

# Portal Triad Clamping or Hepatic Vascular Exclusion for Major Liver Resection

## A Controlled Study

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### Objective

The authors compared operative course of patients undergoing major liver resections under portal triad clamping (PTC) or under hepatic vascular exclusion (HVE).

### Summary Background Data

Reduced blood loss during liver resection is achieved by PTC or HVE. Specific complications and postoperative hepatocellular injury mediated with two procedures have not been compared.

### Methods

Fifty-two noncirrhotic patients undergoing major liver resections were included in a prospective randomized study comparing both the intraoperative and postoperative courses under PTC (n = 24) or under HVE (n = 28).

### Results

The two groups were similar at entry, but eight patients were crossed over to the other group during resection. In the HVE group, hemodynamic intolerance occurred in four (14%) patients. In the PTC group, pedicular clamping was not efficient in four patients, including three with involvement of the cavohepatic intersection and one with persistent bleeding due to tricuspid insufficiency. Intraoperative blood losses and postoperative enzyme level reflecting hepatocellular injury were similar in the two groups. Mean operative duration and mean clampage duration were significantly increased after HVE. Postoperative abdominal collections and pulmonary complications were 2.5-fold higher after HVE but without statistical significance, whereas the mean length of postoperative hospital stay was longer after HVE.

### Conclusions

This study shows that both methods of vascular occlusion are equally effective in reducing blood loss in major liver resections. The HVE is associated with unpredictable hemodynamic intolerance, increased postoperative complications with a longer hospital stay, and should be restricted to lesions involving the cavo–hepatic intersection.

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Operative blood loss is the main factor associated with perioperative prognosis of patients undergoing liver resection.<sup>1-3</sup> It occurs during the dissection phase, during the parenchymal transection, or during the revascularization phase of the procedure. During the transection phase, blood loss can be reduced either by portal triad clamping (PTC), also called Pringle maneuver, or by complete hepatic vascular exclusion (HVE), combining PTC and occlusion of the inferior vena cava (IVC) below and above the liver.<sup>4</sup> Guidelines for vascular control have been reported by several authors but with a recent enthusiasm for HVE. Despite a complex surgical technique and anesthetic management, HVE has been adopted rapidly.<sup>5-8</sup> Both types of vascular occlusion are effective in limiting bleeding, but they also produce liver ischemia. It is not yet fully known how much each type of vascular occlusion influences the amount of parenchymal bleeding, the rate of hepatocyte damage, subsequent recovery, and the surgical outcome.

The purpose of this randomized prospective study was to assess the effects of each type of vascular occlusion on intraoperative and postoperative courses in major liver resections.

## PATIENTS AND METHODS

From November 1991 through March 1994, of a total of 216 patients who underwent an elective liver resection, 52 (25%) consecutive noncirrhotic patients requiring a major liver resection (*i.e.*, removal of 3 liver segments or more) in whom preoperative imaging studies showed no involvement of major hepatic veins or the vena cava were selected for this study. There were 21 men and 31 women. Their mean ( $\pm$  standard deviation) age was  $46 \pm 16$  years (range, 14–72 years). Indications for liver resection were mainly malignant tumors in 40 (77%) (8 hepatocellular carcinomas, 13 secondary malignancies, 18 cholangiocarcinomas, 1 gallbladder carcinoma) and benign disease in 12 (23%) (8 adenomas, 4 miscellaneous). Chronic liver disease was absent from all the remnant livers, including patients with hepatocellular carcinoma. Major liver resections according to the Couinaud classification included 18 right hepatectomies (segments V, VI, VII, VIII), 12 right lobectomies (segments IV, V, VI, VII, VIII, and sometimes I), 12 left hepatectomies (segments II, III, IV), 8 extended left hepatectomies (segments II, III, IV, V, VIII, and sometimes I), and 2 central hepatectomies (segments IV, V, VIII, and sometimes I).<sup>9</sup>

All patients considered for resection underwent preop-

erative assessment. Laboratory tests included liver function tests, coagulation tests, and measurement of serum creatinine and electrolytes. Radiologic workup included liver ultrasonography, computed tomography, and selective celiac and mesenteric arteriography with late-phase portography; magnetic resonance imaging was used selectively. Patients with evidence of involvement of the hepatic veins or the vena cava (*i.e.*, narrowing of the vessel lumen by the tumor) or both were not included in the study.

Before surgery, all patients had a pulmonary artery catheter and a radial arterial line. Monitored variables included mean arterial pressure (MAP), pulmonary arterial pressure (PAP), thermodilution cardiac index (CI), and systemic vascular resistances (SVRs).

An abdominal incision without thoracotomy was used in all patients. When abdominal exploration was negative for extrahepatic spread, patients were randomly allocated to either PTC group or HVE group. Intraoperative ultrasonography was systematically performed to accurately determine the location of the lesions, their relationship to the vascular system, and to rule out other lesions not apparent on preoperative radiologic workup. A careful search for a left hepatic artery arising from the left gastric artery was made to avoid liver congestion during HVE or persistent bleeding during PTC. In the HVE group, the entire retrohepatic vena cava was freed up; if the right adrenal vein entered in this segment of vena cava, it was ligated and divided. In the PTC group, the vascular occlusion never included the hepatic vein draining the parenchyma to be resected. Hemodynamic data were recorded before vascular occlusion and 5 minutes after vascular occlusion. In the HVE group, initial triad vascular exclusion was undertaken for up to 5 minutes after an adequate blood volume expansion with crystalloids to ensure that the procedure would be well tolerated.

Hemodynamic intolerance to HVE was defined as a decrease of MAP  $> 30\%$  or a decrease in CI  $> 50\%$  or both.<sup>10,11</sup>

In all patients, parenchymal transection was performed using a Kelly forceps and ultrasonic dissector; biliary and vascular radicles were secured by sutures and clips and liver cut surface sealed by fibrin glue (Biocol Laboratoires Bio-Transfusion, Roissy, France). In all patients, a silicone rubber closed-suction drain (Drain de Jost et Redon, Pharmacie Centrale des Hôpitaux, Paris, France) was placed.

Duration of warm ischemia and operative time were recorded. Intraoperative blood losses were calculated by adding the blood volume into the suction canister to the blood loss as calculated by weighing the sponges. The indications for peroperative blood transfusion were a decrease in hematocrit to 0.24 in patients without previous cardiac disease or to 0.29 in patients with previous

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**Table 1. CLINICAL AND OPERATIVE CHARACTERISTICS OF PATIENTS UNDERGOING RESECTION IN THE PORTAL TRIAD CLAMPING GROUP (PTC) AND IN THE HEPATIC VASCULAR EXCLUSION (HVE) GROUP**

	PTC (n = 24)	HVE (n = 28)
Age (yr) (mean ± SD)	43 ± 16	48 ± 18
Sex (M/F)	8/16	13/15
No. of benign lesions	7	5
No. of malignant lesions	17	23
No. of resected segments (mean)	4.2	4.6
Mean specimen weight (g)	1342 ± 971	1215 ± 756

cardiac disease or hemodynamic instability. Postoperative parameters of hepatocellular injury and recovery, including serum transaminases levels and prothrombin time, were measured at days 1 and 5. The effect of the type of vascular control on the renal function was assessed by serum creatinine levels at days 1 and 5.

Patients were observed until the day of discharge. Pulmonary complications included chest infection or pleural effusion or both. Routine abdominal ultrasound was carried out at between days 3 and 6 or in any patient with a suspected infected collection. All fluid collections were drained percutaneously with bacteriologic cultures. The mean length of hospital stay was recorded.

The results are expressed as the means (one standard deviation). Comparisons between groups were analyzed by Student's *t* test or the chi square test with Yates's correction for quantitative and qualitative variables as appropriate. Significance was defined as  $p \leq 0.05$ . Patients not following the inclusion assignment were analyzed separately. The protocol was approved by the ethics and research committee of our institution.

## RESULTS

According to the randomization, patients were equally divided in PTC group ( $n = 24$ ) and HVE group ( $n = 28$ ). As listed in Table 1, there were no significant differences between the two groups in terms of age, gender, type of liver lesions, number of resected segments, and mean resected specimen weight ranging between 360 and 4310 g in the PTC group and 1103 and 2250 g in the HVE group (not significant). Eight of the 52 patients who were entered in the study, 4 in each group, were crossed over to the other group. In the PTC group, three patients with malignant tumors (numbers 19, 27, and 44) showed during liver mobilization to have tumor involving the retrohepatic vena cava, including the terminal part of the middle hepatic vein in the one. Resections in these pa-

tients necessitated crossover to HVE. The postoperative course was marked by pulmonary complications in two of these and was associated in one with subphrenic collection. In the same group, one patient (number 40) who was resected for a carcinoid tumor complicated by slight tricuspid insufficiency experienced persistent bleeding during parenchymal transection and was crossed over to HVE, which was not hemodynamically tolerated. Resection was successfully performed under PTC associated with extraparenchymal occlusion of the hepatic veins. The postoperative course was uneventful. In the HVE group, three patients (numbers 26, 29, and 46) showed a poor hemodynamic tolerance during the exclusion trial (more than 50% decrease in CI with a 30% rise in SVR for patient numbers 26 and 29 and more than 30% decrease in MAP with a 40% rise in SVR for patient number 46). Patient numbers 26 and 29, aged 69 and 71 years, respectively, had had a full noninvasive preoperative cardiorespiratory evaluation for previous heart disease that was within normal limits, whereas patient number 46 was a 36-year-old, otherwise healthy, woman. Their resections were successfully performed under PTC. The postoperative course was marked by chest infection in one. In the same group, one patient (number 21) who was operated on for a huge hepatocarcinoma with invasion of the diaphragm experienced liver congestion and bleeding during parenchymal transection that was promptly relieved after unclamping the vena cava. Transection was uneventfully performed under PTC. The postoperative course was marked by pleural effusion.

These eight patients who required crossing over to the other group were not considered for analysis of surgical complications, hemodynamic response, blood loss, and liver and renal tolerance. Overall, 20 patients were analyzed in the PTC group and 24 in the HVE group.

## Hemodynamic Data

Baseline values of MAP, PAP, CI, and SVR were not different between the two groups (Table 2). A mean crystalloid fluid volume of  $1047 \pm 750$  mL (range, 500–2500) in the PTC group versus  $2614 \pm 817$  mL (range, 1250–5000) in the HVE group was infused before vascular occlusion ( $p < 0.01$ ). The PTC was followed by a 13% increase of MAP, 42% increase of SVR, 6% decrease of PAP, and a 9% decrease of CI. The HVE was followed by a 25% decrease of PAP, 38% decrease of CI, and a 86% increase of SVR; MAP did not change (Table 2). During the vascular occlusion phase, MAP was not significantly different between the two groups, whereas PAP and CI were significantly lower and SVR significantly higher in the HVE group ( $p < 0.05$ ).

**Table 2. BASELINE HEMODYNAMIC PROFILES AND HEMODYNAMIC RESPONSE TO PORTAL TRIAD CLAMPING OR HEPATIC VASCULAR EXCLUSION**

	PTC (n = 20)*	HVE (n = 24)*
Baseline		
MAP (mmHg)	90 ± 9	94 ± 13
PAP (mmHg)	15 ± 4	16 ± 5
CI (L · min <sup>-1</sup> · m <sup>-2</sup> )	4.2 ± 1.2	4.0 ± 1.0
SVR (dyne · s · cm <sup>-5</sup> )	947 ± 247	911 ± 264
Vascular occlusion†		
MAP (mmHg)	102 ± 16	93 ± 17
PAP (mmHg)	14 ± 5‡	12 ± 5‡
CI (L · min <sup>-1</sup> · m <sup>-2</sup> )	3.8 ± 1.0‡	2.5 ± 0.5‡
SVR (dyne · s · cm <sup>-5</sup> )	1345 ± 490‡	1699 ± 555‡

MAP = mean arterial pressure; CI = cardiac index; PAP = pulmonary arterial pressure; SVR = systemic vascular resistance.

Values are mean ± standard deviation.

\* Patients who crossed over to another group were not analyzed.

† Five minutes after clamping.

‡ p < 0.05.

**Table 4. INFLUENCE OF PORTAL TRIAD CLAMPING (PTC) AND HEPATIC VASCULAR EXCLUSION (HVE) ON LIVER TESTS AND RENAL FUNCTION**

	PTC (n = 20)*	HVE (n = 24)*
SGOT (units/L)		
Preoperative	51 ± 32	49 ± 28
Day 1	368 ± 240	352 ± 235
Day 5	51 ± 21	50 ± 23
Prothrombin time (%)		
Preoperative	97 ± 5	98 ± 4
Day 1	47 ± 14	42 ± 12
Day 5	68 ± 15	63 ± 16
Creatinine (mmol/L)		
Preoperative	62 ± 4	64 ± 3
Day 1	64 ± 13†	74 ± 12†
Day 5	63 ± 8	68 ± 9

SGOT = serum glutamic oxaloacetic transaminase.

\* Patients who crossed over to another group were not analyzed.

† p < 0.01.

### Blood Transfusions, Ischemia Duration, and Operative Time

The mean duration and the mean operative time of vascular occlusion were significantly longer in the HVE group (p > 0.05), whereas the mean amount of estimated intraoperative blood losses and the mean amount of intraoperative transfusions were not significantly different between the two groups (Table 3). Two (10%) patients in the PTC group versus 1 (4%) in the HVE group required

**Table 3. BLOOD TRANSFUSIONS, ISCHEMIA DURATION, AND OPERATIVE TIME IN THE PORTAL TRIAD CLAMPING GROUP (PTC) AND IN THE HEPATIC VASCULAR EXCLUSION (HVE) GROUP**

	PTC (n = 20)*	HVE (n = 24)*
Intraoperative blood losses (mL)	989 ± 1250	1195 ± 1105
Range	100–5000	200–5000
Blood transfusions (packed red cell units)	2.9 ± 3.9	2.5 ± 3.4
Range	0–13	0–15
Ischemia duration (min)	35 ± 9†	42 ± 12†
Range	17–55	23–78
Operative duration (min)	301 ± 103	366 ± 106†
Range	135–540	40–600

\* Patients who crossed over to another group were not analyzed.

† p < 0.05.

more than 10 packed red cell units. In two of these patients (one of each group), bleeding occurred before liver transection and was related to a difficult liver mobilization. Ten (50%) patients in the PTC group versus 8 (33%) in the HVE group received no blood transfusion (not significant).

### Liver Tests and Renal Function

The postoperative changes in serum transaminase, prothrombin time, and serum creatinine levels are listed in Table 4. After a significant rise of serum glutamic-oxaloacetic transaminase in the two groups at day 1, these returned to preoperative values at day 5. Prothrombin time fell in the two groups at day 1 but was followed by a 45% increase at day 5. The variations in serum glutamic-oxaloacetic transaminase and prothrombin time levels were not significantly different between the two groups. Postoperative creatinine levels were unchanged in the PTC group and showed a minimal rise within normal limits in the HVE group. The mean creatinine level at day 1 was significantly lower in the PTC group (p < 0.01).

### Operative Mortality and Morbidity

As listed in Table 5, one death occurred in the PTC group (patient 9 who underwent a right lobectomy for a hilar cholangiocarcinoma) at day 20 from ascites and renal failure, accounting for an overall operative mortality rate of 2.3%. There was no intraoperative death from

**Table 5. MORTALITY AND MORBIDITY RATES OF PORTAL TRIAD CLAMPING (PTC) AND HEPATIC VASCULAR EXCLUSION (HVE) GROUPS**

	PTC (n = 20)* [n (%)]	HVE (n = 24)* [n (%)]
Death	1 (5)	0 (0)
Preoperative		
Air embolism	2 (10)	0 (0)
Splenic rupture	0 (0)	1 (4)
Pulmonary complications	2 (10)	6 (25)
Pleural effusion	1 (5)	5 (21)
Chest infection	1 (5)	1 (4)
Subphrenic collections	3 (15)	9 (37.5)
Infected	1 (5)	3 (12)
Hematoma	1 (5)	2 (8)
Reoperation	0 (0)	1 (4)
Hospital stay (days) (mean ± SD)	14 ± 6†	22 ± 12†

SD = standard deviation.

\* Patients who crossed over to another group were analyzed.

†  $p < 0.05$ .

massive bleeding. Minimal intraoperative air embolism, detected only by intraoperative capnography, occurred in two patients in the PTC group. In these two patients, attempts to preserve the middle hepatic vein at the transection margin resulted in many tears. Spontaneous splenic rupture occurred in one patient undergoing resection for a liver secondary tumor approximately 1 hour after HVE. A splenectomy was performed and the liver resection was completed. One patient in the HVE group required reoperation for postoperative bleeding originating from a tear of the caudate lobe. Both the rates of postoperative abdominal collections (15% vs. 35%) and pulmonary complications (10% vs. 25%) were 2.5-fold higher in the HVE group compared with the PTC group but without statistical significance. However, the mean length of postoperative hospital stay was significantly longer in the HVE group. Comparable results were obtained if the eight patients who were crossed over after randomization are included in the group of vascular exclusion (HVE or PTC) that was actually performed (mortality after PTC = 4% vs. 0% after HVE; pulmonary complication after PTC = 16% vs. 28% after HVE; subphrenic collection after PTC = 16% vs. 32% after HVE; and duration of in-hospital stay after PTC = 16 ± 7 days vs. 21 ± 11 days after HVE).

## DISCUSSION

It is now accepted that liver parenchyma is more tolerant to prolonged continuous normothermic ischemia

than to the consequences of massive bleeding and blood transfusions.<sup>7,12</sup> The first priority is therefore to reduce intraoperative blood loss. In this series, 40% of major liver resections were performed without any blood transfusion, and this could be achieved either with HVE or with PTC.

The HVE was first described by Heaney et al.<sup>4</sup> and has recently gained wide acceptance, sometimes to the point of overuse. This procedure theoretically provides a bloodless transection and improves the parenchymal tolerance to ischemia.<sup>13</sup> This study confirms the effectiveness of this technique, and the beneficial effect on parenchymal tolerance to ischemia was reflected by the fact that postoperative parameters of hepatocyte damage and recovery were similar between the two groups despite a longer ischemic period in the HVE group. The longer operative period and ischemic period in the HVE group could be related to caval dissection, vascular loading before clamping, exclusion trial, and the three-stage removal of the clamps with intermediate hemostasis.

Although HVE is very effective in limiting bleeding and seems well tolerated by the parenchyma, we found, like others, that HVE requires a specific management, compels a strict surgical technique, can lead to hemodynamic intolerance, and may be associated with complications.<sup>8</sup>

In this series, the hemodynamic response to HVE confirms the results of Delva et al.<sup>13</sup> by showing a significant decrease in CI by 40% to 50% requiring careful hemodynamic monitoring and the infusion of large fluid volumes. However, HVE was not tolerated in 5 (17%) of 29 of our patients (4 of the HVE group and 1 of the PTC group). This rate is similar to that observed by Gavelli et al.<sup>14</sup> Two patients had evident cause of hemodynamic intolerance; the first with right valvular deficiency and the second with incomplete liver mobilization before clamping. We think, like Huguet et al.,<sup>10</sup> that perihepatic adhesions must be completely severed before performing HVE and not after, thus avoiding filling of the liver *via* pathologic venous channels during the clamping period, which would result in severe bleeding and hemodynamic intolerance.<sup>10</sup> The three other patients had hemodynamic failure despite an adequate fluid loading, the observance of a strict technique, and increasing confidence with the method. Our hemodynamic results showed that an inadequate cardiovascular response was responsible for this failure. Unfortunately, this response, which includes patient's reflex responsiveness to increase its vascular tone and the myocardium's ability to maintain an adequate cardiac output in the presence of an elevated afterload, is unpredictable.

Analysis of the detailed morbidity of this series suggests that HVE was associated with specific complications, which may have accounted for the longer hospital stay in this group. These are pulmonary dysfunction, spontaneous splenic rupture, and injury to the caudate

lobe. Although not statistically different, the rate of pulmonary complications in the HVE group was twice that in the PTC group. Pulmonary complications can be related to two factors: 1) the higher amount of crystalloid fluid infused before vascular occlusion and 2) the right hemidiaphragm dysfunction. As previously reported, crush injury to the right phrenic nerve may occur in patients with suprahepatic caval clamping.<sup>15</sup> The resulting hemidiaphragm dysfunction may contribute to the development of postoperative pulmonary problems and abdominal collections. Injury to the caudate lobe during HVE observed in one of our patients has not yet been reported. Axial caval clamping performed to exclude all venous tributaries probably was responsible for this event.<sup>16</sup> This complication would be more likely in the presence of a huge caudate lobe obliterating the lateral aspect of the IVC or during subsequent manipulation of the liver and clamps. Spontaneous splenic rupture during HVE has been seldom reported and occurred in one noncirrhotic patient in this study.<sup>17</sup> Simultaneous occlusion of the portal vein and the vena cava is known to exacerbate the portal venous hypertension as the safety collateral channels between portal and systemic venous circulations are interrupted.<sup>17</sup> Despite the fact that our patients had a normal preoperative renal function, a moderate and temporary rise in serum creatinine level occurred only in the HVE group and was similar to that observed by others.<sup>7,8</sup> Results of this study suggest a cautious approach to HVE in patients with pre-existing renal insufficiency. The current use of venous bypass for patients with poor renal function undergoing liver transplantation under HVE suggests that the renal response of this subgroup to HVE may be deleterious.<sup>18</sup>

In this series, PTC was as effective as was HVE in limiting blood loss and was well tolerated in all patients. The main substantial risk of this method is air embolism if a hepatic vein or the IVC is torn, especially in patients under a low central venous pressure regimen that aims to reduce back flow bleeding.<sup>8,12</sup> In this study, the likelihood of air embolism would have been reduced by avoiding extensive dissection of the lateral aspect of the middle hepatic veins and by placing the patients in Trendelenburg's position at a 15° tilt.<sup>19</sup> Preservation of the hepatic vein draining the cut surface of partial liver grafts seems essential, but its usefulness in standard hepatic resections is still speculative.<sup>20</sup>

Between a radical method of total liver isolation and liver inflow occlusion alone, an intermediate option is represented by liver isolation with preservation of caval flow. This procedure combines a PTC and an extraparenchymal control of the hepatic veins and aims to reduce backflow bleeding and to provide maximal safety with minimal hemodynamic consequences as the caval flow is not interrupted.<sup>19</sup> This type of vascular control was used as a rescue procedure in one patient with increased

central venous pressure who did not respond to PTC and HVE. Although this method of vascular control was reported previously and seems attractive, it has been used infrequently, probably because the dissection of the hepatic veins was considered hazardous.<sup>8</sup> The recent encouraging results of this approach may promote its widespread use.<sup>19,21-24</sup> This occlusion method would be particularly useful in patients with impaired renal function, cirrhotics, and patients with previous intra-arterial hepatic chemotherapy that increases backflow bleeding.<sup>23,24</sup>

In conclusion, during major hepatic resections, a similar reduction in blood loss can be obtained by PTC or HVE. However, hepatic resection under HVE compels a strict technique, a complex anesthetic management, can lead to unpredictable hemodynamic intolerance, and is associated with increased morbidity and with a longer hospital stay in today's economic climate. This occlusion method should therefore be restricted to lesions involving the cavo-hepatic intersection.

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