

## Does clamping during liver surgery predispose to thrombosis of the hepatic veins? Analysis of 210 cases

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### Abstract

**AIM:** To test whether clamping during liver surgery predisposes to hepatic vein thrombosis.

**METHODS:** We performed a retrospective analysis of 210 patients who underwent liver resection with simultaneous inflow and outflow occlusion. Intraoperatively, flow in the hepatic veins was assessed by Doppler ultrasonography during the reperfusion phase. Postoperatively, patency of the hepatic veins was assessed by contrast-enhanced CT angiography, when necessary after 3-6 mo follow up.

**RESULTS:** Twelve patients (5.7%) developed intraoperative liver remnant swelling. However, intraoperative ultrasonography did not reveal evidence of hepatic vein thrombosis. In three of these patients a kinking of the common trunk of the middle and left hepatic veins hindering outflow was recognized and was managed successfully by

suturing the liver remnant to the diaphragm. Twenty three patients (10.9%) who developed signs of mild outflow obstruction postoperatively, had no evidence of thrombi in the hepatic veins or flow disturbances on ultrasonography and contrast-enhanced CT angiography, while hospitalized. Long term assessment of the patency of the hepatic veins over a 3-6 mo follow-up period did not reveal thrombi formation or clinical manifestations of outflow obstruction.

**CONCLUSION:** Extrahepatic dissection and clamping of the hepatic veins does not predispose to clinically important thrombosis.

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**Key words:** CT-angiography; Doppler ultrasound; Liver resection; Pringle maneuver; Radiofrequency; Selective hepatic vascular exclusion

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### INTRODUCTION

Vascular control during liver resection typically involves hepatic inflow occlusion, either continuous or intermittent. However, more complex resections may require both inflow and outflow occlusion, the latter usually being achieved with extraparenchymal control of the major hepatic veins at the hepatocaval junction. This maneuver can significantly reduce backflow bleeding during parenchymal transection and facilitate resection

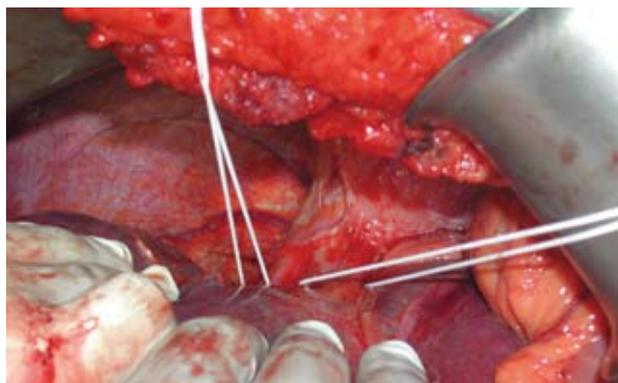
of tumors close to the roots of the major hepatic veins and even reconstruction of a hepatic vein in the liver remnant<sup>[1]</sup>.

Three techniques for vascular control have been widely used: the Pringle maneuver (PM), the selective hepatic vascular exclusion (SHVE) and the total hepatic vascular exclusion (THVE). The PM<sup>[2]</sup> is performed by encircling and clamping the hepatoduodenal ligament<sup>[1]</sup>. Although this is well tolerated, it should always be kept in mind that backflow bleeding and air embolization might occur during parenchymal transection<sup>[3]</sup>. THVE includes clamping of the hepatoduodenal ligament and occlusion of the suprahepatic and infrahepatic inferior vena cava (IVC)<sup>[4]</sup>. This technique has the advantage of a bloodless surgical field, but the serious hemodynamic instability it may cause, makes it inappropriate for 20%-30% of patients. SHVE entails disconnection of the liver from the retrohepatic IVC and inflow occlusion combined with extrahepatic control of hepatic veins. This technique offers bloodless liver transection without the above-mentioned disadvantages of PM and THVE<sup>[5,6]</sup>.

Dissection and clamping of the hepatic veins during the application of SHVE may predispose the major hepatic veins to thrombi formation through the induction of venous stasis and endothelial injury coupled with coagulation disturbances. The scarcity of studies addressing this issue prompted us to test our hypothesis that dissection and clamping of the hepatic veins is associated with an increased risk of thrombosis and liver outflow obstruction.

## MATERIALS AND METHODS

Between 1997 and 2007, 210 consecutive patients underwent hepatectomy with SHVE<sup>[1]</sup>. Briefly, in all cases and irrespective of the type of planned hepatectomy, the abdomen was accessed *via* a bilateral subcostal incision and the liver was fully mobilized after transection of its ligaments. The liver was then disconnected from the retrohepatic IVC by dividing the short perforator hepatic veins. On the right side, dissection along the anterior surface of the IVC continued until the right hepatic vein was isolated, while on the left side, the venous trunks of the left and middle hepatic veins were also dissected free from the surrounding tissues. Control of liver inflow was attained by clamping the porta hepatis with a Satinsky clamp and by occluding any accessory hepatic artery with bulldog clamps. Liver outflow control was achieved by clamping the trunks of the right, middle and left hepatic veins separately (Figure 1). The transection plane was defined with an intraoperative ultrasonographer (Aloka SSD-1400, model IP-1235V, ALOKA CO., LTD., Japan), in order to secure tumor-free margins > 1 cm. Liver splitting was performed using either the clamp crushing technique or by sharp transection with a knife. Hemostasis was achieved by suturing all vascular orifices on the cut surface with 3-0 and 4-0 prolene. After completion of the liver resection, outflow was released first, followed by liver inflow<sup>[5,6]</sup>. Following reperfusion, hemostasis was



**Figure 1** After careful dissection at the hepatocaval junction, the extrahepatic trunk of the right hepatic vein and the common trunk of the left and middle hepatic vein have been isolated and are ready to be clamped.

completed using additional stitches. Flow in the hepatic artery, the portal vein, the hepatic veins and the IVC was assessed by intraoperative Doppler ultrasonography. The negative findings in the first 120 consecutive patients prompted us to restrict our Doppler study to the hepatic veins. Thorough imaging of all liver vasculature was then reserved for cases with liver remnant swelling or signs of hypoperfusion. All operations were performed by the same surgical team, directed by the senior author V.S. All patients had normal imaging of the hepatic veins before liver resection, either on contrast-enhanced CT or MRI.

Postoperative Doppler ultrasonography of the portal vein, hepatic artery and the hepatic veins was performed at the bedside, if the patient exhibited at least one of the following findings: (a) clinically worsening ascites on any postoperative day; (b) persistent or worsening cholestasis (conjugated bilirubin > 3 mg/dL) after the 3rd postoperative day; (c) worsening elevation of transaminases after the 2nd postoperative day (AST and/or ALT > 1st postoperative day levels) or (d) persistent or worsening prolongation of INR > 2 after the 3rd postoperative day.

All patients admitted after 2002 (117 patients-56%) received perioperative thromboprophylaxis with low molecular weight heparin for a median duration of 10 d (range: 4-14 d), according to our new institutional protocol which was initiated at that time. Post-discharge, all patients were invited for a follow-up abdominal CT scan, 3-6 mo after surgery. Helical CT (Philips, The Netherlands) of the abdomen was performed before and after intravenous administration of iodinated contrast material. Contrast enhanced images were obtained in the arterial and portal venous phase and images were evaluated for the presence of hepatic venous thrombosis by two independent observers. Data collection was performed in a prospective manner.

## RESULTS

Clinical, intraoperative and postoperative parameters of the patients are summarized in Table 1. Intraoperatively, 12 (5.7%) patients developed unexpected swelling of the liver remnant. Intraoperative Doppler ultrasonography

**Table 1** Clinical, intraoperative and postoperative parameters of 210 patients undergoing liver resections under selective hepatic vascular exclusion (data are expressed as medians with range)

Clinical, intraoperative and postoperative parameters	
Age (yr)	63 (1-86)
Indication for hepatectomy	
Malignancy	173
Benign (hemangioma, hydatid cyst, <i>etc</i> )	37
Type of hepatectomy	
Right hepatectomy	92
Left hepatectomy	40
Minor hepatectomy (1-2 segments)	78
Intraoperative data	
Warm ischemic time (min)	39 (25-61)
Blood loss (mL)	420 (140-3100)
Transfusions of pRBCs (U)	0 (0-14)
Outcome	
Morbidity (pleural effusion, bile leak, chest infection, post-operative bleeding, wound infection, postoperative liver failure)	34%
Mortality	3 (1.5%) <sup>1</sup>
Hospital stay (d)	12 (4-37)

<sup>1</sup>One death due to postoperative liver failure, 1 due to cardiomyopathy and cardiac arrest and 1 due to postoperative sepsis.

did not reveal evidence of hepatic vein thrombosis in any of these cases. In three of these patients kinking of the common trunk of the middle and left hepatic veins was recognized and was managed by suturing the liver remnant to the diaphragm. In the remaining nine patients, extensive work-up did not show thrombi formation and the liver remnant swelling was attributed to the fact that the portal flow was disproportional to the small liver remnant.

Twenty three (10.9%) patients fulfilled the previously mentioned criteria for postoperative Doppler ultrasonography at the bedside. All these patients were also examined with contrast enhanced CT-angiography. The hepatic veins were visualized in all cases and no evidence of thrombosis was found.

Forty two (20%) patients underwent contrast-enhanced CT scans during their postoperative hospitalization for reasons unrelated to suspected hepatic vein thrombosis (diagnostic work-up for fever, bile collection and chest infection). In all cases, hepatic vein imaging did not reveal thrombi formation or recanalization processes.

Finally, 200 patients (95%) underwent a follow up contrast-enhanced CT scan of the liver at a median time of 150 d (range: 92-205 d) after surgery, without evidence of thrombotic processes or stricture of the hepatic veins.

## DISCUSSION

Our study showed that dissection and clamping of the hepatic veins in hepatectomies under inflow and outflow vascular occlusion of the liver was not complicated with hepatic vein thrombosis either intraoperatively or postoperatively during a 6-mo follow-up period.

Postoperative hepatic venous outflow obstruction is extremely rare in large series of hepatectomies<sup>[7,8]</sup>. On the contrary, in liver transplantation the incidence is high, especially with the piggyback technique (0.5%-2.5%) which has a mortality rate of 24%<sup>[9-14]</sup>. The main causative factors are either technique-related or are associated with coagulation disturbances generated by the underlying disease and graft function.

The only study addressing the risk of hepatic vein thrombosis in liver resection is by Arita *et al*<sup>[15]</sup>, who showed that 10 out of 821 liver resections performed using the intermittent Pringle maneuver developed hepatic vein thrombosis. It is worth noting that the authors had to resort to thrombectomy in the most severe cases. The exposure of major hepatic veins to a length of 3 cm or more and the use of an ultrasonic dissector were postulated to be predisposing factors for vein thrombosis.

Although our technique could be considered more thrombogenic, since it includes dissection and clamping of hepatic veins, the lack of thrombosis in our series is in surprising contrast to the findings of Arita *et al*, who performed only intermittent inflow occlusion. It is possible that the use of the ultrasonic dissection technique used by Arita *et al* could, as the authors themselves admitted, have contributed to the thrombogenic effect, which was further aggravated when the energy was delivered close to the major hepatic veins<sup>[15]</sup>.

Our results are in agreement with the findings of most major clinical series of hepatectomies performed under vascular control, in which hepatic venous thrombosis is scarcely if ever mentioned<sup>[16,17]</sup>. Although SHVE could be considered more thrombogenic, since it involves injurious manipulation of hepatic veins, the lack of confirmed cases of vein thrombosis in our study can be attributed to short warm ischemic time and sharp transection of the liver surface with the scalpel, a technique that is less traumatic to venous epithelium compared to other ablative techniques. Avoidance of radiofrequency ablation in our series may also have contributed to our favorable results, since this technique has been recently associated with damage to the liver remnant<sup>[18]</sup> and hepatic vein thrombosis<sup>[19]</sup>. Venous endothelial trauma has been known to cause platelet aggregation and degranulation, vasoconstriction, thrombin activation and diminished fibrinolysis<sup>[20]</sup>. Therefore, we can not exclude the possibility that some of our patients may have developed small, undetected thrombi postoperatively. However, such thrombi remain clinically silent and resolve spontaneously without increasing morbidity or mortality. It is also possible that ischemia reperfusion of the liver mobilizes mechanisms that attenuate thrombi formation locally. Studies addressing the coagulation-fibrinolysis system during liver resection indicate that the balance leans towards fibrinolysis<sup>[21,22]</sup>.

Regarding diagnosis of hepatic venous thrombosis, Doppler ultrasound is a readily available and inexpensive tool<sup>[23,24]</sup>. It is, however, operator-dependent and

its diagnostic accuracy may be compromised by the presence of bowel gas or ascites. On CT, vein thrombosis is seen as a lack of enhancement on post-contrast images, often associated with peripheral rim enhancement. In hepatic veno-occlusive disease, CT reveals patchy hepatic parenchymal enhancement with lack of normal visualization of the hepatic veins<sup>[25-27]</sup>.

In conclusion, our analysis of a large cohort of patients confirms that extrahepatic dissection and clamping of the hepatic veins for up to one hour is a safe procedure that does not predispose to clinically important thrombosis. Although the technique of selective vascular exclusion used in our series is not advocated for routine use in liver surgery, we suggest that concerns about venous thrombosis are unjustified and should not be a limiting factor in the application of this useful technique, whenever necessary.

## COMMENTS

### Background

Dissection and clamping of the hepatic veins during liver resection may predispose the major hepatic veins to thrombi formation. In this study we test our hypothesis that dissection and clamping of the hepatic veins is not associated with an increased risk of thrombosis and liver outflow obstruction.

### Research frontiers

Postoperative hepatic venous outflow obstruction is extremely rare in large series of hepatectomies. On the contrary, in liver transplantation the incidence is high, especially with the piggyback technique (0.5%-2.5%) which has a mortality rate of 24%. The main causative factors are either technique-related or are associated with coagulation disturbances generated by the underlying disease and graft function.

### Innovations and breakthroughs

The only study addressing the risk of hepatic vein thrombosis in liver resection is by Arita *et al*, who showed that 10 out of 821 liver resections performed with the intermittent Pringle maneuver developed hepatic vein thrombosis. Our study showed that dissection and clamping of the hepatic veins in hepatectomies under inflow and outflow vascular occlusion of the liver was not complicated with hepatic vein thrombosis either intraoperatively or postoperatively during a six-month follow-up period.

### Applications

Although the technique of selective vascular exclusion used in our series is not advocated for routine use in liver surgery, the authors suggest that concerns about venous thrombosis are unjustified and should not be a limiting factor in the application of this useful technique, whenever necessary.

### Terminology

Pringle maneuver: performed by encircling and clamping the hepatoduodenal ligament; Selective hepatic vascular exclusion: inflow occlusion combined with extrahepatic control of hepatic veins; Total hepatic vascular exclusion: clamping of the hepatoduodenal ligament and occlusion of the suprahepatic and infrahepatic vena cava (IVC).

### Peer review

This is an interesting paper about hepatic vein thrombosis.

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