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Effects of Preoperative Platelet Count on Blood Loss for Splenectomy with Esophagogastric Devascularization

Geng Bo, Piyush Kumar Mishra, Luo Chen, Yang Xian Mo, Ting Yan and Shiqiao Luo[*]

Department of Hepatobiliary Surgery, The First Affiliated Hospital, Chongqing Medical University, Yixueyuan Road, Yuzhong District, Chongqing, P. R. China

[*]**Corresponding author:** Shiqiao Luo, Department of Hepatobiliary Surgery, The First Affiliated Hospital, Chongqing Medical University, Yixueyuan Road, Yuzhong District, Chongqing, P. R. China, Tel: 86-23-68485041; E-mail: shiqiaoluo@qq.com

Abstract

Objective: To investigate whether low preoperative platelet count increased blood loss in splenectomy and esophagogastric devascularization for hepatitis B cirrhosis patients, and to discuss the necessity of prophylactic platelet transfusion in patients with platelet count less than 50×10^9/L.

Methods: 105 patients who received splenectomy from January 2008 to July 2014 were divided into three groups based on their preoperative platelet counts: $<30 \times 10^9$/L (group 1), $30\text{-}50 \times 10^9$/L (group 2), $>50 \times 10^9$/L (group 3). Their operation time, blood loss, postoperative platelet count of 1st and 3rd day, drainage volume, postoperative hospital stay and operation associated complications were compared between the 3 groups.

Results: Compared with patients in group 3, patients in group 1 and 2 experienced more blood loss, but the difference was not statistically significant ($P>0.05$). There were no significant differences among 3 groups in terms of operative time, postoperative drainage, postoperative hospital stay and operation-associated complications ($P>0.05$). Compared with preoperative results, PLT count increased significantly after the operation between the 3 groups ($P<0.05$).

Conclusion: It is safe to perform splenectomy and esophagogastric de-vascularization in hepatitis B cirrhosis patients with PLT count less than 50×10^9/L, and also in patients with platelet count lower than 30×10^9/L, it is not necessary to give prophylactic platelet transfusion until patient has any risk of bleeding.

Keywords: Liver cirrhosis; Platelet; Hypersplenism; Portal hypertension; Splenectomy

Introduction

Hepatitis B cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands due to hepatitis B virus (HBV) [1,2]. It has been estimated 1 million deaths yearly worldwide from complications for liver cirrhosis [3,4]. Cirrhosis accounts for 90% of portal hypertension [5]. Hypersplenism and esophagogastric varices are most common clinical manifestations of liver cirrhosis and portal hypertension [6-8]. Hypersplenism leads to decrease in platelet counts, leukocyte counts and rapidly destruct the blood cells [9]. Severe thrombocytopenia due to hypersplenism significantly increases the risk of spontaneous bleeding and can postpone diagnostic or therapeutic procedures for cirrhosis patients, for instance, liver biopsy, interferon therapy and surgery [1].

Splenectomy and esophagogastric devascularization has been considered the effective therapy for liver cirrhosis [6,10,11]. It can not only cure hypersplenism and consequently abolish bleeding tendency due to thrombocytopenia, but also prevent bleeding from esophagogastric varices. Institute of German Medical Association and the American Association of blood banks recommend prophylactic platelet transfusion in liver cirrhosis patients with preoperative platelet counts less than 50×10^9/L [12,13]. On the other side American Society of Clinical Oncology recommends the threshold value of prophylactic platelet transfusion with platelet counts $<10 \times 10^9$/L [14]. But the recommendation remain controversial. We conducted this study to investigate the safety of splenectomy and esophagogastric devascularization for hepatitis B cirrhosis patients with platelet count less than 50×10^9/L.

Materials and Methods

From January 2008 to July 2014 open splenectomy and esophagogastric devascularization were performed for hepatitis B cirrhosis on patients by matured and experienced surgeons at the department of Hepato-Bilio-Pancreatology, 1st Affiliated Hospital of Chongqing Medical University, Chongqing, China. We chose 105 patients, among them 63 were males and 42 were females. For investigation in those 105 patients Preoperative endoscopic ultrasound, CT scan and bone marrow smear test were performed, in which CT scan revealed significant splenomegaly and cirrhosis of the liver in all patients, endoscopic ultrasound showed small to large esophagogastric varices and bone marrow smear excluded hematopoietic disorders [15].

Demographic characteristics, laboratory data and histopathological data for all patients, with preoperative diagnosis of hepatitis B cirrhosis, who underwent splenectomy and devascularization between 2008 to 2014 were retrieved from the medical and histopathological records at the 1st Affiliated Hospital of Chongqing Medical University, Chongqing, China. We collected, Preoperative data including PLT

counts, PT, albumin, spleen size, child-Pugh scores, portal vein diameter, total bilirubin/direct bilirubin. Existence of ascites or hepatic encephalopathy was also revealed preoperatively. Intraoperative data including blood loss, PLT transfusion rate and operation time. Postoperative data including drainage volume, PLT count on 1st and 3rd day, postoperative complications and hospital stays (day). All patients were divided into 3 groups based on their preoperative platelet counts.

Operation procedures

Splenectomy and esophagogastric devascularization were performed by the surgical team of Hepato-Bilio-Pancreatology department. A modified Hassab's surgery was performed to treat esophageal varices in patients with portal hypertension as a result of cirrhosis of the liver [16,17]. Splenic artery was ligated, using traditional ligature and severed before splenectomy, vessels of upper half stomach and 6-10 cm distal esophagus were severed, no pyeloroplasty was carried out and a drainage tube was placed under the left diaphragm [17].

Statistical analysis

Numerical values were expressed as mean ± standard deviation. Statistical analyses were performed by using SPSS20.0 for windows. Statistical comparisons between pre-operative and post-operative platelet count were made by using student's t-test and the chi-square test. Values of p less than 0.05 were considered statistically significant.

Results

Demographic characteristics on comparison of preoperative values among the three groups are shown in Table 1.

Group 1 and group 2 has shown noticeably lower platelet counts on comparison with group 3 (22.4 [range, 7-29] vs. 65.5 [range, 50-152], p<0.001), (41.3 [range, 31-49] vs. 65.5 [range, 50-152], p<0.001), the differences came out on comparison between the three groups in terms of age, HB, PT, Alb, BMI, spleen size, portal vein diameter (PVD) and Child-Pugh score.

Variables	Group 1	Group 2	Group 3	pa	Pb
Cases	26	43	36	-	-
Sex (F/M)	Jun-20	21/22	16/20	NS	NS
Age (y)	49.5 (24-68)	47.0 (21-82)	49.9 (23-73)	NS	NS
Hb (g/L)	96.0 (77-124)	101.4 (70-145)	95.4 (57-128)	NS	NS
PLT (× 10^9/L)	22.4 (7-29)	41.3 (31-49)	65.5 (50-152)	0.001	0.001
PT (s)	16.2 (12.1-19.6)	15.6 (12.4-21.3)	15.5 (12.0-18.0)	NS	NS
Alb (g/L)	34.4 (27-45)	35.8 (21-44)	35.6 (21-51)	NS	NS
BMI (kg/m^2)	22 (18-29)	23 (19-27)	22 (17-28)	NS	NS
Child-Pugh class					
A	15	35	27		
B	11	7	9		
C	0	1	0		
Child-Pugh score	6.3 (5-9)	5.8 (5-11)	5.9 (5-8)	0.085	0.749
Spleen size (cm)	20.1 (10-35)	19.0 (12-25)	18.1(11-27)	NS	NS
Portal vein diameter (mm)	16.9 (11-24)	16.2 (11-22)	16.7 (10-22)	NS	NS
Data are presented as median (range) or n, unless otherwise indicated					
Pa comparison between group 1 and group 3					
Pub comparison between group 2 and group 3					
NS not significant					

Table 1: Demographic characteristics.

A comparison of operative outcomes and postoperative details between three groups are shown in Table 2. Compared with patients in group 3, patients of group 1 had more blood loss (682.7 [range 100-2000] vs. 544.7 ml [range 50-1800], p=0.334), but the difference was not statistically significant. On comparison of group 1 with group 3 in terms of operation time (199.4 [range 95-460] vs. 197.5 min [range 60-360]], p=0.806), drainage volume of the 1st postoperative day (207.9 [range 5-480] vs. 176.6 ml [range 2-970], p=0.477), drainage volume of the 3rd postoperative day (136.9 [range 0-750] vs. 137.1 ml [range 0-610], p=0.996), postoperative hospital stays of the two groups has shown no statistically significant (13.8 [range 8-28] vs. 13.6 day [range 8-32], p=0.888). There were no significant differences on

comparison of group 2 and group 3 in terms of blood loss (678.1 [range 50-3000] vs. 544.7 ml [range 50-1800], p=0.295) operation time (203.8 [range 75-400] vs. 197.5 min [range 60-360], p=0.644), 1st day postoperative drainage (189.4 [range 10-600] vs. 176.6 ml [range 2-970], p=0.437) and hospital stays (14.6 days [range 6-30] vs. 13.6 days [range 8-32], p=0.721), 3rd day postoperative drainage (181.9 ml [range 0-1600] vs. 137.1 ml [range 0-610], p=0.437) and hospital stays (14.1 [range 6-30] vs. 13.6 [range 8-32], p=0.742). In group 1, 6 patients received intraoperative PLT transfusion, among them 3 patients experienced more than 1000 ml blood loss, the other two suffered blood loss of 505 ml, 220 ml. In group 2, 4 patients received intraoperative PLT transfusion, as 2 patients experienced blood loss of more than 800ml and the other two suffered blood loss of 60 0ml, 200 ml respectively. In group 3, 2 patients received PLT transfusion, as their blood loss was 810 ml, 220 ml respectively.

Variables	Group 1	Group 2	Group 3	pa	Pb
Operation (min)	199.4 (95-460)	203.8 (75-400)	197.5 (60-360)	NS	NS
EBL (ml)	682.7 (100-2000)	678.1 (50-3000)	544.7 (50-1800)	NS	NS
Platelet transfusion	May-26	Apr-43	Feb-36	NS	NS
POD 1 PLT	72.2 (20-222)	94.6 (33-240)	100.9 (31-198)	0.009	NS
POD 3 PLT	124.8 (28-336)	177.0 (55-300)	224.3 (58-532)	0.001	NS
POD 1 drain exudates (ml)	207.9 (28-336)	189.4 (10-600)	176.6 (2-970)	NS	NS
POD 3 drain exudates (ml)	136.9 (0-750)	181.9 (0-1600)	137.1 (0-610)	NS	NS
PHS (days)	13.8 (8-28)	14.1 (6-30)	13.6 (8-32)	NS	NS
Data are presented as median (range) or n					
EBL estimated blood loss, POD postoperative day, PHS postoperative hospital stay					
Pa comparison between group 1 and group 3					
Pb comparison between group 2 and group 3					
NS not significant					

Table 2: Operative outcomes and postoperative details.

Postoperative complications of patients among three groups are shown in Table 3. In this study a total number of 31 patients experienced postoperative complications, 11 patients in group 1 (42.3%), 12 patients in group 2 (28%), 8 patients in group 3 (22.2%). No any patient died of operation related complications in our study. One patient in group 1 suffered postoperative bleeding, peripheral vascular hemorrhage of pancreas was found on repeated surgery, bleeding stopped after suturing of vessels, and was discharged on the 10th postoperative day. 3 patients experienced splenic venous thrombus, 2 patients with pancreatic leakage, 2 patients developed pleural fluid postoperatively and were treated with conservative treatment and discharged. One 44 year old male patient in the group 1 with two complications, bacterial peritonitis and lung infection having preoperative PLT count of 24×10^9/L, child-Pugh score 6, operation time 170 min, intraoperative bleeding 500 ml, has not received any blood transfusions during and after surgery. Anti-infection treatment were given to the patient after surgery and discharged from the hospital on 27th day. In group 2, 6 patients were complicated with splenic vein thrombosis and 2 complicated with portal vein thrombosis, 2 patients experienced postoperative wound infection, 1 with pleural fluid, 1 with bacterial peritonitis, all the patients received conservative treatment and discharged from hospital. A prolonged stay in hospital after surgery, a 36 years old male patient with preoperative PLT 45×10^9/L, child-Pugh score 5, operation time 90 min, intraoperative bleeding 100 ml, postoperative wound infection, was given conservative treatment and discharged on the 30th day. In group 3, 2 patients with pleural effusion, 2 cases with pulmonary infection, 2 cases of postoperative wound infection, 1 case of urinary tract infections and 1 case of splenic vein thrombosis, were treated by conservative treatment and discharged from hospital. Overall, among all the patients in three groups, patients of group 1 had much higher operation associated complications than other two groups, but the differences were not statistically significant.

Complications	Group 1	Group 2	Group 3	pa	Pb
Postoperative bleeding	1	0	0		
Splenic vein thrombus	3	6	1		
Pancreatic leakage	2	0	0		
Pleural effusion	2	1	2		

Peritonitis	1	1	0		
Pulmonary infection	1	0	2		
Incision infection	1	2	2		
Portal venous thrombosis	0	2	0		
Ureter infection	0	0	1		
Total	11 (42.3%)	12 (28.0%)	8 (22.2%)	NS	NS
Data are presented as n (%) Pa comparison between group 1 and group 3 Pb comparison between group 2 and group 3 NS not significant					

Table 3: Complications.

Patients of the three groups with postoperative changes in platelets are shown in Table 4. We found significant difference on comparison of preoperative platelet counts with postoperative platelet counts, as platelet counts improved significantly in patients of all the three groups post-operatively. Pre and postoperative platelet counts changes in group 1 to (22.4 [range 7-29] vs. 124.8 [range 28-336], $p<0.001$), group 2 to (41.3 [range 31-49] vs. 177.0 [range 55-300], $p<0.001$), group 3 to (65.5 [range 50-152] Vs. 224.3 [range 58-532], $p<0.001$).

There was significant improvement in platelet count after 72 h of splenectomy (<0.05).

	1 day pre-operation	3 days post operation	P
Group 1	22.4(7-29)	124.8(28-336)	0.001
Group 2	41.3(31-49)	177.0(55-300)	0.001
Group 3	65.5(50-152)	224.3(58-532)	0.001
Data are presented as median (range) P shows comparison between preoperative and postoperative values NS not significant			

Table 4: Changes in platelet counts after the operation.

Discussion

Chronic hepatitis B virus (HBV) infection is a major global public health problem with an estimated 1 million deaths yearly worldwide from complications of liver cirrhosis. The prognosis for patients with decompensated HBV cirrhosis is poor, with a 5-year survival of only 14% compared with 84% in patients with compensated HBV cirrhosis [3]. Hypersplenism, splenomegaly and portal hypertension are common complications of liver cirrhosis associated with HBV. Hypersplenism often led to thrombocytopenia, leukopenia and anemia. Treatment includes drug therapy, liver transplantation, splenic artery embolization and resection of spleen for hypersplenism [18]. However Djordjević et al. [19] reported in his studies that there is no any correlation between spleen size and platelet counts [19]. Splenectomy is indicated when the platelet count goes below 30×10^9/L [20]. In 1950 for the first time open splenectomy was performed and was considered feasible and safe for liver cirrhosis after development of more than 60 years [21-23]. The main purpose of open splenectomy for portal hypertension is: (1) to reduce portal vein blood flow, relieve portal hypertension, to improve esophagogastric varices bleeding [24]. (2) To improve hypersplenism induced thrombocytopenia [10]. (3) To improve the treatment of hepatocellular carcinoma [25]. (4) Splenectomy is favorable for overcoming small-for-size (SFS) graft syndrome in living donor liver transplantation [26,27]. Multiple studies indicate that splenectomy for liver cirrhosis has many benefits. Murata et al. [28] reported albumin, cholinesterase, total cholesterol and liver volume raised 6 months after splenectomy in 12 patients with liver cirrhosis, author considered that splenectomy may be helpful to improve liver function in patients with liver cirrhosis and could be a transitional treatment for patients waiting for liver transplantation [28]. Kawanaka et al. [29] believes that in patients with liver cirrhosis and portal hypertension, splenectomy reduced portal venous pressure. A decrease in splanchnic blood flow, by eliminating splenic blood flow and reduction in intrahepatic vascular resistance, by normalizing hepatic concentrations of ET-1 and NOx, may both have contributed. Anegawa et al. [29] reported that splenectomy significantly decreased portal venous pressure and improves child-Pugh score [29].

Thrombocytopenia induced by hypersplenism increases the risk of spontaneous bleeding caused by rupture of esophagogastric varices, which is the most life-threatening complication of liver cirrhosis and is responsible for approximately 1/3 percent of total number of deaths in cirrhosis after hepatitis B. Acute esophageogastric varices bleeding is

associated with a mortality rate of approximately 25-30% [1]. Although clinical significant spontaneous bleeding does not occur until the platelet count is less than 10×10^9/L [21]. In order to prevent esophagogastric bleeding for liver cirrhosis patients, splenectomy and esophagogastric devascularization is performed for them. Institute of German Medical Association and the American Association of blood banks recommends prophylactic platelet transfusion in liver cirrhosis patients with preoperative platelet counts less than 50×10^9/L [11,12]. However the prophylactic platelet transfusion in patients with preoperative platelet count below 50×10^9/L remains controversial, some scholars believe, it is difficult to assess the role of platelet transfusion in clinical practice, because other potential factors can also cause bleeding during the operation (such as drugs, renal insufficiency, vWF) [30,31]. At present, the platelets are extremely rare blood products and at the same time many adverse effects are associated with platelet transfusion, such as fever, allergies, kidney failure, thrombosis and embolism [32]. In addition, recent studies have shown that, platelet transfusion may cause inflammatory and immune responses and may have negative effects on prognosis of malignant diseases [12].

To investigate the effects of preoperative platelet counts on blood loss for splenectomy and esophagogastric devascularization in hepatitis B associated cirrhosis patients with preoperative platelet counts less than 50×10^9/L, 105 patients were retrospectively divided into 3 groups based on their preoperative platelet counts: $<30 \times 10^9$/L (group 1), $30\text{-}50 \times 10^9$/L (group 2), $>50 \times 10^9$/L (group 3). Liver cirrhosis is often associated with thrombocytopenia, hypersplenism associated with splenomegaly, coagulation disorder and high risk of intraoperative bleeding. As per to reduce the intraoperative bleeding, treatment were given to patients with poor liver function in manner to improve the child-pugh score [33]. In the separation of perisplenic ligaments and blood vessels, careful action were taken for hemostasis to ensure clear vision. We compared three groups to find whether there were differences in operation time, intra-operative bleeding volume, postoperative platelet counts and postoperative hospital stays. Among three groups, group 1 suffered more blood loss than other two groups but the differences were not statistically significant. There were no statistically significant differences between three groups in terms of operation time, drainage volumes, operation associated complications and hospital stays. But, PLT counts increased significantly post splenectomy in all the three groups on comparison with preoperative PLT counts and came to its normal level on 3rd day. Follow-up data requires further investigation whether the platelet counts can be maintained at a normal level for a long time.

In summary, the retrospective study we performed has some limitations. Data are not complete and this limits the power of statistical calculations. Not all the patients characteristics initially planned at the beginning of the study could be addressed in the statistical analysis due to a lack of data. Lack of some evidence like portal venous pressure and number of collateral vessels may affect our study. However, despite these limitations we think that the results of this study can be useful.

The strong relationship between portal venous pressure and number of collateral vessels should be investigated further to explore the role of prophylactic platelet transfusion during intraoperative blood loss. But, we suggest that with sufficient preoperative preparation and careful operation, splenectomy and esophagogastric devascularization can be performed in hepatitis B associated cirrhosis in patients with PLT counts less than 50×10^9/L. Hence, it is not necessary to give prophylactic platelet transfusion until patient has any risk of bleeding,

as it does not bleed until the platelet count is less than 10×10^9/L or 20×10^9/L. But the safe level of platelet count remain uncertain in cirrhosis patients for platelet transfusion pre splenectomy.

Conclusion

According to our study we suggest that performing splenectomy and esophagogastric devascularization in hepatitis B cirrhosis patients with PLT count less than 50×10^9/L and 30×10^9/L, may improve the platelet counts postoperatively and it is not necessary to give prophylactic platelet transfusion until patient has any incidence of bleeding.

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