypercoagulability, remains unclear. We determined if malignancy status affected the coagulation profile following liver resection by assessing perioperative thromboelastogram (TEG) values.

METHODS: Retrospective review of prospectively collected TEG values in patients who received a liver resection was conducted. Values among patients with benign or malignant disease were compared.

RESULTS: Fourteen and 63 patients were resected for benign and malignant disease, respectively. No significant differences in TEG values existed between the groups. Combining the groups, patients developed a relative hypercoagulable state postoperatively with decreased R-times ($P < .05$), although median values remained within the normal range.

CONCLUSION: Following liver resection, no differences in TEG values existed between patients with benign and malignant disease; the relative hypercoagulable state is more likely driven by postoperative coagulopathy rather than the malignancy status of the patient.

Hypercoagulability and the increased risk of venous thromboembolic events (VTE) among cancer patients have been established.[1,2] In autopsy studies, up to 50% of patients with VTEs had a concomitant malignancy.[3–5] However, certain malignancies have a more consistent association with VTE than others. Cancers involving the gastrointestinal tract, breast, and uterus carry the greatest risk.[4]

Although the gastrointestinal tumor often associated with VTEs is pancreatic cancer, the relationship is not as clear among patients with other abdominal malignancies, in particular hepatic malignancies. The liver is unique as the malignant source is not predominantly a primary disease (eg, hepatocellular carcinoma and cholangiocarcinoma), but rather metastatic disease with the most common sites of primary disease being colorectal, lung, and pancreatic carcinomas.[6,7]

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One of the clinically relevant issues of the hypercoagulable state associated with malignancy is the contribution of hypercoagulability in the postoperative state and subsequent risk of developing a VTE. Previous studies have shown that a postoperative hypercoagulable state persists after resection of abdominal malignancies.[8,9] However, none of these patients had benign disease. This raises the question of whether the hypercoagulable state following resection is because of the postoperative state or hypercoagulability associated with malignancy.

Furthermore, the classic teaching following liver resection is that a physiologic insufficiency occurs with an elevated bilirubin and prolongation of the prothrombin time.[10,11] However, our laboratory has used thromboelastography (TEG) to show that a hypercoagulable state exists following liver resection.[12,13] This test uses whole blood to provide a comprehensive assessment of the coagulation profile.

The aim of our previous published studies was focused on elucidating the general coagulation profile of patients who underwent liver resection with the use of TEG. This study aims to determine the coagulation profile of patients with benign versus malignant disease to understand whether a hypercoagulable state following liver resection exists, and if so to ascertain if it is because of the malignancy or the operation.

Methods

This study was a retrospective review of prospectively collected data for a noninterventional trial that was approved by the Institutional Review Board at Oregon Health & Science University. Methods for data collection of demographics, laboratory analysis, and perioperative management were conducted in an identical fashion as described in great detail in our previously published work.[12,13]

The analysis comprised dividing patients into groups with benign or malignant disease. Later, the malignant group was further divided into primary or metastatic disease. The entire cohort was then analyzed as one group to validate our previous studies with more patients. The preoperative management including chemotherapy administration was extracted from the patient record in a retrospective fashion, as it is a known risk factor for hypercoagulability. The type of malignancy was noted by reviewing the final pathology reports after resection. TEG values at 5 separate time points were compared: immediately preoperatively (on the day of surgery), postoperatively, and on postoperative day (POD) 1, 3, and 5.

Statistical analysis was performed using the Statistical Package for the Social Science version 22 (SPSS, Inc, Chicago, IL). Parametric and nonparametric data were compared using a Student *t* test (reported as a mean with standard deviations) and Mann–Whitney *U* test (presented as medians with interquartile ranges), respectively. A Wilcoxon signed-rank test was used to compare TEG values over time (presented as medians with interquartile ranges).

Results

Between November 2010 and January 2013, 101 patients were enrolled in the study. Twenty-four patients were excluded because of nonanatomic wedge resections being conducted (19 patients), or unresectable disease (eg, carcinomatosis) being discovered during the operation (5 patients). The mean age was 57 years (standard deviation ±14 years). Men comprised 52% of the cohort.

A list of confirmed pathologic diagnoses for all the liver resections is depicted in Table 1. The majority of patients, 63/77 (82%), underwent a liver resection for malignant disease. Of these patients, 38/63 (60%) received an operation for metastatic disease. For patients who received a resection for benign disease, the majority were done for either focal nodular hyperplasia or polycystic liver disease. The miscellaneous category for benign disease accounts for 2 patients, one of which underwent a resection for focal nodular hyperplasia or a hepatic adenoma, but was diagnosed with normal hepatic parenchyma with fatty infiltration on final pathology. The other patient received a liver resection because of invading renal cell carcinoma from the adjacent kidney. This patient was not included in the group, with primary or metastatic disease as the invading renal cell carcinoma was neither a primary liver tumor nor the result of systemic disease.

Twenty-eight patients (44%) received preoperative chemotherapy before their liver resection. The median time of the last dose of chemotherapy to the day of operation was 4 weeks. Indications for chemotherapy are listed in Table 2. The majority of these patients had

Table 1 Table of pathology-confirmed diagnoses of the patients who underwent a liver resection

Indication for resection	Number of patients
Benign	
Focal nodular hyperplasia	3
Polycystic liver disease	3
Hepatic adenoma	2
Hemangioma	2
Epithelioid hemangioendothelioma	1
Cystadenoma	1
Misc	2
Primary malignancy	
Hepatocellular carcinoma	17
Cholangiocarcinoma	4
Gallbladder adenocarcinoma	3
PEComa	1
Metastatic malignancy	
Colorectal adenocarcinoma	27
Neuroendocrine tumor	7
Gastrointestinal stromal tumor	2
Cervical cancer	1
Breast cancer	1

PEComa = perivascular epithelioid cell tumor.