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Intermittent Pringle Maneuver and Hepatic Function: Perioperative Monitoring by Noninvasive ICG-Clearance

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Abstract
Background Intermittent Pringle maneuver or selective portal clamping often are used to control inflow during parenchymal liver transection. This study was designed to determinate whether these maneuvers are associated with adverse hepatic function.
Methods Resection was performed without portal clamping in 17 patients (group 1). Selective continuous portal clamping was performed in 11 patients (group 2) and the remaining 33 patients (group 3) had intermittent non-selective portal clamping (occlusion of the main portal trunk). The centers' protocol for total portal occlusion is 15-min occlusion alternated with 5-min reperfusion in patients with normal liver parenchyma or 10 min alternated with 5 min in patients with abnormal parenchyma. ICG elimination tests were conducted concurrently using a noninvasive monitor that tracks the plasma disappearance rate (PDR-ICG-%/min) and 15-min retention rate after administration (ICG-R15-%).
Results There was no statistically difference between the three studied groups in terms of sequential changes of ICG-PDR ($p < 0.625$) or ICG-R15 ($p < 0.398$).
Conclusions Our study indicates that 15 min of intermittent Pringle maneuver or selective hemihepatic continuous portal clamping are safe methods of vascular control during liver resection, with no adverse effects on hepatocellular function.

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Introduction

One of the major advances in liver surgery is the prevention of intraoperative bleeding. This includes several steps: (1) maintain a low central venous pressure, (2) control and division of major portal pedicles and hepatic veins before parenchymal transection, and (3) the use of vascular clamping during transection of parenchyma. Portal clamping or Pringle maneuver (PM) is the most commonly used technique. It significantly decreases bleeding during transection of the parenchyma and it has little effect on systemic hemodynamics or liver function, particularly if applied intermittently [1–5]. Although liver surgeons use different vascular clamping techniques, including PM, the optimal ischemia time has not yet been determined and remains controversial [6–9]. To our knowledge, no prospective clinical study has examined the ideal ischemia time during hepatectomy in relation to severity of ischemia-reperfusion liver injury by using perioperative monitoring of noninvasive indocyanine green (ICG) clearance.

ICG is a nontoxic, water-soluble triacarbocyanime dye. Its elimination rate has been largely used to measure the hepatic function and the hepatic blood flow for the last three decades [10]. Indeed, the ICG is extracted exclusively by the hepatic parenchyma cells and excreted almost entirely into the bile without enterohepatic circulation [11]. Recently, with the LiMON® system (Impulse Medical System, Munich, Germany), the ICG elimination rate is

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monitored by a noninvasive pulse-densitometric method [12, 13]. This monitor expresses the ICG elimination in terms of plasma disappearance rate (PDR-ICG) and retention rate of ICG 15 min after administration (ICG-R15).

This study was designed to estimate the impact of different inflow vascular occlusion techniques on the function of hepatic cells by monitoring the ICG clearance and its plasma disappearance rates in patients undergoing liver resections.

Patients and methods

From January 2006 to March 2008, 61 patients treated in our center were included in the study. Of them, 21 were women and 40 men, with a mean age of 62.5 ± 12.3 (range, 33–84) years. Eleven patients were cirrhotic (Child-Pugh score A). Twelve patients received neoadjuvant chemotherapy.

Type of pathology

Thirty-seven patients had colorectal liver metastases, 13 had hepatocellular carcinoma (HCC), 4 had cholangiocarcinoma, 3 had liver metastases (gastric carcinoma), 1 had hemangioma, 1 had hydatid cyst, 1 had gallbladder carcinoma, and the last patient had liver metastases (GIST).

Surgical procedures

The selection of patients for surgery and type of clamping were based on liver functional status, radiological evidence of tumor resectability, and absence of major contraindications precluding surgery. In addition, patients with HCC had to be outside the Milan criteria [14] and have a Child-Pugh score grade A to be considered for resection [15].

Sixty-one patients underwent right extended hepatectomy ($n = 9$), right hepatectomy ($n = 11$), central hepatectomy ($n = 2$), extended left hepatectomy ($n = 1$), left hepatectomy ($n = 1$), trisegmentectomy ($n = 1$), bisegmentectomy ($n = 3$), left lobectomy ($n = 5$), segmentectomy ($n = 16$), subsegmentectomy ($n = 18$), and pericystectomy ($n = 1$).

We considered as hospital mortality all deaths that occurred during the first two postoperative months. The complications were graded in accordance to the Clavien Score [16].

Resection without portal clamping was performed in 17 patients. Selective continuous portal clamping (occlusion of right or left hepatic artery/portal branch) was performed in 11 patients and the remaining 33 patients had intermittent nonselective portal clamping (occlusion of the main portal trunk). The centers' protocol for total portal occlusion is 15-min occlusion alternated with 5-min reperfusion for patients with normal liver parenchyma, whereas for patients with abnormal parenchyma (cirrhotic, steatosis) the occlusion time is reduced to 10 min. The mean time of the portal clamping was 10 ± 12.01 (range, 0–56) min. The mean transfusion rate was 0 ± 0.77 (range, 0–9 units of red blood cells). Fifty-four (88.5%) patients received no blood transfusion. Table 1 describes the characteristics of patients who had no portal clamping (group 1), selective continuous portal clamping (group 2), and occlusion of the main portal trunk (group 3).

The PDR-ICG and the R15-ICG, hemodynamic status (systolic, diastolic, mean arterial pressure (MAP), central venous pressure, and heart rate), hemoglobin (Hb), platelet count, creatinine and standard liver biochemistry [plasma levels of prothrombin (PT), albumin (Alb), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), total bilirubin (T Bil), lactic acid dehydrogenase (LDH)] were evaluated before induction of general anesthesia (T0), immediately after the end of surgery (T1), and 24 h after hepatectomy (T2).

Measurement of the indocyanine green clearance

ICG elimination tests were conducted by using the LiMON® (Pulsion Medical System, Munich, Germany). Each patient was monitored with an ICG finger clip, which was connected to the liver function monitor (LiMON®) via an optical probe. Injected ICG is detected from fractional pulsatile changes in optical absorption. The optical peak absorption of 805 and 890 nm allows continuous measurements of PDR-ICG.

For each measurement, ICG (5 mg/ml) was administered intravenously at a dose of 0.5 mg/kg body weight of ICG (Infracyanine, Laboratories Serb, France) and given through a peripheral or central vein as a bolus and immediately flushed with normal saline. The monitor determines automatically the PDR-ICG by monoexponential transformation of the original ICG concentration curve and backward extrapolation to the time point "zero" (100%), describing the decay as percentage change per time.

The study protocol was approved by the ethics comity of our hospital. All patients were informed about the study and signed the informed written consent.

Statistical analysis

Continuous data were presented as mean and standard deviation (SD). Skewed and non-Gaussian continuous data were analyzed using nonparametric tests (Mann–Whitney *U* test or the Kruskal–Wallis test, whenever there were two

Table 1 Characteristics of patients without portal clamping (group 1), selective continuous portal clamping (group 2), and intermittent total occlusion of the portal trunk (group 3)

	Group 1($n = 17$)	Group 2 ($n = 11$)	Group 3 ($n = 33$)	p
Age (year)	61.93 ± 11.71	55.3 ± 15.3	61.46 ± 9.28	0.754
Male/female ratio	10/7	7/4	23/10	0.099
Cirrhosis	3	2	4	0.488
Indication of hepatectomy				0.411
Colorectal liver metastases	13	6	18	
Hepatocellular carcinoma	3	2	8	
Cholangiocarcinoma	0	2	2	
Gastric liver metastases	1	0	2	
Hemangioma	0	1	0	
Hydatid cyst	0	0	1	
GIST liver metastases	0	0	1	
Gallbladder carcinoma	0	0	1	
Type of intervention				
Extended right hepatectomy	1	1	7	
Right hepatectomy	2	6	1	
Extended left hepatectomy	0	0	1	
Left hepatectomy	0	1	0	
Central hepatectomy	1	0	1	
Trisegmentectomy	0	0	1	
Bisegmentectomy	3	0	0	
Left lobectomy	4	0	1	
Segmentectomy	3	1	12	
Subsegmentectomy	6	8	4	
Pericystectomy	0	0	1	
Hemodynamic data				
Heart rate (beats/min)	84 ± 10	82 ± 14	83 ± 12	0.880
Systolic blood pressure (mmHg)	133 ± 15	133 ± 22	132 ± 17	0.981
Diastolic blood pressure (mmHg)	66 ± 12	66 ± 10	70 ± 10	0.480
Central venous pressure (mmHg)	8.8 ± 2.4	7.9 ± 1.9	8.4 ± 1.9	0.556
ICU stay (days)	2.7 ± 1.7	2.5 ± 1.8	2.4 ± 1.8	0.588

Data are presented as range (mean ± SD)

ICU intensive care unit

samples, three or more samples to compare); Chi-square test was applied to compare proportions. Serial measurements were compared by repeated measure analysis variance (ANOVA). Statistical analysis was performed using Statistica® version 7, and the value of 5% was considered as a significant level.

Results

Mortality and morbidity

There were no perioperative deaths. Postoperative complications occurred in nine patients. In the intermittent nonselective portal clamping group, complications included bile leak ($n = 1$), intra-abdominal abscess ($n = 1$), and intestinal obstruction ($n = 2$) (Clavien grade I—two patients; Clavien grade II—one patient; and Clavien grade IIIa—one patient). In the selective continuous clamping group, complications included bile leak ($n = 1$) and pneumonia ($n = 1$) (Clavien grade I—one patient; and grade II—one), and lastly in the nonclamping group, complications included biliary fistula ($n = 1$), intra-abdominal abscess ($n = 1$), and intestinal occlusion ($n = 1$) (Clavien grade I—two patients; and Clavien grade IIIa—one patient). No significant statistical difference was obtained for postoperative mobility between different groups.

Sequential changes of clinical parameters

We observed no statistical differences in the evolution of the clinical parameters measured over time between the three studied groups. Table 2 describes the hemodynamic changes before induction of general anesthesia (T0), immediately after intervention (T1), and at 24 h after (T2).

Table 2 Sequential changes of hemodynamic status before induction of general anesthesia (T0), immediately after the end of hepatectomy (T1), and 24 hafter the surgery (T2) for patients without portal clamping (group 1), selective continuous portal clamping (group 2), and intermittent total occlusion of the portal trunk (group 3)

T	Group	T0	T1	T2	p (time × groups)	p (groups)
HR (beats/min)	1	84.00 ± 9.86	87.20 ± 10.69	87.47 ± 8.62	0.066	T0: 0.880
	2	81.67 ± 13.71	90.75 ± 9.92	84.42 ± 12.18		T1: 0.594
	3	82.92 ± 12.06	90.62 ± 11.71	86.58 ± 9.88		T3: 0.729
SBP (mmHg)	1	132.53 ± 14.84	113.00 ± 17.35	133.80 ± 13.63	0.739	T0: 0.981
	2	132.75 ± 21.57	109.67 ± 35.06	130.25 ± 17.98		T1: 0.758
	3	131.69 ± 16.84	115.35 ± 15.86	130.69 ± 14.85		T3: 0.783
DBP (mmHg)	1	66.47 ± 11.96	58.47 ± 11.02	67.53 ± 11.23	0.657	T0: 0.480
	2	65.92 ± 10.13	59.33 ± 11.78	65.75 ± 9.19		T1: 0.640
	3	69.73 ± 9.80	61.42 ± 8.75	70.31 ± 8.13		T3: 0.344
CVP (mmHg)	1	8.80 ± 2.39	7.07 ± 1.71	8.40 ± 1.35	0.382	T0: 0.556
	2	7.92 ± 1.98	6.17 ± 1.59	8.17 ± 0.72		T1: 0.113
	3	8.35 ± 1.98	5.81 ± 1.98	7.88 ± 0.91		T3: 0.294

Results are mean ± SD

HR heart rate (beats/min), *SBP* systolic blood pressure (mmHg), *DBP* diastolic blood pressure (mmHg), *CVP* central venous pressure (mmHg)

Sequential changes of plasma disappearance (PDR-ICG) and retention rate of ICG 15 min (R15-ICG) after administration

There was no statistical difference between the three studied groups in terms of ICG-PDR ($p < 0.625$) or ICG-R15 noninvasive monitoring ($p < 0.398$). Figure 1a and b show sequential changes for the plasma disappearance rate of ICG (PDR-ICG) and retention rate of IGC 15 min (R15-ICG) after administration of ICG, respectively. Table 3 describes sequential changes of plasma disappearance rate (PDR-ICG) and retention rate of IGC 15 min (R15-ICG) after administration of ICG before induction of general anesthesia (T0), immediately after intervention (T1), and at 24 h after (T2).

Sequential changes of biochemical parameters

There was a statistically significant difference for ALT ($p < 0.016$), GGT ($p < 0.003$), and AF ($p < 0.014$) between group 3 (intermittent total occlusion of the main portal trunk) and group 1 (no portal clamping) or group 2 (selective continuous portal clamping). In contrast, there were no differences between the three groups in terms of platelet numbers, creatinine, hemoglobin or prothrombin levels, albumin, AST, total bilirubin, and LDH. Table 3 describes sequential changes of biochemical parameters before induction of general anesthesia (T0), immediately after intervention (T1), and at 24 h after (T2).

Discussion

Hepatic resection is a challenging surgical procedure because of the complicated biliary and vascular anatomy of the liver and the high risk of bleeding. One of the surgical methods applied to reduce blood loss during hepatectomy is inflow occlusion by clamping the portal triad (Pringle maneuver). Several reports have compared continuous versus intermittent pedicle occlusion, and have concluded that intermittent pedicle occlusion may be a superior technique to preserve the function of the future remnant liver and prevent liver failure as a result of prolonged liver ischemia [3, 9, 17, 18].

To date, much of the evidence is experimental and not derived from human studies. The standard clamping time of 10–15 min used at our institution is established empirically based on 30 years of clinical experience with hepatectomies as well as experimental evidence from animal studies.

However, there is still controversy concerning the potential effects of ischemia–reperfusion injury, which may have deleterious consequences on the remnant liver resulting from the activation of Kupffer cells and production of reactive oxygen species and cytokines (tumor necrosis factor and interleukin-8), leading to liver dysfunction due to sinusoidal endothelial and parenchymal injury [19].

To evaluate the effects of clampage-induced ischemia on the liver parenchyma, a noninvasive monitoring (spectrophotometry) of ICG clearance was used in this study (the first to use this method). ICG is a water-soluble, nontoxic tricarbocyanine dye. The principal characteristic

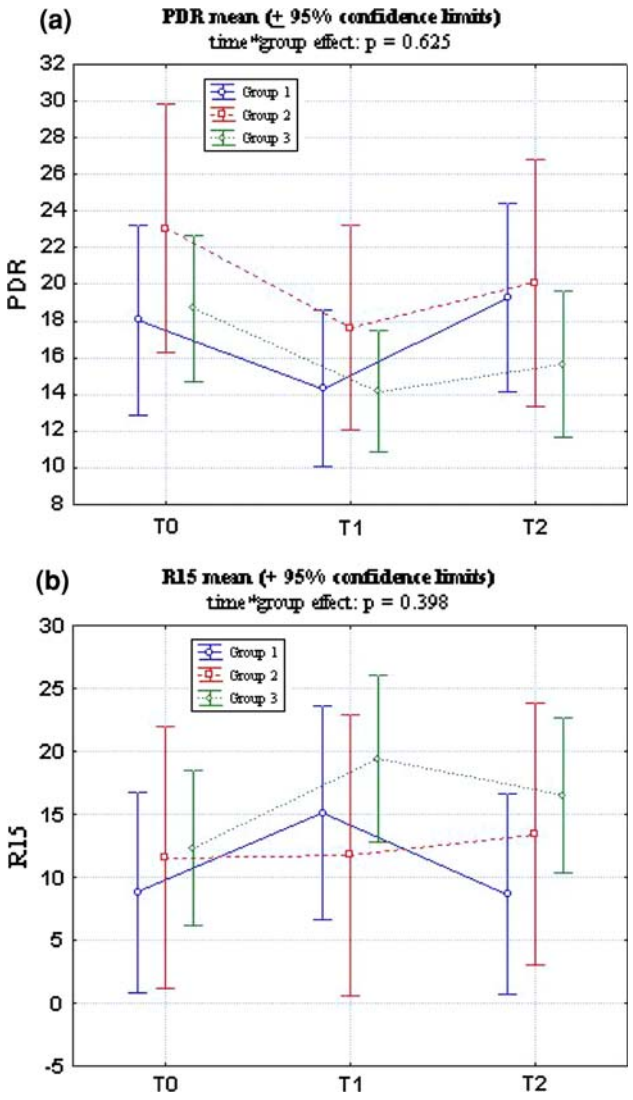

Fig. 1 **a**, **b** Sequential changes of plasma disappearance rate (PDR-ICG) after administration of ICG before induction of general anesthesia (T0), immediately after the end of hepatectomy (T1), and 24 h after the surgery (T2) for patients without portal clamping (group 1), selective continuous portal clamping (group 2), and intermittent total occlusion of the portal trunk (group 3). *ICG* indocyanine green, *PDR-ICG* plasma disappearance rate of ICG (%/min), *R15-ICG* retention rate of indocyanine 15 min after administration (%)

of the ICG is that is extracted nearly exclusively by the hepatocytes and excreted almost entirely into the bile without enterohepatic circulation [11]. Indeed, after injection, the ICG is taken up by hepatocytes, bound by acceptor proteins, and then through them excreted and eliminated with the bile in an unchanged form. The ICG is detectable in the bile 15 min after injection, with a maximum concentration between 30 min and 2 h after injection, depending on the amount injected. The kinetics of ICG plasma disappearance has been described in previous articles [20, 21]. Because of the ICG metabolism, a dynamic test has been used largely to assess hepatic function as well as portal and hepatosplanchnic blood flow [10, 22, 23]. Indocyanine green is safe and well tolerated with no related side effects. However, in patients with iodine allergy or thyrotoxicosis, the use of ICG is not advised because it contains iodine. In addition, rarely ICG can trigger anaphylactic reactions (incidence = 1:40000) [24]. No allergic response related to the injection of ICG was observed in our study.

Various techniques (invasive and noninvasive) have been used to evaluate the ICG elimination, providing different values that quantify its elimination: the clearance, the plasma disappearance rate (PDR-ICG—percentage of ICG eliminated in 1 min), and the retention rate at 15 min (R15-ICG). More recently a noninvasive method (spectrophotometry) has been used for its evaluation. With this noninvasive bedside monitoring, the ICG elimination is determined without time delay (within few minutes, depending on the circulation time).

The pulse dye densitometry method for assessing liver function and hepatic blood flow can be used in both hemodynamically stable and unstable patients [25]. However the ICG-PDR value should be interpreted with caution in some situations [25].

Several prognostic scores have been tested and validated in intensive care patients. In many of them [Simplified Acute Physiology Score (SAPS II), Sequential Organ Failure Assessment (SOFA)], bilirubin was the only variable used to assess liver function. On other hand, the ICG-PDR clearance on admission in ICU is as sensible as other scores, such as APACHE II or SAPS II [26]. In patients with septic shock, the ICG elimination rate is an indicator of hepatocellular dysfunction; indeed, in a recent issue, an association between hepatocellular injury and a reduction in hepatic ICG clearance has been reported [27]. In addition, it has been shown that in patients with septic shock, sequential changes of the elimination rate of ICG could predict survival [27]. The ICG clearance is thought to be an adequate estimate of liver functional reserve in patients with cirrhosis and reflect the degree of sinusoidal capillarization, portovenous shunt/s, and the modification of liver blood flow [10]. In cirrhotic patients, the ICG clearance is significantly lower than in healthy patients, mainly with an intrinsic decrease of ICG hepatic uptake and during the follow-up of cirrhotic patients, the ICG has been used as a significant predictor of survival [28, 29].

In this prospective study, the biochemical variables used to estimate the ischemia–reperfusion injury of the hepatocytes and subsequent recovery include: plasma levels of PT, Alb, total protein, AST, ALT, ALP, GGT, T Bil, and LDH.

Our results demonstrate that there is a statistically significant difference for ALT ($p < 0.016$), GGT ($p < 0.003$),

Table 3 Sequential changes of PDR-ICG, R15-ICG, and biochemical parameters before induction of general anesthesia (T0), immediately after the end of hepatectomy (T1), and 24 h after the surgery (T2) of patients without portal clamping (group 1), selective continuous portal clamping (group 2), and intermittent total occlusion of the portal trunk (group 3)

T	Group	T0	T1	T2	*p* (time × groups)	*p* (groups)
PDR-ICG (%/min)	1	18.36 ± 5.17	14.74 ± 5.8	19.07 ± 6.68	0.625	T0: 0.364
	2	22.5 ± 10.06	17.74 ± 7.29	17.08 ± 12.1		T1: 0.425
	3	18.98 ± 8.73	14.18 ± 7.55	14.48 ± 7.56		T3: 0.160
R15-ICG(%)	1	8.27 ± 6.83	14.35 ± 9.66	8.62 ± 7.45	0.398	T0: 0.383
	2	10.01 ± 18.6	11.05 ± 12.79	16.89 ± 13.94		T1: 0.501
	3	11.1 ± 11.43	18.94 ± 16.39	18.35 ± 15.37		T3: 0.160
HB (gr/dl)	1	12.82 ± 1.68	11.85 ± 1.33	11.37 ± 1.37	0.692	T0: 0.865
	2	12.87 ± 1.89	11.4 ± 1.67	11.78 ± 2.08		T1: 0.850
	3	13.13 ± 2.09	12.12 ± 2.12	11.22 ± 1.52		T3: 0.558
Platelets no ($\times 10^4$)	1	20.4 ± 12.9	16.7 ± 11.9	17.9 ± 10.5	0.070	T0: 0.148
	2	21.2 ± 6.5	14.7 ± 6.9	12.4 ± 6.7		T1: 0.325
	3	14.7 ± 10.1	10.7 ± 10.1	9.5 ± 9.4		T3: 0.023
Protomb (%)	1	85.6 ± 13.04	72.54 ± 10.58	56.5 ± 10.68	0.645	T0: 0.588
	2	83.6 ± 9.9	64.56 ± 9.5	47.91 ± 8.96		T1: 0.348
	3	87.04 ± 14.39	108.59 ± 159.34	61.5 ± 10.79		T3: 0.006
Creat (mg/dl)	1	0.97 ± 0.37	0.85 ± 0.33	0.93 ± 0.4	0.328	T0: 0.923
	2	0.9 ± 0.35	0.93 ± 0.27	0.87 ± 0.35		T1: 0.550
	3	0.88 ± 0.16	0.87 ± 0.22	0.86 ± 0.17		T3: 0.698
TB(mg/dl)	1	0.81 ± 0.30	1.0 ± 0.41	0.9 ± 0.40		T0: 0.789
	2	0.91 ± 0.39	1.10 ± 0.51	1.0 ± 0.51	0.147	T1: 0.302
	3	0.89 ± 9.43	1.12 ± 0.39	1.1 ± 0.52		T3: 0.289
TP (gr(dl)	1	7.4 ± 0.61	5.58 ± 0.89	5.68 ± 0.76	0.916	T0: 0.834
	2	7.28 ± 0.68	5.54 ± 0.72	5.05 ± 0.64		T1: 0.964
	3	7.2 ± 0.74	5.57 ± 0.86	5.39 ± 0.55		T3: 0.087
Alb (gr/dl)	1	4.25 ± 0.49	3.51 ± 0.42	3.21 ± 0.41	0.522	T0: 0.994
	2	4.26 ± 0.3	3.33 ± 0.36	3 ± 0.38		T1: 0.890
	3	4.18 ± 0.48	3.44 ± 0.45	3.38 ± 0.63		T3: 0.097
AST (U/I)	1	32.8 ± 22.64	243.08 ± 178.56	199.93 ± 110.27	0.054	T0: 0.538
	2	35.1 ± 20.1	390.75 ± 153.16	334.4 ± 139.28		T1: 0.039
	3	35.88 ± 16.09	475.88 ± 306.16	443 ± 276.17		T3: 0.001
ALT (U/I)	1	26.47 ± 14.21	210.54 ± 179.72	234.87 ± 200.7	0.016	T0: 0.404
	2	35.5 ± 30.39	330.78 ± 152.91	391.25 ± 183.15		T1: 0.057
	3	32.88 ± 15.28	446.33 ± 320.92	516.36 ± 373.26		T3: 0.015
GGT (U/l)	1	108.87 ± 120.22	75.08 ± 73.18	94.93 ± 106.34	0.003	T0: 0.384
	2	222.4 ± 224.01	159.78 ± 128.17	112.75 ± 93.42		T1: 0.122
	3	99.44 ± 77.48	100.44 ± 81.84	88.52 ± 63.95		T3: 0.660
ALP (U/l)	1	106.8 ± 37.88	82.46 ± 28.41	99.6 ± 86.32	0.014	T0: 0.224
	2	196 ± 163.65	129.5 ± 94.42	110 ± 76.19		T1: 0.541
	3	122.54 ± 70.62	94.06 ± 61.81	82 ± 29.76		T3: 0.613
LDH (U/l)	1	204.4 ± 38.77	350.93 ± 140.7	297.93 ± 110.63	0.935	T0: 0.166
	2	227.4 ± 75.75	415.5 ± 180.72	315.01 ± 80.72		T1: 0.102
	3	335.76 ± 359.29	483.96 ± 29.57	452.96 ± 271.57		T3: 0.025

Results are mean ± SD

ICG indocyanine green, PDR-ICG plasma disappearance rate of ICG, R15-ICG retention rate of indocyanine 15 min after administration of ICG, *HB* hemoglobin, *platelets no* platelets numbers, *Creat* creatinine, *PT* prothrombin, *ALB* albumin, *TP* total protein, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *ALP* alkaline phosphatase, *GGT* gamma-glutamyl transpeptidase, *TB* total bilirubin, *LDH* lactic acid dehydrogenase

and ALP ($p < 0.014$) between group 3 (total occlusion of the portal trunk) and group 1 (no portal clamping) or group 2 (selective continuous portal clamping). In contrast, there are no differences between the three groups for Hb, platelet count, creatinine, PT, Alb, total protein, AST, T Bil, and LDH. Many studies have used aminotransferase levels to assess the severity of hepatic injury resulting from ischemia [30–32]. Although serum AST and ALT levels are currently considered by many clinicians as most sensitive markers reflecting liver ischemic damage they also are influenced by the injury caused by liver transection resulting in much higher levels. In general, hepatobiliary surgeons pay special attention to postoperative serum total bilirubin levels as an indicator of liver failure after hepatectomy. In our study, there is no difference between the three groups in the bilirubin rate. However, a prospective study suggested that dynamic liver function tests, such as indocyanine green clearance, are superior to conventional liver function tests in assessing short-term prognosis in cirrhotic patients [33].

The present investigation demonstrated that statistically there is no difference between the three studied groups in terms of ICG-PDR or ICG-R15 noninvasive monitoring. Our results showed that intermittent 15-min Pringle maneuver (group 1) or selective hemihepatic continuous portal clamping (group 2) are not associated with adverse long-term prognosis.

Although this is a prospective study, the findings may be limited by a selection bias and confounding factors, which would be minimized by performing a randomized, controlled trial. However, the three groups were well matched for clinicopathological features and types of liver resection thereby reducing the influence of any selection bias.

Perhaps with the advent of new surgical devices, news trails to perform bloodless hepatic transection will be opened with no need for inflow or outflow occlusion [34–36]. Nevertheless, our study indicates that 15 min of intermittent Pringle maneuver or selective hemihepatic continuous portal clampage are safe methods of vascular control during liver transection, with no adverse effects on hepatocellular function.

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