Ischemic time by the intermittent occlusion of hepatic inflow (Pringle's maneuver) influences surgical outcome after hepatectomy

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Background: Intermittent occlusion of hepatic inflow, so-called Pringle's maneuver, is a useful technique to control intraoperative bleeding; however, it can lead to ischemia-reperfusion injury. We examined the influence of ischemic time on surgical factors, posthepatectomy liver function and morbidity.

Methods: The clinical records of 296 patients who underwent an elective hepatectomy for liver disease between 2004 and 2013 were retrospectively examined. Univariate and multivariate analyses of clinicopathological and surgical factors associated with hepatic-inflow occlusion time were performed.

Results: The mean and median times of total hepatic-inflow occlusion were 47±23 minutes (5-173 mL) and 45 minutes, respectively. The occlusion time was significantly correlated with increased indocyanine-green retention rate, total operation time, amount of blood loss or red cell transfusion, postoperative morbidity and hospital stay (each p<0.05). Blood loss upon the use of occlusion tended to be lower than that in its absence (568±602 mL vs. 887±841 mL) (p=0.075). The occlusion time was shorter in limited resection and longer in central bi-segmentectomy or sectionectomy (p<0.05). The occlusion time was significantly correlated with the maximum alanine aminotransferase level (r=0.291, p<0.01). The predictive cut-off value of occlusion time for these correlated parameters ranged between 45 and 46.5 minutes (p<0.05). Hepatic-inflow occlusion was not associated with morbidity in cirrhosis.

Conclusion: A longer ischemic time induced increased blood loss or related transfusion, operating time, postoperative liver injury, complication rate and duration of hospital stay.

Introduction

Recent advances in surgical techniques in hepatectomy have provided better patient outcomes (1, 2). However, the possibility of increased blood loss leading to poor postoperative outcomes still remains (3, 4). To control bleeding at the transected parenchyma of the liver during hepatectomy, transient hepatic-inflow (= ischemic) occlusion using clamp-ing devices, so-called "Pringle's maneuver", has been applied worldwide (5). Intraoperative bleeding requiring blood transfusion decreased and surgical outcomes improved as a result of this, according to previous reports (6-8). However, some investigators reported that hepatic-inflow occlusion was not always necessary to control intraoperative bleeding and, furthermore, there were concerns over ischemic-reperfusion injury after de-clamping (9, 10). Such increased blood

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loss might be related to poor patient outcomes (11,12) and blood loss over 1500 mL was described as being significantly associated with poor overall survival in patients with hepatocellular carcinoma or metastatic liver carcinoma in our previous report (13). Thus, our present policy is that the hepatic-inflow occlusion method is still necessary in cases of anatomical liver resection, except for small resections on the surface of the liver. Continuous occlusion over 30-60 minutes was shown to induce severe ischemic damage in liver (14). However, the postoperative adverse effects of intermittent hepatic-inflow occlusion (such as 15-minute clamping and 5-minute de-clamping) and the relationship with the duration of occlusion have not been fully reported yet (15, 16). Although it has been well known that the continuous longer ischemic time obviously influence the liver damage, influences by the frequency of intermittent ischemic clamping has not been confirmed so far, to our knowledge. We often experienced that many frequent clamping led to increase of serum bilirubin or transaminase levels after operation but not lethal. In our previous clinical study examining blood gas sampling of the hepatic venous blood (Japanese article without English abstract), a couple of intermittent clamping did not induce progression of severe liver damage and, thereafter, we experienced a few cases with severe liver damage but not showing remarkable hepatic failure. In these cases, more than nine times or more clamping were undergone. Thus, we concerned the accumulation of liver parenchymal damage by the frequent hepatic inflow occlusion in the clinical setting. We hypothesized that longer intermittent hepatic-inflow occlusion is related to higher rates of liver injury and related morbidity.

The aim of the present study was thus to determine the influence of the duration of intermittent hepatic-inflow occlusion on posthepatectomy liver dysfunction and complications in patients with liver diseases who have undergone various types of hepatectomy. Preoperatively associated factors influencing the duration of hepatic-inflow occlusion and the relationship between this duration and intraoperative blood loss requiring blood transfusion or poor patient outcomes were examined in 296 consecutively selected patients who underwent elective hepatectomy for a decade between 2004 and 2013.

Methods

Patients and methods

The clinical records of 296 consecutively selected patients who underwent various types of hepatectomy without com-bined resection of other organs for liver disease at the Department of Surgical Oncology at Nagasaki University Hospital for 10 years between 2005 and 2014 were retrospectively examined after retrieval from an institutional database. Patients in whom the duration of hepatic-inflow occlusion was not recorded were excluded. Mean age of the patients at the time of surgery was 65.4 ± 13.6 years (range, 29-85 years). In terms of gender, there were 190 males and 106 females. Chronic viral hepatitis was present in 113 patients (including 34 cirrhotic patients), icteric liver in 21 patients, alcoholic liver disease in 1, fatty liver in 11, chemotherapy-associated liver injury in 18 and normal liver in 132. Child-Pugh classification was B in 5 patients (2%) and A in 291 patients. Diseases included hepatocellular carcinoma (HCC) in 113 patients, intrahepatic cholangiocarcinoma (ICC) in 31, metastatic liver tumor in 84, extra-hepatic bile duct carcinoma in 33, gallbladder carcinoma in 14 and benign liver disease in 21. Hepatectomy included hemi-hepatectomy or more in 122 patients, sectionectomy or segmentectomy in 88 and partial resection including laparoscopic partial resection in 86 patients. Radical hepatectomy was performed to remove hepatic tumor without leaving any residual tumor. All study protocols were approved by the Human Ethics Review Board of our institution. Informed consent for data collection was obtained from each patient during this period. Anesthetic and patient data were retrieved from the institutional database. There was no financial support or conflict of interest regarding the present study.

Operative indications and evaluated parameters

The indications for hepatectomy and types of surgical procedure were determined according to functional liver reserve. For hepatectomy, the volume of liver to be resected was estimated according to results of the indocyanine green retention rate at 15 min (ICGR15) using Takasaki's formula (17). Furthermore, hepatic function for hepatectomy was limited to ICGR15 <40%, Child-Pugh classification A or B, and total bilirubin level <2 mg/dL, according to the Tokyo University criteria (18). The expected liver volume for resection, excluding the tumor, was measured by computed tomography (CT) volumetry (19). We examined preoperative clinical parameters, operative procedures, surgical records and postoperative morbidity. The presence of hepatic-inflow occlusion and the sum of the duration (minutes) of occlusion, so-called Pringle's maneuver, were examined (5, 15, 16).

Surgical procedures

Clamping of the hepatoduodenal ligament to occlude total inflow to the liver during transection was intermittently performed (16), in which one cycle consisted of 15-minute total clamping and 5-minute de-clamping. It also included the use of the forceps crush clamping method (20) and an ultrasonic dissector (USU MH-207, Olympus, Tokyo, Japan) at some points around the major vessels for the transection of liver parenchyma. During de-clamping, the transected liver planes were compressed with an absorbable hemostat (Avitene® microfibrillar collagen, Medchem Products Inc., Woburn, MA). Using the Kelly clamp or LigaSure (Valleylab, Boulder, CO) itself, the hepatic parenchyma was widely and gently crushed and it was confirmed that the remnant vessels were divided and tied by absorbable braid (Ethicon Inc., Somerville, NJ), and Glissonian branches near the secondary trunk were also tied to avoid bile leakage. In the case of using a vessel sealer, we used the LigaSure Tissue Fusion System™ for open laparotomy to divide isolated tiny vessels (<2 mm). The transected cut surface was clearly exposed, but no black burning was noted. The LigaSure™ vessel sealing generator was the new ForceTriad™ energy platform that includes a foot switch (Valleylab), which is a full-feature radiofrequency energy system that allows precise automatic management of the energy and the desired tissue effect. The sealing time is only a few seconds. The isolated large hepatic vein was ligated using Endopath-Endocutter ETS-Frex 35 (staple load; 3.0 x 35 mm, white cartilage, Ethicon Endo-surgery, Johnson & Johnson Company, Somerville, NJ) (21).

Hepatectomy was performed by various surgeons, who included two attending surgeons in 210 hepatectomies and resident training surgeons in 86. In the case of trainees, quality control for the operation was supported by the attending surgeons. Autologous blood transfusion was not applied in all patients in the present study. Intraoperative blood transfusion (= red blood cells) was estimated in cases of unstable vital signs or a hemoglobin value of less than 9.0 mg/dl. Fresh frozen plasma was transfused in the patients with liver cirrhosis or those who underwent extended hemi-hepatectomy or more. The patients were divided into two groups according to blood loss.

Hepatic complications were defined as hepatic failure (total bilirubin level over 5 mg/dl at postoperative day 7), uncontrolled ascites or pleural effusion (massive ascites under the use of diuretics over 7 days), intra-abdominal infection and biliary fistula in the present study.

Statistical analysis

Chi-square test was used for the comparison of categorical variables. Differences between groups were analyzed by Fisher's exact test and Scheffe's multiple comparison test.

All continuous data are expressed as mean ± SD. Data for different groups were compared using one-way analysis of variance (ANOVA) and examined by student's *t*-test. The correlation of the continuous data was tested by Spearman's rank correlation test, and its correlation coefficient (r) was indicated. Logistic regression analysis was performed to determine the predictive value of risk factors. Predictive variables were identified by the univariate analysis and the identified factors were then entered into logistic regression analysis to identify risk ratio with 95% confidence intervals. The area under receiver operating characteristic (AUROC) curve analysis was performed to set the cutoff value. A two-tailed *P* value < 0.05 was considered significant. PASW Statistics 18.0.0 for Windows (SPSS Inc., an IBM Company, Chicago, IL) was used for all statistical analyses.

Results

Surgical records

Hemostatic devices for hepatic transection were used in 294 patients (99%). Hepatic-inflow occlusion during hepatic transection was performed in 249 patients, but not in 47 (16%). In the case of non-use of hepatic-inflow occlusion, the extent of hepatectomy was limited resection in 26, segmentectomy in 3, sectionectomy in 18 and more major hepatectomy in none. The mean and median times of total hepatic-inflow occlusion were 47 ± 23 minutes and 45 minutes (range: 5-173 mL), respectively. The mean blood loss and red cell blood transfusion were 982 ± 1033 mL and 278 ± 616 mL, respectively, and transfusion was undergone in 76 patients (24%). Postoperative complications were observed in 108 patients (36%) and hepatic complications were observed in 51 (17%), which included hepatic failure in 14, uncontrolled ascites or pleural effusion in 38, intra-abdominal infection in 26 and biliary fistula in 20 patients. Postoperative hospital death was observed in 7 patients (2%). The mean and median lengths of hospital stay were 23 ± 17 days (range: 5-106 days) and 21 days.

Parameters associated with the estimated blood loss

The correlations of continuous perioperative parameters with occlusion time are shown in Table 1. Using these data,

ICGR15 was shown to be significantly correlated with a longer occlusion time (r=-0.153, p<0.05) and a longer occlusion time was significantly correlated with a longer total operation time (r=0.362), blood loss (r=0.378) and amount of red cell transfusion (r=0.247) (each p<0.01). The occlusion time was also significantly correlated with the posthepatectomy hospital stay (r=0.181, p<0.01). By comparing the use and non-use of hepatic-inflow occlusion in cases of limited resection, segmentectomy or sectionectomy, the blood loss upon the use of occlusion showed a tendency to be lower (568 ± 602 mL vs. 887 ± 841 mL), but the difference was not statistically significant (p=0.075). Table 2 shows the results of univariate analysis between perioperative categorical parameters and occlusion time. Gender, background liver, the main liver disease and liver functions were not associated with occlusion time. In terms of the surgical parameters, the occlusion time did not differ significantly between chief operators and resident surgeons. In a comparison of the extent of hepatectomy, the occlusion time was significantly shorter in limited resection than in each other type of hepatectomy (each p<0.05). In addition, the occlusion time in central bisegmentectomy or sectionectomy was significantly longer than that in hemi-hepatectomy (each p<0.05).

The relationship between occlusion time and postoperative liver functions was also examined. The occlusion time was significantly correlated with the maximum alanine aminotransferase level (r=0.291, p<0.01), although it was not significantly correlated with the maximum total bilirubin level (r=0.049, p=0.55) or prothrombin activity (r=-0.155, p=0.059).

Table 3 shows the relationship between postoperative morbidity or mortality and the occlusion time to clarify the hazard ratio of hepatic-inflow occlusion (Pringle's maneuver). Each of the presence of any complications, hepatic failure and bile leakage was significantly correlated with a longer occlusion time (each p<0.01). Table 4 shows the relationship between postoperative morbidity or mortality and the existence of occlusion in each patient group with non-cirrhotic or cirrhotic liver. Although the ischemic occlusion was significantly associated with any complications (hazard ratio =7.2), hepatectomy-related morbidity (hazard ratio =6.7) and intra-abdominal infection (hazard ratio=3.6), the occlusion was not associated with any morbidity or mortality.

On the basis of the univariate analysis, the predictive value of the occlusion time for the parameters related to the surgical records and morbidity that were significantly correlated with the occlusion time was calculated by receiver operating characteristic curve analysis (Table 5). For all parameters, the cut-off value of occlusion time was significantly predictive, ranging between 45 and 46.5 minutes.

Table 1. Correlation of continuous preoperative and intraoperative parameters with occlusion time

	Correlation (r)	Significance (P value)
Age (years)	-0.061	0.33
Liver function		
IICGR15 (%)	-0.153	0.022
LHL15	0.017	0.81
Total bilirubin (mg/dl)	-0.014	0.83
Prothrombin activity (%)	0.105	0.11
Hyaluronic acid level (ng/mL)	-0.08	0.32
Platelet count (/mm^3)	-0.062	0.34
Surgical records		
Operating time (minutes)	0.362	<0.01
Blood loss (mL)	0.378	<0.01
Red cell transfusion (mL)	0.247	<0.01
Hospital stay (days)	0.181	<0.01

ICGR15, indocyanine green retention rate at 15 minutes; LHL15, liver uptake ratio at 15 minutes in [99m]-technetium galactosyl serum albumin liver scintigraphy

Table 2. Comparison between perioperative categorical parameters and the occlusion time

	Occlusion time (minutes)	Significance (p value)
Gender		
Male (n=190)	48.2 ± 25.0	0.104
Female (n=106)	44.8 ± 19.7	
Background liver diseases		
Normal (n=132)	45.6 ± 20.2	
Alcoholic (n=1)	45	
Fatty (n=11)	46.9 ± 21.3	
Chemotherapy-associated liver injury (n=18)	45.1 ± 20.1	
Viral chronic hepatitis (n=79)	52.7 ± 27.6	NS
Cirrhosis (n=34)	36.4 ± 29.1	
Jaundice (n=21)	47.7 ± 13.3	
Liver diseases		
Hepatocellular carcinoma (n=113)	49.2 ± 28.6	
Intrahepatic cholangiocarcinoma (n=31)	45.1 ± 14.7	
Extrahepatic bile duct carcinoma (n=33)	48.9 ± 13.8	
Gallbladder carcinoma (n=14)	29.7 ± 17.2	NS
Metastatic liver carcinoma (n=84)	45.4 ± 22.6	
Benign diseases (n=21)	52.7 ± 16.8	
Child Pugh classification		
A (465)	47.1 ± 23.3	0.29
B(17)	31.3 ± 23.7	
Surgical records*		0.2
Operator		
Chief	46.7 ± 27.3	0.78
Resident (315/167)	45.8 ± 30.5	
Extend of hepatectomy		
Limited resection (n=86)	27.8 ± 15.9	*p<0.05
Segmentectomy (n=40)	51.3 ± 17.1	
Sectionectomy (n=42)	66.1 ± 31.7	**p<0.05
Central bisegmentectomy (n=6)	85.0 ± 41.4	***p<0.05
Hemi-hepatectomy or more (n=122)	45.8 ± 13.3	

*: *vs*. hemi-hepatectomy or more, bisegmentectomy, sectionectomy and segmentectomy.
: *vs*. hemi-hepatectomy or more, *: *vs*. hemi-hepatectomy or more.
NS: not significant

Table 3. Comparison between postoperative morbidity and the occlusion time

	Occlusion time (minutes)	Significance (p value)
Hospital death		
No (n=289)	46.5 ± 23.4	0.16
Yes (n=7)	55.9 ± 15.0	
Total complications		
No (n=188)	45.6 ± 20.2	<0.01
Yes (n=108)	51.9 ± 26.1	
Hepatectomy-related complications		
No (n=245)	45.2 ± 21.5	0.071
Yes (n=51)	53.6 ± 28.7	
Hepatic failure		
No (282)	45.5 ± 21.3	<0.01
Yes (14)	70.2 ± 40.0	
Long-term ascites or pleural effusion		
No (n=258)	45.5 ± 22.1	0.098
Yes (n=38)	54.4 ± 28.7	
Intra-abdominal infection		
No (n=270)	46.2 ± 23.4	0.17
Yes (n=26)	51.6 ± 21.2	
Bile leakage		
No (n=276)	45.6 ± 23.3	<0.01
Yes (n=20)	59.1 ± 18.8	

Table 4. Comparison of morbidity between the background liver and use of Pringle's maneuver.

	No cirrhosis		Significance p value	Hazard ratio (95%CI)	Cirrhosis		Significance p value	Hazard ratio (95%CI)
	Pringle (n=224)	Non-Pringle (n=38)			Pringle (n=25)	Non-Pringle (n=9)		
Hospital death								
No (n=289)	218	37		1	25	9		1
Yes(n=7)	6	1	1.0	1	0	0	1.0	1.1
Total complication								
No (n=188)	137	34		1	12	5		
Yes(n=108)	87	4	<0.01	7.2*	13	4	1.0	0.7
Hepatectomy-related complications								
No (n=245)	187	37		1	15	6		1
yes (n=51)	37	1	0.023	6.7*	10	3	1.0	0.8
Hepatic failure								
No (n=282)	212	37		1	24	9		1
Yes (n=14)	12	1	0.699	2.0	1	0	0.99	1.3
Ascites								
No (n=258)	198	37		1	16	7		1
Yes (n=38)	26	1	0.145	1.9	9	2	0.682	0.5
Infection								
No (n=270)	200	38		1	23	9		1
Yes (n=26)	24	0	0.032	3.6*	2	0	1.0	1.7
Bile leakage								
No (n=276)	205	38		1	24	9		1
Yes (n=20)	19	0	0.086	2.8	1	0	1.0	1.4

*p<0.05

Table 5. The area under receiver operating characteristic (AUROC) curve analysis between the occlusion time and surgical records and outcomes

Parameters	Area	Standard deviation	Significance	95% confidence interval		Cut-off value of time (minutes)
				Lower limit	Upper limit	
Blood loss >1000 ml	0.768	0.030	<0.001	0.710	0.826	45.0
Blood transfusion, yes	0.718	0.033	<0.001	0.653	0.783	45.0
Operating time > 600 minutes	0.666	0.037	<0.001	0.594	0.738	46.5
Complication, yes	0.596	0.036	0.011	0.524	0.667	45.0
Bile leakage, yes	0.709	0.046	0.002	0.619	0.800	46.0
Hospital stay > 30 days	0.592	0.039	0.037	0.515	0.669	45.0

Discussion

To minimize intraoperative blood loss, various means of preoperative evaluation of hepatic functional reserve, surgical procedures and intraoperative anesthetic management might be attempted (1-8, 16-18, 22, 23). However, our present results show that the amount of blood loss did not significantly decrease over time between 1994 and 2003 (unpublished data). With respect to the surgical procedures to reduce intraoperative blood loss, we applied the liver hanging maneuver and used the latest hemostatic devices from 2004 onwards (21, 24). Basically, we continued to apply intermittent Glissonian pedicle occlusion, so-called Pringle's maneuver, which was shown to be a useful technique to reduce bleeding at the hepatic transected area by controlling ischemic liver injury or intestinal congestion, since 1994 (5, 21, 24). Thus, subjects in the present 10-year series between 2004 and 2013 were selected. Nevertheless, using these techniques for hemostasis, bleeding could not be completely controlled in some cases. However, longer inflow occlusion was supposed to promote liver injury and related posthepatectomy complications (25, 26). Against this background, we examined the relationship of occlusion time with clinicosurgical parameters in the present study.

Despite the hepatic-inflow occlusion method being applied in various types of hepatectomy, the occlusion time ranged widely, with a mean or median time of around 45 minutes, which consisted of three sets of 15-minute intermittent occlusion, similarly to previous reports (15, 16, 18-20). Among the preoperative parameters, a factor that negatively correlated with the occlusion time was ICGR15, which well reflects the severity of chronic liver injury (27). In case of severely injured liver indicated by the increased data of ICGR15, it was speculated that the operator might hesitate times of occlusion to avoid intraoperative liver injury by the operator's decision during hepatectomy. A higher degree of chronic liver injury might influence the difficulty of parenchymal transection and related increased blood loss, which led to the longer occlusion time. In fact, the occlusion time was positively correlated with the amount of blood loss or transfusion and a longer operation time. However, in comparison with the non-occlusion group, the levels of blood loss and transfusion were lower in the occlusion group. Therefore, the usefulness of hepatic-inflow occlusion itself to reduce intraoperative blood loss was observed in the present study, as well as in previous reports (14-16, 25, 26). In the present series, the sectionectomy or segmentectomy and central bisegmentectomy showed the longer ischemic times. Such a complicated hepatectomy with a larger cut planes might be associated with posthepatectomy complications. However, the adequate anatomical resection may not induce biliary fistula or hepatic failure. At this point of view, operative procedures itself might not mainly influence the postoperative complications.

In the recent years, the operative procedures or hemostatic devices has been improved and the blood loss were decreased (21, 24). However, even though these methods developed, the complete control of intraoperative bleeding could not be fully performed at this stage, particularly the severely cirrhotic liver (28). Role of hepatic inflow-occlusion was still important. Selective hepatic inflow occlusion to minimize total hepatic ischemic injury has been reported (29). However, in case of hemi-hepatectomy, the bleeding from the counter part of the liver often occurred through the interlober blood flow or peri-biliary arterial flow in the hepatic hilum. Therefore we basically select the whole inflow-occlusion.

Our major concern of an adverse effect of a longer occlusion period was ischemic-reperfusion liver injury and related morbidity after hepatectomy in the present study. The relationship between a longer intermittent occlusion time and the severity of liver injury has yet to be fully elucidated. Our previous report written in Japanese showed the safety of Pringle's maneuver, in which recovery from liver injury with lactic acidosis immediately occurred after 5-minute declamping in every occlusion cycle (not published in English). Our study showed that a longer occlusion time was correlated with an increased transaminase level after hepatectomy, which reflected increased liver parenchymal injury. However, hepatic functional parameters regarding hepatic failure, such as bilirubin level and prothrombin activity, were not correlated with the occlusion time. Therefore, longer occlusion might not remarkably induce severe liver damage. With respect to the posthepatectomy complications, the occlusion period did not correlate with the presence of hepatic failure or uncontrolled ascites, which were severe posthepatectomy complications. Only the presence of bile leakage was correlated with a longer occlusion time, which might have been caused by the increased injured liver tissues. It was shown previously that bile leakage might be related to injured liver (30). The fact that a longer hospital stay was correlated with the occlusion time might be influenced by this biliary complication (31). Influences of hepatic inflow occlusion in cirrhosis was also concerned and, however, the existence of occlusion did not influence any morbidity or mortality under the present intermittent occlusion method. Thus, the intermittent hepatic inflow occlusion could be safely performed in cirrhosis with preserved liver functional

reserve indicated by the ICGR15. On the other hand, in the present study, influences of Pringle's maneuver with posthepatectomy complications in cirrhosis and non-cirrhosis were examined to clarify the hazard ratio, respectively. As a result, in non-cirrhotic patients, Pringle's maneuver showed increased risks for intraabdominal infection, particularly. In patients undergoing Pringle's maneuver with non-cirrhotic liver, major hepatectomy or hepatectomy for biliary carcinomas, therefore, such a morbidity might increase due to longer ischemic time. In case the comprehensive analysis to clarify the independent factor related to such a morbidity by the multivariate analysis, various other factor except Pringle's maneuver might influence. While, we have to recognize that ischemic occlusion might sometimes lead any infectious complications in patients with impairment of immune-function.

On the basis of the correlations identified by the univariate analysis, multivariate ROC analysis showed that a long occlusion time over 45 minutes significantly influenced various adverse effects, but not severe liver damage. It is important to reduce the total clamping time and use of selective occlusion of the Glissonian pedicle (32, 33). Furthermore, in cases in which the total occlusion time is prolonged over 45 minutes, the presence of biliary leakage at the transected plane must be carefully checked during operation using a sensitive diagnostic method, such as the ICG-photodynamic eye method (32). Attempts to reduce transection and operating time by applying the latest hemostatic devices would be necessary.

In conclusion, we examined the parameters associated with increased hepatic-inflow occlusion time during various types of hepatectomy by retrospective analysis using the clinical records of 296 patients who underwent an elective hepatectomy for liver diseases. The occlusion time and the existence of occlusion was significantly correlated with preoperative ICGR15, intraoperative operating time and the amount of blood loss or related transfusion, postoperative transaminase level, prevalence of biliary complications and the length of hospital stay. Intermittent hepatic inflow occlusion did not influence the increase of morbidity or mortality in cirrhotic liver. By the ROC analysis, the cut-off predictive occlusion time in patients who had increased blood loss, received red cell blood transfusion and had a postoperative biliary fistula was set as an estimated value of 45-46 minutes. It is necessary to reduce the total hepatic-inflow occlusion time to within 45 minutes in patients with the above high-risk factors who undergo hepatectomy by the application of various surgical means during hepatectomy.

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