Effect of preoperative platelet count on liver resection for hepatocellular carcinoma

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Background

Hepatocellular carcinoma is a common cancer, and liver resection is one of the surgical choices for management, but it is associated with morbidity and mortality. Many methods are used as predictors for safety of operation. Preoperative platelet count may be used to evaluate outcomes of liver resection.

Patients and methods

This was a prospective study on 75 patients who were divided into two groups: group A included 25 patients with preoperative low platelet count ($<100\times10^3/mm^3$), and group B included 50 patients with normal preoperative platelet count ($\geq100\times10^3/mm^3$).

Results

In group A, the median postoperative ICU stay was 2 days, with a range of 1.0–12.0, and it was significantly longer than that of group B, which was 1 day, with a range of 1.0–14.0. There were no statistically significant differences between the two groups regarding operative and early postoperative outcomes.

Conclusion

Performing minor liver resection for patients with hepatocellular carcinoma with preoperative low platelet count ($<100\times10^3/mm^3$) in comparison with patients with normal preoperative platelet count ($\geq100\times10^3/mm^3$) is considered safe and is associated with the same operative and short-term postoperative outcomes, except for only increased postoperative ICU stay, with the same overall postoperative morbidity and mortality.

Keywords

hepatocellular carcinoma, liver resection, low platelet count

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Introduction

Hepatocellular carcinoma (HCC) is the fifth common malignancy and the second leading cause of cancer-related death worldwide [1]. Although HCC is a slow-growing tumor, it is usually rapidly fatal after clinical appearance; this is partly because of the asymptomatic nature of small HCCs. HCC cases are usually not discovered until the disease is far advanced. The disease often occurs in individuals with cirrhosis, a condition that increases risk when performing potentially curative surgical therapy [2]. There are a variety of treatment options for HCC, of which resection remains at the forefront, especially for patients with normal livers or well-compensated cirrhosis. In some areas, resection is the mainstay of surgical treatment because of limited organ availability for transplantation [3]. Careful patient selection with assessment of the tumor burden and residual liver function is 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 [4]. Despite dramatic improvements in diagnosis and treatment with improved surgical techniques and perioperative care over the past few decades, the prognosis of HCC is still poor, with an overall 5-year survival rate of ~5–6% [5]. Platelets, the levels of which normally range from 100 to $300\times10^9/l$ in adults, are involved in the inflammatory response by releasing several cytokines, such as platelet-derived growth factors and transforming growth factor-ß. Moreover, platelets are able to transport these substances to specific sites and play roles in angiogenesis, wound healing, and liver regeneration [6]. Low preoperative platelet count is independently associated with increased major complications, postoperative liver insufficiency, and mortality after resection for HCC, even when accounting for standard criteria, such as Child/MELD score and tumor extent, used to select patients for resection [3].

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Aim

The aim of this study was to evaluate the effect of preoperative platelet count on the operative and short-term postoperative outcomes of minor liver resection of HCC.

Patients and methods

This was a prospective study that was done on patients with HCC who underwent elective hepatic resection from January 2018 to December 2021 in the National Liver Institute of Menoufia University.

The study included 75 patients who were divided into two groups:

Group A included 25 patients who were subjected to hepatic resection with low preoperative platelet count (below $100\times10^3/mm^3$).

Group B included 50 patients who were subjected to hepatic resection with normal preoperative platelet count (above or equal $100\times10^3/mm^3$).

Inclusion criteria

Patients with Child A score, with confirmed diagnosis of HCC and scheduled for elective minor (two or less segments) hepatic resection, were included.

Exclusion criteria

Patients with major hepatic resection (resection of more than two segments according to Couinaud's classification), history of previous portal vein embolization or transarterial chemoembolization, Child B and C patients, MELD score above 10, presence of portal vein thrombosis, presence of ascites, and recurrent HCC after resection were the exclusion criteria.

Ethical consideration

A written informed consent was taken from every case before the operation after describing and explaining details of operation and postoperative follow-up and also describing complications of the procedure. Data security and patient's confidentiality were guaranteed.

Patients were subjected to the following.

Preoperative evaluation

Age, sex, history of previous abdominal surgery, clinical presentation, and comorbidities (diabetes mellitus, hypertension, and other comorbid risk factors) were taken.

Laboratory investigations: complete blood count especially platelet count, liver function tests [bilirubin, total proteins, albumin, prothrombin time and concentration, and international normalized ratio (INR)] and liver enzymes (aspartate aminotransferase and alanine aminotransferase), kidney function tests (urea and creatinine), viral markers [hepatitis C virus (HCV) and hepatitis B virus (HBV)], tumor markers (α-FP, CEA, and CA19.9), and Child and MELD classifications were recorded.

Imaging studies: abdominal ultrasonography, triphasic abdominal computed tomography (CT) to confirm the diagnosis of hepatic lesion and for its initial staging, chest radiograph for pulmonary metastasis, CT chest (if needed), dynamic MRI, and CT volumetry (if needed) were done.

Upper gastrointestinal endoscopy was done for assessment of esophageal varices.

In the era of coronavirus disease 2019 pandemic, a routine PCR for coronavirus disease 2019 and CT chest were added to preoperative preparation of all patients according to the updated protocol of evaluation.

Fitness for surgery was evaluated by the anesthesia team before operation.

Operative data

The operation was done under general anesthesia with endotracheal intubation. Both open and laparoscopic approaches were used for patients in our study. Regarding the type of resection, nonanatomical resection (wedge resection of part of liver including the mass) was the commonest type and left lateral resection was done in some cases. Intraoperative ultrasonography was done in some cases if needed to evaluate the presence of other lesions, to assess relation to major vasculature, and also to determine the safety margin of resection. Different techniques were used for parenchyma transection such as traditional technique, Harmonic scalpel, Cavitron ultrasonic surgical aspirator, Habib sealer, and bipolar diathermy. Other procedures were done in the same operation such as cholecystectomy owing to either presence of gall stones or tumor location, and ablation of another lesion by radiofrequency ablation. Insertion of one drain or more was done according to each case in dependent areas and cut surface of liver.

Blood loss was estimated after operation by evaluating suction and towels. Blood transfusion intraoperatively was evaluated including packed red blood cells (PRBCs), plasma, and platelets. Operative time was recorded in minutes.

Postoperative evaluation

All patients were admitted to the ICU for at least 24 h according to hemodynamic stability. ICU stay was estimated. They were managed by intravenous fluids, antibiotics, prophylactic dose of low-molecular-weight heparin, and analgesia. Blood transfusion on need was done, and enteral feeding was mostly instituted on the first postoperative day.

Follow-up of patients was according to hemodynamic criteria, including vital signs, urine output, drain(s) output, and blood or fresh frozen plasma transfusion. Postoperative laboratory data including, LFTs, PT and PC%, and complete blood count, were done on postoperative days 1, 3, and 5 and at the time of discharge. Abdominal ultrasound with Doppler study was done for intraperitoneal collection and portal vein thrombosis on postoperative days 1 and 3 and at the time of discharge. Hospital stay was recorded from the day of operation till the day of discharge. Drain was removed when the amount of the drain fluid was less than 50 ml/day, and it was clear fluid whether the patient was still hospitalized or discharged; if there was any bile tinge, then the drain was not removed.

Assessment of postoperative complications was done.

Major post-hepatectomy complications

Postoperative hemorrhage

The International Study Group of Liver Surgery defines post-hepatectomy hemorrhage as the presence of any one of follows: a postoperative drop in hemoglobin level of more than 3 g/dl compared with the postoperative baseline level, or any need for the postoperative transfusion of PRBC for a falling hemoglobin level, or the need for radiological intervention (such as embolization) and/or repeat laparotomy to stop bleeding. It is graded as grade A in consideration of transfusion of up to two units of PRBCs, grade B in transfusion of more than two units of PRBCs, and grade C when there is a need for invasive interventions such as embolization and/or repeat laparotomy [7].

Post-hepatectomy liver failure

Post-hepatectomy liver failure (PHLF) was diagnosed and graded (grades A, B, or C) according to the proposed definition by the International Study Group of Liver Surgery. In brief, PHLF was defined as an increased INR, the need for coagulation factors to maintain normal INR, and hyperbilirubinemia on or after postoperative day 5. Hyperbilirubinemia was defined as a serum bilirubin concentration greater than 1 mg/dl and increased INR was defined as an INR greater than 1.2. In patients with preoperative hyperbilirubinemia or increased INR, PHLF was defined as an increase in serum bilirubin levels or INR on or after postoperative day 5 [8].

Postoperative bile leak

The diagnosis of postoperative biliary leakage and grading according to the International Study Group of Liver Surgery were based on the findings of one or more of the following: drainage of bile from the abdominal wound or drain (a fluid bilirubin three times the serum bilirubin constitutes a bile leak) or intra-abdominal collection of bile confirmed at the time of percutaneous drainage or reoperation, or cholangiographic evidence of biliary leakage. Grade A bile leak does not affect clinical management, grade B requires a deviation in typical postoperative management such as a percutaneous drainage but does not require surgery, and grade C bile leaks require a return to the operating room [9].

Other complications

Ascites: regarding ascites, grade 1 ascites is mild and is only detectable by ultrasound examination, grade 2 ascites or moderate ascites is manifested by moderate symmetrical distension of the abdomen, and grade 3 ascites is large or gross ascites with marked abdominal distension [10]. Moreover, infected intraperitoneal collection, pleural effusion, chest infection, wound infection, cardiac complication, renal complication, and reoperation (assessment of cause of reoperation) were recorded.

Postoperative morbidity was defined as any other deviation from the normal postoperative course and was graded by the Clavien–Dindo classification. The score was based on the most severe postoperative complication experienced by each patient. Grades I and II morbidities were defined as minor and grades III and IV morbidities were defined as major [11] (Table 1).

Table 1 Classification of surgical complications graded by Clavien–Dindo classification [11]

Grades	Definition
I	Any deviation from the normal postoperative course without pharmacologic treatment or surgical, endoscopic, and radiological interventions
	Allowed therapeutic regimens are drugs such as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy
	This grade also includes wound infections opened at the bedside
II	Requiring pharmacologic treatment with drugs other than ones allowed for grade I complications. Blood transfusion and total parenteral nutrition are also included
III	Requiring surgical, endoscopic, or radiologic intervention
IIIa	Intervention not under general anesthesia
IIIb	Intervention under general anesthesia
IV	Life-threatening complication (including CNS complications) requiring IC/ICU management
IVa	Single organ dysfunction (including dialysis)
IVb	Multiorgan dysfunction
V	Death of a patient

CNS, central nervous system.

Postoperative mortality was defined as death within 90 days after liver resection. Follow-up of patients after discharge was done for 3 months, and follow-up visits in the outpatient clinic was once weekly in the first month and then monthly in the following 2 months.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package, version 20.0 (IBM Corp., Armonk, New York, USA). Categorical data were represented as numbers and percentages. χ^2 test was applied to investigate the association between the categorical variables. Alternatively, Fisher's exact or Monte-Carlo correction test was applied when more than 20% of the cells have expected count less than 5. For continuous data, they were tested for normality by the Shapiro–Wilk test. Quantitative data were expressed as range (minimum and maximum), mean, SD, and median. Student *t* test was used to compare two groups for normally distributed quantitative variables. On the contrary, Mann–Whitney test was used to compare two groups for not normally distributed quantitative variables. Significance of the obtained results was judged at the 5% level.

Results

The study included 75 patients who underwent liver resection for HCC. They were divided into two groups: group A included 25 patients with preoperative low platelet count ($<100\times10^3/mm^3$), and group B included 50 patients with normal preoperative platelet count ($\geq100\times10^3/mm^3$). The demographic data of the study showed a significantly increased number of males in group B (Table 2). There was no statistically significant difference between both groups regarding the presence of liver cirrhosis and HBV status, but group A showed a statistically significant increase in the number of HCV-positive patients (Table 2). No statistically significant difference was noted between both groups regarding the presence of comorbidities (Table 2). In group A, esophageal varices were present in 13 (52%) patients, and it was significantly more than in group B, which included 14 (28%) patients

Table 2 Comparison between the two studied groups according to demographic data and patients' characteristics

	Group A (*N*=25) [*n* (%)]	Group B (*N*=50) [*n* (%)]	Test of significance	*P*
Sex				
Male	15 (60)	44 (88)	χ^2=7.786*	0.005*
Female	10 (40)	6 (12)		
Age (years)				
Minimum–maximum	45–79	23–73	*t*=0.804	0.424
Mean±SD	57.28±7.07	58.88±8.59		
Cirrhosis	25 (100)	48 (96)	χ^2=1.027	^{FE}P=0.550
HCV	25 (100)	42 (84)	χ^2=4.478*	^{FE}P=0.046*
HBV	0	4 (8)	χ^2=2.113	^{FE}P=0.294
Diabetes mellitus	4 (16)	12 (24)	χ^2=0.636	0.425
Hypertension	9 (36)	15 (30)	χ^2=0.276	0.600
Chest comorbidities	1 (4)	3 (6)	χ^2=0.132	^{FE}P=1.000
Cardiac comorbidities	0	1 (2)	χ^2=0.507	^{FE}P=1.000
Esophageal varices	13 (52)	14 (28)	χ^2=4.167*	0.041*
Spleen status				
Normal	7 (28)	28 (56)	χ^2=7.427*	^{MC}P=0.021*
Enlargement	17 (68)	17 (34)		
Removed	1 (4)	5 (10)		
Tumor number				
One	25 (100)	45 (90)	χ^2=2.679	^{FE}P=0.162
Two	0	5 (10)		
Tumor site				
Right	8 (32)	27 (54)	χ^2=3.990	^{MC}P=0.103
Left	17 (68)	22 (44)		
Bilobar	0	1 (2)		
Tumor size				
<5 cm	15 (60)	25 (50)	χ^2=0.670	0.413
≥5 cm	10 (40)	25 (50)		

χ^2, χ^2 test; FE, Fisher exact; HBV, hepatitis B virus; HCV, hepatitis C virus; MC, Monte-Carlo; *t*, Student *t* test.
Group A: low platelet count.
Group B: normal platelet count.
P: *P* value for comparing between the two studied groups.
*Statistically significant at *P* value less than or equal to 0.05.

with esophageal varices. The splenic status showed that there is significant presence of splenic enlargement in group A (Table 2). There was no difference between the two groups regarding tumor characteristics (Table 2). Preoperative laboratory investigations showed a statistically significant difference between the two groups regarding hemoglobin, albumin, bilirubin, INR, and course platelet count (Table 3). There was no statistically significant difference between both groups regarding operative data (Table 4). In group A, the median postoperative ICU stay was 2 days, with a range of 1.0–12.0, and it was significantly longer than that of group B, which was 1 day, with a range of 1.0–14.0, with *P* value less than 0.05. Regarding postoperative hospital stay, no statistically significant difference was noted between the two groups (Table 5). There was no statistically significant difference between both groups regarding postoperative major complications (hemorrhage, liver failure, and bile leak) (Table 5). No statistically significant difference between both groups regarding other complications such as ascites, chest infection, pleural effusion, wound infection, cardiac complications, renal complication, and reoperation (Table 5). Regarding postoperative mortality, there was no statistically significant difference between two groups (Table 5). Regarding overall morbidity according to Clavien–Dindo classification, there was no statistically significant difference between the two groups (Table 6).

Discussion

HCC is the fifth most common cancer. HCC is frequently secondary to infections with hepatitis viruses, such as HBV or HCV, and alcohol use and obesity are also risk factors for HCC [12].

Liver resection is one of the preferred therapeutic options for patients with HCC. Liver resection is still associated with postoperative morbidity and mortality,

Table 3 Comparison between the two studied groups according to preoperative laboratory investigations

	Group A (*N*=25)	Group B (*N*=50)	Test of significance	*P*
Bilirubin (mg/dl)				
Mean±SD	0.85 ± 0.33	0.67 ± 0.31	*U*=398.50*	0.011*
Median (minimum–maximum)	0.8 (0.1–1.5)	0.6 (0.18–1.4)		
ALB (g/dl)				
Mean±SD	3.86 ± 0.31	4.21 ± 0.42	*t*=3.761*	<0.001*
Median (minimum–maximum)	3.9 (3.4–4.5)	4.15 (3.6–5.3)		
INR				
Mean±SD	1.18 ± 0.09	1.11 ± 0.10	*t*=2.713*	0.008*
Median (minimum–maximum)	1.2 (1.0–1.4)	1.1 (0.9–1.39)		
Creatinine (mg/dl)				
Mean±SD	0.79 ± 0.16	0.85 ± 0.21	*t*=1.362	0.177
Median (minimum–maximum)	0.80 (0.56–1.20)	0.83 (0.33–1.26)		
Hb (g/dl)				
Mean±SD	13.03 ± 1.33	13.94 ± 1.47	*t*=2.601*	0.011*
Median (minimum–maximum)	13.0 (10.6–16.0)	14.35 (10.7–16.5)		
PLT ($\times 10^3/mm^3$)				
Mean±SD	75.36 ± 15.04	198.4 ± 81.48	*U*=0.0*	<0.001*
Median (minimum–maximum)	74 (44–98)	185.5 (110–586)		
ALT				
Mean±SD	46.96 ± 26.88	40.52 ± 26.68	*U*=503.50	0.172
Median (minimum–maximum)	40 (9–115)	33 (11–131)		
AST				
Mean±SD	53.44 ± 30.41	46.36 ± 21.20	*U*=578.50	0.601
Median (IQR)	48 (10–121)	41.5 (13–102)		
AFP (ng/ml)				
Mean±SD	125.9 ± 260	71.67 ± 173	*U*=489.50	0.128
Median (IQR)	24 (2.5–1210)	16 (1.6–1100)		
AFP stratification				
<200	21 (84)	47 (94)	χ^2=1.970	^{FE}P=0.213
>200	4 (16)	3 (6)		

χ^2, χ^2 test; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FE, Fisher Exact; Hb, hemoglobin; INR, international normalized ratio; IQR, interquartile range; PLT, platelet; *t*, Student *t* test; *U*, Mann–Whitney test.
Group A: low platelet count.
Group B: normal platelet count.
P: *P* value for comparing between the two studied groups
*Statistically significant at *P* value less than or equal to 0.05.

Table 4 Comparison between the two studied groups according to operative data

Operative data	Group A (*N*=25)	Group B (*N*=50)	Test of significance	*P*
Type of operation				
Open	17 (68)	41 (82)	χ^2=2.624	^{MC}P=0.232
Laparoscopic	6 (24)	8 (16)		
Laparoscopic converted to open	2 (8)	1 (2)		
Type of resection				
Non anatomical	21 (84)	42 (84)	χ^2=0.00	^{FE}P=1.000
Left lateral resection	4 (16)	8 (16)		
Associated procedures				
No	22 (88)	39 (78)	χ^2=1.120	^{MC}P=0.573
Cholecystectomy	3 (12)	9 (18)		
Radiofrequency ablation	0	2 (4)		
Blood loss (ml)				
Mean±SD	424±301	378±211	*U*=602.0	0.794
Median (minimum–maximum)	300 (200–1500)	325 (150–1200)		
Blood transfusion				
No	22 (88)	46 (92)	χ^2=0.889	^{MC}P=1.000
≤2 units PRBCs	2 (8)	3 (6)		
>2 units PRBCs	1 (4)	1 (2)		
Plasma transfusion	3 (12)	4 (8)	χ^2=0.315	^{FE}P=0.680
Platelet transfusion	2 (8)	1 (2)	χ^2=1.563	^{FE}P=0.256
Operative complication (bleeding)	3 (12)	4 (8)	χ^2=0.315	^{FE}P=0.680
Operative time (min)				
Mean±SD	228±80.42	199±66.90	*U*=484.50	0.114
Median (minimum–maximum)	200 (150–440)	180 (90–420)		

χ^2, χ^2 test; FE, Fisher exact; MC, Monte-Carlo; PRBC, packed red blood cell; *U*, Mann–Whitney test.
Group A: low platelet count.
Group B: normal platelet count.
P: *P* value for comparing between the two studied groups.

especially in patients with underlying chronic liver disease. PHLF, a primary cause of hepatectomy-related mortality, is caused by small reserved liver function. It is essential to evaluate appropriately reserved liver function in patients before liver resection [13].

There are several diagnostic tests available to assess reserved liver function in patients undergoing liver resection, including conventional blood examinations such as serum bilirubin concentration, serum albumin concentration, platelet count, and indocyanine green as well as scoring systems such as Child–Pugh classification [14].

Platelets are best known for their role in hemostasis because their major function is the formation of blood clots in the case of a vessel wall injury [15]. A low platelet count serves as a noninvasive indicator of portal hypertension. The value of a low preoperative platelet count to predict perioperative outcomes is not well defined in patients undergoing resection for HCC [3].

Our study was done to evaluate the effect of preoperative platelet count on the operative and early postoperative outcomes of minor liver resection for patients with HCC. It included 75 patients who underwent elective minor liver resection for HCC. Patients were divided into two groups: group A included 25 patients with low preoperative platelet count ($<100\times10^3/mm^3$), and group B included 50 patients with normal preoperative platelet count ($\geq100\times10^3/mm^3$).

All patients in group A had liver cirrhosis, and also all of them were positive for HCV and negative for HBV. In group B, liver cirrhosis was present in 48 (96%) patients, and of patients had who liver cirrhosis, 42 (84%) patients were positive and eight (16%) patients were negative for HCV. Moreover, four (8%) patients were positive and 46 (92%) were negative for HBV. There was a statistically significant increase in group A more than group B regarding HCV, and this showed that the most common cause of HCC in our study was HCV-related liver cirrhosis.

The significant increased number of patients with esophageal varices and splenic enlargement in group A than group B was an indicator for the presence of portal hypertension and hypersplenism, and it caused the low platelet count in patients of the group. These results go in parallel with the study done by Maithel *et al.* [3], which concluded that thrombocytopenia is a

Table 5 Comparison between the two studied groups according to postoperative hospital, ICU stay, and complications

	Group A (*N*=25) [*n* (%)]	Group B (*N*=50) [*n* (%)]	Test of significance	*P*
ICU stay (day)				
Mean±SD	2.84±2.43	1.70±1.99	*U*=370.50*	0.001*
Median (minimum–maximum)	2 (1–12)	1 (1–14)		
Hospital stay (day)				
Mean±SD	6.12±2.24	5.30±1.97	*U*=472.00	0.080
Median (minimum–maximum)	6 (3–12)	5 (3–14)		
Hemorrhage				
No	23 (92)	50 (100)		
Grade A	0	0	χ^2=3.809	^{MC}P=0.113
Grade B	1 (4)	0		
Grade C	1 (4)	0		
Liver insufficiency				
No	22 (88)	45 (90)		
Grade A	1 (4)	4 (8)	χ^2=2.738	^{MC}P=0.594
Grade B	1 (4)	0		
Grade C	1 (4)	1 (2)		
Ascites				
No	22 (88)	43 (86)	χ^2=2.253	^{MC}P=0.407
Grade A	2 (8)	7 (14)		
Grade B	1 (4)	0		
Chest infection	6 (24)	7 (14)	χ^2=1.163	^{FE}P=0.338
Pleural effusion	4 (16)	4 (8)	χ^2=1.119	^{FE}P=0.429
Wound infection	1 (4)	3 (6)	χ^2=0.132	^{FE}P=1.000
Reoperation	1 (4)	0	χ^2=2.027	^{FE}P=0.333
Cardiac complication	1 (4)	1 (2)	χ^2=0.257	^{FE}P=1.000
Renal complication	1 (4)	1 (2)	χ^2=0.257	^{FE}P=1.000
Mortality	1 (4)	1 (2)	χ^2=0.257	^{FE}P=1.000

χ^2, χ^2 test; FE, Fisher exact; MC, Monte-Carlo; *U*, Mann–Whitney test.
Group A: low platelet count.
Group B: normal platelet count.
P: *P* value for comparing between the two studied groups.

Table 6 Comparison between the two studied groups according to overall morbidity (Clavien–Dindo)

Morbidity (Clavien–Dindo)	Group A (*N*=25) [*n* (%)]	Group B (*N*=50) [*n* (%)[	χ^2	^{MC}P
No	14 (56.0)	33 (66.0)		
Grade I	8 (32.0)	13 (26.0)		
Grade II	1 (4.0)	3 (6.0)		
Grade IIIa	0	0	3.107	0.568
Grade IIIb	1 (4.0)	0		
Grade Iva	0	0		
Grade IVb	0	0		
Grade V	1 (4.0)	1 (2.0)		

χ^2, χ^2 test; MC, Monte-Carlo.
Group A: low platelet count.
Group B: normal platelet count.
P: *P* value for comparing between the two studied groups.

good surrogate for the presence of portal hypertension, and in patients with HCC, the etiology of low platelet count was owing to hypersplenism, which was induced by portal hypertension, causing increased platelet sequestration.

Regarding tumor characteristics (number, site, and size of vascular invasion), no statistically significant difference was noted between the two groups.

The preoperative laboratory investigation showed a statistically significant difference between both groups in some values, and of course, the mean value of platelet count was decreased in group A than group B, as it is the subject of our study. Group B showed better values of hemoglobin, bilirubin, albumin, and INR, which reflected better liver condition, but still values were in normal ranges as all patients of both groups in our study were Child A, and these differences did not reflect any clinically significant difference in the outcomes of our study. The other preoperative laboratory investigations did not show any statistically significant difference between the two groups.

Regarding the operative data of our study, nonanatomical resection was the dominant type of resection in both groups, and left lateral resection was done in the rest of patients in our study. Radiofrequency ablation was done intraoperatively for two (4%) patients in group B owing to the presence of another small lesion not in the area of planned resection. Intraoperative transfusion of PRBCs, fresh frozen plasma, and platelets was only done when indicated owing to occurrence of bleeding with restrictions to avoid any unnecessary transfusions. The evaluation of operative data showed that there was no statistically significant difference between both groups of our study in all intraoperative parameters that were recorded, so the presence of preoperative low platelet count in patients in group A did not affect the feasibility and did not add any difficulties to minor liver resection operations in comparison with patients in group B with normal preoperative platelet count.

The overall postoperative hospital stay was comparable in both groups with no statistically significant difference. The long hospital stay in some patients in either group was owing to the presence of postoperative complications, which indicated hospital management and close follow-up. The postoperative ICU stay was significantly longer in group A than group B as the median ICU stay in group A was 2 days, with a range of 1.0–12.0, whereas in group B, the median was 1 day, with a range of 1.0–14.0.

Regarding postoperative major complications, postoperative hemorrhage occurred in two patients in group A. Grade B hemorrhage occurred in one (4%) patient, diagnosed by blood in drain and hemoglobin drop, but the patient was still stable hemodynamically. This patient was managed conservatively with blood transfusion and the hemorrhage was controlled, but the patient developed ascites and postoperative liver failure that did not respond to treatment, ending with patient death in the ICU. The other patient (4%) had grade C hemorrhage. As this patient was hemodynamically unstable with postoperative blood in drains and serum hemoglobin drop in spite of resuscitation and blood transfusion, the patient was explored on the same day of operation and the bleeding was controlled intraoperatively. This patient also developed grade B liver insufficiency and was managed medically, with improved follow-up parameters, and the patient was discharged from the hospital. No postoperative hemorrhage occurred in any patient in group B. These results showed that there was no statistically significant difference between both groups according to postoperative hemorrhage.

Bile leak did not occur in any patients of both groups in our study. This was owing to the type of liver resection as minor liver resections are usually not associated with dissection of porta hepatis and the incidence of major duct injury in minor liver resection is minimal.

In our study, PHLF occurred as follows: in group A, one (4%) patient developed grade A, and the same number had grades B and C. The patient with grade C died in the ICU, and the other two patients improved with medical treatment. In group B, PHLF grade A developed in four (8%) patients; all of them improved on medical treatment. Grade C PHLF developed in one patient who died in the ICU. There was no statistically significant difference between the two groups, and there was no effect of low preoperative platelet count regarding incidence of occurrence of PHLF according to our study results. This goes in parallel with the results of a study done by El Hajji *et al.* [16] on 571 patients, which found that preoperative thrombocytopenia in patients with HCC who were subjected to partial hepatectomy is not a predictor for PHLF. However, Meyer *et al.* [17], in a systematic review and meta-analysis study, found that preoperative thrombocytopenia lower than $150\times10^3/mm^3$ constitutes a risk factor for PHLF, especially in cirrhotic patients. Moreover, our results are not in parallel with a study done by Tomimaru *et al.* [13] on 277 patients, which found that patients with low preoperative platelet count ($<150\times10^3/mm^3$) showed a higher incidence of PHLF than those with platelet count more than or equal to $150\times10^3/mm^3$.

In our study, postoperative ascites grade A occurred in two (8%) patients in group A and in seven (14%) patients in group B, and grade B occurred in only one (4%) patient in group A; these patients were managed by medical treatment. There was no statistically significant difference between the two groups, and there was no effect of low preoperative platelet count regarding incidence of development of postoperative ascites according to our study results. However, the study done by Ishizawa *et al.* [18] concluded that there was an increased incidence of development of large volume ascites in patients with preoperative platelet count less than $100\times10^3/mm^3$ after liver resection.

The incidences of development of other postoperative complications such as chest infection, pleural effusion, wound infection, cardiac complications (in the form of arrhythmia and hypotension), and renal impairment were comparable in both groups, with no statistically significant difference between two groups and no effect of low preoperative platelet count.

Reoperation was indicated in only one patient in our study from group A, and it was explored owing to the presence of postoperative hemorrhage and occurrence of hemoglobin drop, with no statistically significant difference between two groups.

Postoperative mortality occurred in one (4%) patient in group A, and it occurred on postoperative day 12. This patient experienced PHLF and developed renal impairment with no improvement on management. However, in group B, it occurred in one (2%) patient and it occurred on postoperative day 14. This patient developed PHLF, renal impairment, and unexplained hypotension, with no response to medical management. There was no statistically significant difference between the two groups regarding postoperative mortality. However, a study done by Taketomi *et al.* [19] on 213 patients in the period from 1997 to 2002 showed that patients who died during postoperative hospital stay had a low preoperative platelet count. Another study done by Kaneko *et al.* [20] on 198 patients who were subjected to liver resection for HCC concluded that low preoperative platelet count ($\leq 100 \times 10^3/mm^3$) was the strongest independent factor for postoperative mortality.

Regarding overall morbidity according to the Clavien–Dindo classification, there was no statistically significant difference between the two groups and no effect of low preoperative platelet count. However, a study done by Maithel *et al.* [3] concluded that low preoperative platelet count is independently associated with increased incidence of postoperative major complications and mortality after liver resection for HCC. Another study done by Taketomi *et al.* [19] concluded that a low preoperative platelet count was an independent risk factor for postoperative complications and might be a predictor for liver failure in patients with HCC undergoing liver resection. Moreover, the study done by Kaneko *et al.* [20] found that preoperative platelet count independently affects morbidity and mortality after liver resection.

The variability of results in studies are owing to the different parameters of each study as some of these included all types of liver resections (minor and major), also the different periods of performing liver resection as more advancement in techniques of liver resection occurred in recent time, and another factor is the cutoff of the definition of low platelet count, which is not fixed, as some studies considered it below $150 \times 10^3/mm^3$ and another studied consider it below $100 \times 10^3/mm^3$. The good results of our study in comparison with others were owing to selection of only patients with minor liver resection, and Child A patients, and another important factor is doing all cases in highly specialized center in hepatobiliary surgery, which improved the outcomes of liver resection operations.

Conclusion

Performing minor liver resection for patients with HCC with preoperative low platelet count ($<100 \times 10^3/mm^3$) in comparison with patients with normal preoperative platelet count ($\geq 100 \times 10^3/mm^3$) is considered safe and associated with the same operative and short-term postoperative outcomes, except for only increased postoperative ICU stay, with the same overall postoperative morbidity and mortality.

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Conflicts of interest

No conflict of interest.

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