World Journal of Surgery 2005
Published Online: 1 October 2005

World J Surg (2005) 29: 1384–1396
DOI: 10.1007/s00268-005-0025-x

Vascular Control during Hepatectomy: Review of Methods and Results

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Abstract
The various techniques of hepatic vascular control are presented, focusing on the indications and drawbacks of each. Retrospective and prospective clinical studies highlight aspects of the pathophysiology, indications, and morbidity of the various techniques of hepatic vascular control. Newer perspectives on the field emerge from the introduction of ischemic preconditioning and laparoscopic hepatectomy. A literature review based on computer searches in Index Medicus and PubMed focuses mainly on prospective studies comparing techniques and large retrospective ones. All methods of hepatic vascular control can be applied with minimal mortality by experienced surgeons and are effective for controlling bleeding. The Pringle maneuver is the oldest and simplest of these methods and is still favored by many surgeons. Intermittent application of the Pringle maneuver and hemihepatic occlusion or inflow occlusion with extraparenchymal control of major hepatic veins is particularly indicated for patients with abnormal parenchyma. Total hepatic vascular exclusion is associated with considerable morbidity and hemodynamic intolerance in 10% to 20% of patients. It is absolutely indicated only when extensive reconstruction of the inferior vena cava (IVC) is warranted. Major hepatic veins/ and limited IVC reconstruction has been also achieved under inflow occlusion with extraparenchymal control of major hepatic veins or even using the intermittent Pringle maneuver. Ischemic preconditioning is strongly recommended for patients younger than 60 years and those with steatotic livers. Each hepatic vascular control technique has its place in liver surgery, depending on tumor location, underlying liver disease, patient cardiovascular status, and, most important, the experience of the surgical and anesthesia team.

Liver resection may be complicated by intraoperative bleeding. Especially resection of lesions in close proximity or infiltrating major vascular structures (*i.e.*, the cavohepatic junction) or an extended hepatectomy can be unpredictably complicated by life-threatening hemorrhage, leading even to rapid patient demise on the operating table. Moreover, bleeding together with the subsequent blood transfusions increase postoperative morbidity and mortality,[1–5] particularly in cirrhotic patients.[6–8] Furthermore, transfusions have been found to enhance tumor recurrence in patients undergoing hepatectomy for hepatocellular carcinoma, even if the amount of blood transfused is minimal.[7,9,10] The same recurrence-promoting effect attributed to nonspecific suppression of immunity by transfusion has been reported after hepatectomy for colorectal metastases,[3,7,11] not only with banked blood but with

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autologous blood as well.[3,12] That is why every effort is made during hepatic resection to reduce or even abort the need for transfusions. Clinical series have been reported where more than half of the major hepatectomies[13–19] and more than 90% of all hepatectomies, including major and minor ones,[19–23] were performed without any blood transfusion.

Strategies to reduce intraoperative bleeding during hepatectomy include the following:

1. Afferent or complete devascularization of the resected segments before parenchymal transection.[15,24,25]
2. Precise hemostasis during parenchymal transection following avascular planes, aided by newer techniques such as ultrasonic dissection with the Cavitron Ultrasonic Surgical Aspirator (CUSA), heat coagulation, a bipolar vessel-sealing device,[25–27] and the use of intraoperative ultrasonography (IOUS).[28,29]
3. Performance of the hepatectomy under low central venous pressure (CVP) (*i.e.*, 0–5 cm H_2O).[14,15,21,30–33] Low CVP is achieved mainly by restricting the volume of administered fluids. If anesthetic interventions fail to lower the CVP, placing a vascular clamp on the infrahepatic inferior vena cava (IVC) above the renal veins can reduce the CVP from a mean of 13 mmHg to 4 mmHg.[34] The main danger associated with low CVP is that of air embolization during parenchymal transection.[14,32]
4. Temporary occlusion of blood inflow with or without outflow control, of the whole or part of the liver during parenchymal transection, a method called hepatic vascular occlusion or control.

Techniques of vascular control are reviewed in this article. Articles were selected by a MEDLINE literature search according to the following criteria:

1. All prospective randomized studies were thoroughly searched and are presented, as we consider them the most valuable source of information on the outcomes of each method of hepatic vascular control.
2. Large (including more than 40 patients) retrospective studies were also included; smaller studies and case reports are presented only if they highlighted special aspects of each method.
3. Most of the series involved major liver resections. This review was focused on the technical aspects of vascular exclusion methods (*i.e.*, techniques, ischemia time, morbidity, mortality). Results of long-term follow-up and oncologic outcomes (e.g., tumor recurrence) were not investigated. Special attention was given to the application of each method in the pathologic (mainly cirrhotic) liver.

RATIONALE FOR HEPATIC VASCULAR CONTROL

The concept of hepatic vascular control is based on the proven tolerance of liver to warm ischemia and on strong evidence that liver tolerates ischemia better that bleeding.[5,35–42] This has been well illustrated in the series of Man *et al.* where the intermittent Pringle maneuver was prospectively evaluated versus no vascular control at all;[35,37] that of Arnoletti and Brodsky, who compared the continuous Pringle maneuver versus no vascular control;[13] and the retrospective clinical study of Delva *et al.*[5] In the last study, the duration of inflow ischemia up to 90 minutes had no effect on morbidity or length of hospital stay, whereas the amount of blood transfused was adversely correlated with the morbidity and length of hospital stay.[5]

In theory, the reperfusion that takes place after removing the vascular clamps might aggravate the sustained hepatic ischemic injury, particularly during IPM where multiple episodes of ischemia/reperfusion (I/R) take place.[43] However, the results of clinical series contradict this concept.[5,13,35,37] It must also be taken into account that vascular control eliminates bleeding only at the phase of parenchymal transection and is not beneficial during the phase of liver mobilization, when according to some authors most massive hemorrhagic insults during hepatectomy take place.[5,38,40] In addition, reasonable or minimal blood loss has been achieved during major hepatectomy performed without embarking on vascular control at all[16,26] or limiting its use[24,25] by using a combination of vascular pedicle ligation, CUSA, and IOUS.

Hepatic vascular control methods can be categorized as those involving occlusion of only liver inflow and those involving occlusion of both liver inflow and outflow. They can be summarized in the following manner.

- I. Inflow vascular occlusion
  - A. Hepatic pedicle occlusion
    - 1. Continuous Pringle maneuver (CPM)
    - 2. Intermittent Pringle maneuver (IPM)
  - B. Selective inflow occlusion
    - 1. Hemihepatic vascular clamping
    - 2. Segmental vascular clamping
- II. Inflow and outflow vascular occlusion
  - A. Total hepatic vascular exclusion (THVE)
  - B. Inflow occlusion with extraparenchymal control of major hepatic veins: selective hepatic vascular exclusion (SHVE) or hepatic vascular exclusion with preservation of caval flow (HVEPC)

Table 1.
Clinical series of hepatectomies performed with the continuous Pringle maneuver

Study	No. of patients	Type of hepatectomy [a]	Texture of liver [b]	Total ischemia time (min)	Blood transfusion (PRBCU)	Transfused patients (%)	Morbidity/mortality (%)	Postresection liver failure (%)
Delva[5]	50	Major	Normal	36.8 ± 2	6.3 ± 0.7	N/A[5]	44/6	8
Hannoun[42]	15	Major	Normal	70 ± 3	5.0 ± 1.4	N/A	26.6/0	6.67
Kelly MC[89]	20	Major	Normal	16 (8–35)	2.4 (mean)	N/A	20/0	N/A
Arnoletti[13]	34	Major	Normal	N/A	0 (0–3)	21	21/3	3
Belghiti[38]	42	Minor 52.4%	Normal 54.7%	41 ± 13	3 (0–7)	28	31.0/4.8	9.52
Midorikawa[23]	277	Minor 78.0%	Pathologic 67.5%	66 ± 47	45 ± 226 ml	5.7	64.1/0	0
Smyrniotis[18]	55	Major	Normal	32 (25–61)	1 (0–14)	58	52.7/1.9	0
Clavien[19]	100	Major	Normal	37 (30–60)	N/A	6	15/0	N/A

PRBCU: packed red blood cells units; N/A: data not available.
Values are expressed as the mean ± SD or the median (range) if not otherwise specified.
[a]Major hepatectomy is defined as resection of more than two segments according to Couinaud's classification.
[b]Pathologic liver texture involves cirrhosis (mainly), chronic hepatitis, steatosis > 20%, fibrosis after intraarterial chemotherapy, cholestasis.

CONTINUOUS PRINGLE MANEUVER

Hepatic pedicle clamping (Pringle maneuver) is the oldest method of hepatic vascular control.[44] The CPM (Table 1) is performed by encircling the hepatoduodenal ligament with a tape and then applying a tourniquet or a vascular clamp until the pulse in the hepatic artery disappears distally. Prior to placing the occluding clamp or tourniquet, any adhesions around the hepatoduodenal ligament should be freed. If these adhesions are left intact there is a serious risk of injuring the IVC or the duodenum when placing the clamp. Also, the effectiveness of the CPM is lessened if hypervascular adhesions, such as those that develop after preoperative hepatic artery chemoembolization, permit collateral flow toward the liver. An aberrant left hepatic artery originating from the left gastric artery should also be occluded if present.[45]

After pedicle clamping, a moderate decrease in venous return due to pooling of blood in the mesenteric basin results in a 10% decrease in the cardiac index. Simultaneously, a sympathetic reflex produced by clamping causes a 40% increase in systemic vascular resistance and a 40% increase in mean arterial pressure. Unclamping of the hepatic pedicle leads to a transient decrease in blood pressure because of deactivation of the above-mentioned reflex.[34,45–47] CPM is generally well tolerated because caval flow is not interrupted and specific anesthetic management is not required.[40,48] The anesthesiologist should also be alerted to the possibility of intraoperative air embolism, as with any kind of inflow vascular occlusion where the major hepatic veins are left open. Air embolism may occur during parenchymal transection especially if the CVP has been lowered to prevent back-bleeding from hepatic veins or during reperfusion owing to mobilization of air bubbles trapped in opened veins. Air entry can take place even from small venules during liver transection, and it is particularly dangerous when a patent foramen ovale permits migration of the air embolus to the carotid circulation. The consequences of air embolism can be minimized by placing the patient in a 15 degree Trendelenburg position.[14,32,49,50]

A number of clinical studies have established 60 minutes as the safe duration of CPM under normothermic conditions for both normal and pathologic (mainly cirrhotic) livers.[18,23,41,42] Delva *et al.* extended this period to 90 minutes.[5] In their retrospective study Delva *et al.* proved that even in cirrhotic livers the duration of ischemia up to the limit of 90 minutes did not increase morbidity and mortality. On the other hand, the volume in transfusions had a direct adverse effect on morbidity, especially in cirrhotic patients in whom transfusion increased the possibility of postoperative liver failure.[5] Periods of CPM up to 127 minutes in normal livers[42] and 100 minutes in pathologic livers[23] have been reported with favorable clinical outcomes.

The effectiveness of CPM in reducing bleeding during major hepatectomies has been shown in historical controls and also in the prospective study of Arnoletti and Brodsky.[13] CPM cannot prevent bleeding from hepatic veins and should be used cautiously or even avoided for lesions close to or involving the cavohepatic junction. Hemorrhage from hepatic veins can be minimized by operating under low CVP and by complete devascularization of the resected segments before applying CPM.[13] On the other hand, retrograde flow from hepatic veins during the Pringle maneuver seems to contribute to attenuation of hepatic I/R injury, as was demonstrated in a prospective clinical study of CPM versus SHVE regarding plasma levels of interleukin (IL)-6, IL-8, and malondialdehyde.[51] Of course this hepatoprotective effect is diminished when the operation is performed under low CVP.[46]

There is great flexibility during clinical application of CPM. The method has been achieved laparoscopically, mainly for segmentectomies for small tumors located in the left lateral or right anterior segments.[52] CPM has been effectively used in conjunction with previous devascularization of the resected segments[13] or has been converted to THVE or SHVE when difficulties were encountered because the tumor was near the cavohepatic junction.[5,41,42] CPM can also be combined with ischemic preconditioning, an established hepatoprotective method that involves application of a brief period of I/R before initiating long-term inflow occlusion.[46,53–59] Clavien *et al.* in a prospective series involving major resections in noncirrhotic livers,[19] studied the effect of ischemic preconditioning (10 minutes of ischemia followed by 10 minutes of reperfusion) during hepatectomies performed under CPM. The postoperative serum transaminase levels were significantly lower in the ischemic preconditioning group. This hepatoprotective effect was more pronounced in young (< 60 years) patients and in the presence of steatosis.

In conclusion, because of its effectiveness and simplicity, CPM remains the most popular method of vascular control and in our opinion is preferred by less experienced surgeons. CPM is not indicated (1) for lesions involving the major hepatic veins or the IVC; (2) in patients with increased CVP due to right heart failure and pulmonary artery hypertension; or (3) when a patent foramen ovale increases the risk of cerebral air embolus. In the above-mentioned cases and also when significant backflow bleeding ensues during CPM, methods of combined inflow and ouflow occlusion should be considered.[45] Nevertheless, Abdalla *et al.* proposed clamping the infrahepatic vena cava above the renal veins as an adjunct to CPM when persistent backflow bleeding ensues or when anesthetic techniques fail to lower the CVP before embarking on THVE or SHVE.[34]

INTERMITTENT PRINGLE MANEUVER

The intermittent Pringle maneuver (Table 2) involves periods of inflow clamping that last 15 to 20 minutes followed by periods of unclamping for 5 minutes (mode 15–20/5).[20,22,35–38,60–62] An alternative mode of IPM consisting of 5 minutes of clamping and 1 minute of unclamping (mode 5/1) has also been described.[14,32] The initial cycle of clamping/unclamping during IPM could have a preconditioning hepatoprotective effect. Another technical advantage of IPM is that intermittent release of the portal clamp allows gradual hemostasis over smaller transection areas.[35,37,38] On the other hand, repeated clamp removal during IPM may result in fluctuations of systemic blood pressure, multiple episodes of hepatic I/R injury, and repeated bleeding from the transection surfaces. However, prospective clinical studies proved the hepatoprotective effect of IPM.[35,37,38,60] Belghiti *et al.* in a prospective study of IPM (mode 15/5) versus CPM, found no statistical difference in total blood loss or the volume of blood transfused between the two groups, despite significantly higher blood loss during parenchymal transection in the IPM group. In this study, the four cases of serious postoperative liver failure took place in patients with abnormal livers operated on under CPM, prompting the authors to recommend IPM strongly for patients with abnormal parenchyma.[38] Man *et al.* in two prospective studies of IPM (mode 20/5) versus no use of vascular control at all, showed significantly lower total blood loss especially during liver transection, fewer transfusions, and shorter liver transection time in the IPM group. The above-mentioned differences were again more pronounced in cirrhotic patients.[35,37,60]

The proven effectiveness of IPM in reducing bleeding together with its hepatoprotective profile encourage wide application of the method. Also IPM permits a significant increase (almost doubling) of the ischemia times that can be achieved with CPM. IPM can be safely applied up to 120 minutes in both normal and impaired livers.[21,22,31,36,38,60,61] Impressively, ischemic times of 322 minutes in normal livers[22] and 204 minutes in cirrhotic livers have been reported.[61] Furthermore, Wu *et al.* achieved 45.7 ± 27.8

Table 2.
Clinical series of hepatectomies performed with the intermittent Pringle maneuver

Study	No. of patients	Type of hepatectomy [a]	Mode ofIPM [b]	Texture of liver [c]	Totallschemia time (min)	Blood transfusion (PRBCU)	Transfused patients (%)	Morbidity/ mortality (%)	Postresection liver failure (%)
Elias[36]	20	Major	20/5	Pathologic 65%	109 ± 18 (90–150 range)	N/A	N/A	35/0	5.0
Cunningham[32]	100	Major 69%	5/1	Normal	23 (median)	2 (mean)	59.0	27/3	4.0
Wu[61]	83	Minor 83%	15/5	Pathologic	52.95 (mean); 9.5–204 (range)	409.88 ml (mean)	N/A	22.9/2.4	4.8
Man[35]	50	Major 68%	20/5	Pathologic 62%	88 (24–101)	0 (0–8.6)	36.0	26/2	N/A
Takayama[22]	132	Minor 72.7%	15/5	Pathologic 68.9%	61 ± 47 (15–322 range)	N/A	7.6	N/A/0	0
Melendez[14]	496	Major	5/1	Normal	20 min (maximum)	0.9 ± 1.8	52.6	N/A/3.8	0.8
Belghiti[38]	44	Minor 56.8%	15/5	Normal 61.4%	46 ± 18 (20–118 range)	2.3 (0–3)	32.0	26/0	0
Torzilli[21]	329	Minor 58.7%	N/A	Normal 59%	60 (0-248)	N/A	3.9	25/0	0
Man[37]	20	Major 70%	20/5	Pathologic 85%	65 (40-08)	N/A	60.0	25/0	N/A
Wu[31]	28	Major	15/5	Pathologic	96.0 ± 10.9 (62–196 range)	N/A	42.85	28.57/0	N/A

IPM: intermittent Pringle maneuver.
Values are expressed as the mean ± SD or the median (range) if not otherwise specified.
[a]Major hepatectomy is defined as resection of more than two segments according to Couinaud classification.
[b]IPM mode: periods (in minutes) of clamping/unclamping during application of IPM.
[c]Pathologic liver texture involves cirrhosis (mainly), chronic hepatitis, steatosis > 20%, fibrosis after intraarterial chemotherapy, cholestasis.

minutes of liver ischemia in a series of 10 Child C cirrhotic patients.[63] Torzilli *et al.* reported resections of tumors infiltrating major hepatic veins and IVC together with reconstructions of these vessels using IPM in almost all of the cases and never embarking on THVE. These authors liberally used thoracoabdominal incisions together with low CVP and IOUS during liver transection and reported successful performance of major hepatectomies even in patients with abnormal liver parenchyma.[20,21] Lai *et al.* described the resection of large tumors (diameter 10.4 ± 0.7 cm) of the right lobe infiltrating segment I or the diaphragm in 25 patients, by combining afferent devascularization of the right hemiliver, IOUS, CUSA, and in most (72%) patients IPM (mode 15/5). These hepatectomies were accomplished with 4% mortality, 44% morbidity, and 1500 ml mean blood transfusion.[24] Yamamoto *et al.* reported isolated resection of the caudate lobe in five patients combining IPM (mode 15/5) and the anterior transhepatic approach.[64]

In conclusion, IPM permits execution of complex, time-consuming resections even in patients with an abnormal liver. It can be used in conjunction with afferent or total devascularization of the part of the liver to be resected[6,14,32,35,36,60] and with extraparenchymal control of the major hepatic veins.[14,32] IPM can be applied under low CVP to reduce bleeding during parenchymal transection and during unclamping;[14,20,21,32] it has also been applied laparoscopically.[47,62,65] In our experience IPM is an easily applied, flexible method with the inherent risk of bleeding during the reperfusion periods. Thus CPM is preferred if the estimated occlusion time is less than 60 minutes.[18,23,41,42]

HEMIHEPATIC VASCULAR CLAMPING

Hemihepatic vascular clamping (Table 3)—pioneered by Makuuchi *et al.*[66]—selectively interrupts the arterial and portal inflow to the part of the liver (right or left hemiliver) ipsilateral to the lesion that requires resection. It can be combined with simultaneous occlusion of the ipsilateral major hepatic vein. Selective clamping can be achieved after carefully dissecting the right from the left hilar branches or after placing a curved renal pedicle clamp across the right or left portal structures without prior hilar dissection, a technique called the half-Pringle maneuver.[67,68] IOUS can be helpful during hilar dissection and when tattooing liver parenchyma with dye (indigo carmine) when performing subsegmentectomies.[66,69,70]

The advantages of hemihepatic clamping include avoidance of ischemia in the remnant liver, prevention

Table 3.
Clinical series of hepatectomies performed with selective inflow occlusion

Study	No. of patients	Type of vascular occlusion [a]	Type of hepatectomy [b]	Textureof liver [c]	Total ischemia time (min)	Blood transfusion (PRBCU)	Transfused patients (%)	Morbidity/ mortality (%)	Postresection liver failure (%)
Makuuchi[70]	45	Hemihepatic, intermittent (30/5)	All kinds	Pathologic 71.1%	45 ± 4 cirrhotic, 30 ± 4 normal liver	N/A	N/A	N/A	N/A
Takenaka[4]	280	Hemihepatic, intermittent (15/5)	Minor 70%	Pathologic 52%	281.57 (mean)	N/A	N/A	50/2	4
Takayama[22]	26	Hemihepatic, intermittent (30/5)	Minor 80.7%	Pathologic 57.7%	95 ± 47 (21–207 range)	N/A	7.7	N/A/0	N/A
Malassagne[15]	43	Hemihepatic, continuous	Major	Normal	221 (150–360)	0 (0–4)	35	19/2	6
Wu[31]	30	Hemihepatic, intermittent (30/5)	Major	Pathologic	94.9 ± 9.9 (64.5–188.0 range)	N/A	16.66	33.33/0	N/A
Castaing[72]	15	Segmental, continuous	Minor	Normal 53.34%	47 mean (22–80 range)	1.3 mean (0–7 range)	33.33	33.33/0	13.33
Goseki [73]	18	Segmental, intermittent (15/5)	Minor	Pathologic 61.1%	N/A	N/A	N/A	22.22/0	N/A

Values are expressed as the mean ± SD or the median (range) if not otherwise specified.
[a]Numbers in parenthesis represent periods (in minutes) of clamping/unclamping during intermittent application of selective inflow occlusion.
[b]Major hepatectomy is defined as resection of more than two segments according to the Couinaud classification.
[c]Pathologic liver texture involves cirrhosis (mainly), chronic hepatitis, steatosis > 20%, fibrosis after intraarterial chemotherapy, cholestasis.

of splanchnic congestion, and maintenance of hemodynamic stability during liver transection.[70] This kind of vascular control also permits clear demarcation of the resection margins, which is crucial during central bisegmentectomy and during resection of the right anterior segment. In that case hemihepatic clamping can be applied in an alternate manner (*i.e.*, occlusion of the right portal branches for liver transection on the right side of a lesion that lies across the main scissura and then occlusion of the left branches when working on the left side of the lesion).[70,71]

Hemihepatic clamping can also be performed in an intermittent manner—in modes 15/5[4] and 30/5 [20,22,31,71]—prolonging the ischemia time. Intermittent hemihepatic occlusion is particularly useful in cirrhotic livers, where a mean ischemia time of 90 minutes [22,31] and a maximum time of 207 minutes [22] have been reported. It has also been applied in Child B and C cirrhotic patients.[6,63] In normal livers ischemia times under continuous hemihepatic occlusion can be long (median 221 minutes, range 150–360 minutes).[15] In prospective studies of both normal and cirrhotic livers, intermittent hemihepatic occlusion was associated with significantly reduced blood loss and need for transfusion compared to IPM [4] and to no application of vascular control.[70]

The only drawback of the method is bleeding during transection from the remnant (nonoccluded) liver. Bleeding may be more pronounced when limited resections are performed.[20] Low CVP helps minimize bleeding, as does complete occlusion of the common hepatic artery together with selective unilateral portal vein clamping.[15,31,45] If hemorrhage is significant, conversion to the Pringle maneuver is imperative. A conversion rate of 21% has been reported in 43 patients.[15]

Hemihepatic clamping is particularly indicated when dealing with tumors located peripherally in a liver with abnormal parenchyma especially in cirrhotic patients,[15,22,70] when operating on tumors straddling the main scissura, and during central hepatectomy.[31,71] Torzilli *et al.* has also used the method when operating on large posteriorly located tumors close to or infiltrating the cavohepatic junction.[21]

In conclusion, hemihepatic clamping is a useful approach when dealing with cirrhotic livers and wide resection planes (> 60 cm^2). The method is contraindicated (1) for tumors approaching or infiltrating the liver hilum, (2) when dense adhesions around the hepatoduodenal ligament (due to prior operation or chemoembolization) make portal dissection dangerous, and (3) when anatomic variations of the portal vein or hepatic artery exist.[31,70]

Table 4.
Clinical series of hepatectomies performed with total hepatic vascular exclusion.

Study	No. of patients	Type ofhepatectomy[a]	Textureof liver[b]	Total ischemia time (min)	Blood transfusion (PRBCU)	Transfused patients (%)	Morbidity/ mortality (%)	Postresection liverfailure (%)
Delva[48]	24	Major	Normal 83.4%	39 mean (24–65 range)	3650 ml mean	N/A	29.2/25.0	N/A
Delva[5]	35	Major	Normal	40.0 ± 2.2	8.0 ± 1.4	N/A	43.0/8.9	5.7
Bismuth[49]	50	Major	Normal	46.5 ± 5.0	4.5 ± 1.0	N/A	16/2	N/A
Yamaoka[79]	20	Major	Normal 60%	36.48 mean (8–70 range)	N/A	N/A	65/5	5.0
Emre[76]	16	Major	Normal	29.0 ± 10. 7	N/A	N/A	N/A/12.5	0
Hannoun[42]	15	Major	Normal	72.0 ± 3.0	5.8 ± 1.2	N/A	53.3/0	6.66
Emond[84]	60	Major 93%	Normal 80%	37.72 mean	2.2 mean	58.33	21/0	N/A
Belghiti[40]	24	Major	Normal	42 ± 12	2.5 ± 3.4	67.0	70.8/0	N/A
Hannoun[78]	12	Major	Pathologic	121 ± 54	4.3 ± 4.0	66.6	27.0/8.3	9
Stephen[77]	99	Major 59.59%	Normal 86.7%	9–38 range	0–18 range	61.61	12.12/6.06	0
Kelly[89]	23	Major	Normal	16 mean (8–35)	2.3 mean	N/A	17/0	N/A
Grazi[85]	19	Major 79%	Normal	44.3 ± 12.8	1267.8 ± 578.3 ml	73.7	N/A/0	N/A
Berney[39]	41	Major 63.4%	Normal 92.7%	95 (5–58)	2 (0–26)	65.85	24/0	29.27
Huguet[80]	47	Major 87%	Normal	51.2 ± 16.5	9.4 ± 9.8	N/A	57.4/ 6.4	N/A
Smyrniotis[33]	18	Major	Normal	32 ± 12	3.0 ± 2.5	N/A	33.33/0	N/A

Values are expressed as the mean ± SD or the median (range) if not otherwise specified.
[a]Major hepatectomy is defined as resection of more than two segments according to the Couinaud classification.
[b]Pathologic liver texture involves cirrhosis (mainly), chronic hepatitis, steatosis > 20%, fibrosis after intraarterial chemotherapy, cholestasis.

SEGMENTAL VASCULAR CLAMPING

Segmental vascular clamping (Table 3) entails occlusion—after hilar dissection—of the right or left branch of the hepatic artery ipsilateral to the segment that is to be resected together with balloon occlusion of the portal branch of that segment. The branch of the portal vein draining the resected segment is identified by IOUS and punctured by a cholangiography needle. A flexible guidewire is introduced through the needle into the portal branch, and a balloon catheter is directed over this wire to the origin of the branch. The corresponding branch of the hepatic artery is clamped and the portal branch occluded by inflating the balloon of the catheter. Methylene blue then injected into the portal catheter allows more precise identification of the segment by tattooing the liver parenchyma. In this way selective inflow occlusion is achieved followed by transection of the stained segment.[72] The occlusion has been applied in both continuous[72] and intermittent (15/5) modes.[73]

Segmental vascular clamping is useful when dealing with small, peripheral hepatocellular carcinomas in cirrhotic patients. It minimizes ischemic injury to the abnormal liver and delineates precisely the segment to be resected. The method permits removal of the tumor along with the involved portal venous bifurcation, thereby conferring a theoretical oncologic advantage because the portal route is the main route of spread of hepatocellular carcinoma.[72]

TOTAL HEPATIC VASCULAR EXCLUSION

Total hepatic vascular exclusion (THVE) (Table 4) combines total inflow and outflow vascular occlusion of the liver, isolating it completely from the systemic circulation. It is achieved after complete liver mobilization, application of inflow occlusion as with the Pringle maneuver, and then placing a clamp across the infrahepatic IVC above the renal veins and the right adrenal vein followed by placing a suprahepatic IVC clamp above the ostia of the major hepatic veins.[74] After completing the parenchymal transection and hemostasis, the clamps are removed in the reverse order in which they were placed.

Application of THVE is associated with significant hemodynamic changes and warrants close invasive monitoring and anesthetic expertise. Suppression of IVC flow causes marked (40–60%) reduction of venous return and cardiac output, with a compensatory 80% increase in systemic vascular resistance and 50% increase in heart rate. Also, depending on the anesthesia technique, a 10% decrease in mean arterial pressure and a 40% decrease in cardiac index have been reported.[33,40,46,48,75,76] A fall in cardiac output exceeding 50% or a decrease in mean arterial pressure exceeding 30% (*i.e.*, less than 80 mmHg) in a euvolemic patient is defined as hemodynamic intolerance to THVE. It occurs in 10% to 20% of patients and is unpredictable preoperatively as it is caused by failure of the patient's adrenergic cardiovascular reflexes to increase cardiac output in the presence of decreased preload.[33,40,41,74] This is why a trial of exclusion lasting 2 to 5 minutes after adequately expanding blood volume is strongly recommended, which ensures that THVE can be tolerated. Hemodynamic intolerance usually leads to discontinuation of THVE; alternatively, supraceliac aortic clamping or venovenous bypass can be applied. Supraceliac aortic clamping leads to an increase in systemic vascular resistance and mean arterial pressure and has been applied to 25% to 50% of patients in some THVE series.[5,48,76,77] It was routinely used by Stephen *et al.* in a study of 99 major hepatectomies,[77] where it was accompanied by high mortality in cirrhotic patients with portal hypertension. Venovenous bypass has been used in cases of hemodynamic intolerance to THVE, during resection of tumors infiltrating the IVC or the major hepatic veins,[78–80] or routinely when the anticipated ischemia time under THVE exceeded 60 or 30 minutes.[78,81] Venovenous bypass has been also used safely in cirrhotic patients, provided the ischemic THVE time was less than 60 minutes.[79] Hannoun *et al.* combined venovenous bypass and hypothermic perfusion with University of Wisconsin solution when THVE exceeded 1 hour in patients with abnormal liver parenchyma.[78] Hypothermic perfusion was achieved preferably through a hilar branch of the hepatic artery, and the solution was vented through an anterior cavotomy.[78,82] Azoulay *et al.* have also used venovenous bypass together with in situ hypothermic perfusion through the portal vein during complex resections warranting prolonged (> 1 hour) application of THVE.[83]

The high volume of crystalloid fluids infused during THVE leads to increased postoperative liver, renal, and pulmonary dysfunction and increased postoperative abdominal collections. Pulmonary dysfunction due to atelectasis can also be caused by traumatic injury to the phrenic nerve during application of the suprahepatic IVC clamp. Splanchnic congestion during THVE contributes to postoperative liver and pancreatic dysfunction, expressed mainly by abnormal liver function tests and hyperamylasemia; and it can infrequently causes automatic splenic rupture.[33,40,48,75]

In a prospective study of THVE versus CPC, postoperative abdominal collections and pulmonary complications were 2.5-fold higher after THVE.[40] In a similar study of THVE versus SHVE, creatinine, amylase, bilirubin, and aspartate aminotransferase (AST) were significantly higher in the THVE group during the first postoperative day.[33] Increased morbidity in THVE patients also leads to an increased postoperative hospital stay.[33] Belghiti *et al.* suggested that inflow occlusion combined with extraparenchymal control of major hepatic veins should be used instead of THVE in patients with impaired renal function, cirrhotic patients, and patients with previous chemoembolization.[40] However, Emond *et al.* proposed that THVE can be tolerated by cirrhotic patients provided they have good liver function.[84] Yamaoka *et al.* suggested that major hepatectomy involving even IVC reconstruction can be performed under THVE in cirrhotic patients provided venovenous bypass is used and the ischemia period does not exceed 60 minutes.[79]

The safely achieved ischemia time under THVE for normal livers under normothermic conditions is 60 minutes,[39,41,42] although a maximum of 90 minutes has been reported.[5,80] In abnormal liver (usually cirrhotic) a normothermic ischemia time of 34.2 ± 12.6 minutes has been reported[84] and a maximum time of 70 minutes has been achieved using venovenous bypass,[79] whereas under hypothermic conditions the time limits have been prolonged to a mean of 121 minutes of ischemia (maximum 250 minutes).[78]

THVE is mainly indicated for tumors approaching or infiltrating the major hepatic veins or the IVC. It is particularly useful when a tumor thrombus is present in the IVC, as application of THVE prevents intraoperative thrombus migration.[39,76,78–81,85] major hepatic veins or IVC reconstruction can be safely performed under THVE[81,85–87] with the possible use of thoracotomy[80] or venovenous bypass.[78,79] On the other hand, Okada *et al.* noted that imaging modalities demonstrating IVC invasion by tumors are unreliable, and in most cases the tumor can be peeled from the IVC without embarking on THVE.[88] Torzilli *et al.* suggested that THVE be restricted to patients in whom the IVC requires total replacement with a graft.[21] Except for posteriorly situated tumors, THVE has been also used for large centrally located tumors,[40] benign hypervascular tumors > 10 cm (hemangiomas, angiomyolipomas),[89] trauma involving the cavohepatic junction,[85] and when the CVP cannot be lowered during CPM (*i.e.*, concomitant right heart failure).[40]

In conclusion, THVE is a technically demanding technique that requires surgical and anesthetic expertise. THVE associated with hemodynamic intolerance has been observed in 10% to 20% of patients as well as increased morbidity and hospital stay versus CPM[40,41] and SHVE.[33]

Table 5.
Clinical series of hepatectomies performed with inflow and outflow vascular occlusion with preservation of inferior vena cava flow.

Study	No. of patients	Type of hepatectomy[a]	Type of occlusion	Texture of liver[b]	Total ischemia time (min)	Blood transfusion (PRBCU)	Transfused patients (%)	Morbidity/ mortality (%)	Postresection liver failure (%)
Elias[93]	16	Major	Intermittent	Pathologic 56.25%	60.2 mean (37–140 range)	N/A[5]	N/A	40/6.25	6.25
Elias[90]	41	Major	Intermittent	Pathologic 56%	69.2 mean (37–140 range)	N/A	N/A	26.83/4.87	0
Cherqui[17]	40	Major	Intermittent 45%	Normal 60%	27(10–45) in continuous; 45 (30–90) in intermittent clamping	0 (0-4)	30	17.5/0	5.0
Smyrniotis[33]	20	Major	Continuous	Normal	38 ± 15	1.5 ± 2.0	N/A	25/0	N/A
Smyrniotis[18]	50	Major	Continuous	Normal	34 (24–58)	0 (0–12)	33	49/0	N/A

Values are expressed as the mean ± SD or median (range) if not otherwise specified.
[a]Major hepatectomy is defined as resection of more than two segments according to the Couinaud classification.
[b]Pathologic liver texture involves cirrhosis (mainly), chronic hepatitis, steatosis > 20%, fibrosis after intraarterial chemotherapy, cholestasis.

Nevertheless, it is a useful method for lesions infiltrating the cavohepatic junction or when major IVC reconstruction must be performed. In some cases parenchymal transection can begin under IPM followed by THVE when approaching the cavohepatic junction.[39,90] In our experience its use should be limited to selected cases, as inflow occlusion alone or combined with extraparenchymal control of major hepatic veins permits safe execution of complex hepatectomy and even IVC or major hepatic vein reconstruction with considerably less morbidity.[21,33,34,40,85,88]

INFLOW OCCLUSION WITH EXTRAPARENCHYMAL CONTROL OF MAJOR HEPATIC VEINS

Inflow occlusion with extraparenchymal control of major hepatic veins (Table 5) results in total liver isolation from the systemic circulation (similar to THVE) but without interruption of caval flow. Thus it is not associated with the hemodynamic and biochemical drawbacks of THVE. The technique has been called hepatic vascular exclusion with preservation of caval flow (HVEPC) by Cherqui *et al.* [17] and selective hepatic vascular exclusion (SHVE) by Smyrniotis *et al.*[18,33]

The pioneering work of Makuuchi and colleagues showed that extraparenchymal control of major hepatic veins is feasible.[91,92] The trunks of the major hepatic veins were safely looped in 90% of patients in a series reported by Elias *et al.*[90] The technique demands full mobilization and disconnection of liver from the IVC by dividing liver ligaments and short hepatic veins. The trunk of the main hepatic vein and any accessory right hepatic veins, the common trunk of the middle and left hepatic veins, or the separate trunks of the middle and left hepatic veins (15% of cases) are then dissected free and looped. Finally, the Pringle maneuver is applied followed by occlusion of the major hepatic veins after tightening the loops [90,93] or applying bulldog clamps.[18,33]

The technique is quite flexible, as it can be applied in a continuous or intermittent manner. When applied intermittently, it was called complete intermittent vascular exclusion of the liver (IVEL) by Elias *et al.*[90,93] IVEL in modes of 20/5 or 15/5 is strongly recommended when operating on abnormal liver (fibrotic after chemotherapy, cirrhotic) or when the anticipated ischemic time exceeds 40 minutes.[17,93] The maximum ischemia time reported under IVEL is 140 minutes,[90] and that under continuous occlusion is 58 minutes.[18] Also total, partial, or alternate application of the method is feasible. Partial application of the technique is particularly useful when defining resection planes, but it is accompanied by increased bleeding during the parenchymal transection phase.[17,93]

The hemodynamic and biochemical profile of SHVE has been similar to that of CPM.[17,33] In a prospective study comparing SHVE to CPM in patients with major hepatectomies, those in the SHVE group had significantly decreased intraoperative blood loss, transfusion requirements, and postoperative hospital stay, together with better postoperative liver function.[18] The same authors, in a prospective study of SHVE versus THVE, found the two methods to be equally effective for bleeding control, but SHVE was better tolerated in terms of postoperative pulmonary, liver, renal, and pancreatic function, leading to fewer complications and a shorter hospitalization stay.[33] Extraparenchymal control of major hepatic veins is strongly indicated when THVE intolerance develops or is anticipated because of unstable cardiovascular status (*i.e.*, a history of myocardial infraction or stroke, treatment with β-blockers, heart failure).[90] It is also preferred to THVE in patients with impaired renal function and when the liver parenchyma is pathologic.[40] SHVE is particularly useful in cases of cirrhosis, cholestasis, and intraarterial chemotherapy that result in high intrahepatic venous pressure and significant backflow bleeding if hepatic veins are not occluded or the CVP is not lowered prior to liver transection. Furthermore, in cases where the CVP cannot be lowered (*i.e.*, right heart failure, poor cardiovascular status), extrahepatic occlusion of major hepatic veins remains the only option during major resections in abnormal liver parenchyma.[17,33,40,90] SHVE or IVEL can be also applied in the presence of tumors approaching the cavohepatic junction and even infiltrating the major hepatic veins far from their IVC ostia, especially if preservation of a major hepatic vein is mandatory. In such cases major hepatic vein reconstruction under SHVE has been performed successfully.[17,90,94]

In conclusion, SHVE requires surgical expertise similar to that required for THVE. Infrequently, accidental tears during looping of major hepatic veins require rapid conversion to THVE. Also, there may be moderate bleeding from segment I if it has not been fully disconnected from the IVC, the operation is performed under high CVP, or the liver parenchyma is fibrotic due to cirrhosis or previous chemoembolization.[17,90] In our institution, we favor SHVE as one of the standard methods of vascular control because it provides a bloodless surgical field similar to THVE but is much better tolerated by patients. The method is particularly useful for performing complex hepatectomies on impaired liver parenchyma and in patients with poor cardiovascular status.

CONCLUSIONS

Each hepatic vascular occlusion technique has its place in liver surgery. Tumor location, underlying liver disease, patient cardiovascular status, and most important the experience of the surgical and anesthetic team should be taken into account to select the most appropriate method for achieving hepatic vascular control in a given patient. The Pringle maneuver is the simplest and oldest method of hepatic vascular control. When performed intermittently, it allows execution of complex lengthy resections in patients with abnormal parenchyma, even enabling reconstruction of major hepatic veins or the IVC. In cirrhotic livers, hemihepatic vascular occlusion is useful for central hepatectomies, and segmental vascular occlusion can be applied for segmentectomies. THVE is useful for resecting large tumors, especially those involving the cavohepatic junction or the IVC. However, it demands high surgical and anesthesia skills, is hemodynamically not tolerated by 10% to 20% of patients, and may be accompanied by considerable morbidity. Inflow occlusion with extraparenchymal control of the major hepatic veins (SHVE or HVEPC) also requires significant surgical expertise but is tolerated by most patients, resulting in a favorable intraoperative and postoperative hemodynamic and metabolic profile. It permits safe execution of complex resection of abnormal livers or in patients with poor cardiovascular status, facilitating also major hepatic vein reconstruction. It is preferred to THVE except in uncommon cases when extensive IVC reconstruction is required.

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