Relationship between platelet count and hepatic failure and residual liver regeneration after hemihepatectomy in patients with hepatitis B-related primary hepatocellular carcinoma

Chuhui Ye
The First Affiliated Hospital of Guangxi Medical University
Banghao Xu
The First Affiliated Hospital of Guangxi Medical University
Kaiyi Lu
The First Affiliated Hospital of Guangxi Medical University
Tingting Lu
The First Affiliated Hospital of Guangxi Medical University
Ling Zhang
The First Affiliated Hospital of Guangxi Medical University
Jingjing Zeng
The First Affiliated Hospital of Guangxi Medical University
Ya Guo
The First Affiliated Hospital of Guangxi Medical University
Minhao Peng
The First Affiliated Hospital of Guangxi Medical University
Zhang Wen (wenzgxmu@163.com)
The First Affiliated Hospital of Guangxi Medical University

Research article

Keywords: Hepatitis B virus, correlation of primary hepatocellular carcinoma, Half liver resection, Platelet counts, Liver failure, Liver regeneration

Posted Date: October 31st, 2019

DOI: https://doi.org/10.21203/rs.2.16653/v1

Abstract

Objective A retrospective analysis of the influences of platelet (PLT) counts on liver failure and liver regeneration in patients with primary hepatocellular carcinoma (HCC) provides a treatment strategy for clinical prevention and treatment of postoperative liver failure and residual liver regeneration.

Method The clinical data of 111 patients with a background of hepatitis B virus infection and who underwent (expanded) half liver resection at the First Affiliated Hospital of Guangxi Medical University from June 2012 to June 2017 were collected and statistically analyzed.

Results On the basis of the International Study Group of Liver Surgery liver failure-grading standards and Dino–Clavien postoperative complication criteria, the incidence of grade B and above liver failure was 55%, and complication II level and above was 47.5% in the PLT decline group after semihepatectomy. The incidence rates in the normal group were 26.8% and 23.9%. A statistically significant difference was determined in the two groups (P1=0.003, P2 = 0.011). The average volumes of liver hyperplasia (residual liver volume (RLV)80.4 days − RLV) in the PLT decline and normal groups were 132.09 ± 61.89 cm3 and 190.89 ± 91.98c cm3, respectively; the average rates of hyperplasia ((RLV80.4days−RLV)/RLV) were 16.59%± 7.36% and 24.78% ± 10.82%. The difference between the two groups was statistically significant (PProliferation = 0.001, PProliferation rate = 0.001). Univariable and multivariable logistic regression analyses of postoperative liver failure grade and proliferation rate in patients who underwent semihepatectomy suggested that the decrease in postoperative PLT count (PLT < 125 × 109/L) might be an independent risk factor of severe posthepatectomy liver failure (PHLF) (PHLF-B or above) and residual liver regeneration rate for patients with primary HCC after half liver resection. No death occurred.

Conclusions A correlation existed between PLT count and postoperative PHLF or liver regeneration. Monitoring PLT counts after liver resection may help us predict the suffering from PHLF-B or above and severe postoperative complications.

Background

Hepatitis B virus (HBV) infection is widespread worldwide. Approximately one-fifth of the world's 6 billion people have been infected with HBV, and chronic infections have reached 248 million. Some patients with chronic HBV develop from hepatitis, liver fibrosis, or cirrhosis to liver cancer and eventually die from primary liver cancer[1].

For early primary hepatocellular carcinoma (HCC), surgical resection remains the most fundamental and effective treatment[2]. Hepatocyte function in patients with hepatitis B-related primary liver cancer has been impaired to varying degrees. Large-scale liver resection may lead to postoperative liver failure and serious complications because the remaining liver tissue is insufficient to compensate for normal physiological functions. Liver failure is an important cause of increased mortality after partial hepatectomy. The liver is one of the organs of the body that can regenerate. Certain indicators after most liver resection are used to predict postoperative liver failure and the incidence of complications, and residual liver regeneration rate has important clinical significance. Previous studies have shown that PLT and their derivatives have important effects on liver function recovery after partial hepatectomy[3−5]. Most patients with liver cancer in China have a hepatitis background. No reports exist on the factors that affect liver failure and regeneration after hepatectomy in patients with hepatitis B-related primary liver cancer. Therefore, this study was designed to investigate the association between PLT count and liver failure after hepatectomy in patients with hepatitis B-related primary liver cancer and residual liver regeneration.

Methods

Normal information: A total of 111 patients with primary liver cancer who have HBV background and underwent hepatectomy (right or left hepatectomy) were enrolled from June 2012 to June 2017 at the First Affiliated Hospital of Guangxi Medical University. The inclusion criteria were as follows: 1 The diagnostic criteria for liver cancer were in accordance with the 2017 Chinese primary liver cancer diagnosis and treatment criteria, and postoperative pathology confirmed HCC[6]; 2 No obvious organic organ diseases, such as heart, lung, and kidney, occurred before operation; 3 Surgical records and postoperative imaging studies were confirmed as hemihepatectomy (left and right hemihepatectomy);4 The PLT count must not be affected by medication; 5 Patients aged between 18 and 80 years; 6 Patients had HBV background; 7 Patients did not receive PLTs during the perioperative period. The patients

included 94 males and 17 females. The age ranged from 20 years to 74 years, with an average age of 47.3 ± 11.6 years. Hepatitis B surface antigen HBsAg was positive in 86 cases, and no anti-HCV antibody positive cases existed. Postoperative pathology confirmed different degrees of liver fibrosis or cirrhosis, and the classification was judged by Ishak pathological scoring system[7]. V-P typing of portal vein tumor plugs was conducted[8]. The preoperative liver function was Child–Pugh A grade. The mean value of PLT counts <125×10^9/L was observed in the observation group at 3 days postoperatively, and PLT≥ 125×109/L was used for the control group. Forty cases were included in the observation group and 71 cases in the control group.

Surgical approach

Opening the half of the liver or expanding the hepatectomy

A patient was placed in the supine position, and the anti-"L"-shaped incision was layered into the abdominal cavity to explore the abdominal cavity and exclude distant metastatic lesions. The round ligament of the liver was cut, and the right (or left) hepatic pedicle was separated by external sheath or intrathecal method. The hepatic ischemic plane was marked, and the hepatic vein was preserved (the right hepatic resection did not preserve the hepatic vein). Breaking the deep liver parenchyma, and cuting the right (or left) hepatic vein. The half of the liver was completely removed, and the specimen was removed.

PLT count detection method

On the first, second and third day after operation, fasting venous blood was drawn from patients in the morning. An anticoagulant tube containing dipotassium ethylenediaminetetraacetate was added. PLT counts were measured using a fully automated hematology analyzer (Beckman Coulter LH780) (reference range 125–350 × 109/L).

Liver and kidney function and blood coagulation function detection method

On the 1st, 3rd, 5th, 7th, 10th, and 14th days after the operation, 3 ml of fasting venous blood was extracted into an ordinary drying tube. After centrifugation, the upper serum was collected and detected by the automatic blood analysis line system (Abbott α3600), with serum total bilirubin (TB, reference range 3.40–20.50 μmol/L), alanine aminotransferase (reference range 9–60 U/L), aspartate aminotransferase (reference range 15–45 U/L), alkaline phosphatase (reference range 45–125 U/L), and glutamyl transpeptidase (reference range 10.0–60.0 U/L). At the same time, 2 ml of whole blood was added to the anticoagulant tube containing sodium citrate, and the coagulation function was detected by a fully automatic coagulation analyzer (Beckman Coulter ACL-TOP700). Prothrombin time (reference range 9.00–15.00 S) and international standardized ratio (reference range 0.80–1.40) were set.

Postoperative liver function and complication observation indicators

Grades were evaluated using the International Liver Study Group of Liver Surgery postoperative hepatic failure (PHF) grading criteria[9] and Dino–Clavien postoperative grading criteria[10]. Grade A of liver failure and grade I postoperative complications do not require special treatment. Thus, this study focused on the incidence of grade B and above and grade II and above complications of liver failure.

Measurement and analysis of postoperative liver volume

CT images of the upper abdomen were collected from the 2nd day to the 9th day (average 5.2 days) and 53–97 days (average 80.4 days) after hepatectomy. The two residual liver volumes (RLVs) were measured using the IQQA liver three-dimensional imaging system of the First Affiliated Hospital of Guangxi Medical University. The remaining liver volume hyperplasia ($RLV_{80.4\ days}$ − RLV) and proliferation rate (($RLV_{80.4\ days}$ − RLV)/RLV) were calculated. Surgical observation indicators included operative time, hepatic blood flow blockage, intraoperative blood loss and blood transfusion volume, mean daily drainage of drainage tube, and hospitalization time.

Statistical analysis

Data analysis was performed using IBM SPSS 20.0. The measurement data were expressed as mean ± standard deviation. The t-test was used for comparison between groups. The percentage of count data was used. The comparison between groups was performed by X2 test. Risk factor analysis was performed using logistic regression model for single-factor and multivariate analyses. $P < 0.05$ indicates a statistical difference.

Results

Surgery and postoperative liver function and complications

In this study,no statistically significant difference in preoperative general baseline data existed between the two groups ($P > 0.05$) (Table 1).In the observation group, 22 patients underwent right hepatectomy, and 18 patients underwent left hepatectomy. In the control group, 47 patients underwent right hepatectomy, and 24 patients underwent left hepatectomy. Intraoperative blood flow blockage included 22 cases of hepatic occlusion in the observation group and 18 cases of the first hepatic occlusion (Pringle method). In the control group, 49 cases of hepatic occlusion and 22 cases of first hepatic occlusion were observed (Pringle method). The postoperative observation group had PHF classification, with 2 cases of grade C, 20 cases of grade B, and 18 cases of grade A. The incidence of postoperative PHF grade B and above was 55.0%. The control group had 0 cases of grade C, 19 cases of grade B, and 52 cases of grade A. The incidence rate of PHF grade B and above was 26.8%. The difference between the two groups was statistically significant ($P = 0.003 < 0.05$). The postoperative complications were graded in the observation group, with 1 case of grade III, 18 cases of grade II, and 21 cases of grade I. The incidence rate of grade II and above was 47.5%. The control group presented 0 cases of grade III, 17 cases of grade II, and 54 cases of grade I. The incidence rate of grade II and above was 23.9%. The difference between the two groups was statistically significant ($P = 0.011 < 0.05$) (Table 2).

Residual liver volume

The average postoperative Residual liver volume (RLV) of the observation group was 800.19 cm^3 (441.72–1174.81 cm^3). The control group was 801.07 cm^3 (340.38–1415.73 cm^3). The average liver volume ($RLV_{80.4\ days}$) in the observation group was 933.48 cm^3 (489.49–1399.45 cm^3) after an average of 80.4 days. The control group was 991.96 cm^3 (428.55–1688.75 cm^3). The mean hepatic hyperplasia volumes ($RLV_{80.4\ days} - RLV$) in the observation and control groups after hemisection were 132.09 ± 61.89 cm^3 and 190.89 ± 91.98 cm^3, and the mean proliferation rates (($RLV_{80.4\ days} - RLV$)/RLV) were 16.59% ± 7.36% and 24.78% ± 10.82%, respectively (Table 3).

Factors affecting the classification of postoperative liver failure

Univariate and multivariate logistic regression analyses were performed according to the classification of postoperative PHF grades. The results suggested that postoperative PLT count decreased (OR = 3.18 (1.16, 8.75) P = 0.025), preoperative liver fibrosis or cirrhosis was observed (Ishak score) > 4) (OR = 2.85 (1.04, 7.81) P = 0.043), and the TB value was higher than the upper limit on the seventh day after surgery (OR = 5.71 (1.68, 19.46) P = 0.005). TB might be an independent risk factor for severe PHF (PHF-B grade and above) after hepatectomy in patients with primary HCC (Table 4).

Factors affecting the rate of residual liver regeneration after surgery

We performed single-factor and multifactor logistic regression analyses with the average liver proliferation rate (21.83%) as the baseline. The results suggested that postoperative PLT count decreased (OR = 2.83 (1.06, 7.56) P = 0.038). Postoperative PLT count might be an independent risk factor for the reduction of residual liver regeneration rate after hepatectomy in patients with primary HCC (Table 5).

Discussion

Primary HCC is a common malignant tumor in China, and surgical resection remains the preferred treatment option. Most of the liver cancer patients in China have a background of hepatitis B cirrhosis. Hepatocyte reserve function is lower than normal population. Partial hepatectomy, especially after extensive hepatectomy, has a high risk of PHF and residual liver hyperplasia. Studies have shown that the incidence of PHF after partial hepatectomy is 2%–32%[11,12]. The liver is one of the organs with regenerative potential in the body. Liver regeneration is the premise and basis for liver resection. With the increase in extensive liver resection, identifying a predictive index of posthepatectomy liver failure (PHLF) and assessment of residual liver regeneration after hepatectomy have great clinical significance.

PLT counting is one of the routine blood tests, which promotes liver regeneration by increasing the release of hepatocyte growth factor[13]. Thrombocytopenia after partial hepatectomy is an important factor in delaying liver function recovery[14]. Margonis[15] reported that early PLT count after major liver resection exerts an important effect on the incidence of perioperative complications, but the study included not only malignant tumors, such as primary liver cancer and liver metastases, but also hepatic hemangioma, such as focal nodular hyperplasia. Most of the subjects had no pathological changes, such as hepatitis B background, liver fibrosis, or cirrhosis, and the scope of surgical resection was not uniformly defined. Therefore, the current study selected patients with primary HCC who underwent hepatectomy with hepatic cirrhosis. The combined determination of RLV, hepatocyte function, and coagulation function reflected postoperative liver function recovery and liver volume hyperplasia. PHLF is one of the important factors that lead to an increase in perioperative mortality during hepatectomy. The factors affecting PHLF are complex and diverse. In this study, the incidence of PHF-B grade and above was 55%, and the incidence of complications grade II and above was 47.5%. The normal PLT counts were 26.8% and 23.9%. The incidence of PHLF-B and above and that of complications of grade II and above were higher than those reported in previous literature[11,16]. The difference may be related to the inclusion of patients with hepatoprotective cirrhosis, liver reserve function, liver flotation after hemihepatectomy, and the incidence of postoperative complications.

Liver regeneration is a complex process that requires the involvement of hepatogenic cytokines, inflammatory stimulators, and nutrients. This process is affected by multiple factors, such as intraoperative hepatic blood flow blockade and postoperative portal hemodynamics. Lesurtel[17] also found a significant increase in PLT-derived serotonin receptors after hepatectomy through animal experiments. PLT-derived serotonin plays an important role in the initial stage of liver regeneration. However, Meyer[18] found that PLT-derived serotonin may indirectly act on hepatocytes and promote liver regeneration by increasing the release of PLT alpha particles.

Tucker[19] showed that after liver transplantation or hepatectomy, RLV/standard liver volume (SLV) ≥ 25% (normal liver), ≥ 40% (cirrhosis and other pathological changes in the liver), or RLV/weight (kg) ≥ 0.5% (normal liver), 0.8% (cirrhosis and other pathological changes in the liver) is an important prerequisite to ensure smooth liver cell regeneration without severe PHLF. The current study indicated that the ratio of RLV/SLV in the PLT-reducing group and the PLT-normal group was theoretically sufficient to stimulate the hepatocyte regeneration procedure without the occurrence of small-for-size syndrome. The PLT decline group was significantly lower than the normal PLT group in RLV hyperplasia and proliferation rate after 75 days. The residual liver regeneration rate in this study was lower than that reported in the literature[20] and might be related to extensive hepatectomy (≥3 liver segments). After operation, most of the hepatocytes and interstitial cells entered the mitosis state, and the hepatocytes rapidly proliferated to form “hepatocyte islands.” In the early stage, a large number of “hepatocyte islands” could not exert the normal physiological functions of hepatocytes due to lack of energy. Certain pressure was induced on the surrounding liver sinus and portal area, thereby resulting in increased portal pressure and poor bile excretion. High portal perfusion might cause mechanical damage to normal liver parenchyma, which might affect the process of liver regeneration and lead to the occurrence of PHLF. Logistic single-factor and multivariate model regression analyses found that postoperative PLT count decline (PLT < 125 × 109/L) was an independent risk factor for PHLF-B grade and above and slow liver regeneration rate. Therefore, monitoring the trend of PLT count after surgery could predict the incidence of PHF-B grade and above and serious complications after hemi-hepatectomy and the rate of residual liver regeneration. Early intervention in patients with thrombocytopenia after hepatic resection may promote regeneration of the remaining liver. Excessive PLTs cause an increase in blood viscosity and an increased risk of thrombosis. Strictly controlling the indications for infusion of PLTs and their derivatives and considering the risk of portal thrombosis are necessary. A multicenter large sample study should be conducted to clarify the optimal mechanism of PLT promoting hepatocyte regeneration mechanism, determine its adverse effects, and guide the clinical application of PLTs and their derivatives. This study focused on the effect of

postoperative PLT count on recent PHLF, severe complications, and liver regeneration. Long-term effects, such as postoperative recurrence rate and 1-, 3-, and 5-year survival rates, were not elaborated.

Conclusions

A correlation existed between PLT count and postoperative PHLF or liver regeneration. Monitoring PLT counts after liver resection may help us predict the suffering from PHLF-B or above and severe postoperative complications. Early intervention in patients with thrombocytopenia after hepatic resection may promote regeneration of the remaining liver. which provides a feasible strategy for preventing and reducing the incidence of postoperative severe liver failure and promoting the regenerational rate of the residual liver.

Abbreviations

Platelet (PLT)

Hepatocellular carcinoma (HCC)

Posthepatectomy liver failure (PHLF)

Hepatitis B virus(HBV)

Postoperative hepatic failure (PHF)

Declaration

Ethics approval and consent to participate

The specimen is the blood specimen of the patient, and the method of collection is venous blood collection. The research project is a routine test item for admitted patients with liver tumor, so the informed consent obtained from study participants was verbal.The study was approved by the Ethics Review Committee of Guangxi Medical University, Guangxi, China (NO2018,KY-E–079).

Availability of data and material

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no conflict of interest.

Consent for publication

Not Applicable

Funding

This work was supported by the National Natural Science Foundation of China (No.81560387) and”Medical Excellence Award” funded by the creative research development grant from the first affiliated hospital of Guangxi Medical University NO.180327

Authors’ contributions

CY, KL, TL, LZ and JZeng analyzed the patient data, and BX,YG, MP, ZW was a major contributor in writing the manuscript,All authors read and approved the final manuscript.

Acknowledgements

We are grateful to the members of the Department of ultrasound,radiology and pathology at The first affiliated hospital of Guangxi Medical University, Guangxi, People's Republic of China.

References

1.Global epidemiology of hepatitis B virus infection:new estimates of age-specific HBsAg seroprevalence and endemicity[J].Vaccine, 2012, 30 (12):2212–2219.

2.Cucchetti A, Ercolani G, Vivarelli M, et al. (2006) Impact of model for end-stage liver disease (MELD) score on prognosis after hepatectomy for hepatocellular carcinoma on cirrhosis. Liver Transpl 12(6):966–971

3.Jarnagin WR, Gonen M, Fong Y, DeMatteo RP, Ben-Porat L, Little S, Corvera C, Weber S, Blumgart LH. Improvement in perioperative outcome after hepatic resection: analysis of 1,803 consecutive cases over the past decade. Ann Surg 2002; 236: 397–406

4. Poon RT, Fan ST, Lo CM, Liu CL, Lam CM, Yuen WK, Yeung C, Wong J. Improving perioperative outcome expands the role of hepatectomy in management of benign and malignant hepatobiliary diseases: analysis of 1 222 consecutive patients from a prospective database. Ann Surg 2004; 240: 698–708

5.Lesurtel M, Graf R, Aleil B, et al. Platelet-Derived Serotonin Mediates Liver Regeneration[J]. Science, 2006, 312(5770):104.

6. Guidelines for Diagnosis and Treatment of Primary Liver Cancer in China (2017 Edition) , Liver Cancer 2018;7:235–260.

7.Ishak K, Baptista A, Bianchi L, et al. Histological grading and staging of chronic hepatitis[J]. Journal of Hepatology, 1995, 22(6):696.

8.JaPan L C S G O. The general rules for the clinical and Pathological study of Primary liver cancer[J]. JaPanese Journal of Surgery, 1989, 19(1):98- 129.

9.Rahbari NN, Garden J, Padbury R, et al. PosthePatectomy liver failure: a definition and grading by the International Study GrouP of Liver Surgery(ISGLS). Surgery, 2011, 149(5): 713–724.

10.Rahbari NN, Garden J, Padbury R, et al. PosthePatectomy liver failure: a definition and grading by the International Study GrouP of Liver Surgery(ISGLS). Surgery, 2011, 149(5): 713–724.

11. Ome Y, Hashida K, Yokota M, et al. Efficacy of laparoscopic hepatectomy in patients with liver cirrhosis[J]. European Surgery, 2018.

12.Paugam-Burtz C, Janny S, Delefosse D, et al. Prospective validation of the "fifty-fifty" criteria as an early and accurate predictor of death after liver resection in intensive care unit patients[J]. Annals of Surgery, 2009, 249(1):124.

13.Tomikawa M, Hashizume M, Highashi H, et al. The role of the sPleen, Platelets, and Plasma hePatocyte growth factor activity on hePatic regeneration in rats.[J]. Journal of the American College of Surgeons, 1996, 182(1):12.

14.Takahashi K, Kurokawa T, Oshiro Y, et al. PostoPerative Decrease in Platelet Counts Is Associated with Delayed Liver Function Recovery and ComPlications after Partial HePatectomy[J]. Tohoku Journal of ExPerimental Medicine, 2016, 239(1):47.

15.Margonis G A, Amini N, Buettner S, et al. Impact of early postoperative platelet count on volumetric liver gain and perioperative outcomes after major liver resection[J]. Br J Surg, 2016, 103(7):899–907.

16. Takenaka K, Kanematsu T, Fukuzawa K, et al. Can hepatic failure after surgery for hepatocellular carcinoma in cirrhotic patients be prevented?[J]. World Journal of Surgery, 1990, 14(1):123–127.

17.Lesurtel M, Graf R, Aleil B, et al. Platelet-Derived Serotonin Mediates Liver Regeneration[J]. Science, 2006, 312(5770):104.

18.Meyer J, Lejmi E, Fontana P, Morel P, Gonelle-Gispert C,Buhler L. A focus on the role of platelets in liverregeneration: do platelet–endothelial cell interactionsinitiate the regenerative process? J Hepatol 2015; 63:1263–1271.

19.Tucker O N, Heaton N. The 'small for size' liver syndrome.[J]. Current OPinion in Critical Care, 2005, 11(2):150.

20.Klink T, Simon P, KnoPP C, et al. Liver remnant regeneration in donors after living donor liver transPlantation: long-term follow-uP using CT and MR imaging.[J]. Fortschr Röntgenstr, 2014, 186(6):598.

Tables

Table 1 Summary of general baseline data of preoperative patients

	Platelet drop group (observation group)	Normal platelet group(control)	*t(X²) value*	*P value*
Age	45.8±9.5	48.2±12.5	1.072	0.286
Gender（man/female）	37/3	57/14	2.945	0.086※
Interventional therapy (yes/no)	4/36	9/62	0.177	0.674※
Preoperative portal vein tumor thrombus using VP typing (I/IIIII/IV/None)	0/12/1/0/27	0/18/3/0/50	0.103	0.748※
Hepatitis B surface antigen positive (yes/no)	31/9	54/17	0.030	0.863※
Hepatitis B DNA replication (yes/no)	22/18	38/33	0.023	0.881※
Liver trematode(yes/no)	9/31	12/59	0.523	0.470※
Number of tumors (single/multiple)	35/5	58/13	0.636	0.425※
Tumor diameter (<5cm/≥5cm)	11/29	10/61	3.002	0.083※
Postoperative liver fibrosis or cirrhosis (Ishak score)	5.0±1.0	4.7±1.1	-1.669	0.098
Preoperative platelet count（$\times 10^9$/L）	194.9±58.9	210.9±43.8	1.500	0.138
Preoperative alanine aminotransferase ALT (U/L)	36.6±10.2	41.5±13.5	0.837	0.404
Preoperative aspartate aminotransferase AST (U/L)	42.1±17.1	47.6±19.3	1.506	0.135
Preoperative alkaline phosphatase ALP (U/L)	107.7±67.4	127.2±59.0	-1.334	0.185
Preoperative glutamate transpeptidase GGT (U/L)	122.5±63.6	143.1±69.3	1.551	0.124
Preoperative prothrombin time PT(S)	11.8±1.1	11.7±1.3	-0.256	0.799
Preoperative international standardized ratio INR	1.01±0.10	0.99±0.11	-0.442	0.660

Note:※ indicates the use of X-test

Table 2 Patients with postoperative liver failure and complication classification

	Platelet drop group (Observer Group)	Normal platelet group (control group)	t(X^2) value	P value
Surgery(right half liver / left half liver)	22/18	47/24	1.364	0.243※
Time of operation(min)	301.6±110.6	308.0±117.4	-0.285	0.776
Surgical blood loss(ml)	947.5±379.1	1008.4±457.2	0.287	0.775
Liver flow obstruction(HIO/Pringle method)	22/18	49/22	2.18	0.140※
Inoperative plasma transport(ml)	226.4±83.8	275.1±93.3	0.851	0.397
Intraoperative erythrocyte transfusion(U)	5.0±2.7	5.6±2.9	0.654	0.517
Postoperative PHLF classification(A / B and above)	18/22	52/19	8.759	†0.003※
Postoperative complication classification(level I/II and above)	21/19	54/17	6.749	†0.011※
Average daily drainage(ml/day)	404.3±132.9	269.3±136.3	2.486	†0.014
Average length of stay(days)	25.7±17.2	19.3±8.0	2.215	†0.009

Table 3 Comparison of residual hepatic volumetric hyperplasia after operation

	Platelet drop group (Observer Group)	Normal platelet group (Control group)	t(X^2) value	P value
RLV/SLV□%□	77.25±15.11	79.91±20.74	0.709	0.480
GRWR	1.39±0.40	1.32±0.27	1.033	0.304
Postoperative pathology VEGF(+ /-)	41/30	20/20	0.620	0.431※
Time of upper abdominal CT examination after first reexamination(days)	5.3±1.6	5.2±1.6	0.211	0.833
Time of upper abdominal CT examination after second reexamination(days)	80.6±14.5	80.0±13.9	0.196	0.845
CT interval between two reviews of the upper abdomen(days)	75.3±14.6	74.8±13.9	0.171	0.864
Postoperative liver volume hyperplasia(cm^3)	132.09±61.89	190.89±91.98	3.360	†0.001
Postoperative hepatic volumetric hyperplasia(%)	16.59±7.36	24.78±10.82	3.543	†0.001

†P<0.05 indicated that the difference was statistically significant.

Table 4 Grades of hepatic failure in patients with hepatitis B associated primary hepatocellular carcinoma after hysterectomy

	classification	Number	*Single-factor analysis*		*Multifactorial analysis*	
			OR value (95 % trusted interval)	P value	OR value (95 % trusted interval)	P value
Gender	man	94				
	female	17	1.24（0.43,3.54）	0.694	-	-
Age	≥60	93				
	（60	18	0.43（0.13,1.42）	0.158	-	-
Preoperative intervention	No	13				
	Yes	98	0.73（0.21,2.55）	0.624	0.52（0.08,2.26）	0.309
High cholesterol	No	11				
	Yes	100	0.35（0.07,1.69）	0.175	-	-
Portal cancer suppository	No	34				
	Yes	77	0.92（0.40,2.12）	0.851	-	-
Hepatosomiasis	No	21				
	Yes	90	0.46（0.17,1.19）	0.103	-	-
Preoperative AFP	（400	42				
（ng/ml）	≥400	69	0.78（0.35,1.74）	0.539	-	-
Hepatitis B virus DNA payload	（10^3	49				
	≥10^3	52	1.12（0.49,2.53）	0.790	-	-
Postoperative hepatic fibrosis(ishak score)	≤4.0	46				
	（4.0	65	2.28（1.01（5.18）	0.046	2.85（1.04,7.81）	0.043
Number of tumours	Single	93			-	
	≥2（	18	1.46（0.52（4.04）	0.471		-
Tumor diameter	（5cm	69				
	≥5cm	42	1.03（0.39,2.72）	0.950	1.02(0.27,3.25)	0.910
Surgical procedure	right half liver.	69				
	Left half liver.	42	0.92（0.41,2.04）	0.835	-	-
Blood flow blockade during surgery	Halfliver block	71				
	First hepatic occlusion(Pringle method)	40	1.23（0.55,2.73）	0.616	-	-
Surgical blood loss（ml）	（1000	72				
	≥1000	39	1.11(0.50,2.47)	0.807	1.55（0.12,2.60）	0.452
Preoperative TB	（20.5	100				
（umol/L）	≥20.5	11	1.48（0.42,5.19）	0.537	-	-

Preoperative ALT	60	93				
U/L	≥60	18	1.10(0.39,3.12)	0.851	-	-
Preoperative AST	45	69				
U/L	≥45	42	1.28(0.58,2.81)	0.547	-	-
Preoperative ALP	125	68				
U/L	≥125	43	1.02(0.46,2.25)	0.962	-	-
Preoperative GGT	60	14				
U/L	≥60	97	0.39(0.12,1.21)	0.094	-	-
Preoperative PLT	No	102				
whether decline	Yes	9	1.19(0.28,5.03)	0.815	-	-
Postoperative PLT	No	71				
whether decline	Yes	40	3.35(1.48,7.56)	0.003	3.18(1.16,8.75)	0.025
Total bilirubin after surgery(umol/L)	20.5					
	≥20.5					
TB-POD1		-	3.44(1.34,8.82)	0.008	1.58(0.45,5.49)	0.473
TB-POD3		-	4.00(1.39,11.49)	0.007	2.20(0.50,9.70)	0.297
TB-POD5		-	3.04(1.12,8.25)	0.024	1.46(0.10,2.10)	0.317
TB-POD7		-	5.33(2.21,12.87)	0.000	5.71(1.68,19.46)	0.005
TB-POD10		-	2.45(1.10,5.44)	0.026	1.96(0.30,3.07)	0.939
Postoperative	60					
ALT(U/L)	≥60					
		-	1.79(0.18,17.81)	0.092	-	-
ALT-POD1		-	1.11(1.03,1.20)	0.737	-	-
ALT-POD3		-	1.87(0.67,5.21)	0.226	-	-
ALT-POD5		-	1.11(0.51,2.40)	0.788	-	-
ALT-POD7		-	0.753(0.31,1.81)	0.525	-	-
ALT-POD10						
Postoperative	45					
AST(U/L)	≥45					
		-	-	-	-	-
AST-POD1		-	0.90(0.83,0.97)	-0.036	-0.75(0.11,5.09)	0.770
AST-POD3		-	1.42(0.61,3.33)	0.414	-	-
AST-POD5		-	1.66(0.75,3.64)	0.208	-	-

AST-POD7		-	1.57（0.66,3.71）	0.306	-	-
AST-POD10						
Postoperative ALP（U/L）	<125					
	≥125	-				
ALP-POD1		-	1.30（0.48,3.55）	0.608	-	-
ALP-POD3		-	1.91（0.69,5.28）	0.210	-	-
ALP-POD5		-	1.17（0.44,3.16）	0.754	-	-
ALP-POD7		-	1.77（0.70,4.49）	0.224	-	-
ALP-POD10			0.90（0.33,2.48）	0.843	-	-
Postoperative GGT(U/L)	<60					
	≥60					
GGT-POD1		-	1.23（0.55,2.73）	0.616	-	-
GGT-POD3		-	1.78（0.81,3.88）	0.147	-	-
GGT-POD5		-	1.11（0.47,2.61）	0.810	-	-
GGT-POD7		-	1.40（0.58,3.35）	0.453	-	-
GGT-POD10		-	1.62（0.69,3.77）	0.264	-	-

Table 5 Risk factors for residual liver regeneration rate after hysterectomy

	classification	Number	*Single-factor analysis*		*Multifactorial analysis*	
			OR value (95 % trusted interval)	P value	OR value (95 % trusted interval)	P value
Gender	man	94				
	female	17	1.70（0.56,5.22）	0.349	-	-
Age	（60	93				
	≥60	18	1.04（0.37,2.92）	0.943	1.637（0.50,5.36）	0.416
Preoperative intervention	No	98				
	Yes	13	1.06（0.32,3.47）	0.926	1.43（0.35,5.81）	0.621
High cholesterol	No	100				
	Yes	11	1.85（0.46,7.41）	0.377	-	-
Portal cancer suppository	No	77				
	Yes	34	1.10（0.40,2.08）	0.826	-	-
Hepatosomiasis	No	90				
	Yes	21	1.50（0.58,3.90）	0.406	-	-
Preoperative AFP	（400	41				
（ng/ml）	≥400	70	0.76（0.35,1.66）	0.482	-	-
Hepatitis B virus DNA payload	（10^3	49				
	≥10^3	52	1.02（0.46,2.28）	0.964	-	
Postoperative hepatic fibrosis(ishak score)	≤4.0	46				
	（4.0	65	2.46（1.12（5.37）	0.023	2.07（0.82,5.20）	0.122
Histopathological VEGF	negative	50			-	
	positive	61	1.80（0.83,3.93）	0.136		-
P53	negative	52			-	
	positive	59	0.81（0.38,1.74）	0.590		-
P21	negative	102			-	
	positive	9	2.02（0.51,7.98）	0.309		-
Number of tumours	Single	93			-	
	≥2（	18	2.17（0.78（6.02）	0.132		-
Tumor diameter	（5cm	22				
	≥5cm	89	2.65（0.90,7.82）	0.070	-	-
Surgical procedure	right half liver.	69				
	Left half liver.	42	0.46（0.20,1.05）	0.063	-	-
Blood flow	Halfliver block	71				

blockade during surgery	First hepatic occlusion(Pringle method)	40	1.36（0.61,3.03）	0.453	-	-
Surgical blood loss（ml）	<1000	72				
	≥1000	39	2.11(0.95,4.67)	0.065	1.91（0.73,5.01）	0.186
Preoperative TB（umol/L）	<20.5	100				
	≥20.5	11	1.85（0.46,7.41）	0.377	-	-
Preoperative ALT（U/L）	<60	93				
	≥60	18	2.17（0.78,6.02）	0.132	-	-
Preoperative AST（U/L）	<45	69				
	≥45	42	1.24（0.57,2.71）	0.589	-	-
Preoperative ALP（U/L）	<125	68				
	≥125	43	2.57（1.17,5.67）	0.018	1.89（0.73,4.87）	0.189
Preoperative GGT（U/L）	<60	14				
	≥60	97	4.58（0.97,21.59）	0.038	-	-
Preoperative PLT whether decline	No	102				
	Yes	9	1.34（0.32,5.68）	0.687	-	-
Postoperative PLT whether decline	No	71				
	Yes	40	3.35（1.40,8.04）	0.006	2.83（1.06,7.56）	0.038
Total bilirubin after surgery（umol/L）	<20.5					
	≥20.5					
TB-POD1		-	1.79（0.77,4.15）1.19（0.50,2.82）	0.175	-	-
TB-POD3		-	2.16（0.92,5.07）	0.697	-	-
TB-POD5		-	1.78（0.82,3.83）	0.073	-	-
TB-POD7		-	2.16（0.95,4.91）	0.141	-	-
TB-POD10		-		0.063	-	-
Postoperative ALT（U/L）	<60					
	≥60					
ALT-POD1						
ALT-POD3		-	4.83（0.49,47.99）	0.341	-	-

ALT-POD5		-	2.13（0.45,10.03）	0.563	-	-
ALT-POD7		-	1.03（0.40,2.63）	0.955	-	-
ALT-POD10		-	1.13（0.53,2.42）	0.756	-	-
Postoperative		-	1.98（0.85,4.59）	0.108	-	-
AST（U/L）	<45					
AST-POD1	≥45	-	-	-	-	-
AST-POD3		-	1.15（0.25,5.42）	0.857	-	-
AST-POD5		-	1.44（0.64,3.25）	0.375	-	-
AST-POD7		-	1.36（0.63,2.96）	0.208	-	-
AST-POD10		-	2.05（0.82,5.17）	0.123	-	-
Postoperative						
ALP（U/L）	<125					
ALP-POD1	≥125	-	1.47（0.54,3.96）	0.449	-	-
ALP-POD3		-	2.17（0.78,6.02）	0.132	-	-
ALP-POD5		-	1.02（0.38,2.74）	0.971	-	-
ALP-POD7		-	1.03（0.40,2.63）	0.955	-	-
ALP-POD10		-	1.27（0.46,3.49）	0.639	-	-
Postoperative						
GGT（U/L）	<60					
GGT-POD1	≥60	-	1.92（0.84,4.36）	0.119	-	-
GGT-POD3		-	4.19（1.79,9.85）	0.001	2.55（0.76,8.48）	0.128
GGT-POD5		-	2.95（1.14,7.63）	0.022	1.82（0.35,9.46）	0.479
GGT-POD7		-	4.08（1.41,11.76）	0.006	2.40（0.47,12.26）	0.292
GGT-POD10		-	3.77（1.40,10.18）	0.007	1.91（0.48,7.64）	0.359