Research Article

Selective Inflow Vascular Control in Resection of Hepatic Focal lesions.

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Abstract

Purpose: In this study, we prospectively evaluated the selective inflow vascular control during and afterresection of hepatic focal lesions and compare this technique with Pringle's maneuver. **Methods:** Between November ٢٠١٣ and November ٢٠١٥.Thirty patients with hepatic focal lesion were prospectively randomized into two groups by means of sealed envelope,group A, ١٤ patients were subjected to surgical resection using Pringle's maneuver (PM) and group B ,١٦ patients were subjected to surgical resection using selective inflow vascular control.The intraoperative (operative time, blood loss, hemodynamic changes, etc.) and postoperative parameters (complications, recovery of normal liver function, etc.) were measured and compared between the two groups. Liver function of all these patients was detected by blood test at ١-day preoperation, and at ١, ٣, and ٧ days postoperation. **Results:** Both of the two surgeries were successfully performed without any mortality. The intraoperative systolic arterial pressure and pulse in PM group were much higher than that in selective inflow vascular control group ($P < ٠.٠١$). The postoperative liver function parameters such as alanine transaminase (ALT), aspartate transaminase (AST), and total bilirubin (TBIL) increased much more in the PM group than that in the selective inflow vascular control group group compared with preoperation results ($P < ٠.٠٥$). Intraoperative bleeding, blood transfusion were more in the selective inflow vascular control group than in the PM group but the difference was not significant. There were no statistical differences in, hepatic inflow occlusion time and incidence of complications between the two groups ($P > ٠.٠٥$). **Conclusion:** Selective inflow vascular control is safer with less ischemia reperfusion injury than PM surgery for resection of hepatic focal lesions.

Keywords: Hepatic focal lesions, liver resection, Pringle maneuver (PM), selective inflow vascular control, Ischemia reperfusion injury.

Introduction

Liver resection is performed mainly for benign and malignant liver tumors, especially for hepatocellular carcinoma. It is a potential curative treatment option in patients with early stage carcinoma[١]. Intraoperative bleeding is a main concern during liver resections, and mortality and morbidity are clearly correlated with the amount of blood loss and the subsequent blood transfusions[٢]. Many methods of hepatic vascular control have been introduced to control intraoperative blood loss. In ١٩٠٨, Pringle applied inflow vascular occlusion technique (the Pringle maneuver) at the hepatic hilar for the first time. It is a technique of total compression of the hepatoduodenal ligament and the most commonly used and relatively easy method for controlling afferent blood flow[٣]. However, the Pringle maneuver also carries the risk of global ischemic damage to the liver and intestinal congestion, especially in patients with chronic liver diseases, the degree of which is likely to be accentuated by a prolonged period of vascular inflow occlusion[٤,٥]. In ١٩٨٧, Bismuth and Makuuchi proposed a hemihepatic vascular occlusion (HHO) technique to reduce the severity of visceral congestion and total liver ischemia, especially for the remaining liver[٦,٧]. By this method, visceral congestion is considered to be limited, because consider-

able portal blood flow is preserved and only portions of the liver are rendered anoxic[٨]. The technique with occlusion of vessels supplying the hemiliver containing the tumor, has been suggested to reduce intraoperative bleeding and postoperative liver functional disturbances because of the interruption of blood flow to the liver[٩]. But, portal vein and artery dissection to perform selective clamping is time consuming and may result in another blood loss[١٠]. Many prospective randomized controlled trials (RCTs) and retrospective clinical trials have evaluated the feasibility, safety andefficacy of HHO and total hepatic inflow occlusion (THO), however, the clinical significance between the two vascular control methods remain inconsistent. So, the optimal method of vascular control during hepatic resection continues to be debated.

Patients and Methods

After obtaining approval of the local ethics committee in El- Minia university hospital and written informed consent from the first degree relatives of the patients prior to entry into the study, ٣٠ patients (according to sample size) of either sex, aged between ٢٥-٧٠ years old with hepatic focal lesion admitted to hepatobiliary surgery unit, were enrolled in this prospective randomized study. They were randomly allocated into two groups by means of sealed envelope, group A, ١٤ patients were subjected to surgical resection using Pringle's maneuver and group B, ١٦ patients were subjected to surgical resection using selective inflow vascular control. This study carried out between November ٢٠١٣ to November ٢٠١٥.

Inclusion criteria

١. Age range was ٢٥-٧٠ years old
٢. Patient with hepatic focal lesion indicated for surgical resection bydecision of our surgical committee staff and according to guidelinesthat necessitate sectionectomy or less
٣. Child-Pugh class A and early B patients were included.

Exclusion criteria

Patients were excluded from the study if they were Child-Pugh late B & C

١. Multiple lesions in both hepatic lobes
٢. Portal vein thrombosis
٣. Patients with distant metastasis
٤. Patients with congestive heart failure or chronic renal failure.
٥. Patients with highly elevated preoperative liver enzymes.
٦. Previous treatment for hepatic focal lesion.

Preoperative Evaluation

All patients had a chest X-ray, abdominal ultrasonography, and triphasic computed tomography. Preoperative laboratory blood tests included hemoglobin, platelet count, alanine aminotransferase (ALT), aspartate amino transferase (AST), serum albumin, serum total bilirubin, creatinine, prothrombin time (PT), and serum alpha-fetoprotein. Child–Pugh score was used to assess hepatic function for each patient.

Surgical Procedure

All surgical procedures were accomplished by the one surgical team from the same department, ensuring procedures performed in a standardized manner. The hepatic parenchyma was transected using crush-clamp, ligasure or by harmonic scalpel. Liver resections based on segmental anatomy were performed in all patients.

In Pringle group, hepatic vascular control was performed through encircling the hepatoduodenal ligament with an umbilical tape and then applying a tourniquet until the pulse in the hepatic artery disappears distally. The portahepatis was intermittently clamped with cycles of ١٥ minutes of inflow occlusion followed by ٥ minutes of reperfusion.

In Selective inflow vascular control group, a small incision was made in the base of the Glisson's sheath. Then the right-angle forceps was gently passed through the plane between the hilar plate and the liver to dissect the hilar plate outside the Gilsson's sheath, and the ٨-Fr catheter was introduced. Finally, the vascular occlusion was achieved by tighten the catheter during hepatic resection with cycles of ١٥ minutes of inflow occlusion followed by ٥ minutes of reperfusion.

Anesthetic management was accomplished by general anesthesia, and blood loss was estimated by taking into account suction volume minus rinsing fluids. Indications for red blood cell transfusion included blood loss exceeding ٨٠٠ mL or the hematocrit value became less than ٣٠٪ during operation or within ٤٨ hours after surgery.

Postoperative Management

All patients received the same postoperative care. Liver function was monitored by ALT, AST, albumin, bilirubin, on post-operative days ١, ٣, and ٧.The tumors were diagnosed histopathologically. Post-operative complications and mortality within hospital stay postoperatively were recorded.

Statistical Analysis

Continuous, normally distributed variables are expressed as mean (±SD) or median (range), as appropriate. Student's t test was performed for continuous data, and Chi Square test was used for categorical data. All statistical tests were ٢-sided. P value less than ٠.٠٥ was considered statistical significant. All statistical analysis was performed with SPSS ٢٣.٠ statistical software (SPSS, Chicago, IL).

Results

Baseline of Patient Characteristics

In total, ١٤ patients were included in Pringle group and ١٦ patients in Selective inflow vascular control group. There was no significant difference between the ٢ groups in rates of age, sex ratio, liver function status and preoperative laboratory test (Table ١).

Clinicopathological Characteristics and Type of Hepatectomy

There were no significant differences between the ٢ groups regarding condition of liver parenchyma, pathology of the resected hepatic focal lesion and type of hepatectomy between ٢ groups (Table ٢).

Table ١: Clinical Characteristics of patients

Variable	Group A Pringle Maneuver (n =١٤)	Group B Selective Inflow Occlusion (n =١٦)	P value
Age, year	٤٩.٠٠(٢٥-٥٩)	٥٠.٩٤(٣٠-٦٤)	٠.٦
Sex (male %)	٧(٥٠.٠٪)	١٠(٦٢.٥٪)	٠.٧١
Liver function status			٠.٦١
Child–Pugh A	١١(٧٨.٦٪)	١٣(٨١.٣ %)	
Early Child–Pugh B	٣ (٢١.٤ %)	٣(١٨.٧٪)	
Preoperative laboratory tests			
ALT, U/L	٧٠.٣٦(±٣٦.٨٢)	٥٦.٨٨(±٢٦.٢٢)	٠.٢٥
AST, U/L	٥٨.٩٣(±٣٠.٢٥)	٦٥.٥٠(±٣٠.٩٥)	٠.٥٦
Albumin, g/L	٤.١٠(±٠.٦٩)	٤.٠٠(±٠.٧٤)	٠.٧١
Bilirubin, mg/dl	٠.٨٩(±٠.٣٨)	٠.٩٣(±٠.٤٤)	٠.٨٠
INR	١.٠٧١(±٠.١٢)	١.٠٥٦(±٠.١٢)	٠.٧٠

ALT = alanine aminotransferase, AST= aspartate aminotransferase,
INR=International Normalized Ratio.

Table ٢: Pathological Factors of Patients

Variable	Group A Pringle Maneuver (n =١٤)	Group B Selective Inflow Occlusion (n =١٦)	P value
Condition of Liver parenchyma			٠.٤٨٤
Normal liver parenchyma	٥(٣٥.٧٪)	٨ (٥٠.٠ %)	
Abnormal liver parenchyma	٩(٦٤.٣ %)	٨ (٥٠.٠ %)	
Pathology of the resected hepatic focal lesion			٠.٨٨
HCC	٦(٤٢.٨٪)	٦(٣٧.٥٪)	
CRC metastasis	٣(٢١.٤٪)	٣(١٨.٧٥٪)	
Other organ metastasis	١(٧.١٤٪)	٢(١٢.٥٪)	
Hydatid cyst	٢(١٤.٢٨٪)	٤(٢٥٪)	
Other benign lesions	٢(١٤.٢٨٪)	١(٦.٢٥٪)	
Hepatectomy procedures			٠.٩٣
Segmentectomy	٤(٢٨.٥٧ %)	٥(٣١.٢٥ %)	
Sectionectomy	٥(٣٥.٧٪)	٥(٣١.٢٥ %)	
Non anatomical	٥(٣٥.٧٪)	٦(٣٧.٥ %)	

HCC=Hepatocellular Carcinoma, CRC=Colorectal Carcinoma.

Influence of Type of Clamping on Postoperative Laboratory Test Results

The liver function parameters such as alanine transaminase (ALT), aspartate transaminase (AST), albumin (ALB), and total bilirubin (TBIL) are presented in Table ٣. The results showed that all these liver function parameters were significantly different between the Selective vascular control group and Pringle's group after surgery. ALT, AST, and TBIL increased much more in the Pringle's group than that in the Selective vascular control group compared with preoperation results ($P < ٠.٠٥$) Figure ١,٢.

Table ٣: Postoperative Laboratory Test Results and Outcome Data

Variable	Group A Pringle Maneuver (n =١٤)	Group B Selective Inflow Occlusion (n =١٦)	P value
ALTin١st post Opday	٦٤٥.٧١(±٢٧٢.٤٥)	٣٩٥.٥٦(±١٩١.٢٢)	٠.٠٣
ALTin٣rd post Op day	٤٢٢.١٤(±٢٦١.١٤)	٢٨٠.٦٩(±١٢٨.٥٧)	٠.٠١
ALTin٧th post Op day	١٧٧.٥٠(±١٢٠.٣١)	١٠٠.٠٦(±٣٣.١٧)	٠.٠٤
AST in ١st post Op day	٦٣٧.١٤(±٢٦٦.٥٨)	٤٧٩.٠٠(±١٩٤.٩٥)	٠.٠١
AST in ٣rd post Op day	٣٢٥.٦٤(±١٩٩.٩٣)	٢٤٥.٠٠(±٩٥.٠٧)	٠.٠٣
AST in ٧th post Op day	١٦٩.٥٠(±٨٥.٧٥)	٨٩.٩٤(±٣٨.٨٩)	٠.٠٢
Postoperative Albumin level	٣.٠٣(±٠.٣٢)	٣.٥٦(±٠.٥٣)	٠.٠٤
Post-operative bilirubin level	١.٦٦(±٠.٥٨)	١.١٩(±٠.٣٥)	٠.٠٤

ALT =alanine aminotransferase, AST = aspartate aminotransferase, Op=operative.

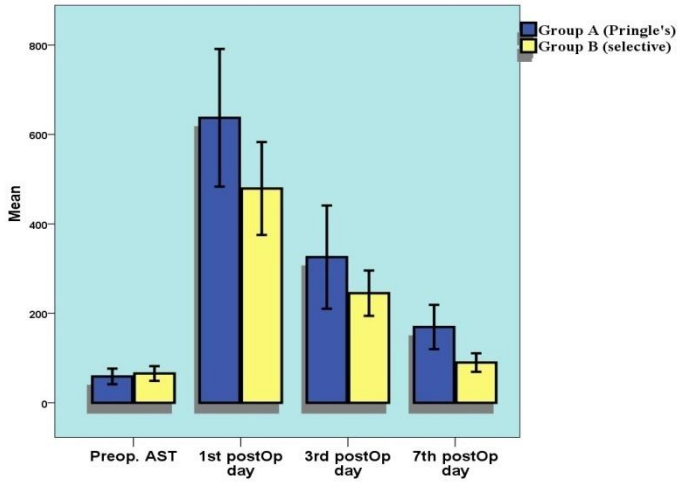

Figure ١: Serial changes in AST levels in both groups

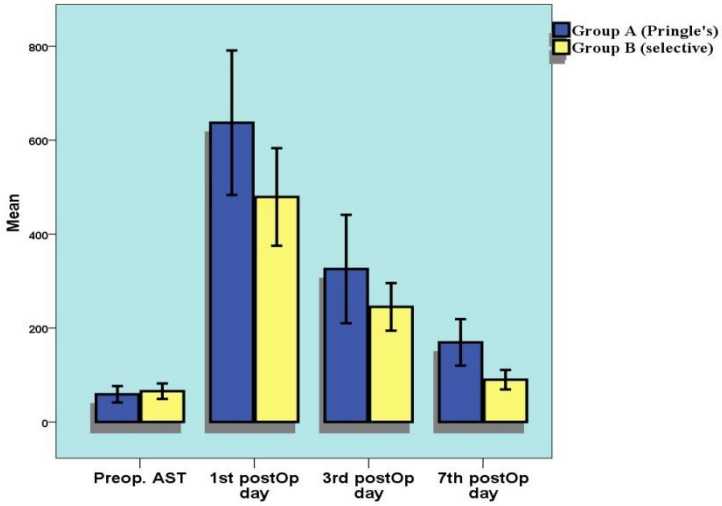

Figure ٢: Serial changes of ALT levels in both groups

Influence of Type of Clamping on Operative Parameter

The intraoperative data including operative time, ischemic duration, intraoperative blood loss, and blood transfusion are shown in Table ٤. The operating time in selective clamping group was significantly higher (P =٠.٠١٣) than the Pringle's group. The total amount of blood loss was more in the selective clamping group (P= ٠.٠٨) than the Pringle's group and also the amount of blood transfusion (P=٠.٢٣); but the results was not significant (P> ٠.٠٥). Significant difference was found between the two groups in systolic arterial pressure and pulse (P = ٠.٠١) and (P=٠.٠٠٤) respectively, indicating that the effect of hemodynamics

caused by Selective inflow control surgery was much less than that caused by Pringle's maneuver surgery. Several patients suffered from different complications (٥٠% vs٣١.٢٥%, Table ٤). No operative mortality in any group. But one patient in group A died in the ١٠th postoperative day most probably due to pulmonary embolism. One patient was found to have early postoperative bleeding requiring reexploration in group A. few patients suffered complications of bile leak, Ascites, Pleural effusion or portal vein thrombosis. There was no significant

difference in hospital stay between the ٢ groups.

Table ٤: Comparison of Operative Parameters and Outcomes of Patients

Variable	Group A Pringle Maneuver (n =١٤)	Group B Selective Inflow Occlusion (n =١٦)	P value
Pulse (time)			٠.٠٠٤
١-min before occlusion	٨١.٣٢(± ١٠.٦٤)	٧٩.١٩ (± ١٠.٣٥)	
١-min after occlusion	٩٦.١٤(± ١٤.٣٦)	٨١.٧٧(± ٨.٦٨)	
١-min after opening	٨٢.٢٨(± ١٢.٥٩)	٧٩.٠٤ (± ١٣.٢٣)	
Systolic arterial pressure (mmHg)			٠.٠١
١-min before occlusion	١١٩.٢٩(± ١١.٥٦)	١٢١.٦٥(± ١١.٣٠)	
١-min after occlusion	١٤٥.١٣(± ١٧.٢٠)	١٢٢.١٥(± ١٢.٢٣)	
١-min after opening	١١٦.٢٦(± ١٣.٣٧)	١١٩.٠٤(± ١٢.٧٨)	
Operative time (Min)	١٦٩.٢٩(±٣٥.٤٠)	٢٠٩.٣٨(± ٤٥.٣٨)	٠.٠١
Total blood Loss(Liters)	٠.٨٨٨(±٠.٦٨)	١.٢٥٧(± ١.٠٢)	٠.٠٨
Total Ischemia duration (Min)	٩٣.٥٧(±٣٢.٢٥)	٩٩.٠٦(±٣٥.٦٩)	٠.٦٦
Post-operative complications	٥٠٪	٣١.٢٥٪	٠.٠٥
Ascites or Pleural effusion	٢	٢	
biliary fistula	١	٠	
hyperbilirubinemia	٣	٠	
portal thrombosis	٠	٣	
Reoperation	١	٠	
Hospital Stay indays	١٦.٧١(±٦.٨٤)	١٩.١٩(±٦.٥٧)	٠.٣٢

Discussion

Excessive blood loss during hepatectomy requiring perioperative blood transfusion has a negative impact on morbidity and mortality,[٢, ١١, ١٢] particularly in patients with cirrhosis. Using modern technology, hepatic parenchymal transection can be carried out with little blood loss. A Japanese survey revealed that only a minority (٧٪) of surgeons never use inflow occlusion, whereas ٢٥٪ apply a Pringle maneuver on a routine basis even in cirrhotic patients.[١٣] Although inflow occlusion is not necessarily accepted as routine practice, many surgeons still prefer to use hepatic vascular inflow occlusion with, or without outflow occlusion during parenchymal transection,[١٤-١٧] especially in those cirrhotic patients with irregular branches and collateral circulations of vessels. The Pringle maneuver is sufficient in most situations[١٣] to control bleeding from the hepatic artery or portal vein during hepatectomy. However, it is hard to avoid ischemic injury in the remnant liver after Pringle maneuver and may result in postoperative liver dysfunction.

The degree of ischemic injury to the hepatocytes may be accentuated in the presence of underlying liver disease [١٨].

To avoid adverse effects of the Pringle maneuver such as hepatic warm ischemia and splanchnic congestion, selective inflow control technique[٩,١٩] has been advocated tocontrol hemorrhage from the liver parenchyma without causing ischemia in the contralateral hepatic lobe or splanchnic congestion.

However, this method is time consuming and, more important, can destroythe pericholedochal collateral vessels, which can lead to biliary complications. Furthermore, in case of majorhepatectomy selective inflow vascular control is not always applicable, and bleeding from the contra lateral liver may make necessary the conversion to portal triad clamping in as much as ٢٠٪ of cases[١٦].

Until now there has been no consensus on the indications and outcomes of different hepatic vascular occlusion methods[٢٠]
This study evaluated the intraoperative and postoperative outcome of selective inflow vascular control and Pringle's maneuver surgeries and found no significant difference between the groups in preoperative profiles, the results showed that the intraoperative systolic arterial pressure and pulse in the Pringle's group were much higher than that in the selective inflow vascular control group, indicating that the effect of hemodynamics caused by selective inflow vascular control surgery was much less than that caused by Pringle's maneuver, And these results are in accordance with those presented by Li et al., ٢٠٠٥[٢١] and Hasselgren et al., ١٩٨٧[٢٢].

The operating time was significantly higher (P=٠.٠١٣) in the selective clamping group. And these results are in accordance with those presented by Makuuchi et al., ١٩٨٧[٩]. But in conflict with those presented by Wang et al., ٢٠١١[٢٣].

One of the concerns about selective inflow vascular control is the risk of bleeding fromthe contralateral liver[٢٤].We have compared the bleeding rates depending on the performed hepatectomy, and we have found that the total amount of blood loss and the amount of blood transfusion were more in the selective clamping group than in the Pringle's group but the difference was not significant. These results are in accordance with those presented by Königsrainer et al., ٢٠٠٦[٢٥] and Figueras et al., ٢٠٠٥[٢٦]. But in conflict with those presented by Gar-Yang et al., ٢٠٠٥[٢٧] who found no difference in these findings between the two groups.

Liver injury due to ischemia and subsequent reperfusion are major concerns in inflow vascular occlusion[٢٨,٢٩] and are usually monitored after surgery by measuring aminotransferase levels[٣٠]. We found significant higher peak in ALT and AST levels on postoperative days ١, ٣ and ٧ in the Pringle's maneuver group than in the selective inflow vascular control (P= ٠.٠٣ - ٠.٠١ - ٠.٠٤ respectively).

Three RCTs Si-Yuan et al., ٢٠٠١[١٥] Takayama et al., ١٩٩٧[١٩] and Chauet al., ٢٠٠٥ [٣١]and one retrospective study by Wu et al., ١٩٩٦[٥] drew the same conclusion. Meta-analysis by Wang et al., ٢٠١١[٢٣] also showed that AST levels on postoperative day ١ were also higher in the Pringle's group.

Figueras et al., ٢٠٠٥[٢٦] Wen et al., ٢٠٠٧[٣٢] and Liang et al., ٢٠٠٨[٣٣] found no significant difference on ALT and AST levels on postoperative days ١, ٣ and ٧ in the two groups.

No statistically significant difference was found in either peri-operative mortality, peri-operative morbidity, ischemic duration or hospital stay. These results were in accordance with results by Figueras et al., ٢٠٠٥[٢٦], Liang et al., ٢٠٠٨[٣٣], Si-Yuan et al., ٢٠٠١[١٥].

Conclusions in summary, our study compared the short-term outcomes of selective inflow vascular control and Pringle's maneuver surgeries on patients with hepatic focal lesions and demonstrated that selective inflow vascular control is safer with less ischemia reperfusion injury than Pringle's maneuver surgery. However, further studies with more patients and long-term follow-up durations are required to compare the safety and effectiveness of the two techniques.

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