Observational Study

Medicine®

OPEN

A study on risk factors and diagnostic efficiency of posthepatectomy liver failure in the nonobstructive jaundice

He Wang, MD[a], Shi-Chun Lu, MD[a], Lei He, MD[a], Jia-Hong Dong, MD[a,b,*]

Abstract

Liver failure remains as the most common complication and cause of death after hepatectomy, and continues to be a challenge for doctors.

t test and χ^2 test were used for single factor analysis of data-related variables, then results were introduced into the model to undergo the multiple factors logistic regression analysis. Pearson correlation analysis was performed for related postoperative indexes, and a diagnostic evaluation was performed using the receiver operating characteristic (ROC) of postoperative indexes.

Differences in age, body mass index (BMI), portal vein hypertension, bile duct cancer, total bilirubin, alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), operation time, cumulative portal vein occlusion time, intraoperative blood volume, residual liver volume (RLV)/entire live rvolume, ascites volume at postoperative day (POD)3, supplemental albumin amount at POD3, hospitalization time after operation, and the prothrombin activity (PTA) were statistically significant. Furthermore, there were significant differences in total bilirubin and the supplemental albumin amount at POD3. ROC analysis of the average PTA, albumin amounts, ascites volume at POD3, and their combined diagnosis were performed, which had diagnostic value for postoperative liver failure (area under the curve (AUC): 0.895, AUC: 0.798, AUC: 0.775, and AUC: 0.903).

Preoperative total bilirubin level and the supplemental albumin amount at POD3 were independent risk factors. PTA can be used as the index of postoperative liver failure, and the combined diagnosis of the indexes can improve the early prediction of postoperative liver failure.

Abbreviations: ALP = alkaline phosphatase, ALPPS = associating liver partition and portal vein ligation for staged hepatectomy, AUC = area under the curve, BMI = body mass index, BSA = body surface area, HBSAg = hepatitis B surface antigen, INRs = international standardization ratios, PTA = the prothrombin activity, PVE = portal vein embolization, PVL = portal vein ligation, rGt = r-glutamyl transferase, RLV = residual liver volume, ROC = receiver operating characteristic, SLV = standard liver volume, TBIL = total bilirubin.

Keywords: diagnostic efficiency, nonobstructive jaundice, posthepatectomy liver failure, risk factors

1. Introduction

With the putting forward of the concept of precision surgery and the application of its procedures, the safety of surgical treatment has been further enhanced. However, liver failure remains as the most common complication and cause of death after hepatectomy, and continues to be a challenge for doctors. When determining the best efficacy of surgical treatment, the safety of patients should be guaranteed at the maximum degree. To unify the contradiction, the controllable factors such as the preoperative assessment of patients, surgical injury control, and perioperative management should be nuanced. The concept of precision would be considered throughout the treatment consistently, and the treatment procedures would provide the guidance. Currently, there are no accepted conclusions on the evaluation of the risk factors of postoperative liver failure due to many factors, such as the single classification of the diseases that were studied individually, the individual research factors, and the different understanding of the definition of postoperative liver failure and so on. In the clinical practice, the relevant factors should be analyzed and controlled according to the protocols of diagnosis and treatment of the center. Furthermore, determining the signs of liver failure after hepatectomy at the earliest possible time, as well as effective and timely treatment, is particularly urgent and important for the reduction of the occurrence of hepatic failure and its progression.

Editor: King-Wah Chiu.

Ethic statement: complied with the ethical standards.

The authors have no conflicts of interest to disclose.

[a] Department of Hepatobiliary Surgery, The General Hospital of the People's Liberation army, [b] Beijing Tsinghua Changgung Hospital, Beijing, China.

[*] Correspondence: Jia-Hong Dong, Department of Hepatobiliary Surgery, The General Hospital of the People's Liberation army, No. 28 of Fuxing Road, Haidian District, Beijing 100853, China, Beijing Tsinghua Changgung Hospital, No. 168 of Litang Road, Changping District, Beijing 102218, China (e-mail: dongjh1218@163.com).

Medicine (2018) 97:8(e9963)

Received: 8 August 2017 / Received in final form: 9 November 2017 / Accepted: 30 January 2018

http://dx.doi.org/10.1097/MD.0000000000009963

2. Materials and methods

This study was conducted in accordance with the Declaration of Helsinki. This study was conducted with the approval from the Ethics Committee of The General Hospital of the People's Liberation. Written informed consent was obtained from all the participants.

2.1. Research objects

The data of patients who underwent hepatectomy in the Department of Hepatobiliary Surgery of the General Hospital of People's Liberation army from November 2009 to November 2014 were retrospectively analyzed. A total of 1767 cases with relatively complete clinical data were selected, in which 303 cases were preoperatively combined with obstructive jaundice, and 1464 cases were not preoperatively combined with obstructive jaundice.

2.2. Inclusion criteria

Screening criteria for nonobstructive jaundice patients: patients with jaundice induced by all other causes except for preoperative intrahepatic or extrahepatic bile duct obstruction confirmed through medical history and imaging results; nonobstructive jaundice patients with liver lesions that should be surgically resected; a total of 1464 patients whose bilirubin values at the 5th and 7th day, and postoperative international standardization ratios (INRs) met the recorded requirements for preoperative nonobstructive jaundice were screened based on the recorded data; liver transplantation donor.

2.3. Exclusion criteria

Patients with obstructive jaundice; 208 nonobstructive jaundice patients who could not be determined whether to be patient with liver failure due to the lack of postoperative data at the 5th or/and 7th day, or/and INR; death cases not caused by postoperative hepatic failure.

2.4. Diagnostic criteria

At present, there is no unified and clear definition for posthepatectomy liver failure. Hence, the following criteria proposed by the liver surgical team in May 2011 was selected as the diagnostic criteria for this study: serum bilirubin levels >3 mg/dL and/or INR value > the normal value (>1.5) for 5 days or more after operation, and the cases that elevated bilirubin levels were caused by tumor compression-induced biliary obstruction were excluded.[1]

2.5. Factors planned to be studied

Preoperative factors: age, gender, body mass index (BMI), type of disease, hepatitis B surface antigen (HBSAg) (±), the presence or absence of liver cirrhosis (confirmed according to postoperative pathological results), the determination of whether or not this was combined with portal hypertension, the determination of whether or not this was combined with history of smoking, diabetes and hepatectomy, total bilirubin (TBIL), alkaline phosphatase (ALP), and r-glutamyl transferase (rGt).

Intraoperative factors: operation duration (hours), surgical resection range (segmentation), intraoperative cumulative portal vein occlusion time (minutes), surgical approach, intraoperative blood loss (mL), residual liver volume/standard liver volume (RLV/SLV).

$$\text{Standardized residual liver rate} = (\text{standard liver volume} - \text{postoperative liver volume determined in pathology})/\text{standard liver volume} \times 100\%$$

Urata[2] formula was used to calculate the standard liver volume: $SLV = 706.2 \times BSA\ (m^2) + 2.4$

(1) The DuBois[3] formula was used to calculate the body surface area (BSA)
(2) $BSA = \text{body weight (kg)}^{0.425} \times \text{height (cm)}^{0.725} \times 0.007184$

Postoperative indexes and intervention factors: total ascites volume (mL) within 3 days after operation, total supplemental albumin amount within 3 days after operation (g) (supplied according to body weight if it was less than 30 g/L daily), total infused plasma volumes within 3 days after operation (mL), and the prothrombin activity (PTA) and its average value.

2.6. Statistical methods

The *t* test of independent samples was used to compare the means of the continuous variable data of the studied factors. The χ^2 test was used to compare categorical variables (calibration χ^2 test or Fisher exact probability method). Single factor analysis and binary logistic multivariate analysis were used for preoperative, intraoperative, and postoperative indexes and intervention factors. Pearson correlated coefficient was used for correlation analysis, and receiver operating characteristic (ROC) curve analysis was performed to the postoperative indexes (ROC was used to evaluate the diagnostic value). SPSS 21.0 software was used for analysis and $P < .05$ was considered statistically significant.

3. Results

3.1. General description of statistical data

A total of 1464 patients were screened for nonobstructive jaundice between 2009 and 2014. Among them, 916 cases were males (62.6%) and 548 cases were females (37.4%); and the average age was 52.41 years old (1–83 years). Furthermore, 336 cases were combined with bad habits of smoking, 104 cases were combined with underlying diabetes with an average BMI of 23.80 (11.7–38.7), 408 cases were combined with liver cirrhosis, 20 cases were combined with portal hypertension, 557 cases were positive for hepatitis B HBsAg, 69 patients underwent interventional treatment before hepatectomy, and 24 patients had a history of hepatectomy. In addition, average preoperative TBIL concentration was 17.98 umol/L (2–463 umol/L), average ALP concentration was 123.84 u/L (7–1,373 u/L), average GGT activity was 152.49 u/L (9–3,221 u/L), average operation duration was 4.29 hours (1–18 hours), surgical resection segments were <3 in 237 cases (20.5%), surgical resection segments were <5 and ≥3 in 809 cases (70%) and the segments were ≥5 in 109 cases (9.5%), the intraoperative average portal vein occlusion time was 18.87 minutes (0–218 minutes), 594 cases did not occlude the portal vein during surgery (40.8%), and mean perioperative blood loss volume was 634.5 mL (10–10,000 mL). Furthermore, 1352 cases underwent open hepatectomy (92.4%), 85 cases underwent laparoscopic hepatectomies (5.8%), and 27 cases underwent robot hepatectomy (1.8%). In addition, 590 cases had hepatocellular carcinoma (40.3%), 225 cases had bile duct carcinoma, 224 cases had bile duct calculi (15.4%), 79 cases had liver metastatic carcinoma (5.4%), 58 cases had gallbladder carcinoma (4.0%), 64 cases had hemangioma (4.3%), 23 cases had focal nodular hyperplasia (1.5%), and the rest of the 201 cases had liver diseases of other classifications (13.7%). Moreover, average ascites volume within 3 days after operation

Table 1

Postoperative single factor analysis of continuous variables for patients with nonobstructive jaundice.

	Hepatic failure	N	Mean value	Standard deviation	t	P
Age (years old)	No	1237	52.88	12.417	2.302	.021
	Yes	227	50.81	12.701		
BMI (body mass index)	No	1231	23.944	3.4137	3.494	.000
	Yes	225	23.081	3.3569		
TBIL (total bilirubin) (umol/L)	No	1212	15.35	23.070	−7.378	.000
	Yes	222	32.25	58.872		
Alkaline phosphatase AKP (u)	No	1185	117.06	114.098	−5.080	.000
	Yes	219	161.64	144.405		
r-glutamyltransferase (u)	No	1182	142.05	239.140	−3.849	.000
	Yes	216	211.68	271.954		
Operative time (h)	No	1229	3.91	1.578	−13.842	.000
	Yes	224	5.72	2.720		
Portal vein occlusion (min)	No	1229	16.78	21.208	−7.654	.000
	Yes	226	29.68	32.304		
Amount of bleeding (mL)	No	1193	539.06	659.122	−10.409	.000
	Yes	222	1086.89	985.666		
Residual liver volume/ standard liver volume	No	700	0.63	0.28	3.851	.000
	Yes	112	0.52	0.27		
Hospital stays (d)	No	1236	11.45	6.452	−8.755	.000
	Yes	225	16.24	11.897		
Volume of ascites at 3rd day after operation (mL)	No	1230	676.02	631.322	−15.000	.000
	Yes	225	1433.49	979.461		
Amount of albuminsupplement at 3rd day after operation (g)	No	1219	24.821	28.6784	−17.828	.000
	Yes	225	64.256	38.8625		
Average creatinine at 3rd day after operation (umol)	No	1089	60.58	16.881	−.090	.928
	Yes	223	60.70	22.860		
Average PTA	No	715	72.55	10.93	20.693	.000
	Yes	216	53.29	14.99		
PTA1	No	675	71.57	11.817	16.12	.000
	Yes	205	52.20	15.926		
PTA2	No	372	69.56	11.616	15.173	.000
	Yes	152	51.22	14.610		
PTA3	No	236	76.03	12.578	9.411	.000
	Yes	94	57.94	16.86		

PTA = the prothrombin activity.

was 785.57 mL (0–6350 mL), average amount of supplemental albumin for 3 days after operation was 30.952 g (0–210 g), average value of creatinine within 3 days after operation was 60.59 umol/L (23–238 umol/L), average value of INR within 3 days after operation was 1.357 (0.65–5.1), average postoperative hospital stay was 12.32 days (1–134 days), and 227 cases had liver failure after the operation.

3.2. Postoperative single factor analysis

t tests of independent samples were performed for continuous variables of the studied factors (Table 1). The χ^2 test was performed for categorical variables (calibration χ^2 test or Fisher exact probability method was used) (Table 2).

Among the nonjaundice patients, there were statistical differences in age (years), BMI, TBIL, ALP, GGT, operation duration (hours), portal vein occlusion time (minutes), bleeding volume (mL), resection range, the volume ratio of remnant liver after surgical resection and standard liver (RLV/SLV), hospitalization time (days), cholangiocarcinoma, portal vein hypertension, plasma transfusion amount within 3 days after operation (mL), the supplemental amounts of albumin within 3 days after operation (g), the volumes of ascites within 3 days after operation (mL), and PTA ($P < .05$). However, the rest of the indexes had no significant differences.

3.3. Hierarchical comparison of results of partial variables with statistical significance in single factor analysis

1. The odds ratio (OR) of liver failure in the different age groups was analyzed (Table 3). All the *P* values were >.05. Therefore, it could not be considered that the OR values for liver failure in the different age groups were different.
2. BMI grouping: The *P* value was <.05 in groups with BMI ≥28 and OR value was 0.422, suggesting that the risk of liver failure reduced in groups with BMI≥28, compared with groups with BMI <18.5.
3. Time grouping: With the increase in time, the risk of liver failure significantly increased; and the OR value of the third group was 25.291. Therefore, longer time durations may be a possible risk factor.
4. Resection range: The value of OR increased significantly with the increase in the resection range, and $P < .05$. The OR value of the third group was at the maximum.
5. Occlusion grouping: The value of OR significantly increased with the increase in occlusion, and all was $P < .05$. The OR value of the third group was at the maximum.

3.4. Postoperative multiple factors analysis

All significant variables were introduced into the logistic regression model. The significant effects of TBIL and the

Table 2

Postoperative single factor analysis of categorical variables for patients with nonobstructive jaundice.

	Hepatic failure				
	No	Yes	Total	χ^2	P
Sex					
Male	779	137	916	0.56	.45
Female	458	90	548		
Hepatic sclerosis					
No	897	156	1053	1.23	.27
Yes	338	70	408		
Portal hypertension					
No	1223	218	1441	7.53	.01
Yes	12	8	20		
HBSAg					
No	770	135	905	0.67	.41
Yes	465	92	557		
Smoking					
No	960	168	1128	1.4	.24
Yes	277	59	336		
Diabetes					
No	1152	208	1360	0.65	.42
Yes	85	19	104		
Preoperation intervention					
No	1180	215	1395	0.2	.66
Yes	57	12	69		
Hepatectomy history					
No	1216	224	1440	0.02	.90
Yes	21	3	24		
Resection range (segment)					
(<3)	219	18	237	26.37	.00
(>=3,<5)	655	154	809		
(>=5)	78	31	109		
Operation method					
Open surgery	1135	217	1352	4.95	.08
Laparoscopy	79	6	85		
Robot	23	4	27		
Hepatocellular carcinoma					
No	734	138	872	0.15	.70
Yes	501	89	590		
Cholangiocellular carcinoma					
No	1056	182	1238	4.08	.04
Yes	180	45	225		
Gallbladder carcinoma					
No	1186	220	1406	0.54	.46
Yes	51	7	58		
Biliary stone					
No	1070	197	1267	0.01	.91
Yes	167	30	197		
Hemangioma					
No	1175	225	1400	7.83	.50
Yes	62	2	64		

HBSAg = hepatitis B surface antigen.

supplemental albumin amount within 3 days after operation on liver failure were found (Table 4).

4. Discussion

In the present study, the prevalence of liver failure after hepatectomy in patients with nonobstructive jaundice was 15.5%, in which 2 patients with liver failure died in the hospital and 5 cases were discharged voluntarily; and the fatality rate was 3%. In the present study, there was no significant difference in the risk of liver failure among the different age groups. Data from several large medical centers showed that advanced age was not associated with the incidence of liver failure. In a study involving 129 patients with partial hepatectomy, there was no correlation between the incidence of postoperative liver failure and mortality in patients with age >70 years.[4] The reason may be that the operative tolerance of the elderly population, including underlying disease, nutritional status, and pathophysiological characteristics, was fully assessed, and personalized surgery program was developed. The purpose of these measures was to control operative injury, to reduce the incidence of liver failure by means of combined multidisciplinary therapies, while the purpose of the treatment was achieved.

Malnutrition patients with BMI <18.5 had poor tolerance to surgery. Furthermore, the liver disease was chronic and consumptive, and the immune mechanism was disordered, which resulted in the dys-synthesis of postoperative liver cells.[5]

Most patients with portal hypertension had severe liver cirrhosis and poor hepatic function, and there were significant differences in hemodynamic changes after hepatectomy, compared with patients with nonportal hypertension.

Furthermore, elevated ALP and GGT levels may be related to the release of huge tumors themselves or the repeated cholangiolitis of patients with nonobstructive jaundice that resulted from biliary tract infection and the bile accumulation of bile capillaries caused by immune factors. These may have a certain reference value for the preoperative evaluation of the liver. Prolonged operation duration makes the body stay at a lower temperature for a long time, which causes the coagulation mechanism to be disordered. In addition, the damage and exposure of tissues and organs during operations with long time durations increases postoperative infection risk. The different portal vein occlusion technologies, the single control of occlusion time during the operation, and the cumulative occlusion time in the present study are the main factors that affect liver failure. The long-term repeatedly occlusion-induced ischemia and hypoxia would cause ischemia reperfusion injury to the liver. The liver is rich in blood supply; hence, portal vein occlusion during hepatectomy is an effective way to reduce bleeding. The occlusion time is determined by the site and size of the resected liver, and mode of operation. The hepatic ischemia-reperfusion injury is induced by the complement activation cascade, which activates Kuffer cells to produce oxygen-free radicals, to induce inflammation, and finally to induce endothelial cell injury. During reperfusion, other phenomena such as upregulation of other cell adhesion molecules, cytokine release, agglutination and activation of T lymphocytes and polymorphonuclear cells also occur, which lead to liver cell death.[6]

The increased volume of bleeding would cause the disorder of the coagulation mechanism, and induce changes in hemodynamics, which would aggravate the liver ischemia reperfusion injury.[7] A precise surgery can assess the resection range of the liver individually, and increase and protect the remaining functional liver volume; which are the decision factors of the postoperative liver compensatory function.[8] This study confirms that the range of hepatectomy is the influencing factor of liver failure. In the present study, individualized surgical design was performed according to the size of tumor and preoperative liver function, and transcatheter arterial chemoembolization, portal vein embolization (PVE), portal vein ligation (PVL), associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) and other means were used, to ensure that the tumor margin is negative, the operation is safe, and liver failure is reduced after hepatectomy.

Table 3

Hierarchical comparison of results of partial variables with statistical significance in single factor analysis.

	Hepatic failure				
	No	Yes	Total	χ^2	P
Age (years old) 0–30	55 (0.80)	14 (0.20)	69	7.67	.02
31–60 (1)	783 (0.83)	160 (0.17)	943		
61–90 (2)	399 (0.88)	53 (0.12)	452		
BMI <18,5	59 (0.75)	20 (0.25)	79	10.08	.02
≧18.5–24 (1)	588 (0.83)	117 (0.17)	705		
≧24–28 (2)	433 (0.86)	68 (0.14)	501		
≧28 (3)	148 (0.89)	19 (0.11)	167		
Operative time (h) <5	948 (0. 91)	96 (0.09)	1044	151.3	.00
5–10 (1)	276 (0.72)	110 (0.29)	386		
>10 (2)	5 (0.22)	18 (0.78)	23		
Resection range (segment) <3	219 (0.92)	18 (0.08)	237	26.37	.00
≧3,<5 (1)	655 (0.81)	154 (0.19)	809		
>=5 (2)	78 (0.72)	31 (0.28)	109		
Occlusion time (min) nonocclusion	522 (0.88)	72 (0.12)	594	59.87	.00
<30 (1)	435 (0.89)	54 (0.11)	489		
30–60 (2)	218 (0.77)	67 (0.24)	285		
>60 (3)	54 (0.62)	33 (0.38)	87		

BMI = body mass index.

Cirrhosis of the liver is the most widely recognized and the most important limiting factor for liver regeneration.[9] There was no statistical difference in several concerned factors such as cirrhosis. This reason may be that the identification of liver cirrhosis was based on the pathological results, in which more microscopic histological standards were included. Furthermore, no hierarchical analysis of cirrhosis degree was performed to them, which affected the results of the analysis. However, in our medical center, measures of the full preoperative evaluation of surgical treatment feasibility in patients with cirrhosis, the reasonable choice of operation mode, full reservation of residual functional liver volume after surgical resection, damage control during operation, and much attention given to perioperative management are of great significance to reduce the incidence of liver failure. It is noteworthy to mention that the disease classification in the data of nonobstructive jaundice is considered an influence factor, as a result to drew the conclusion that bile duct cell carcinoma had a statistical significance. The reason may be determined by the pathological characteristics of the disease. Huang[10] presented that the enlarged hepatectomy range is the inevitable trend of the radical operation for bile duct cancer due to tumor staging, vascular invasion, lymph node metastasis, neural invasion, and biological characteristics. Furthermore, the complexity of the surgery relatively increases the incidence rate of

Table 4

Postoperative multiple factors analysis.

						95% CI of OR	
	B	S.E	Walds	P	OR	Lower limit	Upper limit
Age (years old)	.013	.029	.202	.653	1.013	.957	1.073
Portal hypertension	2.733	1.882	2.108	.146	15.372	.384	614.588
BMI (body mass index)	−.044	.098	.199	.655	.957	.790	1.159
TBIL (total bilirubin)	.014	.006	5.697	.017	1.014	1.003	1.026
Alkaline phosphatase	.002	.002	1.369	.242	1.002	.998	1.006
r-glutamyltransferase	.001	.001	.738	.390	1.001	.999	1.002
Operative time	.800	.635	1.587	.208	2.225	.641	7.726
Resection range			2.360	.307			
Resection range (1)	2.042	1.381	2.187	.139	7.708	.515	115.417
Resection range (2)	1.388	1.690	.675	.411	4.008	.146	110.040
Hepatic portal occlusion time	.003	.011	.075	.785	1.003	.982	1.024
Amount of bleeding	.001	.000	2.833	.092	1.001	1.000	1.002
Residual liver volume/standard liver volume	.186	1.235	.023	.880	1.205	.107	13.560
Hepatocellular carcinoma	−1.332	.813	2.687	.101	.264	.054	1.298
Volume of ascites at 3rd day after operation	.000	.000	.009	.925	1.000	.999	1.001
Amount of albuminsupplement at 3rd day after operation	.020	.007	9.018	.003	1.020	1.007	1.034
Average PTA	.020	.027	.544	.461	1.020	.968	1.075
Constant	28.831	25415.422	.000	.999	.000		

Resection range (<3 segment) as the control group, resection range (1) (>=3, <5 segment), resection range (2) (>=5 segment).

hepatic failure after hepatectomy. The formation of ascites was closely associated with increased portal vein perfusion pressure and postoperative liver anatomical changes.

These results of binary logistic multifactoral analysis revealed that preoperative bilirubin level and the supplemental albumin amount within 3 days after operation were independent factors of postoperative liver failure. Preoperative bilirubin level has important significance in evaluating the liver function of patients with liver tumor and postoperative tolerance.[11] The elevated preoperative bilirubin level in patients with nonobstructive jaundice may be due to factors on bile duct secretion function, bile duct inflammation, immune injury, and other factors. These can reflect liver function before the operation, and has an important effect on residual and functional liver volume after resection. Peri-operative albumin level in patients with liver diseases was significantly lower than that in normal persons, the more severe the disease was, the lower the synthesis ability became.[12] The postoperative supplemental amounts of albumin were closely related to the preoperative liver disease course, nutritional status, liver cirrhosis degree, the amount of albumin lost during hepatectomy, postoperative stress, and the short time synthesis inhibition after surgery. Furthermore, the amount of albumin cannot meet the needs of the body in a short period of time; and the extraneous source of supplemental albumin significantly increased. These are the main effects of the influencing factors on patients with liver failure after surgery.

The results of the analysis revealed that as a single indicator, the average value of PTA within 3 days after surgery has the diagnostic value in the ROC analysis; and its accuracy was higher. As a common coagulation index, PTA is the most important indicator of the severity of liver disease and the prognosis.[13,14] The reason may be that inflammatory reactions and polyorganic insufficiency can result in disorders of coagulation mechanism.[15,16] Among the diagnostic criteria of the present study, the definition of postoperative liver failure is determined according to the value of INR. The result of the correlation analysis of PTA versus INR revealed that these 2 indexes were highly and negatively correlated (correlation coefficient $r=-0.816$, $P=.000$) (Fig. 1). In the postoperative early stage, the judgment of liver function was interfered due to INR, which was influenced by various factors (liver function, blood volume, drugs, and so on). The average value of PTA within 3 days after operation cooperates with INR, and can be considered the diagnostic index of early liver failure. A PTA (mean) <56.42 suggests the occurrence of early liver failure, and the prognosis can be determined through a sustainable observation of the tendency. The amounts of plasma infusion within 3 days after operation were usually determined according to clinical experience and the supply conditions of blood products. However, this was relatively informal, and was not discussed in the present study.

The amount of albumin and ascites within the 3 days after operation were more objective. ROC analysis was performed to these 2 indexes, which had diagnostic significance to liver failure; and the results revealed that they were not perfect in AUC, sensitivity and specificity, and the combined diagnosis of these 2 indexes did not have advantages either. However, the efficiency of the diagnosis is greatly increased when these 2 indexes were combined with the average value of PTA (AUC value was 0.903, *P* value was.000<.05; when predictive probability was 0.39, Se was 0.826, and Sp was 0.948) (Fig. 2 and Table 5).

Therefore, in the study of the early diagnosis of patients with nonobstructive jaundice, multiple indicators combined with clinical manifestations are still needed to determine the occurrence of liver failure. It also requires surgeons to fully assess the risks before surgery, and improve systemic conditions and liver function. Therefore, it is very important to control the injury during the operation and correctly interpret the relevant indexes at different stages after the operation. In the present study, the risk factors associated with liver failure were obtained by a statistical analysis of a large sample. The risk factors were various, including the incidence of diseases, benign and malignant nature, specificity of surgical methods, surgical trauma size, which will bias the results. Therefore, stratification of the disease, and related factors such as the use of the drugs, the occurrence of infection, and the implementation of enteral nutrition were studied. This would make the result more meaningful. In addition, the present study was a retrospective study, due to the influence of confounding factors, the bases of evidence-based medicine for the association of the early predictors for postoperative liver failure with the occurrence

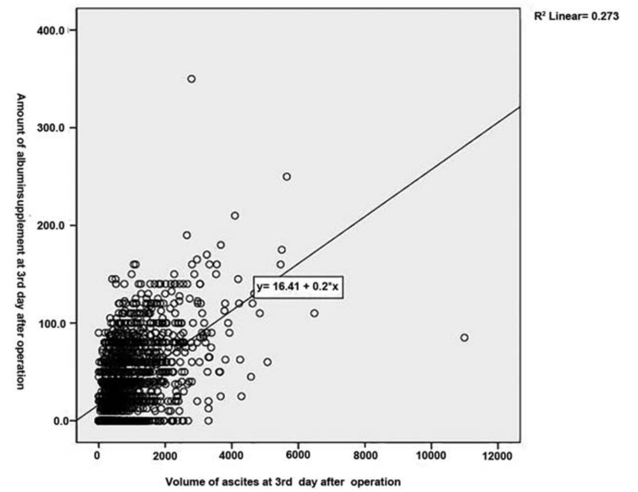

Figure 1. Scatter diagram for analysis of the correlation between average INR and average PTA of PoD3. INR = international standardization ratio, PTA = the prothrombin activity.

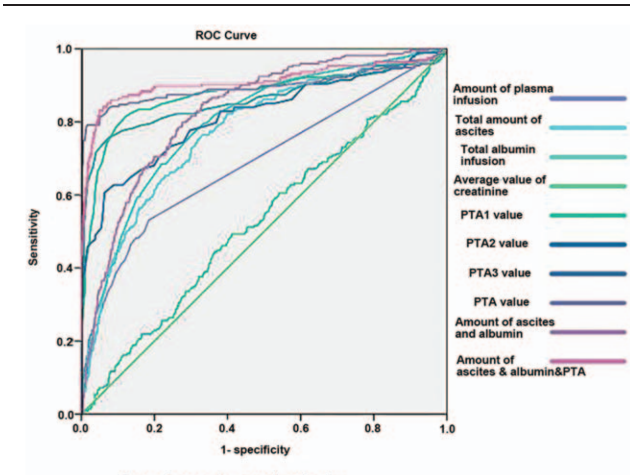

Figure 2. ROCs of various postoperative indexes. ROC = receiver operating characteristic.

Table 5

Diagnosis efficiency of the postoperative index for patients with nonobstructive jaundice.

Postoperative index	AUC	*P* value	Cut-off value	Se	Sp	Diagnostic value
PTA1	0.874	.000	58.50	0.815	0.879	Yes
PTA2	0.863	.000	55.50	0.757	0.925	Yes
PTA3	0.817	.000	59.50	0.606	0.936	Yes
PTA (MEAN)	0.895	.000	56.42	0.792	0.983	Yes
PoD3 total albumin infusion (g)	0.798	.000	48.75	0.684	0.780	Yes
PoD3 total amount of ascites (mL)	0.775	.000	731	0.756	0.677	Yes
PoD3 ascites and albumin	0.833	.000		0.799	0.817	Yes
PoD3 ascites and albumin and PTA (mean)	0.903	.000		0.826	0.948	Yes
PoD3 amount of plasma infusion (mL)	0.690	.000	60	0.531	0.816	Yes
PoD3 average value of creatinine	0.526	.224		No		

AUC = area under the curve, PTA = the prothrombin activity.

and prognosis of liver failure were not as persuasive as rigorous, normative prospective studies.

References

[1] Rahbari NN, Garden OJ, Padbury R, et al. Posthepatectomy liver failure: a definition and grading by the International Study Group of Liver Surgery (ISGLS). Surgery 2011;149:713–24.

[2] Urata K, Kawasaki S, Matsunami H, et al. Calculation of child and adult standard liver volume for liver transplantation. Hepatology 1995; 21:1317–21.

[3] Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight be known. 1916. Nutrition 1989;5:303–11.

[4] Aldrighetti L, Arru M, Caterini R, et al. Impact of advanced age on the outcome of liver resection. World J Surg 2003;27:1149–54.

[5] Awad S, Constantin-Teodosiu D, Macdonald IA, et al. Short-term starvation and mitochondrial dysfunction—a possible mechanism leading to postoperative insulin resistance. Clin Nutr 2009;28:497–509.

[6] Zhang DX, Jiang S, Dong JH. Research progress of liver failure after extensive hepatectomy. Chin J Curr Adv Gen Surg 2015;04:295–9.

[7] Xiong BW, Hou K. Risk factors of the perioperative liver failure after hepatectomy. China Mod Med 2013;20:12–3+16.

[8] Yin TS, Yi YY, Mao XX, et al. Meta-analysis of risk factors for posthepatectomy liver failure in patients with hepatocellular carcinoma. J Clin Hepatol 2014;30:1009–14.

[9] Lafaro K, Buettner S, Maqsood H, et al. Defining post hepatectomy liver insufficiency: where do we stand. J Gastrointest Surg 2015;19:2079–92.

[10] Huang ZQ. Current situation and my opinion of surgical treatment for Hilar cholangiocarcinoma. Chin J Pract Surg 2007;341–6.

[11] Geng XP, Zhao ZH. A clinical investigation on factors influencing postoperative serum bilirubin level in patients with primary liver cancer. Chin J Gen Surg 2010;23:1314–5.

[12] Zeng DX, Pan LH, Xiang CX. The clinical significance of detection of serum prealbumin in patients with hepatopathy. J Med Theory Pract 2010;1314–5.

[13] Lv RY, Li SX, Wu JZ. Relation between serological indicators and prognosis in patients with severe hepatitis. Appl J Gen Pract 2012; 10:1520–1.

[14] Lv RY, Li SX, Wu JZ, et al. Development of a prognostic factors model for severe hepatitis. J Clin Hepatol 2012;28:789–92.

[15] Levi M. The coagulant response in sepsis and inflammation. Hamostaseologie 2010;30: 10–2, 14–16.

[16] Cheng T, Mathews K, Abrams-Ogg A, et al. The link between inflammation and coagulation: influence on the interpretation of diagnostic laboratory tests. Compend Contin Educ Vet 2011;33:E4.