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Effect of the Intermittent Pringle Maneuver on Residual Liver Function after Hepatectomy: A Retrospective Case-Controlled Study

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Abstract

Background: The Pringle Maneuver (PM) interrupts the blood flow through the hepatic artery and the portal vein to help control bleeding. This study analyzes the effects of the Intermittent Pringle Maneuver (IPM) on the surgical process and the liver function recovery.

Methods: This case-control study retrospectively evaluated 257 patients who underwent hepatectomy. In the IPM group, the hepatic vascular flow was intermittently clamped, with cycles of 10 minutes of inflow occlusion followed by 5 minutes of reperfusion that were repeated until the end of the surgery. In the non-IPM group, liver resection was performed without hepatic blockage.

Results: Surgery with IPM has advantages over surgery without IPM in terms of operation time and bleeding volume. The postoperative hospitalization time and ICU time were significantly lower in the IPM group than in the non-IPM group. The first day after the operation, the level of aspartate amino transferase (AST, p=0.0221), the level of total bilirubin (p=0.0171), the pro Thrombin Time (PT, p=0.0257), and the Activated Partial Thromboplastin Time (APTT, p=0.0063) were significantly higher in the non-IPM group than in the IPM group.

Conclusion: The IPM does not negatively affect postoperative liver function recovery; the use of the IPM results in shorter operation times, lower bleeding volumes, and shorter hospital and ICU stays compared to surgeries without the use of the IPM.

Keywords: Hepatectomy; Pringle maneuver; Liver function; Retrospective; Clinic

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Introduction

Hepatectomy is the most effective way to treat hepatobiliary cancer, such as hepatic carcinoma. Massive bleeding is usually the major problem in hepatectomy. During the operation, a variety of surgical techniques are used to prevent possible turbulent bleeding. Although a successful hepatectomy does not necessarily require blocking hepatic blood flow [1], controlling the hepatic blood flow is helpful for providing a relatively bloodless surgical environment, facilitating liver disconnection, reducing intraoperative bleeding, and shortening the operation time. The Pringle Maneuver (PM) is a surgical maneuver used to interrupt the blood flow through the hepatic artery and the portal vein to help control bleeding from the liver; the PM is technically easy to implement and often used by surgeons [2]. However, injuries to hepatocyte morphology and liver function caused by hepatic ischemia-reperfusion after blood flow blocking by the PM is the main factor affecting its clinical application. However, there is still controversy about the advantages and disadvantages of the PM [3,4]. Unlike the effect of PM on liver dysfunction in animal experiments [5], in clinical practice, although blocking hepatic blood flow leads to hepatic ischemia, metabolism in the human liver is not significantly affected [6]. The main reason may be the more abundant collateral circulation of the human liver compared with the livers in animal models. In addition, the tolerance of the liver to warm ischemia and ischemia-reperfusion injury induced by the PM may be related to the duration of hepatic ischemia [7]. An Intermittent PM (IPM) can partially reduce residual hepatic ischemic damage, thereby prolonging the total tolerance time of the residual liver to ischemia. The ability of the residual liver to regenerate is another important aspect of evaluating the success of a hepatectomy, and the effect of intraoperative hepatic blood flow occlusion on liver regeneration remains controversial [8]. Thermal ischemia of the liver may lead to protein synthesis

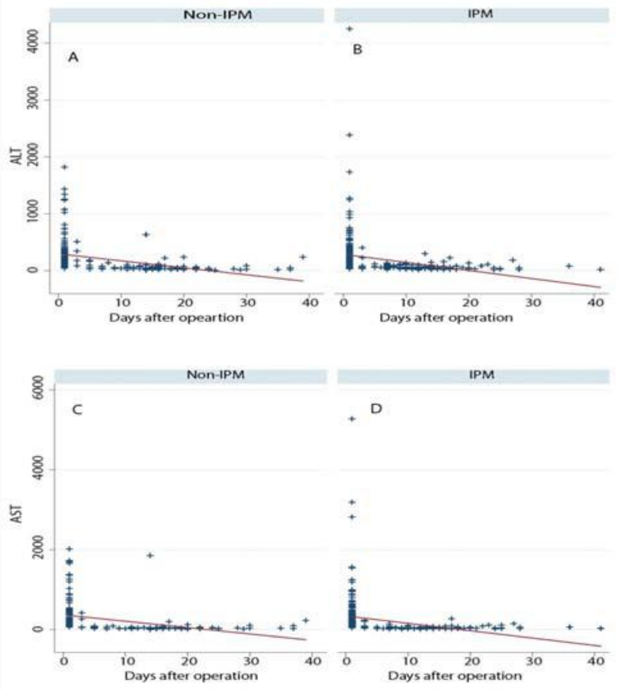

Figure 1: Regression analysis of ALT/AST recovery with postoperative time in non-IPM and IPM patients.
A: ALT change in Non-IPM patients; B: ALT change in IPM patients; C: AST change in Non-IPM patients; D: AST change in IPM patients

dysfunction in hepatocytes. However, a study has shown that the PM does not affect liver regeneration after hepatectomy, and short-term thermal ischemia can even accelerate liver regeneration [9]. In this study, we retrospectively analyzed the effects of the IPM on the surgical process and the recovery of postoperative liver function and compared hepatectomy with IPM to hepatectomy without IPM.

Patients and Methods

Patients

This case-control study retrospectively evaluated 257 patients who underwent hepatectomy in the hepatological surgery department of the Army Medical University (Third Military Medical University) First Affiliated Hospital (Southwest Hospital) from 2012 to 2016. The patient age range was 12 to 84 years old, with 185 males and 72 females. In total, 145 patients were in the IPM group, and 112 patients were in the non-IPM group. The inclusion criteria were as follows: patients undergoing hepatectomy, including those with hepatic carcinoma, gallbladder cancer, other cancers (such as intrahepatic neuroendocrine cancer, and metastatic cancer), and other non-cancer diseases (such as hepatoliths and hepatic abscess necrosis), who provided informed consent. The following patients were excluded from this study: patients undergoing major operations on the liver or adjacent areas, patients who did not provide informed consent and patients who did not undergo liver resection. All included patients were consecutive patients who met the inclusion criteria. This study was approved by the Ethics Committee for Clinical Pharmacology.

Table 1: Characteristic of included patients.

	Non-IPM	IPM	p value
n	112	145	
Age (year)	50.76 ± 11.99	50.97 ± 13.31	0.898
Sex (Male/Female)	80/32	105/40	0.862
Diagnosis			
Hepatic carcinoma	74	108	
Gallbladder cancer	17	7	
Other cancer	2	0	
No cancer	19	29	0.013
Liver related basic disease			
Cirrhosis	26	45	0.164
Portal hypertension	10	13	0.992
Hypersplenism	11	15	0.89
HbsAg(+)	66	86	0.951
HBV DNA(+)	49	54	0.291
AFP>40	36	55	0.948
Others	31	31	0.242
Non-liver combined disease			
Hypertension	10	8	0.288
Diabetes	9	18	0.256
Others	23	24	0.413
Liver function reserve			
ALT (U/L)	43(24-84)	38.45(21.65-68.5)	0.2797
AST (U/L)	48(29-89)	43.75(28.35-71.6)	0.327
Albumin (g/L)	40.5(28.8-439.4)	41.3(38.1-45)	0.1882
Total bilirubin (μmol/L)	17(5.7-1436)	15.8(11.8-23.3)	0.1885
Child-pugh classification			
5	77	112	
6	8	9	
7	15	12	
8	6	5	0.421
Coagulation function			
Prothrombin time(seconds)	11.70 ± 1.10	11.67 ± 1.10	0.8992
Platelet ($\times 10^9$/L)	192.77 ± 83.31	199.81 ± 98.42	0.7748
Characteristics of Hepatic carcinoma patients			
TNM stage			
1	42	63	
2	13	18	
3	13	20	
4	8	6	0.666
Cancer embolus	20	25	0.898
Lymphatic metastasis	7	6	0.444

Abbreviations: AFP: Alpha-Feto Protein; ALT: Alanine Transaminase; AST: Aspartate Amino Transferase; IPM: Intermittent Pringle Maneuver; TNM stage: Tumor, Lymph Node, Metastasis stage

Preoperative evaluation

The gender, age and clinical diagnosis of each patient were recorded before the operation. Liver-related complications and other comorbidities were also recorded. The preoperative laboratory blood tests included the Level of Alanine Aminotransferase (ALT), the Level of Aspartate Amino Transferase (AST), the level of serum albumin, the level of total bilirubin, the platelet count, the Prothrombin Time (PT), the level of Hepatitis B Surface Antigen (HBsAg), the presence of Hepatitis B Virus (HBV) DNA, and the Level of Alpha-Fetoprotein

(AFP). The Child-Pugh classification scheme was used to assess the liver reserve function of patients [10]. For patients with hepatic carcinoma, TNM staging was evaluated.

Surgical procedure

All surgical procedures were performed by our departmental doctors to ensure consistency. The extent of liver resection was precise segmental resection. The hepatoduodenal ligament was clinched to control the hepatic vasculature until the pulse of the hepatic artery disappeared distally. In the IPM group, the hepatic vasculature was intermittently clamped, with cycles of 10 minutes of inflow occlusion followed by 5 minutes of reperfusion that were repeated until the end of the surgery. In the non-IPM group, liver resection was performed without hepatic blockage. The duration of hepatic vascular occlusion (excluding the open period), the number of occlusions, the duration of the operation, and the amount of bleeding during the operation were recorded.

Postoperative management

Postoperative complications and the durations of hospital and ICU stays were collected. The leukocyte count, neutrophil ratio, platelet count, level of ALT, level of AST, level of serum albumin, level of total bilirubin, PT, Activated Partial Thromboplastin Time (APTT), and level of D-Dimer (D-D) were measured on the 1st, 3rd, 5th, and 7th postoperative days and at discharge. No results were recorded when the test was normal or the patient refused the test.

Statistical analysis

The qualitative data are expressed as frequencies (percentages), and statistical significance was evaluated using the χ^2 test. Quantitative data were expressed as the mean ± standard deviation and the groups were compared using Analysis of Variance (ANOVA) if the data were normally distributed. If the data were non-normally distributed, the data were compared with the Kruskal-Wallis test and are expressed as medians and quartiles. Linear regression analysis was used to analyze the blocking time and postoperative liver function. The recovery of liver function with increasing postoperative time in IPM patients and non-IPM patients was further analyzed. This seemingly unrelated estimation was used to test the difference in regression equation coefficients [11]. The subgroup results of patients with hepatic carcinoma and those with cirrhosis were analyzed. All the calculations were performed with STATA 14.0 software (StataCorp LLC, TX, US), and results with p<0.05 were considered to be significant.

Results

There was no difference in the mean age or sex ratio between the IPM and non-IPM groups. For the disease type, there was a significant difference between the two groups (p=0.013). There were no significant differences between the two groups in terms of hepatic comorbidities, such as cirrhosis, portal hypertension and hypersplenism. There were also no significant differences between the two groups in terms of the incidence of hypertension and diabetes. With regard to the laboratory tests, there were no significant differences in the level of ALT, the level of AST, the level of albumin, the level of total bilirubin, the PT, the platelet count, the level of HBsAg, the amount of HBV DNA, or the AFP between the two groups (Table 1). The operative time and bleeding volume of the IPM group were significantly superior to those of the non-IPM group. The duration of portal occlusion was 60.25±40.68 minutes and 50 (40-80) minutes and the number of occlusions was 5.89 ± 3.99 and 5 (3-8) in the IPM group. There were differences between the two groups in terms of the performance of cholecystectomies (p=0.044) and other accessory operations (p=0.05) (Table 2). In terms of the postoperative complications, there were no significant differences between the two groups in postoperative bleeding, bile leakage, incision infection, abdominal abscess, incision effusion, ascites, pulmonary infection, hepatic insufficiency/liver failure, or death. The incidences of pleural effusion and respiratory failure in the IPM group were significantly lower than those in the non-IPM group. The postoperative hospitalization time and ICU time in the IPM group were significantly lower than those in the non-IPM group (Table 2). On the first day after the operation, the leukocyte count, neutrophil ratio, platelet count, level of ALT, level of albumin and level of D-D were not significantly different between the two groups, but the AST in the non-IPM group was significantly higher than that in the IPM group (p=0.0221). The level of total bilirubin in the non-IPM group was significantly higher than that in the IPM group (p=0.0171). The PT in the non-IPM group was also significantly higher than that in the IPM group (p=0.0257). The APTT in the non-IPM group was significantly higher than that in the IPM group (p=0.0063). On the third day after operation, only the neutrophil ratio remained significantly higher in the non-IPM group than in the IPM group (p=0.0021), and there were no significant differences in the other indexes. On the fifth and seventh postoperative days and at discharge, there were no significant differences in any of the indexes between the two groups (Table 3). The effects of hepatic occlusion time on the levels of ALT and AST after operation were analyzed by regression (Table 4). The Univariate regression analysis results showed that the prolongation of interruption time was related to an increase in the levels of ALT (coef=2.11, p<0.001) and AST (coef=2.29, p=0.003) on the first day after operation. On the fifth day after surgery, the interruption time was correlated with

Table 2: Characteristic of patients during and after surgery.

	Non IPM	IPM	p value
Surgery time(min)	351(261-465)	305(236-387)	0.0134
Amount of bleeding(ml)	500(300-800)	400(200-700)	0.0015
Hepatic portal occlusion time (min)	0	50(40-80)	NA
Count of occlusion	0	5(3-8)	NA
Attach surgery			
Cholecystectomy	80	86	0.044
Others	48	45	0.05
Postoperative complication			
Bleeding	2	2	0.794
Biliary fistula	3	2	0.455
Incision infection	4	4	0.71
Intra-abdominal abscess	3	5	0.725
Sectional effusion	6	17	0.076
Ascites	29	24	0.066
Pulmonary infection	37	37	0.187
Pleural effusion	69	68	0.019
Respiratory failure	3	0	0.047
Liver failure/dysfunction	1	0	0.254
Death	0	3	0.126
Hospital duration (day)	15(13-19.5)	12(10-16)	<0.001
ICU duration (day)	3(2-3)	2(2-3)	0.0206

Abbreviations: ICU: Intensive Care Unit; IPM: Intermittent Pringle Maneuver

Table 3: Results of blood biochemistry and coagulation function after operation.

	Non IPM	IPM	p value
First day after operation			
WBC	11.42(9.14-14.47)#	12.64(10.02-15.39)	0.072
NLR	88.05(85.55-91.25)	88.3(84.7-91.05)	0.775
PLT	143(111-192)	157(114-221)	0.119
ALT	218(125-338)	159.85(97.7-348.1)	0.123
AST	252(163-464)	203.9(121.2-386)	0.022
ALB	32.32 ± 5.12#	31.94 ± 5.71	0.592
TB	26.9(17.6-50.2)	22.8(15.5-34.9)	0.017
PT	14.9(13.8-16.5)	14.2(13.4-15.7)	0.026
APTT	36.3(31-44.2)	33.2(28.7-38.7)	0.006
D-Dimer	3.39(0.867-4.43)	3.74(2.35-5.28)	0.066
Third day after operation			
WBC	9.36(6.39-11.34)	8.84(6.59-11.66)	0.976
NLR	84.4(80.4-89.6)	81.6(78-84.9)	0.002
PLT	122(82-165)	130.5(99-169)	0.416
ALT	136(82-266)	99.2(68.3-224)	0.087
AST	84(59-134)	81.3(54.6-140.2)	0.393
ALB	37.8(34.5-41.2)	37.35(32.9-40.1)	0.313
TB	26(16.1-42)	25.5(15.3-35.2)	0.458
PT	14.7(12.6-16.8)	14.1(12.9-16.8)	0.67
APTT	40(32.95-53.2)	37.8(30.3-48.2)	0.129
D-Dimer	3.84(2.2-6.57)	4.93(3.09-9)	0.077
Fifth day after operation			
WBC	7.81(5.92-10.6)	7.99(6.29-9.64)	0.916
NLR	76.63 ± 8.98	73.99 ± 7.45	0.118
PLT	142(77-216)	166(110-207)	0.271
ALT	66.5(39.5-106)	79.95(53-123.4)	0.302
AST	49(31-62.5)	49.15(31-70.9)	0.422
ALB	37.15 ± 5.14	37.3 ± 4.22	0.872
TB	26.95(15.65-60.3)	22.05(16.9-33.6)	0.21
PT	15.35(13.45-17.15)	13.8(13.1-16)	0.272
APTT	40.2(30.9-46.7)	36.3(30.9-38.8)	0.152
D-Dimer	6.86 ± 5.91	9.53 ± 6.92	0.237
Seventh day after operation			
WBC	8.7(7.14-11.815)	9.045(7.73-12.465)	0.8
NLR	73.74 ± 8.88	70.98 ± 8	0.146
PLT	173.32 ± 85.33	191.71 ± 96.65	0.384
ALT	65.5(43-93)	56.3(42-84.2)	0.97
AST	34.5(26.5-62)	37.4(29-53.9)	0.803
ALB	36.69 ± 5.25	35.47 ± 3.75	0.208
TB	30.55(16-76.3)	20.9(16.1-34.7)	0.117
PT	15.36 ± 3.02	14.67 ± 2.77	0.624
APTT	33.3(27.8-47.2)	37.5(29.7-50.8)	0.824
D-Dimer	6.92 ± 5.86	11.8 ± 9.33	0.142
Discharge from hospital			
WBC	6.46(4.76-8.2)	6.745(5.265-8.585)	0.221
NLR	67.57 ± 10.59	67.78 ± 7.38	0.869
PLT	199.5(137-275)	189.5(139.5-270)	0.588
ALT	41(29-61)	50(31.05-67.7)	0.056
AST	38(26-48)	36.8(27.4-50.15)	0.961
ALB	36.9(33-39.9)	35.15(32.3-38.65)	0.077
TB	18.6(13-32.9)	16.75(12.25-25.45)	0.399
PT	13(12.1-14.2)	13.15(11.95-14.25)	0.953
APTT	28.8(27.4-33.6)	30.5(28-35.9)	0.36
D-Dimer	7.55 ± 5.59	7.98 ± 5.17	0.816

Abbreviations: WBC: White Blood Cell; NLR: Neutrophil To Lymphocyte Ratio; PLT: Platelet; ALT: Alanine Transaminase; AST: Aspartate Transaminase; ALB: Albumin; TB: Total Bilirubin; PT: Prothrombin Time; APTT: Activated Partial Thrombin Time

#: Normal distribution quantitative data is expressed as mean ± standard deviation and compare the group comparison using analysis of variance; non distribution data is expressed as median and quartile, and compare the group comparison using Kruskal-Wallis test.

the level of ALT (coef=0.46, p=0.036). No correlation was found between the interruption time and the levels of ALT and AST on the seventh day after surgery or at discharge. After adjusting for age, sex, preoperative ALT level and preoperative AST level, multivariate analysis revealed similar results to those of the univariate analysis. In the subgroup analysis of hepatic carcinoma patients, univariate regression showed that the prolongation of interruption time was related to the increase in the levels of ALT (coef=1.66, p=0.001) and AST (coef=2.00, p=0.002) on the first day after the operation. On the fifth day after operation, the interruption time was significantly correlated with the level of ALT (coef=0.41, p=0.038). No correlation was found between the interruption time and the levels of ALT and AST on the seventh day after operation or at discharge. Multivariate analysis showed similar results. For cirrhosis patients, univariate regression analysis showed that the prolongation of interruption time was related to the increase in the level of ALT (coef=3.94, p<0.001) and AST (coef=3.24, p=0.002) on the first day after operation. In addition, a correlation was found between the interruption time and the level of ALT on the third day after surgery (coef=1.86, p=0.022). No correlation was found between the interruption time and the levels of ALT or AST on the fifth and seventh days after surgery and at discharge. Multivariate analysis showed similar results (Table 4). Regression analysis was used to analyze the relationships between the levels of ALT and AST and postoperative time in the IPM group and the non-IPM group. The levels of ALT and AST on the first day after operation and at discharge were selected. The regression results of the levels of ALT (y= -12.29x+294.41, p<0.001) and AST (y= -15.92x+369.09, p<0.001) with postoperative time were significant in the non-IPM group (Figure 1A,1C). The regression results of the levels of ALT (y= -14.19x+285.04, p<0.001) and AST (y= -18.44x+341.28, p<0.001) with postoperative time were also significant in the IPM group (Figure 1B,1D). There were no significant differences in regression coefficients between the IPM and non-IPM groups (ALT: p=0.5247; AST: p=0.5152). In hepatic carcinoma patients, the regression relationships between the levels of ALT (y= - 14.44x+301.35, P<0.001) and AST (y = -17.88x+350.36, p<0.001) and postoperative time were significant in the non-IPM group. In the IPM group, the regression relationships between the levels of ALT (y= -14.21x+272.46, p<0.001) and AST (y= -18.41x+322.44, p<0.001) and postoperative time were also significant. There was no significant difference in the regression coefficients between the two groups (ALT: p=0.9387; AST: p=0.8901). In cirrhotic patients, the regression relationship between the levels of ALT (y= -16.24x+346.23, p<0.001)

Table 4: Univariate and multivariate analysis of hepatic vascular occlusion time and postoperative ALT AST results.

All included patients		Univariate analysis		Multivariate analysis#	
After operation	Index	coef. (95% CI)	p value	coef.(95% CI)	p
1st day	ALT	2.11(0.95,3.28)	0	1.91(0.8,3.03)	0.001
	AST	2.29(0.79,3.78)	0.003	2.16(0.66,3.66)	0.005
3rd day	ALT	0.56(-0.24,1.35)	0.17	0.51(-0.25,1.28)	0.188
	AST	0.19(-0.42,0.79)	0.543	0.18(-0.43,0.78)	0.562
5th day	ALT	0.46(0.03,0.89)	0.036	0.45(0.05,0.85)	0.028
	AST	0.1(-0.05,0.25)	0.181	0.13(-0.02,0.27)	0.09
7th day	ALT	0.17(-0.09,0.43)	0.193	0.1(-0.13,0.34)	0.388
	AST	-0.01(-0.14,0.12)	0.874	-0.02(-0.15,0.12)	0.812
Discharge	ALT	0.03(-0.15,0.21)	0.759	0.02(-0.17,0.2)	0.861
	AST	-0.19(-0.6,0.22)	0.371	-0.23(-0.65,0.19)	0.278
Cirrhosis patients		Univariate analysis		Multivariate analysis	
After operation	Index	coef. (95% CI)	p value	coef. (95% CI)	p
1st day	ALT	3.94(2.02,5.87)	0	3.94(1.97,5.91)	0
	AST	3.24(1.21,5.26)	0.002	3.2(1.08,5.33)	0.004
3rd day	ALT	1.86(0.3,3.42)	0.022	2.17(0.58,3.76)	0.01
	AST	0.65(-0.02,1.33)	0.057	0.63(-0.1,1.37)	0.087
5th day	ALT	1.07(-0.69,2.83)	0.211	1.48(-0.58,3.54)	0.14
	AST	0.35(-0.2,0.89)	0.196	0.43(-0.21,1.07)	0.166
7th day	ALT	-0.05(-0.57,0.46)	0.837	0.02(-0.55,0.6)	0.927
	AST	-0.03(-0.27,0.21)	0.784	-0.04(-0.29,0.21)	0.73
Discharge	ALT	0.19(-0.19,0.57)	0.308	0.19(-0.19,0.58)	0.311
	AST	-0.05(-0.19,0.1)	0.503	-0.04(-0.19,0.12)	0.634
Hepatocellular carcinoma patients		Univariate analysis		Multivariate analysis	
After operation	Index	coef. (95% CI)	p value	coef. (95% CI)	p
1st day	ALT	1.66(0.67,2.65)	0.001	1.61(0.6,2.63)	0.002
	AST	2(0.76,3.24)	0.002	1.8(0.5,3.1)	0.007
3rd day	ALT	0.36(-0.37,1.09)	0.332	0.42(-0.34,1.18)	0.277
	AST	0.24(-0.06,0.54)	0.118	0.26(-0.04,0.55)	0.088
5th day	ALT	0.41(0.02,0.8)	0.038	0.41(0.01,0.81)	0.043
	AST	NA		0.11(-0.04,0.26)	0.14
7th day	ALT	NA		NA	NA
	AST	NA		NA	NA
Discharge	ALT	0.08(-0.08,0.24)	0.315	0.1(-0.06,0.26)	0.213
	AST	-0.01(-0.13,0.1)	0.817	-0.04(-0.17,0.08)	0.526

Adjust for age, sex, and preoperative ALT/AST variants.

and AST (y= -20.95x+427.96, p<0.001) and postoperative time were significant in the non-IPM group. In the IPM group, the regression relationships between the levels of ALT (y= -15.89x+288.09, p<0.001) and AST (y= -19.39x+322.91, p<0.001) and postoperative time were also significant. There was no significant difference in the regression coefficients between the two groups (ALT: p=0.9498; AST: p=0.8183).

Discussion

This study retrospectively analyzed 257 patients who underwent hepatectomy and evaluated the effect of the IPM on postoperative liver function. In our study, the IPM was revealed to have advantages over surgery without IPM in terms of operation time and bleeding volume. The incidences of pleural effusion and respiratory failure were also higher in the non-IPM group than in the IPM group. The hospitalization time and ICU time of the IPM group were clearly shorter than those of the non-IPM group. The level of AST, level of total bilirubin, PT, and APTT in the non-IPM group was significantly higher than those in the IPM group on the first day after operation. On the third day after operation, the neutrophil ratio in the non-IPM group was significantly higher than that in the IPM group. Other indicators showed no significant differences between the two groups. In the regression analysis of the levels of ALT and AST and the total hepatic occlusion time, the levels of ALT and AST on the first day after operation increased with the prolongation of the occlusion time, regardless of whether all hepatectomy patients were considered or only those with hepatic carcinoma or cirrhosis. In the analysis of changes in the levels of ALT and AST during the postoperative period, the levels of ALT and AST of the two groups decreased significantly with increasing postoperative time, but there were no significant differences between the two groups. The same results were found in patients with hepatic carcinoma and cirrhosis.

In this study, we found that the level of AST, level of total bilirubin, PT, and APTT in the non-IPM group were significantly higher than those in the IPM group. The longer operation time and increased blood loss in the non-IPM group compared to the IPM group may explain the increase in the AST and the level of total bilirubin in the non-IPM group. A prospective study also suggested that the PM could reduce bleeding during hepatectomy, reduce hemodynamic disturbance, and protect liver function in the early postoperative period [12]. The PM is even considered safe for patients with severe cirrhosis [6]. In addition, intermittent occlusion of the hepatic hilu may result in hepatic tissue tolerance of and protection against ischemia-reperfusion injury [7]. Liver ischemia preconditioning before PM has also been shown to enhance liver tolerance [13]. For liver transplantation, intermittent interruption still has no significant effect on liver function [14,15].

This study only compared hepatectomies with and without IPM in this study; however, there is still controversy regarding continuous and intermittent PM. A study suggested that continuous PM could more successfully reduce liver injury and promote liver recovery than IPM [16]. However, another study suggested that there was no significant difference in liver function between patients undergoing continuous and intermittent interruption of the hepatic blood flow [17]. This finding may be related to the duration of the interruption time. If the duration of a single interruption event does not exceed the threshold for liver ischemia-reperfusion injury, it will not cause liver damage. Once the threshold is exceeded, the interruption will cause liver damage. Therefore, the effect of the duration of a single interruption event on liver postoperative recovery may exceed that of the total interruption time. In a clinical prospective RCT, performance of the IPM with intervals of 30 min was still considered safe [18]. In retrospective clinical studies, it was concluded that IPM clamping exceeding 60 min to 120 min was still safe [19-21]. In this study, more intensive circulation was used with an intermittent strategy using cycles of 10 min of inflow occlusion followed by 5 min of reperfusion. This intermittent strategy did not cause significant liver damage in this study, and liver function was more strongly affected in the non-IPM group than in the IPM group on the first postoperative day. Therefore, it is recommended that the interruption strategy be clearly stated in future reports on IPM to allow comparisons among studies. With regard to the recovery of liver function after operation, the levels of ALT and AST decreased gradually as the postoperative time increased in both the IPM and non-IPM groups; there was no significant difference in the recovery of liver function between the two groups in this study. In terms of postoperative complications, this study found that there were higher incidences of pleural effusion and respiratory failure in the non-IPM group than in the IPM group. In a RCT with patients with liver tumors, the population receiving the IPM had more subclinical ascites and pleural effusion than the non-IPM population [22]. Finally, whether the ischemia-reperfusion injury caused by the PM can promote the recurrence and metastasis of hepatic tumors and affect patient prognosis remains controversial in the clinical setting. More results suggest that the IPM is safe for patients with liver cancer [23-25]. This study mainly analyzed the role of the IPM in the recovery of liver function after surgery, and the impact of the IPM on liver cancer patients still requires long-term follow-up results. There were some limitations in this study. This study was a retrospective analysis, so the level of evidence is lower than in studies with prospective designs. This study included patients who underwent hepatectomy with and without IPM, and there were significant differences in the clinical diagnoses between the two groups. Therefore, in the regression analysis, we further analyzed the patients with hepatic carcinoma and cirrhosis. This study focused on the impact of the IPM on liver function and did not analyze the metastasis and recurrence of hepatocellular carcinoma. In the future, the IPM strategies should be stated in detail in related studies to facilitate a comparative analysis.

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