Excerpta Medica

The American Journal of Surgery

The American Journal of Surgery 190 (2005) 75–86
Review

Vascular occlusion to decrease blood loss during hepatic resection

Elijah Dixon, M.D., B.Sc., M.Sc., F.R.C.S.C.[a,*], Charles M. Vollmer, Jr., M.D.[b], Oliver F. Bathe, M.D., M.Sc., F.R.C.S.C.[a], Francis Sutherland, M.D., F.R.C.S.C.[a]

[a]*Department of Surgery, Faculty of Medicine, University of Calgary, Calgary, Alberta, Canada*
[b]*Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA*

Manuscript received March 11, 2004; revised manuscript October 5, 2004

Abstract

Background: Historically, the primary hazard with liver surgery has been intraoperative blood loss. This led to the refinement of inflow and outflow occlusive techniques. The utility of the different methods of inflow and outflow techniques for hepatic surgery were reviewed.
Methods: A search of the English literature (Medline, Embase, Cochrane library, Cochrane clinical trials registry, hand searches, and bibliographic reviews) using the terms "liver," "hepatic," "Pringle," "total vascular exclusion," "ischemia," "reperfusion," "inflow," and "outflow occlusion" was performed.
Results: A multitude of techniques to minimize blood loss during hepatic resection have been studied. The evidence suggests that inflow occlusion techniques are generally well tolerated. These should be used with caution in patients with cirrhosis, fibrosis, steatosis, cholestasis, and recent chemotherapy, and for prolonged time intervals.
Conclusions: Harmful effects of intraoperative blood loss and transfusion occur during hepatic resection. Portal triad clamping (PTC) is associated with less blood loss compared with no clamping. In procedures with ischemic times <1 hour in length, PTC-C (continuous) is likely equal to PTC-I (intermittent). In patients with chronic liver disease or undergoing lengthy operations, PTC-I is likely superior to PTC-C. PTC is superior to total vascular exclusion except in patients with tumors that are large and deep seated, hypervascular, and/or abutting the hepatic veins or vena cava and in patients with increased right-sided heart pressures.

Keywords: Hepatic; Pringle; Surgery; Total vascular exclusion

Primary and metastatic hepatic neoplasms can be safely resected, in many cases altering their natural course [1]. In the 1960s, operative mortality rates of up to 36% were common [2–11]. Recently, operative mortality rates have approached 0% [12]. The reasons for this improvement are several and include advances in perioperative care, improved management of cirrhotic patients, improved understanding of liver anatomy, and technical advances that decrease operative blood loss.

Historically, the major pitfall of liver surgery has been control of intraoperative blood loss. The amount of blood loss has been clearly linked to morbidity and mortality [13]. This has led to the refinement of inflow occlusion techniques as originally described by Hogarth Pringle [14] and further evolution with the introduction of new approaches such as total vascular exclusion (TVE) [15–17]. These techniques are now commonly employed. A recent survey of Japanese surgeons revealed that 25% use the Pringle maneuver routinely, whereas only 7% never use inflow occlusion [18]. Control of hepatic inflow and outflow have allowed major hepatic resections to be carried out without blood transfusion [15,19], but it has done so at the expense of liver damage from warm ischemia and reperfusion [20,21]. This review summarizes pertinent reports investigating the pathophysiologic effects of hepatic inflow and outflow occlusion.

Methods

A comprehensive literature search was performed. Our objective was to identify articles pertaining to intraoperative techniques used to decrease blood loss. Literature examining hepatic ischemia–reperfusion (I-R) was also reviewed. Articles focusing on medications, fibrin glue, and parenchy-

* Corresponding author. Tel.: +403-944-8323; fax: +403-283-1651.
E-mail address: elijah.dixon@calgaryhealthregion.ca

0002-9610/05/$ – see front matter
doi:10.1016/j.amjsurg.2004.10.007

mal transection techniques and instrumentation to decrease blood loss were excluded. MEDLINE was searched, without limitations, using the PubMed search engine. Embase, the Cochrane library, and the Cochrane clinical trials registry were all searched as well; hand searches and bibliographic reviews were also performed. Search terms used included "surgery," "blood loss," "transfusion," "liver," "hepatic," "Pringle," "total vascular exclusion," "inflow," "outflow," and "ischemia–reperfusion." The Boolean operator "and" was used. The search was exploded using the "related articles" function on PubMed when a pertinent article was identified. Abstracts and proceedings from meetings were excluded. Emphasis was placed on pertinent articles published in the last 15 years and important landmark articles published before our period of review. Articles were categorized into levels of evidence according to guidelines supported by the Journal of the American Medical Association Evidence-Based Medicine Working Group and the Oxford Center for Evidence-Based Medicine. Special consideration was placed on larger studies with >100 patients.

Results

Blood loss and its clinical consequences

Catastrophic blood loss during liver surgery has always been a feared complication. It may occur during liver mobilization, dissection of the vasculobiliary structures, or hepatic transection, and bleeding may persist after completion of the procedure. Major hepatic resections historically require blood transfusions between 40% and 100% of the time [20], and blood loss ranges as high as 1964 to 4880 mL [20]. Major blood loss increases morbidity and mortality by causing massive fluid shifts, hypotension, ischemia, and shock. Carson reported that patients with <500 mL blood loss had a mortality rate of 8%, whereas those with blood loss >2000 mL had a mortality rate of 42.9% [22–25]. Operative mortality in patients refusing blood transfusions was found to be 7.1% for patients with a preoperative hemoglobin levels >10 g/dL and 61.5% for patients with hemoglobin levels <6 g/dL [22–28]. Mortality rates are also linked to operative blood loss [24–28].

Aside from the obvious effects of major intraoperative blood loss, blood transfusions have been found to have profound effects on postoperative complication rates and tumor recurrence [29,30]. Furthermore, the use of allogenic blood transfusions after trauma has also been linked to increased rates of infectious complications [29,31–37]. The immunosuppressive effects of allogenic blood transfusions have been recognized since the late 1970s when they were found to increase graft survival after renal transplantation [38]. Allogenic blood transfusions decrease natural killer-cell activity and T-lymphocyte blastogenesis and enhance suppressor T-lymphocyte activity [39]. Perhaps related to these immunosuppressive effects, perioperative blood transfusions are associated with a worse prognosis after surgery for lung cancer [40], cervical cancer [41,42], breast cancer [42], soft tissue sarcomas [43], colorectal cancer [44,45], hepatocellular cancer [30], and colorectal liver metastases [46]. The need for allogenic transfusion is also associated with increased operative mortality, complications, and length of stay [47].

Hepatic: Ischemia, reperfusion, and ischemic preconditioning

The mechanisms by which I-R and ischemic preconditioning (IP) function at a cellular level are complicated, partially understood, interrelated, and occur at multiple levels. This process involves the interplay of many components including the vascular endothelium, cytokines (acting in an autocrine, paracrine, and endocrine fashion), adhesion molecule activation and expression, the complement cascade, and the generation of reactive oxygen species. Fig. 1 lists what are presently believed to be the key components of this process.

Compared with liver transplantation in which cold ischemia is the main type of ischemic injury to the liver, resective liver surgery often involves interruption of portal venous and hepatic arterial blood flow to a portion of the liver without cooling, so-called warm ischemia. Ischemia results in mitochondrial dysfunction [48] and subsequent depletion of the cell's energy source, adenosine triphoshate. This results in the activation of degradative enzymes and the impairment of cellular membrane function, which result in the loss of intracellular ionic homeostasis and the subsequent accumulation of intracellular calcium. Both processes may lead to cellular injury. The depletion of energy also results in the conversion of xanthine dehydrogenase to xanthine oxidase. This scenario contributes to an environment in which an oxidative stress results from the re-establishment of blood flow [48,49]. Reperfusion leads to further cellular injury and death which results from (1) the development of reactive oxygen species, (2) early Kuppfer cell activation, (3) the so-called no-reflow microvascular disturbance [50], and (4) neutrophil activation. The sum product of these 4 processes is hepatocyte death resulting from apoptosis and necrosis.

Mechanisms that may protect, attenuate, or alleviate this injurious sequence include IP. This refers to the phenomenon in which tissues are rendered resistant to the deleterious effects of I-R by previous exposure to brief periods of vascular occlusion [51] and was first appreciated in myocardial tissue [52]. Although still controversial, it is presently believed that IP is mediated by the release of adenosine into the extracellular space by ischemic tissues [53]. Adenosine provides a protective effect by preservation of tissue ATP, inhibition of neutrophil activity, antioxidant and anti–free-radical activity, antiplatelet activity, inhibition of the no-reflow phenomenon, decrease of intracellular calcium levels, and premature degranulation of mast cells [53].

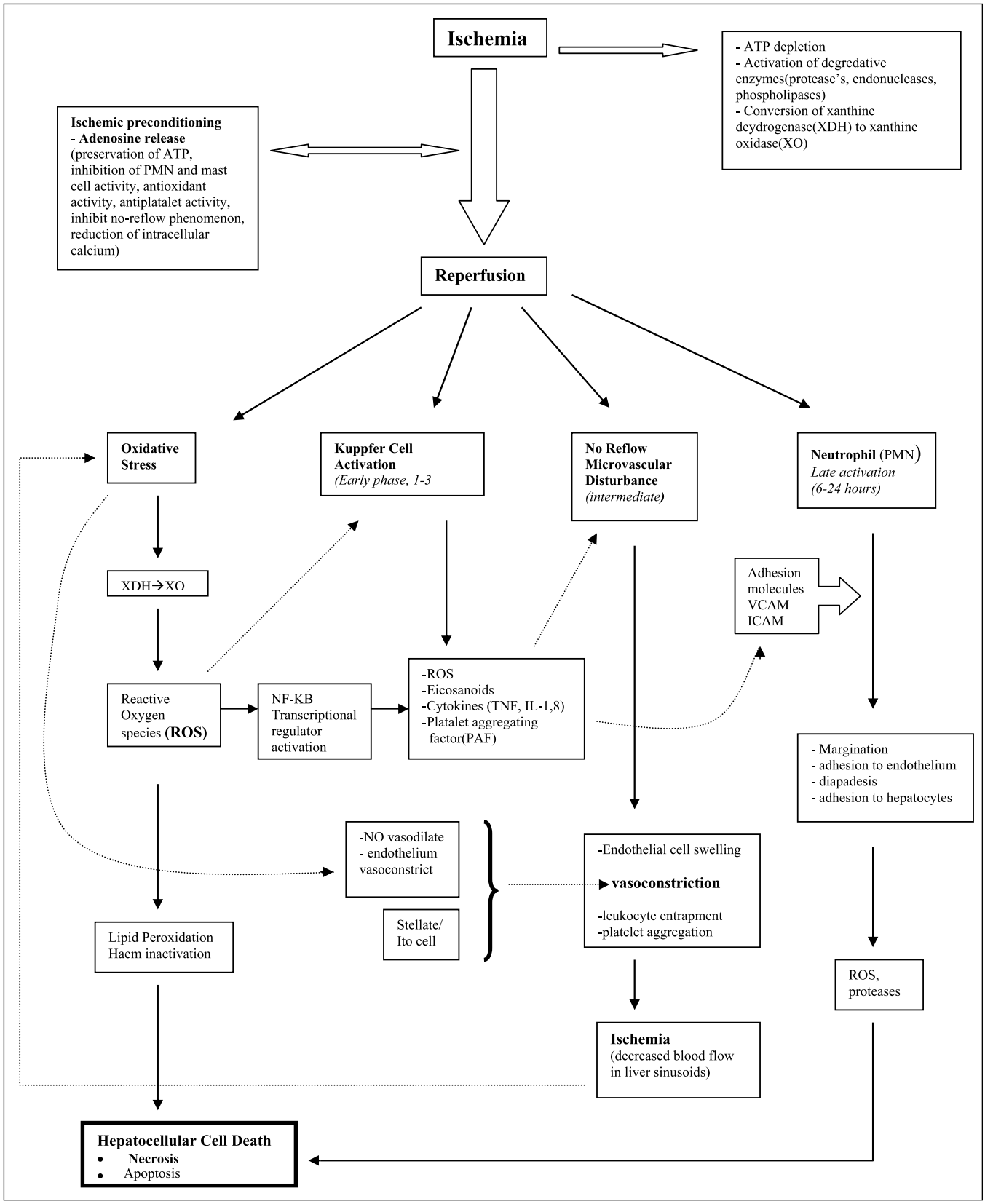

Fig. 1. I-R cycle including mechanisms of ischemic preconditioning.

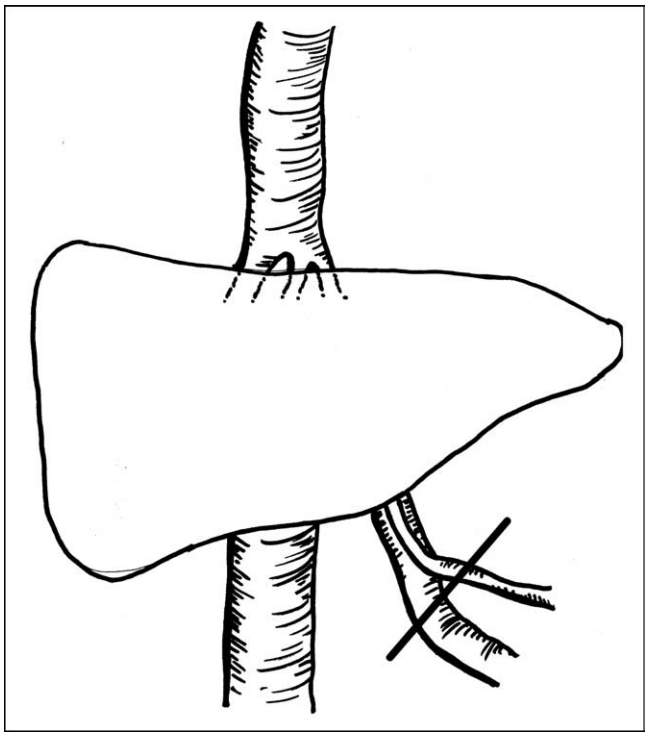

Fig. 2. Pringle occlusion (PTC). Note the interruption of flow to liver by way of the hepatic artery and portal vein. PTC = portal triad clamping.

Human research in this topic as it relates to liver surgery continues and has been pioneered by Clavien [54,55].

Apart from IP, many other areas of the reperfusion injury cycle have been studied with the goal of attenuating cellular injury. The list of possible compounds and mechanisms of protection/inhibition as adapted from Sakon et al [56] includes gadolinium chloride (Kuppfer cells), adenosine administration, antibodies against adhesion molecules and cytokines [57,58], immunosuppressant administration to decrease transcription of key cytokines (FK506, cyclosporin) [59], allopurinol (XO inhibitor) [60], antioxidants and redox-modulating drugs (*N*-acetylcysteine, multivitamins, pentoxyfylline, etc.) [61], calcium-channel blockers [62], antiapoptotic agents [63], inhibition of the coagulation pathway [64], alternate energy sources [65], liver cooling [56], and ischemic and heat-shock preconditioning [66]. The multitude of various compounds and mechanisms studied to date is a testament to the lack of a single good therapy and the complexity of this process.

Inflow occlusion

Vascular inflow to the liver accounts for approximately 25% of cardiac output. This blood flow is divided between the portal vein (70%) and the hepatic artery (30%). The site for inflow occlusion (Fig. 2) is the porta hepatus between the first part of the duodenum and the hilum of the liver. Occasionally, a posterior accessory or replaced right hepatic artery arising off the superior mesenteric artery can be found posterolateral to the common bile duct. Approximately 10% of the time, an accessory (or aberrant) left hepatic artery can also arise from the left gastric artery. The branching pattern of the hepatic artery and portal vein in the porta hepatis is quite variable [67–75].

Techniques of inflow occlusion

In 1908, Hogarth Pringle reported 8 patients who died of hemorrhage from liver trauma [10,11]. During this experience he conceived that digital occlusion of the hepatic pedicle would help control hemorrhage. Although many liver surgeons have come to rely on portal triad clamping (PTC), it was not until 1997 that its effectiveness was confirmed in a randomized trial by Man et al [76].

There are 3 modern methods to perform PTC. The individual portal vein and hepatic artery can be dissected and occluded. This technique does not always occlude all hepatic arteries because an anomalous left or right hepatic artery may be present. Collaterals in the porta hepatis may be well developed in the cirrhotic patient. A second technique for PTC is occlusion of the porta hepatus with a large vascular clamp. If used, the clamp should be used over a Penrose drain or other such device to evenly distribute the pressure and prevent vessel injury. A more recently developed technique involves placing a soft cloth tape around the porta hepatis and constricting the vessels with a Rummel tourniquet [77–79]. This provides effective control of all vessels in the porta hepatis, is less traumatic than a vascular clamp, is very secure, and does not hinder or obstruct the operation.

More selective approaches to inflow occlusion of either the total right- or left-sided Glissonian sheaths have also been described [80]. These techniques serve well those patients with cirrhosis and poor hepatic reserve in whom decreasing the amount of ischemic insult is advantageous. With selective inflow occlusion there is also less stasis and venous hypertension in the mesentery and bowel. The "posterior approach," as described by Launois et al, can be used to gain rapid access to the Glissonian sheaths for early vascular control of a hemiliver or segment [81]. The use of a disposable plastic band as a hepatic clamp has been described [82] as a modification of the Pringle maneuver. As well, resectional devascularization (RD), or dissection of the vessels supplying the liver to be resected, can be performed in the porta hepatus, thus allowing ligation and division before parenchymal transection [83]. Inflow occlusion is generally well tolerated. Belghiti et al described the hemodynamic changes (10% to 15% increase in mean arterial pressure, a 40% to 44% increase in systemic vascular resistance, and a 10% to 11% decrease in cardiac index) experienced when occlusive vascular techniques are used [84,85], which then result in a moderate increase in systolic, diastolic, and mean arterial pressure.

Inflow occlusion literature

The concept that human livers are sensitive to warm ischemia is directly derived from canine experimentation in the 1950s [86]. This model is the reason for limiting warm

ischemia to 15 to 20 minutes in humans. However, dog liver differs from human liver in that it has hepatic vein sphincters as well as bacteria in the portal blood flow, both of which result in hepatic necrosis and gangrene when the hepatic artery is occluded. Eventually, Mackenzie et al established that splanchnic venous stasis was the main factor causing the poor canine tolerance to hepatic ischemia and that if this bed were decompressed, ischemic times could be extended up to 60 minutes [87]. Using portal decompression in pigs, Huguet et al [88] showed that 120 minutes of continuous ischemia was tolerated, but all pigs subjected to 180 minutes of ischemia died of hepatic necrosis. Pigs are more closely related to humans anatomically because they have no hepatic vein sphincters. Huguet et al [26,88,89] successfully challenged the time limit in humans by extending continuous warm ischemic times up to 1 hour. However, in this study they noted a high (77.8%) complication rate in those patients with chronic liver disease. For this reason studies, were undertaken to see whether intermittent PTC-I would ameliorate some of the ischemic damage, especially in patients with chronic liver disease. Protective preconditioning ischemia has been of proven value in the human heart [90]. Since then, Yoshizumi et al [91] showed that a 10-minute IP period can protect against prolonged 40-minute ischemia by decreasing transaminase elevation and increasing bile output in the rat. This effect may explain why PTC-I is tolerated better than PTC-C in the rat [92] and the pig when ischemic times are >90 minutes [93]. No difference in outcomes were noted with a 15-versus 30-minute ischemic insult with a 5-minute reperfusion in the rat [92].

It has been shown in humans that PTC-I can be undertaken for up to 322 minutes [94] and that TVE can be extended up to 116 minutes [95]. However, patients with abnormal liver parenchyma experience high complication rates including liver failure and death. Factors that may impair the regenerative capacity of the liver and need to be taken into account when using occlusive vascular techniques on the liver include cirrhosis, fibrosis, steatosis, cholestasis, previous chemotherapy, and inadequate residual liver volume [96,97].

Table 1 lists the evidence surrounding the use of these techniques. There is level-1 evidence examining inflow occlusion for hepatic resection. Man et al [76] were the first to show in a prospective randomized study that using PTC-I with a cycle of 20-minutes on and 5-minutes off resulted in less intraoperative blood loss less alteration in postoperative liver function versus patients with no inflow occlusion. No significant difference in mortality or complication rate could be demonstrated. There have also been randomized controlled trials of PTC vs. resectional Devascularization (RD); the results are conflicting in terms of blood loss [76,98]. Subsequently, Belghiti et al compared PTC-I with PTC-C in a prospective randomized trial [95]. They demonstrated that PTC-I caused less postoperative liver dysfunction than did PTC-C. As the length of PTC-C time increased, so too did the increase in liver enzymes and serum bilirubin. Furthermore, this response was most marked in the patients with cirrhosis in the PTC-C group. Increased blood loss in PTC-I group was demonstrated. Overall, there was no significant difference in complication rate or mortality, but there was a trend toward increased rates in the PTC-C group.

Outflow occlusion

There are two basic outflow tracts from the liver, the caudate lobe veins and the hepatic veins (Figs. 3 and 4). The caudate lobe veins can vary in number. Occasionally, a larger inferior right hepatic vein drains segments 4, 6, and 7 directly into the inferior vena cava (IVC) [99]. The paracaval portion of the caudate lobe can be dissected off the vena cava to expose these veins for ligature and division. This dissection is a requisite step in obtaining the inferior exposure for extrahepatic control of the hepatic veins.

The hepatic veins are the source of the most difficult-to-control hemorrhage during hepatic surgery. These 3 veins lie between the 4 classical hepatic sectors and the dorsal sector of the liver (caudate lobe). They are accessible for only a short extrahepatic length. The right vein is dissected as a single trunk separate from the common trunk of the middle and left (truncus communis of Rex), which is present in 95% [68,99–103] of cases. After dissecting the right triangular ligament and separating the caudate lobe off the cava, the origin of this vein can be delineated. The superior aspect of the IVC below the diaphragm passes through a fibrous ring that extends posteriorly around the cava from the encompassing caudate lobe. This thick, fibrous sheath (inferior vena caval ligament) must be divided before the lateral aspect of the right hepatic vein can be visualized. Between the right and middle vein there is a space that can be dissected close to the liver substance and parallel to the vena cava connecting the superior dissection with the aforementioned inferior plane developed between the vena cava and caudate lobe. The right vein can then be encircled and controlled.

The middle and left hepatic veins have a shorter extrahepatic course and are broad based because of their common trunk. Segments 2 and 3 are rotated toward the right, which exposes the caudate lobe beneath the gastrohepatic ligament. Dissection is carried out at the cephalad border of the caudate lobe anterior to the IVC, and a plane is developed that connects with the bare area between the right hepatic vein and the right side of the common middle-left hepatic vein orifice. This allows control of the common middle-left trunk with a tourniquet.

Techniques of outflow occlusion

Classical liver resection as described by Lortat et al involves extrahepatic ligation of the left or right portal structures individually followed by control of the hepatic veins within the liver substance toward the end of the parenchymal dissection. Care must be taken to avoid the creation of any large holes in

Table 1
Review of hepatic resective surgery: Inflow occlusion literature

Reference	Year	N	Technique (n)	Age (y)	Major hepatectomy (%)	Morbidity (%)	Mortality (%)	Clamp time (min)	Cirrhosis (%)	CVP	Blood loss	Transfusions (%)
Level-1 evidence												
95	1995–1996	86	CVP (42)	51	>50	43	5	16–118	15	<5	1.18 L	28
			IP (44)	52		29	0		14		1.29 L	32
76	1995–1997	100	IP (50)	59	68	38	2	88 (24–201)	26		1.28 L (0.33–9.42)	36
			RD (50)	52	70	50	4	NA	32		1.99 (0.26–13.9)	58
15	1991–1994	52	CVP (24)	43	100	29	4	35 (17–55)	0		989 mL (100–5000)	
			TVE (28)	48		57	0	42 (23–78)	0		1195 mL (200–5000)	
98	1996–2001	58	IP (28)	57	100	29	0	96 (62–196)	100	5	1685 mL (50–4800)	43
			RD (30)	53		33	0	94 (65–188)	100	5	1159 mL (400–4200)	17
Level-2 evidence												
55	2000	24	IP (12)	60	100	17	0	30	0			13
			CVP (12)		100	34	0	30	0			
114		42	TVE (18)	56	100	33	0	32			850 mL	
			TVECP (20)	58	100	25	0	38		<5	650 mL	
115	1995–1997	112	RD (50)	52	70	13	2	NA	15		1.99 L (.26–13.9)	
			IP (62)	51	69	17	1	(24–201)	18		(.23–9.42)	
104	1992–1998	49	RD (15)	58	92	27	0	NA	0		1600 mL (250–8000)	73
			CVP (34)	64		21	3	<20	0		500 mL (25–2000)	29
Level-3 evidence												
116	1994–2000	72	IP	47	81	24	7					57
Level-4 evidence												
12	1989–1997	330	RD (199)		>60		6		49	>10		35
			IP (131)							>10		
117	1990–1997	747	TVE (58)	50.2	>50	22	4.4		32			23
			IP (541)									
			(148)									
118	1979–2000	101	RD		100	20	5	NA	1		3836 mL	
119		158	CVP (132)		>70	20	0	61			831 mL	
			RD (26)								1035 mL	
120	1979–1998	168	RD (90)	60	40	22	10		2		2300 mL (50–20000)*	
			IP (78)		60	10	3		14	<5	725 mL (50–6000)*	
121	1986–1996	100	CVP (70)	52	53	23	3		10			
17	1980–1985	142	CVP (107)	54	60	32	6	32 (8–90)	11			89
			TVE (35)									
122	1984–1997	245	CVP/IP (125)	56	53	22	3	39 (7–107)	15	<5		34
			(120)		38				14	<5		60

123	1984–2000	141	IP (85)	58		19	1				625 mL	21
			TVE (20)	59		29	5				931 mL	29
			Long. (21)	62		10	0				572 mL	15
			(15)	62		13	0				303 mL	7
124	1994–1999	329	IP	62	71	26	0	69 (0–248)	41		853 mL	3.9
107	1991–2001	1803	IP	59	>70	45	3	31	9	<5	871	49
125	1986–1999	100		61	52	22	%		0		913 mL (80–7000)	
106	1986–1996	100	IP	51	60				10	>5	1000	
										<5	200	
126	1986–1995	150	IP	58	89	23	1			<4	814 mL (70–10000)	
127	1988–1996	133	RD	59*	79	45	5		4	<5		40
128	1984–1999	254	CVP (12%)	51	25	26	3.9	24 (10–50)	8			
			RD (88%)									
129	1995–2001	168	IP (46)	34	100			52 (12–118)	0		427 (195–1100)	
			RD (121)					NA	0		460 (205–1650)	
130	1989–2001	155	IP (50%)	52	100	55	8	60 (20–280)	35		2 L (0.2–20)	
			RD (50%)						14	<5	2300 mL (50–20000)*	
131	1964–1987	411	None	(1–81)	73	12	3	NA	4			
132	1989–1995	200	CVP (28%)	56	76	37	5	34 (22–39)	10		1700 mL	61
			TVE (72%)									
133	1990–1992	100	IP	55	80				29		755 mL (100–4500)	22
134	1984–1992	226		62	70	19	1		0			
135	1994–1997	163	RD (48)	58	80	33	2		100		2562 mL (650–4160)	30
			RD ± IP (115)			15	1		100		801 mL (50–2350)	20

CVP = central venous pressure; IP = ischemic preconditioning; Long = Longmire clamp; RD = resectional devascularization; TVE = total vascular exclusion; TVECP = total vascular exclusion with preservation of caval flow.

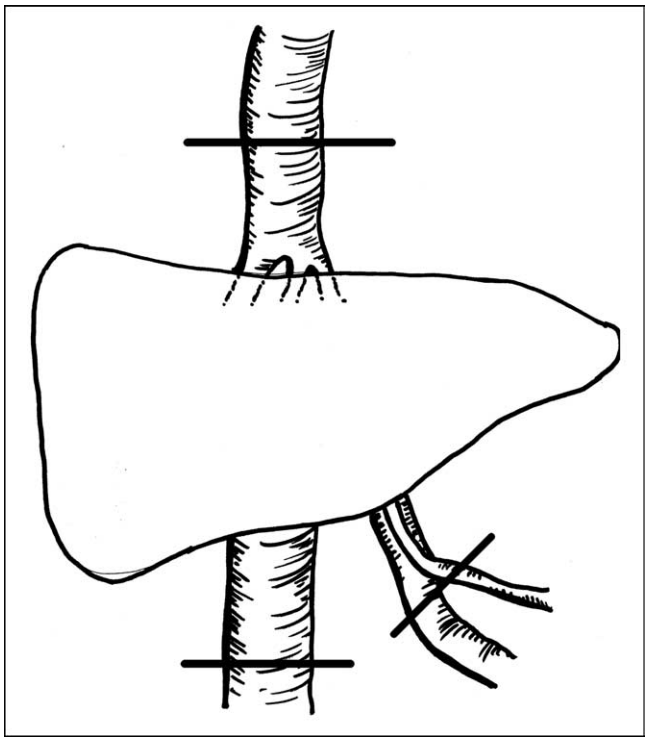

Fig. 3. TVE. Note the interruption of the portal vein and hepatic artery blood flow as well as vena cava clamping above and below the liver. TVE = total vascular exclusion.

these veins because this risks catastrophic hemorrhage and air embolism. Outflow occlusion of the hepatic veins can be accomplished in any number of ways including (1) TVE by clamping of the supra and infrahepatic IVC with or without clamping of the aorta, (2) division and oversewing between clamps of selective hepatic veins, (3) suture ligation, or (4) occlusion with a vascular clamp or tourniquet occlusion [77]. Recently, the use of a long endovascular stapler has been described as a way to occlude and divide the hepatic veins simultaneously [103–105].

Maintenance of low CVP may decrease backflow bleeding from the hepatic veins [16,106]. Bismuth was the first to show that low CVP in the range of 8 to 10 cm water may decrease bleeding during parenchymal transection [16]. In a subsequent study of 100 patients by Jones et al, it was shown that patients with CVP $<$ 5 cm water underwent a median blood loss of 200 mL, whereas those with CVP $>$ 5 cm H2O underwent a median blood loss of 1000 mL [106]. Therefore, a CVP monitor is a useful adjunct to decrease preload and minimize blood loss. Low CVP, however, places the patient at increased risk of air embolism. Measures to prevent this include keeping the patient in 15° Trendelenberg position as well as replacing the liver into its natural anatomic position and increasing ventilation pressures before attempting repair of any injury to the IVC or hepatic veins. Proper exposure and care in dividing the parenchyma as one approaches the hepatic veins is essential. Use of parenchymal dissection devices (eg, ultrasonic dissector, Water-jet dissector) may be helpful in the atraumatic dissection along the vein wall. Control of the hepatic veins to the area of resection may precede parenchymal transaction. If so, inflow control must be employed once the outflow occlusion has been achieved to control congestion, bleeding, and problems with exposure of the transection plane [83,103,105,107,108].

TVE

TVE of the liver, initially introduced by Heaney in the 1960s and popularized by Huguet [88] in the 1970s, is an effective technique to control hemorrhage during hepatectomy (Fig. 3). Most hepatic surgeons use this technique selectively for large tumors that are centrally located or for cancers on or near the hepatic veins or vena cava. This technique involves control of the vena cava above and below the liver and PTC. To completely isolate the liver, the right adrenal vein must be divided in advance or be encompassed by the clamp. Mobilization of the IVC out of the retroperitoneum allows complete control of all venous drainage from the liver. Although most surgeons cross-clamp the vena cava above and below the liver, Huguet et al used long vascular clamps to vertically occlude the vena cava behind the liver from above and below [88]. This effectively controls lumbar and right adrenal veins and can be applied with less thorough dissection of the cava. With TVE, the parenchyma can be divided more rapidly either by conventional dissection or with a scalpel [109]. Before

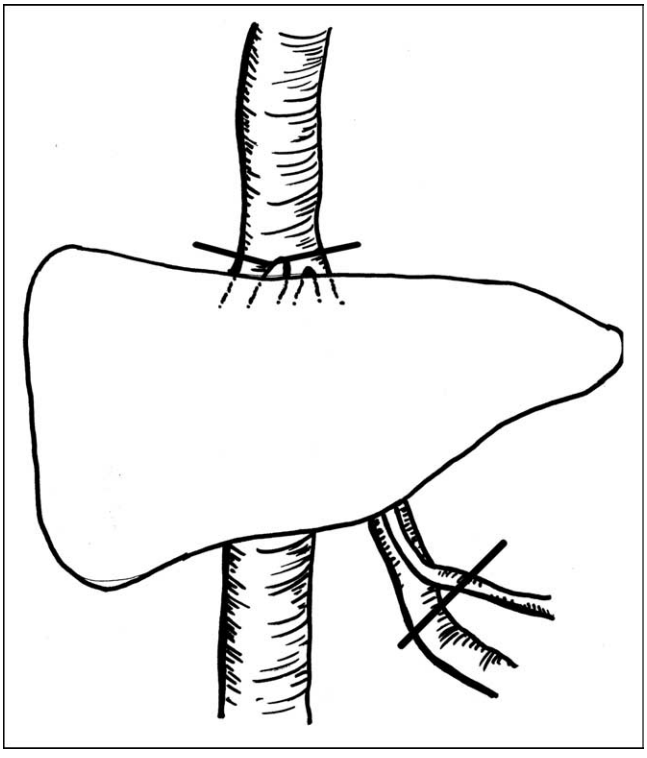

Fig. 4. TVE with preservation of caval flow. Note the interruption of the portal vein and hepatic artery blood flow as well as hepatic vein occlusion. TVE = total vascular exclusion.

removal of the upper caval clamp, the lower clamp may be partially released if there have been large venous openings to flush out any air that can lead to air embolus once the upper clamp is removed.

A trial period of clamping is required to determine patient tolerance to the decrease in venous return. The cardiac index generally decreases by 40% to 50% and infusion of large volumes may be required in preparation [17]. Belghiti et al [15] and Bismuth et al [16] reported that 14% and 6% of their patients, respectively, did not tolerate this clamping. Coordination with the anesthetic team is of critical importance in this procedure; anesthetic teams with liver transplant experience are ideal. For patients who do not tolerate caval clamping, either venovenous bypass or infradiaphragmatic aortic occlusion can be used. Stephen et al [110] reported 99 patients who underwent successful TVE with aortic clamping. Problems with aortic clamping include hypertension, spinal cord ischemia, dislodgment of atheromatous emboli, and postclamp fibrinolysis and coagulopathy. The main risks and complications associated with TVE include lack of familiarity with retrohepatic caval mobilization from the retroperitoneum, potential lumbar and adrenal vein injury, hemodynamic compromise and/or intolerance, and edema of the small bowel with prolonged clamp times.

Hemodynamic and anesthetic management in TVE

The IVC generally delivers two thirds of the cardiac output back to the heart. For this reason, it was feared that interruption of caval flow would result in cardiovascular collapse [85]. The hemodynamic changes associated with TVE include decreases in mean arterial pressure by 14%, pulmonary artery pressure by 19% to 25%, and cardiac index by 40% to 52% and an increase in systemic vascular resistance by 80% [26,84,85]. Before placement of clamps, the patient is volume loaded with crystalloid to a CVP of 12 to 15 mm Hg [111] to prevent intolerance of the clamping. A trial exclusion for 5 minutes is performed to ensure stability. Clamps are applied in the following order; hepatoduodenal ligament, infrahepatic IVC, and then suprahepatic IVC. They are removed in opposite order. Throughout clamping, blood pressure is maintained with volume administration. If properly volume loaded, it is rare that a supraceliac aortic clamp will be required to maintain blood pressure [111]. Monitoring should include an arterial line, a CVP monitor, and—in patients with comorbid medical conditions—a pulmonary artery catheter [111]. Changes recognized with TVE include hypokalemia, coagulation abnormalities, and metabolic academia, all of which resolve without treatment [85]. There is some evidence that interruption of "backflow" from the hepatic veins during TVE may impair the liver's ability to tolerate ischemia (ie, this may suggest that open hepatic veins provide a form of liver perfusion during inflow occlusion) [112].

Outflow occlusion literature

Belghiti et al [15] compared TVE and PTC-C in a prospective randomized study that represented the only level-1 evidence examining the role of TVE. Patients with tumors impinging on the cavohepatic junction were excluded. Fifty-two noncirrhotic patients were randomly assigned to 2 groups (Table 1). Of note, 14% of patients could not hemodynamically tolerate TVE and were crossed over to the PTC-C group. The PTC-C group also included 4 patients who were crossed over to the TVE group, 3 because of tumors involving the cavohepatic junction and 1 patient with bleeding secondary to tricuspid insufficiency. There was no significant difference in ischemic time or blood loss between the groups. Postoperative abdominal collections and pulmonary complications were 2.5 times higher in the TVE group (this did not reach statistical significance). The study confirms that TVE is superior in controlling bleeding in certain patients with large deep-seated tumors, tumors that abut the hepatic veins or vena cava, or hypervascular lesions and in patients with increased right-sided heart pressures.

Elias et al [79] and Cherqui et al [77] have used intermittent TVE with preservation of caval flow (TVECP). In this procedure, isolating and controlling them extrahepatically can achieve selective or complete occlusion of the hepatic veins. Both studies showed that this procedure was well tolerated hemodynamically by patients; in 1 study [77], 70% of patients did not require a blood transfusion. Advantages of this procedure include preservation of caval blood flow, the ability to control single hepatic veins, and intermittent application. Disadvantages of this procedure include the hazard involved in retrohepatic dissection, the time needed for this dissection, and the likelihood that it will not provide adequate control for tumours that encroach on the hepatic veins and vena cava.

Comments

Resective liver surgery remains a technically demanding undertaking. The need to decrease the harmful effects of intraoperative blood loss and transfusion during hepatic resection by controlling hepatic inflow and outflow outweighs the potential risks of ischemia and subsequent reperfusion injury. Complication rates listed in Table 1 range from 11% to 60% [15,113]. Most studies examined postoperative liver enzymes and serum bilirubin; in general, these reached a peak on postoperative day 1 or 2 and returned to normal by days 7 to 10. The degree of increase generally correlates with the length of ischemia and underlying liver disease. Mortality rates range from 0% to 10% and average between 2% and 3%.

To date, some high-quality randomized controlled trials have been conducted by Belghiti et al [15] and others. However, the majority of published literature examining these topics is level-4 evidence. The preponderance of the evidence suggests that some form of inflow occlusion (PTC or RD) does decrease operative blood loss and transfusion requirements. There is also good evidence that IP may ameliorate liver cell injury during inflow occlusion. When

ischemic times are <1 hour, there is little evidence that PTC-I is advantageous compared with PTC-C. However, if ischemic times are expected to be >1 hour, or if the liver may have characteristics reflective of impaired regenerative ability (ie, cirrhotic, fibrotic, steatotic, cholestatic, extended resection, preoperative chemotherapy), then there is evidence that PTC-I may be better tolerated.

Control of hepatic outflow may be accomplished in a number of ways: TVE, TVECP, ligation before parenchymal transection, and control within the substance of the liver at the end of the resection. There is little doubt that if not controlled properly, the hepatic veins are the major source of blood loss during hepatectomy. There is no evidence that TVE should be used routinely; in fact, it may be associated with higher complication rates. However, in the following certain circumstances, it is the procedure of choice: for patients whose tumors are large and deep-seated, hypervascular, or abutting the hepatic veins or vena cava and in patients with increased right-sided heart pressures. If TVE is not required, then a low-operating CVP—or, alternatively, TVECP—should be used in combination with intraparenchymal control of the veins and control of the veins before transection.

References

[1] Iwatsuki S, Sheahan DG, Starzl TE. The changing face of hepatic resection. Curr Probl Surg 1989;26:281–379.

[2] Bourgeon R, Guntz M, Poncelet J, et al. How to direct the surgical therapy of malignant tumors of the liver. Mem Acad Chir (Paris) 1965;91:421–9.

[3] Brunschwig A. Hepatic lobectomies. Am J Gastroenterol 1965;44: 245–53.

[4] Couinaud C. The fissural method in hepatic surgery. Tijdschr Gastroenterol 1965;8:577–90.

[5] Kizhaev VI. On surgical therapy of primary cancer of the liver. Khirurgiia (Mosk) 1965;41:85–9.

[6] McDermott WV Jr. Surgery of the liver and portal circulation. Adv Surg 1965;1:247–84.

[7] Quattlebaum JK, Quattlebaum JK Jr. Technique of hepatic resection. Surgery 1965;58:1075–80.

[8] Stucke K. Clinical experience with hemihepatectomy and liver resection. Taiwan Yi Xue Hui Za Zhi 1965;64:325–35.

[9] Ton TT. Experiences with partial liver resection for malignant and benign tumors of the liver. Zentralbl Chir 1965;90:1499–505.

[10] Troitskii RA. Current aspects of liver surgery. Review of the literature. Eksp Khir Anesteziol 1965;10(4):48–50.

[11] Velasco SC. 40 years of hepato-biliary surgery. Acad Peru Cir 1965;17:385–90.

[12] Fan ST, Lo CM, Liu CL, et al. Hepatectomy for hepatocellular carcinoma: toward zero hospital deaths. Ann Surg 1999;229:322–30.

[13] Nagorney DM, van Heerden JA, Ilstrup DM, et al. Primary hepatic malignancy: surgical management and determinants of survival. Surgery 1989;106:740–9.

[14] Franco D, Smadja C, Meakins JL, et al. Improved early results of elective hepatic resection for liver tumors. One hundred consecutive hepatectomies in cirrhotic and noncirrhotic patients. Arch Surg 1989;124:1033–7.

[15] Belghiti J, Noun R, Zante E, et al. Portal triad clamping or hepatic vascular exclusion for major liver resection. A controlled study. Ann Surg 1996;224:155–61.

[16] Bismuth H, Castaing D, Garden OJ. Major hepatic resection under total vascular exclusion. Ann Surg 1989;210:13–9.

[17] Delva E, Camus Y, Nordlinger B, et al. Vascular occlusions for liver resections. Operative management and tolerance to hepatic ischemia: 142 cases. Ann Surg 1989;209:211–8.

[18] Nakajima Y, Shimamura T, Kamiyama T, et al. Control of intraoperative bleeding during liver resection: analysis of a questionnaire sent to 231 Japanese hospitals. Surg Today 2002;32:48–52.

[19] Jamieson GG, Corbel L, Campion JP, et al. Major liver resection without a blood transfusion: is it a realistic objective? Surgery 1992;112:32–6.

[20] Cherqui D, Alon R, Lauzet JY, et al. Limitation of blood transfusions during hepatectomies. Study of 150 consecutive hepatic resections on healthy and pathological livers. Gastroenterol Clin Biol 1996;20:132–8.

[21] Miyagawa S, Makuuchi M, Kawasaki S, et al. Criteria for safe hepatic resection. Am J Surg 1995;169:589–94.

[22] Carson JL. Morbidity risk assessment in the surgically anemic patient. Am J Surg 1995;170(suppl 6A):32S–6S.

[23] Carson JL, Chen AY. In search of the transfusion trigger. Clin Orthop 1998;357:30–5.

[24] Carson JL, Duff A, Berlin JA, et al. Perioperative blood transfusion and postoperative mortality. JAMA 1998;279:199–205.

[25] Carson JL, Hill S, Carless P, et al. Transfusion triggers: a systematic review of the literature. Transfus Med Rev 2002;16:187–99.

[26] EU Hernia Trialists Collaboration. Repair of groin hernia with synthetic mesh: meta-analysis of randomized controlled trials. Ann Surg 2002;235:322–32.

[27] Carson JL, Duff A, Poses RM, et al. Effect of anaemia and cardiovascular disease on surgical mortality and morbidity. Lancet 1996; 348(9034):1055–60.

[28] Carson JL, Noveck H, Berlin JA, et al. Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. Transfusion 2002;42:812–8.

[29] Agarwal N, Murphy JG, Cayten CG, et al. Blood transfusion increases the risk of infection after trauma. Arch Surg 1993;128:171–7.

[30] Yamamoto J, Kosuge T, Takayama T, et al. Perioperative blood transfusion promotes recurrence of hepatocellular carcinoma after hepatectomy. Surgery 1994;115:303–9.

[31] Edna TH, Bjerkeset T, Svinsas M, et al. Association between transfusion of stored blood and bacterial infective complications after biliary operations. Eur J Surg 1994;160:357–62.

[32] Ford CD, Van Moorleghem G, Menlove RL. Blood transfusions and postoperative wound infection. Surgery 1993;113:603–7.

[33] Blumberg N, Heal JM. Effects of transfusion on immune function. Cancer recurrence and infection. Arch Pathol Lab Med 1994;118:371–9.

[34] Ikuta S, Miki C, Hatada T, et al. Allogenic blood transfusion is an independent risk factor for infective complications after less invasive gastrointestinal surgery. Am J Surg 2003;185:188–93.

[35] Pereira A. Deleterious consequences of allogenic blood transfusion on postoperative infection: really a transfusion-related immunomodulation effect? Blood 2001;98:498–500.

[36] Spence RK. Emerging trends in surgical blood transfusion. Semin Hematol 1997;34(3 Suppl 2):48–53.

[37] Taylor RW, Manganaro L, O'Brien J, et al. Impact of allogenic packed red blood cell transfusion on nosocomial infection rates in the critically ill patient. Crit Care Med 2002;30:2249–54.

[38] Glass NR, Miller DT, Sollinger HW, et al. A four-year experience with donor blood transfusion protocols for living-donor renal transplantation. Transplantation 1985;39:615–9.

[39] Nielsen HJ. Detrimental effects of perioperative blood transfusion. Br J Surg 1995;82:582–7.

[40] Tartter PI, Burrows L, Kirschner P. Perioperative blood transfusion adversely affects prognosis after resection of stage I (subset N0) non-oat cell lung cancer. J Thorac Cardiovasc Surg 1984;88:659–62.

[41] Blumberg N, Agarwal MM, Chuang C. Relation between recurrence of cancer of the colon and blood transfusion. Br Med J (Clin Res Ed) 1985;290:1037–9.
[42] Tartter PI, Burrows L, Papatestas AE, et al. Perioperative blood transfusion has prognostic significance for breast cancer. Surgery 1985;97:225–30.
[43] Rosenberg SA, Seipp CA, White DE, et al. Perioperative blood transfusions are associated with increased rates of recurrence and decreased survival in patients with high-grade soft-tissue sarcomas of the extremities. J Clin Oncol 1985;3:698–709.
[44] Burrows L, Tartter P. Effect of blood transfusions on colonic malignancy recurrent rate. Lancet 1982;2(8299):662.
[45] Voogt PJ, van de Velde CJ, Brand A, et al. Perioperative blood transfusion and cancer prognosis. Different effects of blood transfusion on prognosis of colon and breast cancer patients. Cancer 1987;59:836–43.
[46] Stephenson KR, Steinberg SM, Hughes KS, et al. Perioperative blood transfusions are associated with decreased time to recurrence and decreased survival after resection of colorectal liver metastases. Ann Surg 1988;208:679–87.
[47] Kooby DA, Stockman J, Ben-Porat L, et al. Influence of transfusions on perioperative and long-term outcome in patients following hepatic resection for colorectal metastases. Ann Surg 2003;237:860–70.
[48] Gutierrez G. Cellular energy metabolism during hypoxia. Crit Care Med 1991;19:619–26.
[49] Hasselgren PO. Prevention and treatment of ischemia of the liver. Surg Gynecol Obstet 1987;164:187–96.
[50] Henrion J. Ischemia/reperfusion injury of the liver: pathophysiologic hypotheses and potential relevance to human hypoxic hepatitis. Acta Gastroenterol Belg 2000;63:336–47.
[51] Serracino-Inglott F, Habib NA, Mathie RT. Hepatic ischemia-reperfusion injury. Am J Surg 2001;181:160–6.
[52] Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. Circulation 1986;74:1124–36.
[53] Lee HT. Mechanisms of ischemic preconditioning and clinical implications for multiorgan ischemic-reperfusion injury. J Cardiothorac Vasc Anesth 1999;13:78–91.
[54] Clavien PA, Harvey PR, Strasberg SM. Preservation and reperfusion injuries in liver allografts. An overview and synthesis of current studies. Transplantation 1992;53:957–78.
[55] Clavien PA, Yadav S, Sindram D, et al. Protective effects of ischemic preconditioning for liver resection performed under inflow occlusion in humans. Ann Surg 2000;232:155–62.
[56] Sakon M, Ariyoshi H, Umeshita K, et al. Ischemia-reperfusion injury of the liver with special reference to calcium-dependent mechanisms. Surg Today 2002;32:1–12.
[57] Colletti LM, Cortis A, Lukacs N, et al. Tumor necrosis factor up-regulates intercellular adhesion molecule 1, which is important in the neutrophil-dependent lung and liver injury associated with hepatic ischemia and reperfusion in the rat. Shock 1998;10:182–91.
[58] Kelly KJ, Williams WW Jr, Colvin RB, et al. Intercellular adhesion molecule-1-deficient mice are protected against ischemic renal injury. J Clin Invest 1996;97:1056–63.
[59] Schreiber SL, Crabtree GR. The mechanism of action of cyclosporin A and FK506. Immunol Today 1992;13:136–42.
[60] Saugstad OD. Role of xanthine oxidase and its inhibitor in hypoxia: reoxygenation injury. Pediatrics 1996;98:103–7.
[61] Li C, Browder W, Kao RL. Early activation of transcription factor NF–kappaB during ischemia in perfused rat heart. Am J Physiol 1999;276(2 Pt 2):H543–52.
[62] Takei Y, Marzi I, Kauffman FC, et al. Increase in survival time of liver transplants by protease inhibitors and a calcium channel blocker, nisoldipine. Transplantation 1990;50:14–20.
[63] Daemen MA, van't Veer C, Denecker G, et al. Inhibition of apoptosis induced by ischemia-reperfusion prevents inflammation. J Clin Invest 1999;104:541–9.
[64] Jones A, Geczy CL. Thrombin and factor Xa enhance the production of interleukin–1. Immunology 1990;71(2):236–41.
[65] Nieminen AL, Dawson TL, Gores GJ, et al. Protection by acidotic pH and fructose against lethal injury to rat hepatocytes from mitochondrial inhibitors, ionophores and oxidant chemicals. Biochem Biophys Res Commun 1990;167:600–6.
[66] Peralta C, Hotter G, Closa D, et al. The protective role of adenosine in inducing nitric oxide synthesis in rat liver ischemia preconditioning is mediated by activation of adenosine A2 receptors. Hepatology 1999;29:126–32.
[67] Akgul E, Inal M, Soyupak S, et al. Portal venous variations. Prevalence with contrast-enhanced helical CT. Acta Radiol 2002;43:315–9.
[68] Couinaud C. The anatomy of the liver. Ann Ital Chir 1992;63:693–7.
[69] De Dato M, Sebastiani M, Riccardi M. Anatomic variations of the portal venous bed. Biol Lat 1969;22:177–83.
[70] Gadzijev EM. Surgical anatomy of hepatoduodenal ligament and hepatic hilus. J Hepatobiliary Pancreat Surg 2002;9:531–3.
[71] Kawarada Y, Das BC, Taoka H. Anatomy of the hepatic hilar area: the plate system. J Hepatobiliary Pancreat Surg 2000;7:580–6.
[72] Nakamura T, Tanaka K, Kiuchi T, et al. Anatomical variations and surgical strategies in right lobe living donor liver transplantation: lessons from 120 cases. Transplantation 2002;73:1896–903.
[73] Peri G, Zanoli PG, Trivellini G. Variations and anomalies of the portal trunk. Arch Ital Chir 1969;95:442–53.
[74] Rothlin M, Largiader F. The anatomy of the hepatoduodenal ligament in laparoscopic sonography. Surg Endosc 1994;8:173–80.
[75] van Leeuwen MS, Fernandez MA, van Es HW, et al. Variations in venous and segmental anatomy of the liver: two- and three-dimensional MR imaging in healthy volunteers. AJR Am J Roentgenol 1994;162:1337–45.
[76] Man K, Fan ST, Ng IO, et al. Prospective evaluation of Pringle maneuver in hepatectomy for liver tumors by a randomized study. Ann Surg 1997;226:704–13.
[77] Cherqui D, Malassagne B, Colau PI, et al. Hepatic vascular exclusion with preservation of the caval flow for liver resections. Ann Surg 1999;230:24–30.
[78] Elias D, Dube P, Bonvalot S, et al. Intermittent complete vascular exclusion of the liver during hepatectomy: technique and indications. Hepatogastroenterology 1998;45:389–95.
[79] Elias D, Lasser P, Debaene B, et al. Intermittent vascular exclusion of the liver (without vena cava clamping) during major hepatectomy. Br J Surg 1995;82:1535–9.
[80] Makuuchi M, Mori T, Gunven P, et al. Safety of hemihepatic vascular occlusion during resection of the liver. Surg Gynecol Obstet 1987;164:155–8.
[81] Launois B, Maddern G, Tay KH. The Glissonian approach of the hilum. Swiss Surg 1999;5:143–6.
[82] Matsumata T, Kanematsu T, Shirabe K, et al. Modified technique of Pringle's maneuver in resection of the liver. Surg Gynecol Obstet 1991;172:245–6.
[83] Gallinger S, Langer B. Primary and secondary hepatic malignancies. Curr Opin Gen Surg 1993:257–64.
[84] Belghiti J, Marty J, Farges O. Techniques, hemodynamic monitoring, and indications for vascular clamping during liver resections. J Hepatobiliary Pancreat Surg 1998;5:69–76.
[85] Delva E, Barberousse JP, Nordlinger B, et al. Hemodynamic and biochemical monitoring during major liver resection with use of hepatic vascular exclusion. Surgery 1984;95:309–18.
[86] Nitta N, Yamamoto S, Ozaki N, et al. Is the deterioration of liver viability due to hepatic warm ischemia or reinflow of pooled-portal blood in intermittent portal triad cross-clamping? Res Exp Med (Berl) 1988;188:341–50.
[87] Mackenzie RJ, Furnival CM, Wood CB, et al. The effects of prolonged hepatic ischaemia before 70 per cent partial hepatectomy in the dog. Br J Surg 1977;64:66–9.

[88] Huguet C, Nordlinger B, Galopin JJ, et al. Normothermic hepatic vascular exclusion for extensive hepatectomy. Surg Gynecol Obstet 1978;147:689–93.
[89] Huguet C, Gavelli A, Bona S. Hepatic resection with ischemia of the liver exceeding one hour. J Am Coll Surg 1994;178:454–8.
[90] Yellon DM, Alkhulaifi AM, Pugsley WB. Preconditioning the human myocardium. Lancet 1993;342(8866):276–7.
[91] Yoshizumi T, Yanaga K, Soejima Y, et al. Amelioration of liver injury by ischaemic preconditioning. Br J Surg 1998;85:1636–40.
[92] Isozaki H, Adam R, Gigou M, et al. Experimental study of the protective effect of intermittent hepatic pedicle clamping in the rat. Br J Surg 1992;79:310–3.
[93] van Wagensveld BA, van Gulik TM, Gelderblom HC, et al. Prolonged continuous or intermittent vascular inflow occlusion during hemihepatectomy in pigs. Ann Surg 1999;229:376–84.
[94] Sakamoto Y, Makuuchi M, Takayama T, et al. Pringle's maneuver lasting 322 min. Hepatogastroenterology 1999;46:457–8.
[95] Belghiti J, Noun R, Malafosse R, et al. Continuous versus intermittent portal triad clamping for liver resection: a controlled study. Ann Surg 1999;229:369–75.
[96] Vauthey JN, Chaoui A, Do KA, et al. Standardized measurement of the future liver remnant prior to extended liver resection: methodology and clinical associations. Surgery 2000;127:512–9.
[97] Wakabayashi H, Ishimura K, Okano K, et al. Application of preoperative portal vein embolization before major hepatic resection in patients with normal or abnormal liver parenchyma. Surgery 2002;131:26–33.
[98] Wu CC, Yeh DC, Ho WM, et al. Occlusion of hepatic blood inflow for complex central liver resections in cirrhotic patients: a randomized comparison of hemihepatic and total hepatic occlusion techniques. Arch Surg 2002;137:1369–76.
[99] Couinaud C. Surgical approach to the dorsal section of the liver. Chirurgie 1993;119:485–8.
[100] Chevallier JM. Anatomic basis of vascular exclusion of the liver. Surg Radiol Anat 1988;10:187–94.
[101] Elias D, Lasser P, Rougier P, et al. Frequency, technical aspects, results, and indications of major hepatectomy after prolonged intraarterial hepatic chemotherapy for initially unresectable hepatic tumors. J Am Coll Surg 1995;180:213–9.
[102] Fan MH, Chang AE. Resection of liver tumors: technical aspects. Surg Oncol 2002;10:139–52.
[103] Voyles CR, Vogel SB. Hepatic resection using stapling devices to control the hepatic veins. Am J Surg 1989;158:459–60.
[104] Arnoletti JP, Brodsky J. Reduction of transfusion requirements during major hepatic resection for metastatic disease. Surgery 1999;125:166–71.
[105] McEntee GP, Nagorney DM. Use of vascular staplers in major hepatic resections. Br J Surg 1991;78:40–1.
[106] Jones RM, Moulton CE, Hardy KJ. Central venous pressure and its effect on blood loss during liver resection. Br J Surg 1998;85:1058–60.
[107] Jarnagin WR, Gonen M, Fong Y, et al. Improvement in perioperative outcome after hepatic resection: analysis of 1,803 consecutive cases over the past decade. Ann Surg 2002;236:397–407.
[108] Ramacciato G, Balesh AM, Fornasari V. Vascular endostapler as aid to hepatic vein control during hepatic resections. Am J Surg 1996;172:358–62.
[109] Habib N, Zografos G, Dalla Serra G, et al. Liver resection with total vascular exclusion for malignant tumours. Br J Surg 1994;81:1181–4.
[110] Stephen MS, Sheil AG, Thompson JF, et al. Aortic occlusion and vascular isolation allowing avascular hepatic resection. Arch Surg 1990;125:1482–5.
[111] Emond JC, Kelley SD, Heffron TG, et al. Surgical and anesthetic management of patients undergoing major hepatectomy using total vascular exclusion. Liver Transpl Surg 1996;2:91–8.
[112] Kim YI, Ishii T, Aramaki M, et al. The Pringle maneuver induces only partial ischemia of the liver. Hepatogastroenterology 1995;42:169–71.
[113] Nagasue N, Yukaya H, Ogawa Y, et al. Segmental and subsegmental resections of the cirrhotic liver under hepatic inflow and outflow occlusion. Br J Surg 1985;72:565–8.
[114] Smyrniotis VE, Kostopanagiotou GG, Gamaletsos EL, et al. Total versus selective hepatic vascular exclusion in major liver resections. Am J Surg 2002;183:173–8.
[115] Man K, Fan ST, Ng IO, et al. Tolerance of the liver to intermittent pringle maneuver in hepatectomy for liver tumors. Arch Surg 1999;134:533–9.
[116] Giovanardi RO, Giovanardi HJ, Bozetti M, et al. Intermittent total pedicular clamping in hepatic resections in non-cirrhotic patients. Hepatogastroenterology 2002;49:764–9.
[117] Belghiti J, Hiramatsu K, Benoist S, et al. Seven hundred forty-seven hepatectomies in the 1990s: an update to evaluate the actual risk of liver resection. J Am Coll Surg 2000;191:38–46.
[118] Helling TS. Ruminations of an ordinary hepatic surgeon: a journey through the pitfalls of major liver resections. J Gastrointest Surg 2002;6:625–9.
[119] Nakai T, Koh K, Funai S, et al. Comparison of controlled and Glisson's pedicle transections of hepatic hilum occlusion for hepatic resection. J Am Coll Surg 1999;189:300–4.
[120] Takayama T, Makuuchi M, Inoue K, et al. Selective and unselective clamping in cirrhotic liver. Hepatogastroenterology 1998;45:376–80.
[121] Descottes B, Thognon P, Valleix D, Mendler MH. Major liver resections without vascular clamping: retrospective study of 84 cases. Hepatogastroenterology 1998;45:364–7.
[122] Nuzzo G, Giuliante F, Giovannini I, et al. Liver resections with or without pedicle clamping. Am J Surg 2001;181:238–46.
[123] Buell JF, Koffron A, Yoshida A, et al. Is any method of vascular control superior in hepatic resection of metastatic cancers? Longmire clamping, pringle maneuver, and total vascular isolation. Arch Surg 2001;136:569–75.
[124] Torzilli G, Makuuchi M, Midorikawa Y, et al. Liver resection without total vascular exclusion: hazardous or beneficial? An analysis of our experience. Ann Surg 2001;233:167–75.
[125] Nagasue N, Ono T, Yamanoi A, et al. Prognostic factors and survival after hepatic resection for hepatocellular carcinoma without cirrhosis. Br J Surg 2001;88:515–22.
[126] Rees M, Plant G, Wells J, Bygrave S. One hundred and fifty hepatic resections: evolution of technique towards bloodless surgery. Br J Surg 1996;83:1526–9.
[127] Finch MD, Crosbie JL, Currie E, Garden OJ. An 8-year experience of hepatic resection: indications and outcome. Br J Surg 1998;85:315–9.
[128] Alfierie S, Carriero C, Caprino P, et al. Avoiding early postoperative complications in liver surgery. A multivariate analysis of 254 patients consecutively observed. Dig Liver Dis 2001;33:341–6.
[129] Imamura H, Takayama T, Sugawara Y, et al. Pringle's manoeuvre in living donors. Lancet 2002;360:2049–50.
[130] Wei AC, Tung-Ping Poon R, Fan ST, Wong J. Risk factors for perioperative morbidity and mortality after extended hepatectomy for hepatocellular carcinoma. Br J Surg 2003;90:33–41.
[131] Iwatsuki S, Starzl TE. Personal experience with 411 hepatic resections. Ann Surg 1998;208:421–34.
[132] Brancatisano R, Isla A, Habib N. Is radical hepatic surgery safe? Am J Surg 1998;175:161–3.
[133] Mariette D, Smadja C, Naveau S, et al. Preoperative predictors of blood transfusion in liver resection for tumor. Am J Surg 1997;173:275–9.
[134] Choti MA, Sitzmann JV, Tiburi MF, et al. Trends in long-term survival following liver resection for hepatic colorectal metastases. Ann Surg 2002;235:759–66.
[135] Wu CC, Kang SM, Ho WM, et al. Prediciton and limitation of hepatic tumor resection without blood transfusion in cirrhotic patients. Arch Surg 1998;133:1007–10.