ISSN 2618-1584 Vol. 1, Issue 4: 35-43, DOI: 10.25236/FMSR.2019.010406

Recovery of platelet count in patients with liver primary carcinoma after hepatectomy and its clinical significance

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ABSTRACT. Objective: *To analyze platelet count after resection of liver primary carcinoma and its clinical significance. Methods: This study is a retrospective analysis of the clinical data of 128 patients with liver primary carcinoma who underwent hepatectomy in the Department of Hepatobiliary Surgery, Medical School the First Affiliated Hospital of School of Medicine, Shihezi University from August 20 to August 2019.According to platelet count levels (PLT), the patients were grouped on the first day after surgery, platelet counts <100×109/L were divided into low platelet groups, normal groups at 100-300×109/L, and correlation between platelet count and postoperative liver failure was analyzed for a diagnostic value. Results: Among the 128 patients, 35 of them were grouped as with low platelet counts on the first day after surgery, and the other 93 patients were normal. There were 20 cases of liver failure within six months after the patient underwent surgery.In the single factor analysis of liver failure, the age of liver failure group, the PLT value one day after surgery and the preoperative liver function B grade were higher than the non-hepatic failure group, the difference was statistically significant (P>0.05); In the multivariate analysis, both the PLT count on the first postoperative day and the preoperative liver function grading are independent risk factors for the complications of hepatic failure after hepatectomy. The PLT count on the first day after surgery has a good predictive value for hepatic failure after liver carcenoma complications. The ROC curve was drawn. When the Jordan count was 0.431, the sensitivity and specificity were 0.60 and 0.83 respectively. The area AUC=0.753 (0.651 to 0.854). Conclusion: Age and postoperative PLT count and preoperative liver function were important pathogenic factors for liver failure after hepatectomy. Platelet count has diagnostic value for predicting liver failure after resection of primary liver carcinoma.*

KEYWORDS: *Primary liver carcinoma; Platelet count Clinical significance Diagnostic value*

Liver malignant tumors risk patients' life and harm their bodily functions,

ISSN 2618-1584 Vol. 1, Issue 4: 35-43, DOI: 10.25236/FMSR.2019.010406

especially primary malignant ones with high morbidity and harm, and the pathogenesis is still unclear. Liver carcinoma is a common malignant tumor in clinics. At present, the most effective treatment for this disease is radical resection, but some patients may suffer other complications after surgery, including liver failure (PHLF), the most serious complication [1-2]. Among various treatment methods of liver carcinoma, hepatectomy is the first choice in early treatment, and the treatment effect is more significant. The main cause of liver failure after hepatectomy is due to insufficient liver reserve and the basis of cirrhosis. In general, there is a significant regeneration 2 weeks after liver resection, which is to be completed within three months and accompanied by apoptosis of hepatocytes during regeneration. According to relevant data, platelet (PLT) plays an important role in liver regeneration, and low platelet count level will have a certain restriction on hepatocyte regeneration [3]. Based on this, this paper mainly investigates 128 patients with primary liver carcinoma and analyzes the correlation between platelet count and liver failure. The specific clinical data is reported as follows.

1. General information and Methods

1.1 General Information

In this study, we will retrospectively analyze the clinical data of 128 patients with primary liver carcinoma who underwent hepatectomy in our hospital from August 20 to August 2019, including 61 males and 67 females, ageing from 47 to 75, the average was (65.27±1.42), and there was no statistically significant difference in gender and age. On the first day after the surgery, those with platelet count less than 100×109/L were divided into low platelet group, and those from 100×109/L to 300×109/L were divided into normal group. Criteria: (1) Those diagnosed as with primary liver carcinoma by clinical pathology; (2) The follow-up has complete case data; (3) Patients are enrolled in the study volunteered and had good compliance, and they have signed informed consent for the study. Exclusion criteria: (1) Patients with secondary liver carcinoma or other malignant tumors; (2) Those with severe heart and brain diseases and endocrine diseases and with a survival period of less than 3 months; (3) Patients with poor compliance and unwilling to be involved in the research; (4) Those with incomplete clinical data. The study was in compliance with ethical standards and was approved by the Ethics Committee of the First Affiliated Hospital of School of Medicine,Shihezi University.

1.2 Methods

Relevant medical staff first checked the platelet count and liver function indicators of the two groups of patients. The specific checking of platelets is as follows: All patients were enrolled in the venous blood collection. One day before the and after the surgery, the patients were subjected to fasting for venous blood collection of 1.8 mL to 2.0 mL, 0.2 ml of 109 mmol/L(sodium citrate for anticoagulating), and the blood samples were centrifuged for 10 minutes at 3000

ISSN 2618-1584 Vol. 1, Issue 4: 35-43, DOI: 10.25236/FMSR.2019.010406

rpm, then analyzed for serum and finally stored at -70 ℃. Relevant medical personnel were to operate a Mindray-6800 automatic blood analyzer to assay for platelet counts in blood samples. The specific test contents of liver function are as follows: Fasting venous blood samplings were collected on the 1st day before the surgery and on the 1st, 3rd, 5th, 7th, and 14th day after the surgery, followed by PUZS 300A/ X automatic biochemical analyzer for the analysis of aspartate aminotransferase (AST), serum alanine aminotransferase (ALT) and serum total bilirubin (TBiL) in blood samples. Meanwhile, CP The -2000 blood coagulation instrument is used to measure prothrombin time (PT) on blood samples.

1.3 Observation indicators

Platelet counts and incidences of liver failure were observed in both groups. The normal range of platelet counts is from 100 x 109/L to 300 x 109/L. Platelet count abnormalities are those above 300×109/L and below 100×109/L. The liver failure in two groups of patients was observed and recorded, and the standard of liver failure was judged by reference to the delayed standard of liver function recovery [4]. That is, prothrombin time exceeds 20s within 5 days after surgery, or serum total bilirubin exceeds 50umol/L.

1.4 Statistical processing

The data measured and statistically analyzed in this study were calculated using SPSS20.0 statistical software. The measurement data consistent with the normal distribution is subjected to the T test, the non-normal distribution to the Mann-Whitney U test, and the counting data uses the chi-square test. Prognosis-related parameters are analyzed by univariate and multivariate logistic regression models. $P < 0.05$ indicates that the difference is statistically significant.

2. Results

2.1 Basic information were analyzed on preoperative subjects

According to the collection of 128 patients who were admitted to the hospital for the first time to improve the blood platelet count, the two groups were not statistically significant in gender, and there was no significant difference in male and female ages. (P>0.05)

Table 1 General information of the subjects before hospitalization

Grouping	Number of cases	Low platelet group	Normal platelet group	Age (x±s)
gender Male n (%	61	5(8.20)	56(91.80)	66.76±1.61

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		5 (8.20)	56 (91.80)	66.76±1.61
Female n (%	67	4(6.00) 4 (6.00)	63(94.00) 63 (94.00)	63.61±8.95 63.61±8.95
Z value	0.85			15.67
P value	0.43			0.96 0.96

2.2 Platelets and liver function indicators

Among the 128 patients, 9 of them were judged as suffering from low platelets before surgery, and all of them received normal symptomatic support for ascending platelets to the normal value. The platelet counts of 128 patients with primary liver cancer were analyzed on the first day after resection, and 35 cases (27.34%) were counted as low platelet ones, and 93 cases (72.66%) were judged as normal platelet ones. In the six months after the patient was followed up for surgery, 20 patients developed liver failure (15.63%). (See Table 2)

2.3 Single factor analysis of liver failure

According to Table 2, in the single factor analysis of liver failure, there were no significant differences between the two groups in terms of gender, time of blocking blood flow into the liver, preoperative ALT, AST, and TBiL (P>0.05).). The age of the liver failure group, the PLT value on the first day after surgery, and the preoperative liver function B grade were higher than those in the non-hepatic failure group, the difference was statistically significant (P>0.05).

Table 2 Single factor analysis of liver failure after hepatectomy

project		Number of cases	Liver failure group (n=20)	Non-hepatic failure group (n=108)	*t/x2*	P
gender	male	61	11(18.03) 11 (18.03)	50(81.97) 50 (81.97)	0.663	0.416
	female	67	9(13.43) 9 (13.43)	58(86.56) 58 (86.56)		
age	≤50 years old	93	2(2.15) 2 (2.15)	91(97.85) 91 (97.85)	18.533	＜ 0.001 <0.001
	>50 years old	35	18(51.43) 18 (51.43)	17(48.57) 17 (48.57)		
1 days after surgery	$\geq 100\times10^9$/L ≥100×109/L	35	12(34.28) 12 (34.28)	23(65.72) 23 (65.72)	12.724	＜ 0.001 <0.001
	＜ 100×10^9/L <100×109/L	93	8(8.60) 8 (8.60)	85(91.40) 85 (91.40)		

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Preoperative liver function grading	A 级 Class A	89	13(14.60) 13(14.60)	76(85.40) 76 (85.40)	10.273	0.001
	B 级 Class B	39	7(17.94) 7 (17.94)	32(82.06) 32 (82.06)		
Hepatic blood flow blocking time			13.15±3.65 13.15±3.65	12.42±6.31 12.42±6.31	3.523	0.741
Preoperative ALT (U/L)			58.15±5.62 58.15±5.62	57.15±2.65 57.15±2.65	2.654	0.815
Preoperative AST (U/L)			62.15±4.26 62.15±4.26	61.75±3.15 61.75±3.15	3.256	0.764
Preoperative TBiL (umol/L)			15.42±3.01 15.42±3.01	14.25±3.87 14.25±3.87	4.256	0.912

2.4 Multifactor analysis of liver failure

According to Table 3, logistic regression analysis runs on multiple factors which is derived of statistical significance in the single factor analysis (age, preoperative liver function grading, and postoperative first day PLT values). Hepatic failure occurred as an independent variable, with age (≤50 years = 0, >50 years = 1), and postoperative day 1 PLT count (100 ×109 / L ~ 300 ×109 / L = 0, <100×109/L=1) and preoperative liver function grading (A grade=0, B grade=1) were used as dependent variables and assigned at the same time. Logistic regression model analysis showed that age, 1st-day postoperative PLT count and preoperative liver function Grade B were independent risk factors for liver failure after hepatectomy. **Error! Hyperlink reference not valid.**

Table 3 Logistic regression analysis of liver failure after hepatectomy

Risk factor	B	SE	Waldx^2	P	OR(95%CI)
Age	1.135	0.417	8.615	0.002	2.687 (0.978 ~ 3.405)
PLT value 1 day after surgery	3.265	0.769	7.425	0.012	4.185 (2.358~8.541)
Preoperative liver function grading	1.425	0.425	6.125	0.001	3.256 (1.562~4.615)

2.5 Diagnostic value of postoperative platelet count changes for liver failure

Univariate and multivariate analysis of prognostic indicators in patients with primary liver cancer resection singles out PLT count on the first postoperative day as an independent risk factor for predicting complications of liver failure. The PLT count on the first day after surgery had a significant predictive value for the occurrence of hepatic failure after resection. The ROC curve was drawn. When the

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Yoden count was 0.431, the sensitivity and specificity were 0.60 and 0.83, respectively. AUC = 0.753 (0.651 to 0.854) (Fig. 1).

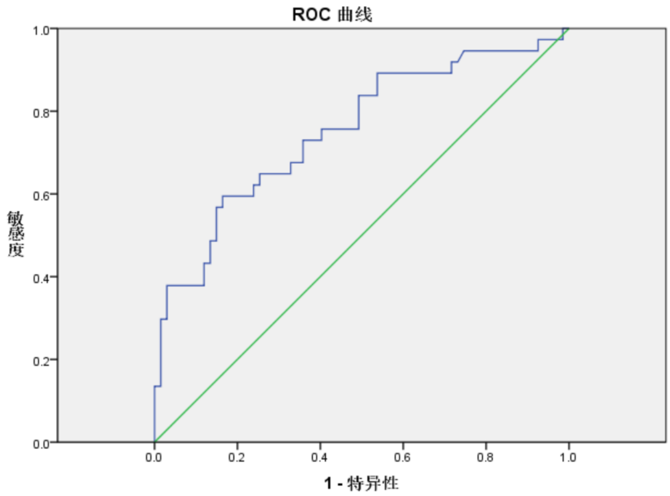

Figure.1 Postoperative platelet counts are applied to diagnose the area under the ROC curve for liver failure.

3. Discussion

Primary liver carcinoma is a very common malignant disease in China, with rapid progress and high incidence in the southeast coastal areas. The median level of liver cancer patients in China is 40 to 50 years old, and there are relatively more male patients.The etiology and pathogenesis of primary liver carcinoma are not yet clear. In recent years, with the early diagnosis and early treatment of primary liver carcinoma, the overall therapeutic effect has been significantly improved. In the treatment of primary liver carcinoma, different treatment plans for different stages of conditions is an important approach to improve the clinical treatment effect. Its major treatment methods include surgery, transcatheter arterial chemoembolization, hepatic artery ligation, radiofrequency, laser, chemotherapy and radiation therapy. In biological therapy, traditional Chinese medicine is also widely applied, while surgical treatment is the preferred treatment and also the most effective one. Normal liver cells in the human body have strong regenerative capacity. However, if accompanied by cirrhosis, the ability to regenerate will be hindrinced. Unfortunately, most patients with liver carcinoma are accompanied by a certain degree of cirrhosis, and the preferred treatment for hepatocellular carcinoma is hepatectomy. The recovery of liver function in patients after surgery depends mainly on the remaining liver cells. Studies have shown that PLT may play an important role in liver pathophysiology by controlling hepatocyte growth factor (HGF) for regeneration, and if the PLT is <100×10^9/L, the remnant liver will suffer obstruction, which in turn leads to liver failure [3-4].

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The formation of platelet count is mainly dependent on macrophages in bone marrow hematopoietic tissue, which can play a role in hemostasis and blood coagulation, and they also have a significant impact on the formation of blood clots and hemostasis effects [3]. In patients with primary liver carcinoma after liver resection, the remaining hepatocyte regeneration affects the recovery of liver function, and restoring liver function in time is a key factor in preventing liver failure [5] .Platelet count has a positive effect on hepatocyte regeneration ability, and it has an important influence on the recovery of liver function in postoperative patients.Therefore, strengthening postoperative platelet count management in patients with primary liver cancer is beneficial to improve long-term prognosis. There are current studies on the risk of postoperative platelet techniques and complications after hepatectomy in patients with primary liver carcinoma. Deng Liping pointed out that [6] when the patient's platelet count was less than 100 × 109 / L before liver resection, the patient's delayed liver function recovery and the risk of hepatic ascites increased significantly [6].Cheng Houpi's study [7] showed that postoperative low platelet count can be used as one of the independent risk factors affecting the prognosis of patients after hepatectomy. After liver resection, nearly 34.00% of patients had platelet count less than 100× 109/L, and compared with the patients with normal postoperative platelet count, the liver function indexes AST, ALT and TBil levels were significantly increased [7].There are also studies[8] say that the follow-up of patients with platelet counts less than 100*109 / L after hepatectomy showed a more than three-fold increase in the risk of delayed liver function recovery.Therefore, abnormal platelet parameters in patients with primary liver cancer resection have certain clinical significance for monitoring the severity of liver damage and pre-empting bleeding tendency [9,10].

After liver resection in patients with primary liver carcinoma, the patient's platelet count remains at a normal level, which is beneficial to shorten the recovery time of liver function in patients. After the surgery, sufficient platelets can play a certain role in liver function cell protection and can improve patient prognosis and prolong survival time. Hepatectomy may cause complications such as portal hypertension and liver failure. Among them, the rate of liver failure is higher, and it accounts for 23% to 76% of the cause of death after hepatectomy and poses serious threat to the patient's life [11]. Based on this, research on liver regeneration and effective intervention strategies for liver failure after partial hepatectomy is a hot topic in liver surgery. Deng Xiangping [1] and others reported that 5 days after hepatectomy, the time of thromboplastin exceeded 20s, serum bilirubin exceeded 50umol / L. The two factor existing at the same time bespeak strong predictor for lethality after liver resection. In this study, in 128 patients, 35 cases with low platelet counts were grouped on the first day after surgery, and 93 with normal platelet counts were grouped. Hepatic failure occurred in 20 patients within six months of the operation. Logistic regression model analysis showed that age, postoperative PLT value and preoperative liver function grading were independent risk factors for liver failure after hepatectomy. The ROC curve was drawn on the change of PLT on the first postoperative day. It was found to have significant predictive value for the diagnosis of postoperative hepatic failure. When the maximum Yoden count was 0.431, the sensitivity and specificity were 0.60 and 0.83 respectively. The area under

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the curve AUC=0.753 (0.651 to 0.854). This result is consistent with the results concluded by scholars such as Ding Shuxin [12]. The reasons for postoperative hepatic failure may be (1) preoperative liver function grading: The higher the level of liver function, the more severe the degree of liver function damage and the degree of cirrhosis, and the longer the recovery time of liver function; (2) Severe hypoxemia status: Factors such as surgical anesthesia will increase the hypoxic state of hepatocytes and aggravate liver cell damage; (3) Age: The older, the slower recovery of the organ function, and the less conducive to liver regeneration; (4) Platelet count: Infusion of platelet stimulating factor to patients with low platelet values to stimulate platelet production and improve liver regeneration. Therefore, monitoring platelet levels after surgery is essential. However, in this study, some Grade A patients also suffered liver failure. Therefore, the preoperative evaluation of liver function has certain limitations. The sample size should be expanded for subgroup analysis to provide treatment and prognosis for patients with primary liver cancer.

In summary, liver failure is one of the complications associated with surgical resection of patients with primary liver carcinoma. The mortality rate is high, which poses serious threat to patients' life. Therefore, in the clinical diagnosis and treatment of liver cancer patients. It is especially important to prevent liver failure after liver resection. In this study, the independent risk factors for liver failure are patient ages, PLT count on the first day after surgery, and preoperative liver function grading. The more aged the patient, the worse the prognosis of the disease, the greater the incidence of liver failure. Besides preoperative liver function grading in predicting the value of postoperative liver failure, and platelet count also has a certain value in predicting liver failure as a complement. Lower platelet counts may cause obstacles in the regeneration of liver cells, resulting in slower recovery of liver function. Therefore, platelet count can be used as one of the indicators for evaluating liver cell regeneration after surgery.

Acknowledgement

Fund Project: Innovation Team Project of the First Affiliated Hospital of Medical College, Shihezi University, No: TD201801.

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