ORIGINAL ARTICLE

Prediction and Limitation of Hepatic Tumor Resection Without Blood Transfusion in Cirrhotic Patients

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Background: The need for blood transfusion in cirrhotic liver resection is difficult to determine because of inaccurate estimation of operative blood loss. Moreover, blood transfusion is detrimental to cirrhotic patients.

Objective: To investigate the predictors and limitations of hepatectomy without blood transfusion for cirrhotic patients.

Design: Retrospective study.

Setting: University hospital, a tertiary referral center.

Patients: A consecutive 163 cirrhotic patients underwent resection for liver tumor(s) under a policy of restrictive blood transfusion.

Interventions: Estimated blood losses and clinicopathological features of patients who received and those who did not receive a blood transfusion were compared.

Main Outcome Measures: Estimated operative blood losses, preoperative assessments, and operative procedures.

Results: There were 48 patients in the group who received a blood transfusion, with 1275 ± 650 mL (mean ± SE) of blood transfused, and 115 patients in the group who did not receive a blood transfusion. From discriminant analysis, the cutoff value of estimated blood loss for blood transfusion was 1685 mL. Tumor size and site of hepatectomy were found to be independent variables influencing blood transfusion under logistic regression analysis.

Conclusions: Most cirrhotic patients tolerate hepatectomy without blood transfusion when the estimated operative blood loss is less than 1600 mL. Hepatectomy can be performed in cirrhotic patients without blood transfusion if the tumor is small (<5 cm), and/or the resection area is confined to Couinaud segments II, III, and VI. In this study, the largest amount of estimated blood loss in cirrhotic liver resection without blood transfusion was 2350 mL, but the uppermost limit remains to be determined.

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LIVER RESECTION in cirrhotic patients is usually associated with large amounts of operative blood loss and blood transfusion.[1-3] However, cirrhotic patients do not tolerate homologous blood transfusion well.[1-4] Adverse effects of blood transfusion, such as transmission of infectious diseases, reduction in immunity, and poor prognosis of malignant diseases, are more apparent in cirrhotic patients than in noncirrhotic patients, even when the transfusion amount is minimal.[5-9]

Management of blood transfusion in cirrhotic liver resection is difficult because conventional methods for estimating operative blood loss, ie, measuring the amount of blood from suctioning of the operative field and from soaked gauzes,[1,3,10] are usually inaccurate. A restrictive blood transfusion policy during hepatectomy on cirrhotic liver, proposed by Makuuchi et al,[3] has been used by many hepatic surgeons.[1,6-8] Under this policy, total replacement of estimated blood loss with homologous blood is unnecessary.[1,3,6-9] However, the extent of estimated blood loss that can be tolerated by cirrhotic patients, without receiving a blood transfusion, is undetermined. In addition, the question of whether resection of cirrhotic liver without providing a blood transfusion can be predicted has yet to be investigated.

We adopted the policy of restrictive blood transfusion during resection of cirrhotic livers. To elucidate the predictors and limitations of hepatectomy without blood transfusion for cirrhotic liver tumors, a retrospective review of hepatectomies on cirrhotic patients was carried out and the clinicopathological features of patients who received (BT group) and those who did not receive (non-BT group) a perioperative blood transfusion were compared.

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PATIENTS AND METHODS

From January 1994 to September 1997, 163 consecutive cirrhotic patients who underwent elective liver resection for liver tumor(s) were enrolled in this study. Patients who required repeat liver resection for recurrent malignant neoplasms, simultaneous resection of gastrointestinal cancers, or resection for ruptured liver tumor were excluded, because in these patients, blood losses may be unrelated to hepatectomy procedures. All operations were performed or guided by the same surgeon (C.-C.W.).

Preoperatively, all patients underwent the following: a routine hemogram, conventional liver function tests (including Child-Pugh grading for cirrhotic liver function[11]), indocyanine green clearance test, and imaging studies (including abdominal ultrasonography, computed tomography, and angiography). Endoscopic sclerotherapy was performed if severe esophageal varices emerged. Couinaud's definition of liver segmentation[12] was used to describe the tumor location and extent of liver resection. The resectional extent was based on liver function and indocyanine green clearance test results.[13,14] Operative ultrasonography[4,13,14] was routinely carried out to detect all lesions and to determine the resection line.

Intermittent hepatic inflow blood occlusion techniques, either unilateral[4,13] or bilateral,[2,3,6,13,14] were performed if necessary. For classic major hepatectomy,[2,13] the hepatic artery and portal vein were divided at the liver hilum before parenchymal transection. Right or left hepatic vein was also divided extrahepatically if possible.[2,13] Liver parenchymal transection was conducted by Kellyclasy technique.[4,7,14] The liver cut surface was packed with oxidized regenerated cellulose (Surgicel, Johnson-Johnson Co, Arlington, Tex) after hemostasis. Total vascular exclusion technique,[15] hypothermia,[1] intraoperative hemodilution,[8] cell saver,[1] and autologous blood transfusion[9] were not used.

Operative blood loss was estimated as the sum of the blood absorbed from gauzes and from suctionings.[1,3,10] The need for blood transfusion was determined by the anesthesiologists (S.-M.K. and W.-M.H.) under intraoperative monitoring of blood loss, hematocrit, vital signs, urinary output, and blood gas analysis. Blood transfusion was carried out when intraoperative hematocrit fell below 0.24 in patients with normal cardiopulmonary function, or below 0.27 in the patients aged 70 years or older or with correctable heart or lung diseases. This policy was continued to the early postoperative period, when fresh frozen plasma, albumin, or both were infused to keep the serum albumin level at 30 g/L or more.[1-4]

Operative morbidity and mortality were defined as complications and deaths that occurred within 30 days after operation or during the same hospitalization.

The clinicopathological data, before and during operation, of BT group and non-BT group patients were compared. The continuous variables presented as mean ± SE were compared using the Student *t* test. Pearson χ^2 test was used for comparison of frequencies. $P<.05$ was defined as significant. Significant variables were selected for a forward stepwise logistic regression analysis, to determine the independent factors that influenced blood transfusion. The estimated blood losses in BT group and non-BT group patients were evaluated by discriminant analysis to find the cutoff value at which blood transfusion was unnecessary. All statistical analyses were performed using commercially available computer software (SPSS/PC+, SPSS Inc, Chicago, Ill)

RESULTS

OPERATIVE BLOOD LOSS AND BLOOD TRANSFUSION

There were 48 patients (29.4%) in the BT group and 115 patients (70.6%) in the non-BT group. The estimated operative blood loss was 2562 ± 980 mL (reference range, 650-4160 mL) in the BT group, with 1275 ± 650 mL of blood transfused. The estimated blood loss in the non-BT group was 801 ± 547 mL (reference range, 50-2350 mL). From discriminant analysis, the cutoff value of estimated blood loss for blood transfusion in cirrhotic liver resection was 1685 mL, with sensitivity of 87.5% (42/48 patients), specificity of 87.6% (103/115 patients), and accuracy of 89.0% (145/163 patients).

PATIENT DEMOGRAPHICS AND INTRAOPERATIVE RESULTS

The operative indications and patient background are given in **Table 1**. Patients in the non-BT group had a better Child-Pugh grade and smaller tumors. No significant differences were found for any other preoperative assessment variable.

The operative procedures are listed in **Table 2**. Hepatic inflow blood occlusion techniques were not used in 1 BT group patient and 9 non-BT group patients ($P=.15$). Patients who required less extensive liver resection, without additional procedures, and with the resection area confined to right posterior inferior area (Couinaud segment VI) and left lateral segment (Couinaud segments II and III) had significantly lower incidences of blood transfusion.

POSTOPERATIVE RESULTS

The operation time was longer (6.4 ± 1.7 hours vs 4.3 ± 1.4 hours, $P<.001$), the morbidity rate was higher (16 of 48 patients vs 17 of 115 patients, $P=.003$), and the postoperative hospital stay was longer (16.7 ± 9.4 days vs 12.8 ± 5.3 days, $P=.001$) in the BT group than in the non-BT group. Two postoperative deaths ensued. A male BT group patient who received 1000-mL blood transfusion for 3000-mL blood loss, had profound hypothermia and ventricular fibrillation that were overlooked during the surgical procedure. He died of heart failure 4 days later. The other patient from the non-BT group with an operative blood loss of 900 mL, received an overdose of hypnotics on postoperative day 10, and died of pneumonia on day 34 after a prolonged somnolent period.

MULTIVARIATE ANALYSIS

Among the significant preoperative and intraoperative variables, the significant independent factors that influ-

Table 1. Operative Indications and Background Factors of 163 Cirrhotic Patients Undergoing Hepatectomy*

	Non-BT Group (n = 115)	BT Group (n = 48)	P
Surgical indications			
Hepatocellular carcinoma	105	48	
Metastatic colon cancer	4	0	.11
Miscellaneous	6†	0	
Background			
Sex, M/F	93/22	38/10	.80
Age, y	58.6 ± 11.5	57.1 ± 13.1	.47
Associated with EV, No. of patients	22	4	.09
Serum HBsAg (+)	65	31	.34
Serum Anti-HCV (+)	36	17	.61
Etiology of cirrhosis			
Posthepatitic	104	42	
Alcoholic	8	4	.82
Others	3	2	
Child-Pugh grade			
A	98	36	
B	12	11	.04
C	5	1	
ICG R15, %	15.72 ± 6.61	14.77 ± 6.87	.41
Hemoglobin, g/L	135.1 ± 16.3	129.3 ± 26.7	.16
Platelet count, $\times 10^9$/L	15.92 ± 7.24	16.98 ± 8.16	.41
Bilirubin μmol/L (mg/dL)	20.0 ± 10.6 (1.17 ± 0.62)	19.8 ± 7.3 (1.16 ± 0.43)	.93
Albumin, (g/L)	39.1 ± 4.2	38.3 ± 4.2	.25
AST, U/L	34.9 ± 25.8	37.3 ± 22.9	.59
ALT, U/L	55.9 ± 58.2	45.3 ± 29.8	.13
Alkaline phosphatase, U/L	160.5 ± 141.5	162.2 ± 79.4	.94
LDH, U/L	221.0 ± 73.4	224.2 ± 99.6	.10
Prothrombin time, % of control	94.9 ± 4.6	94.2 ± 4.3	.34
Tumor size, cm	5.18 ± 3.45	8.43 ± 3.85	<.001
Multiple tumors, ≥2 tumors	24	10	.99

*BT group indicates those cirrhotic patients who received a blood transfusion during hepatectomy; non-BT group, those cirrhotic patients who did not receive a blood transfusion during hepatectomy; EV, esophageal varices; HBsAg, hepatitis B surface antigen; anti-HCV, antihepatitis C antibody; ICG R15, indocyanine 15-minute retention rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; and LDH, lactic dehydrogenase. Values expressed as mean ± SE unless otherwise indicated.

†Includes metastatic esophageal carcinoma, 1 patient; hemangioma, 2 patients; and focal nodular hyperplasia, 3 patients.

Table 2. Intraoperative Results*

	Non-BT Group (n = 115)	BT Group (n = 48)	P
Extent of liver resection, No. of segments			
≥3	21	15	
1-3	30	16	.05
≤1	64	17	
Additional procedures, total No.	**16**	**16**	.004
Resection of diaphragm	11	10	
Resection of pancreas and spleen	0	2	
Colon resection	1	0	
Resection of main bile duct	1	2	
Splenectomy	2	1	
Adrenectomy	0	1	
Embolectomy of portal vein	1	2	
Segment site of liver resection, No.			
VI or II + III	28	4	.02
Other locations	87	44	
Mean ± SE volume of liver resection, mL	191.5 ± 282.4	487.1 ± 587.7	.002
Need for mobilization of right lobe, No. of patients	71	31	.90
Need for multiple hepatectomies,† No. of patients	19	10	.51

*BT group indicates those cirrhotic patients who received a blood transfusion during hepatectomy; non-BT group, those cirrhotic patients who did not receive a blood transfusion during hepatectomy.

†Number of separate liver resections greater than or equal to 2.

enced the need for blood transfusion were tumor size and site of liver resection (**Table 3**).

COMMENTS

Due to hemolysis and increased hepatocyte loading on heme metabolism,[1,6] hyperbilirubinemia inevitably occurs after resection of cirrhotic liver if homologous blood transfusion is required.[1,3,4,6-8] To accomplish the goal of liver resection without blood transfusion, procedures and equipment that reduce operative blood loss in hepatectomy, such as hepatic inflow vascular occlusion,[4,6,13,14] total vascular exclusion,[15] liver clamps,[1] microwave coagulator,[1] and ultrasonic dissector[1,10] have been developed. Moreover, use of cell savers,[1] intraoperative hemodilution,[8] and preoperative autologous blood donation[9] have also been proposed to avoid homologous blood transfusion. Recently, many authors[3-9] have reported that less than 50% of their patients undergoing hepatectomy require homologous blood transfusion. Using hepatic inflow blood occlusion techniques and restrictive blood transfusion policy, our incidence of blood transfusion in cirrhotic liver resection was similar to that of previous reports[4-9,13] despite the fact that, in most of our patients, tumor size was large.

Blood loss during cirrhotic liver resection is usually overestimated. Although hepatic inflow blood occlusion technique decreases operative blood loss in hepatectomy,[3,4,14] it may cause bowel edema and exsanguination of extracellular fluid if used for a prolonged period.[3,4,14] Moreover, mobilization of cirrhotic liver usually causes leakage of lymphs or ascites following division of the dilated perihepatic lymphatic vessels. These leaked body fluids may be counted as blood loss by conventional estimation methods.[3,7,10] Because cirrhotic patients may tolerate some degree of anemia,[3,7] it is unnecessary to replace all of the estimated blood loss by homologous blood transfusion, if the hemodynamic condition and peripheral tissue oxygen concentration are stable.[3,6,7] We found that no blood transfusion was needed in some patients even when estimated blood loss exceeded 2000 mL.

The uppermost limit of estimated blood loss for cirrhotic liver resection without blood transfusion has never been clearly defined. Originally, Makuuchi et al[3] reported that blood loss of up to 1680 mL did not require blood transfusion in cirrhotic patients. They later performed blood transfusion in liver resection when estimated blood loss exceeded 1500 mL.[13] Fan et al[10] transfused hepatectomized patients when hemoglobin level fell to 90 g/L. In addition to transfusion of preoperatively donated autologous blood,

Table 3. Results of Stepwise Logistic Regression Analysis for Hepatectomy With Blood Transfusion in 163 Cirrhotic Patients*

Variables	β	SE	*P*	Odds Ratio, 95% Confidence Interval
Tumor size	0.2520	0.0561	<.001	1.2866 (1.1445-1.4072)
Site of resection	–1.837	0.6900	.007	0.1592 (0.0593-0.7814)
Constant	–9.2223	15.362	. . .	. . .

**Ellipses indicate not applicable.*

Kajikawa et al[9] performed blood transfusion on cirrhotic patients undergoing liver resection when blood loss exceeded 2000 mL. Nevertheless, the generally reported safe lowest hematocrit level without blood transfusion is around 0.20 to 0.30 for cirrhotic patients without cardiopulmonary disease, and somewhat higher in aged patients or patients with accompanying heart or lung disease.[1-10,13]

Due to difficulties in estimating the actual operative blood loss during resection of cirrhotic liver, blood transfusion was carried out on a case-by-case basis by monitoring intraoperative vital signs and hematocrit. The causes of 2 deaths in this series were unrelated to our blood transfusion strategy. By discriminant analysis, about 90% of cirrhotic patients did not require blood transfusion during hepatectomy when estimated blood loss was less than 1685 mL. This cutoff value was very similar to that reported by Makuuchi et al.[3] Although the largest amount of estimated blood loss without blood transfusion was 2350 mL in this study, the uppermost limit of estimated blood loss in cirrhotic patients undergoing liver resection without need for blood transfusion remains undetermined and requires further investigation.

Because unexpected conditions, such as dilated perihepatic lymphatics, abundant collateral vessels, and torsion of liver anatomy, may be encountered during cirrhotic livers resection,[1,2] prediction of hepatectomy without blood transfusion is rather difficult. Gozzetti et al[6] reported that serum albumin and bilirubin levels significantly affected the need for blood transfusion in cirrhotic liver resection. However, in this study, none of the preoperative liver function test variables were found to influence the need for blood transfusion.

Cirrhotic patients with a poor Child-Pugh class are usually associated with some coagulopathy and portal hypertension.[1,11] In our study, cirrhotic patients with a poor Child-Pugh class seemed to have higher rates of blood transfusion. However, if we look at the patient number in each grade, we noted that the Child-Pugh class is not truly "predictive," as the class A patients had decreased need for blood transfusion, but class B and C patients did not have increased blood requirement. Other variables that affected the need for blood transfusion were related to the pathological characteristics of the tumor itself and could be evaluated by preoperative assessments and imaging studies.[1-3,13,16] Thus, preoperative prediction of blood transfusion requirement in cirrhotic liver resection is possible.

Multivariate analysis by logistic regression method was used to determine the most powerful predictors. Due to the economic extent of liver resection,[14] similar to the results of a previous report,[7] the tumor size independently affected the need for blood transfusion under multivariate analysis.

The site of resection was the other independent factor that influenced blood transfusion in cirrhotic patients. The liver parenchyma at left lateral segment and segment VI is usually not thick,[12] and the cut surface of the liver created after resection in these areas is narrow. Moreover, these areas are peripherally located, and extensive liver mobilization is not required. Resection and control of operative bleeding in these areas were easier, and could be achieved without blood transfusion.

As in other reports,[6,7,9] hepatectomy in cirrhotic patients who receive a blood transfusion was associated with higher morbidity rate and longer hospital stay. From our study, the need for blood transfusion in cirrhotic liver resection can be predicted; thus, suitable management can be selected for cirrhotic patients with liver tumor. Prediction of blood transfusion requirement is useful for particular groups of patients, such as Jehovah's Witnesses[17] or those with rare blood types, in whom liver resection should be performed without blood transfusion.

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