Vascular Occlusions for Liver Resections

Operative Management and Tolerance to Hepatic Ischemia: 142 Cases

ERIC DELVA, M.D.,* YVON CAMUS, M.D.,* BERNARD NORDLINGER, M.D.,† LAURENT HANNOUN, M.D.,† ROLLAND PARC, M.D.,† HUGUES DERIAZ, M.D.*, ANDRÉ LIENHART, M.D.,* and CLAUDE HUGUET, M.D. ‡

The intra- and early postoperative courses of 142 consecutive patients who underwent liver resections using vascular occlusions to reduce bleeding were reviewed. In 127 patients, the remnant liver parenchyma was normal, and 15 patients had liver cirrhosis. Eighty-five patients underwent major liver resections: right, extended right, or left lobectomies. Portal triad clamping (PTC) was used alone in 107 cases. Complete hepatic vascular exclusion (HVE) combining PTC and occlusion of the inferior vena cava below and above the liver was used for 35 major liver resections. These 35 patients had large or posterior liver tumors, and HVE was used to reduce the risks of massive bleeding or air embolism caused by an accidental tear of the vena cava or a hepatic vein. Duration of normothermic liver ischemia was 32.3 ± 1.2 minutes (mean ± SEM) and ranged from 8 to 90 minutes. Amount of blood transfusion was 5.5 ± 0.5 (mean ± SEM) units of packed red blood cells. There were eight operative deaths (5.6%). Overall, postoperative complications occurred in 46 patients (32%). The patients who experienced complications after surgery had received more blood transfusion than those with an uneventful postoperative course ($p < 0.001$). The length of postoperative hospital stay was also correlated with the amount of blood transfused during surgery ($p < 0.001$). On the other hand, there was no correlation between the durations of liver ischemia of up to 90 minutes and the lengths of postoperative hospital stay. The longest periods of ischemia were not associated with increased rates of postoperative complications, liver failures, or deaths. There was no difference in mortality or morbidity after major liver resections performed with the use of HVE as compared with major liver resections carried out with PTC alone, although the lesions were larger in the former group. It is concluded that the main priority during liver resections is to reduce operative bleeding. Vascular occlusions aim at achieving this goal and can be extended safely for up to 60 minutes.

INTRAOPERATIVE BLEEDING is the main risk during liver resections. Hepatic inflow occlusion is one of the methods that can be used to reduce this risk.

Presented in part at the First World Congress of Hepatico-Pancreatico Biliary Surgery, June 9–13, 1986, Lund, Sweden.

Reprint requests and correspondence: Eric Delva, M.D., Département d'Anesthésie-Réanimation, Hôpital Saint-Antoine, 184, rue du Faubourg Saint-Antoine, 75571 Paris Cedex 12, France.

Submitted for publication: April 28, 1988.

From the Departments of Anesthesia and Intensive Care and Digestive Surgery,† Saint-Antoine Hospital, Paris, France, and the Department of Surgery,‡ Princess Grace Hospital, Monaco*

Temporary portal triad clamping (PTC), the Pringle maneuver,[1] can minimize the bleeding from the raw surface of the liver during parenchymal transection. But it has no effect on the bleeding from branches of the hepatic veins. Hepatic vascular exclusion (HVE) associates PTC and occlusion of the inferior vena cava below and above the liver.[2-4] It completely isolates the liver and the retrohepatic vena cava from the rest of the circulation. Its aim is to reduce the risks of massive hemorrhage and air embolism caused by a tear of the vena cava or a hepatic vein during the removal of large or posterior liver tumors.

Both types of vascular occlusions result in liver ischemia. The duration of ischemia depends on the extent of liver resection and varies within a relatively wide range, sometimes exceeding 1 hour. Although it is now accepted that the human liver can tolerate a period of normothermic ischemia extending beyond the classical limit of 15–20 minutes,[3-6] it is not yet known if the duration of ischemia influences the surgical outcome.

The aim of this study is to evaluate the role of different factors, particularly the duration of liver ischemia, in intraoperative and early postoperative courses. For this purpose our experience with 142 liver resections performed with vascular occlusions is reported.

Patients and Methods

Patients

Between January 1980 and November 1985, 153 patients underwent liver resections. Eleven minor liver resections were performed without the use of vascular oc-

TABLE 1. *Indications for 142 Liver Resections*

Indications	No. of Patients
Malignant diseases	
Primary liver neoplasms	31
Metastatic neoplasms	64
Direct invasion	10
Benign diseases	
Benign liver tumors	18
Trauma	2
Miscellaneous	17

clusion and were not included in the study. The intra- and early postoperative courses of the 142 patients who underwent liver resection using hepatic vascular arrest were analyzed. There were 72 men and 70 women, with a mean age of 54 ± 1 years (plus minus values are mean ± SEM). Indications for liver resection were malignant tumors in 105 patients and benign disease in another 37 patients (Table 1). Remnant liver parenchyma was normal in all but 15 patients, who had liver cirrhosis. A loss of weight was observed before surgery in 37 patients (6.2 ± 0.7 kg), seven of whom received preoperative parenteral or continuous enteral nutrition.

Intraoperative Management

Anesthesia. Anesthesia was induced and maintained with a combination of thiopental, narcotic, and pancuronium. In addition, 62 patients received droperidol, and 49 received enflurane (0.4–0.8%). Ventilation was controlled throughout anesthesia with a nitrous oxide/oxygen mixture (60/40). Radial artery pressure was monitored in 128 patients, and central venous pressure was monitored in 113; the pulmonary artery pressure was measured through a Swan-Ganz® (Edwards Laboratory) catheter in 91 patients, and cardiac output determined by thermodilution in 84.

Dextrose and crystalloids were infused at a mean rate of 14 $ml/kg^{-1}/hour^{-1}$, and 49 patients received colloids (745 ± 69 ml). We have abandoned prophylactic alkalinization;[4] sodium bicarbonate was administered rarely, ccording to the results of blood gas analysis only. Prophylactic betalactamas was administered to 113 patients (cefoxitin to 90 patients) in association with aminoglycoside or metronidazole in 20 patients.

Operative Procedure. The abdomen was opened through a bilateral subcostal incision in 118 patients, which was extended by a right thoracotomy in seven. An upper midline incision was used in the remaining 24 patients. Eighty-five patients underwent major liver resections: 47 right lobectomies, 25 extended right lobectomies, and 13 left lobectomies. Fifty-seven patients underwent minor liver resections: 21 left lateral segmentectomies and 36 segmental or subsegmental resections.

PTC alone was used in 107 cases. HVE was used for 35 major liver resections. In seven of the patients, the supraceliac aorta had been cross-clamped before HVE. Neither topical refrigeration nor hypothermic perfusion of the liver was used. Duration of normothermic liver ischemia was 32.3 ± 1.2 minutes and ranged from 8 to 90 minutes : 30.4 ± 1.4 minutes under PTC (8–70 minutes) and 40.0 ± 2.2 minutes under HVE (18–90 minutes). Duration of liver ischemia was longer for major liver resections (38.2 ± 1.5 minutes) than for minor liver resections (24.7 ± 1.5 minutes; $p < 0.001$). During liver ischemia, mean body temperature was 34.9 ± 0.1 C.

Liver transection was carried out by hemostat or finger fracture without previous ligation of hilar vessels or hepatic veins. Main vascular or biliary tracts were individually secured by vascular clips or ligatures on the raw surface of the liver.

Synchronous Procedures (n = 18). The biliary continuity was restored with a hepaticojejunostomy after liver resection in seven patients, one of whom also required a tangential resection of the portal vein. A portacaval shunt was concomitantly performed in a cirrhotic patient. Nine patients with secondary liver deposits or a tumor invading the liver had synchronous excision of the primary tumor/intestinal resection (n = 4), total gastrectomy and splenectomy (n = 3), and adrenalectomy and right nephrectomy in continuity (n = 2) necessitating complete resection with reconstruction of the suprarenal inferior vena cava in one patient. Complete resection without reconstruction of the retrohepatic inferior vena cava was associated with an extended right lobectomy in one patient.

The mean duration of the procedure was 4 hours 9 minutes ± 7 minutes: 3 hours and 28 minutes for minor liver resections, 4 hours and 38 minutes for major liver resections ($p < 0.001$)

Blood transfusion. The mean amount of intraoperative blood transfusions was 5.5 ± 0.5 units of packed red blood cells (PRBC) and 5.6 ± 0.5 units of fresh frozen plasma (FFP). Sixteen patients did not receive any unit of PRBC. Two patients required platelet concentrates. Blood transfusions were greater in major liver resections (7.0 ± 0.7 units of PRBC) than in minor liver resections (3.3 ± 0.4 units of PRBC; $p < 0.001$). Massive intraoperative hemorrhage (defined as requiring more than 10 units of PRBC) occurred in 15 patients. In eleven patients, bleeding began before liver transection and was due to a synchronous procedure (n = 3), or to a difficult liver mobilization (n = 8), which resulted mostly from previous liver surgery. In two patients, PTC failed to prevent bleeding from branches of the hepatic veins during liver transection. Clamps were applied to the inferior vena cava in order to complete HVE. They were well-tolerated in one patient, allowing the resection to be finished safely, but had to be released in the second patient because of a poor hemo-

TABLE 2. *Operative Mortality*

Patient No.	Age/Sex (years)	Diagnosis	Procedure	Cause of Death	Day
1	69/F	Metastatic neoplasm	RL	Uncontrollable hemorrhage	Intraoperative
2	72/M	Hilar sclerosing cholangitis	ERL Hepaticojejunostomy	Persistent bleeding	0
3	63/M	Cholangiocarcinoma	ERL	Ruptured esophageal varices; portal thrombosis	23
4	69/M	Metastatic neoplasm	ERL	Unknown	1
5	55/M	Metastatic neoplasm	ERL	Liver failure	27
6	56/M	Malignant retroperitoneal tumor	ERL Right nephrectomy Inferior vena cava resection	Acute renal failure; pulmonary edema	5
7	72/F	Hepatocarcinoma in cirrhotic liver	Segmental resection	Liver failure	6
8	55/M	Hepatocarcinoma in cirrhotic liver	Double segmental resections	Liver failure; gastric bleeding	6

RL = right lobectomy. ERL = extended right lobectomy.

dynamic tolerance. In the remaining two patients, massive bleeding appeared after removal of the clamp on the portal triad and was responsible for the only intraoperative death. Massive bleeding resulted in hemorrhagic shock in seven patients, who required vasopressors and sodium bicarbonate.

Postoperative Management

One hundred nineteen patients were extubated in the recovery room and thirteen were extubated the following morning. After surgery, all of the patients were admitted to the surgical intensive care unit. Eight were ventilated after the first postoperative day for 4.6 ± 0.8 days. Swan-Ganz catheters were almost always removed during the first 24 hours.

Within the 24 first hours, FFP was administered to 55 patients (3.1 ± 0.4 units) and albumin to 13 patients (34 ± 4 g). After Day 1, FFP was given to 72 patients (4.3 ± 0.4 units) and albumin to 49 patients (60 ± 6 g). All patients received intravenous infusion of dextrose (214 ± 3 g/day) for a mean duration of 6.1 ± 0.4 days. Total parenteral nutrition was administered to 19 patients for 5 ± 1 days, and continuous enteral nutrition was used in twelve patients for 14 ± 2 days. Insulin was required in 59 patients during the 24 first hours (20 ± 1 units) and was continued in 13 patients for 6 ± 2 days.

Antibiotics were administered after surgery in 115 patients (betalactamin alone or in association with aminoglycaside and/or metronidazole).

Statistical Analysis

Any death that occurred within 30 days after liver resection, as well as any death that occurred during the initial hospitalization for liver resection, was included in operative mortality. The length of stay in surgical intensive care unit (ICU stay) and the length of postoperative stay in the hospital are reported for patients who survived surgery.

Different factors were analyzed in order to determine any correlation between operative mortality and morbidity: patient age, presence or absence of liver cirrhosis, extent of liver resection (major *vs.* minor liver resections and weight of specimen), amount of blood transfused during surgery, and duration of liver ischemia.

Differences between groups were tested with analysis of variance and Fisher's least significant difference. The chi-square test was used to determine statistical significance of difference in the frequency of variables between groups. Correlation was evaluated by standard linear regression analysis. All values are presented as mean ± SEM. A p value of less than 0.05 was considered statistically significant.

Results

Operative Mortality

As shown in Table 2, there were eight deaths, accounting for an overall operative mortality of 5.6%. Massive bleeding from the raw surface of the liver was responsible for the only intraoperative death (Patient 1) and for one death caused by persistent hemorrhage despite early reoperation (Patient 2). Three patients, two of whom had cirrhosis, died of liver failure (Patients 5, 7, and 8). One patient (Patient 3) died of ruptured esophageal varices caused by a portal vein thrombosis. The patient who underwent an extended right lobectomy associated with a right nephrectomy and complete resection with reconstruction of the suprarenal inferior vena cava died of acute renal failure and pulmonary edema (Patient 6). One patient died suddenly of an unknown cause after an un-

TABLE 3. *Biochemical Liver Tests Before and After Liver Resections**

	Before Surgery	Day 1	Day 3	Day 7
Serum alanine transaminase (IU/l)	44.8 ± 6.3	197.5 ± 19.5†	100.5 ± 10.6†‡	55.4 ± 4.9‡
Serum aspartate transaminase (IU/l)	41.3 ± 6.5	189.9 ± 16.8†	52.6 ± 3.5‡	41.2 ± 4.8‡
Prothrombin (per cent of normal)	85.5 ± 1.2	58.5 ± 1.2†	68.6 ± 1.6†‡	67.7 ± 2.7†‡
Proaccelerin (per cent of normal)	94.7 ± 1.1	61.3 ± 1.6†	71.4 ± 2.2†‡	75.4 ± 3.9†‡
Albumin (g/l)	38.5 ± 1.0	34.3 ± 0.7†	33.7 ± 0.7†	33.8 ± 0.8†
Total Protein (g/l)	69.9 ± 0.8	57.8 ± 0.7†	58.8 ± 0.8†	59.7 ± 1.0†
Platelet Count (10^3/ml)	285 ± 12	185 ± 9†	189 ± 11†	225 ± 24†

* Values are mean ± SEM.
† $p < 0.05$ *versus* before surgery.
‡ $p < 0.05$ *versus* Day 1.

eventful extended right lobectomy (Patient 4). Postmortem examination of this patient could not be obtained.

Postoperative Morbidity

Including the lethal complications, 46 patients (32%) had one or more postoperative complications. Nine patients required reoperation for postoperative bleeding and one for hemothorax. Fourteen patients had subphrenic abscesses, which in seven instances were drained by reoperation. Subphrenic abscesses occurred and required reoperation more frequently in patients who did not receive intraoperative antibiotic (eight of 39 patients; six reoperations) than in the others (five of 103 patients; no reoperation; $p < 0.001$). Hepatic failure occurred in nine patients and was more frequent in patients with cirrhosis (five of 15 patients) than in patients without cirrhosis (four of 127; $p < 0.001$). Other complications included pleural effusion (17 patients), pneumonia or atelectasis (four patients) major gastrointestinal hemorrhage (four patients) bile leakage (four patients), wound infection (four patients), renal insufficiency requiring only conservative therapy (three patients), and wound rupture (one patient).

The mean length of stay in the ICU and in the hospital was 6.3 ± 0.6 days (range of 0–41 days) and 17.7 ± 0.8 days (range of 5–69 days), respectively. Length of stay was longer for patients with complications (ICU stay of 9.5 ± 1.7 days, hospital stay of 25.0 ± 1.9 days) than for patients without complication (ICU stay of 5.0 ± 0.4 days, $p < 0.001$; hospital stay of 14.8 ± 0.6 days, $p < 0.001$).

Liver Function Tests

Changes in biochemical liver tests are presented in Table 3. Levels of serum alanine transaminase and serum aspartate transaminase showed a peak on the first postoperative day (five times the preoperative levels) and rapidly decreased within a few days. No correlation was observed between the level of transaminases on Day 1 and the duration of liver ischemia or the extent of liver resection. Prothrombin and proaccelerin levels decreased on Day 1 and then increased, but remained below the preoperative levels during the first week. The fall in prothrombin and proaccelerin levels was greater after major liver resections than after minor resections. Serum albumin concentrations decreased after surgery and remained low during the first week. No statistically significant difference in serum albumin concentration was observed when comparing the patients who had minor liver resections with those who had undergone major resections. However, after surgery,this latter group received a larger amount of FFP and albumin ($p < 0.01$). In patients with cirrhosis, the levels of prothrombin, proaccelerin, and serum albumin remained lower throughout the postoperative stay than they did in patients without cirrhosis. The fall in platelet count on Day 1 correlated with the amount of blood transfused during surgery ($r = 0.481$ $p < 0.001$).

Incidence of Several Factors on Mortality and Morbidity

Age of the patients. No patients under 50 years of age died. Patients who died after surgery were older than survivors (63.9 ± 2.7 *vs.* 52.9 ± 1.3 years; $p < 0.05$). However, there was no increase with age in the complications rate or the lengths of ICU stay and hospital stay.

Liver cirrhosis. Age of the patients, ratio of major/minor liver resections, specimen weight, amount of blood transfusion, and duration of liver ischemia were similar in patients both with and without cirrhosis (Table 4). Liver failure occurred more frequently in patients with cirrhosis ($p < 0.001$). Although the difference in mortality was not significant when compared with patients without cirrhosis, the mortality rate reached 13.3% in patients with cirrhotic liver.

Extent of liver resection. For all patients, the length of ICU stay and postoperative stay were correlated with the weight of liver specimen ($r = 0.418$, $p < 0.001$, and $r = 0.232$, $p < 0.05$, respectively). Patients who had undergone major liver resections stayed for a longer period in the surgical department, and their complications rate was greater than after minor liver resections (Table 5). Except in two cirrhotic patients, no death occurred after minor liver resections.

Amount of blood transfused. The amount of blood

TABLE 4. *Influence of Liver Cirrhosis**

Variables	Normal Liver	Cirrhosis
Number of patients	127	15
Major liver resection	78 (61%)	7 (47%)
Intraoperative blood transfusion (units of PRBC)	5.3 ± 0.5	7.3 ± 0.9
Ischemia duration (minutes)	32.6 ± 1.2	34.1 ± 4.2
Length of ICU stay (days)	6.2 ± 0.6	7.1 ± 1.4
Length of hospital stay (days)	17.5 ± 0.9	19.1 ± 1.5
Patients with complication	39 (31%)	7 (47%)
Liver failure	4 (3%)	5 (33%)†
Mortality	6 (4.7%)	2 (13.3%)

* Plus-minus values are mean ± SEM.
† $p < 0.001$ *versus* normal liver.

TABLE 5. *Influence of the Extent of Liver Resections**

Variables	Minor Liver Resections	Major Liver Resections
Number of patients	57	85
Cirrhosis	8 (14%)	7 (8%)
Intraoperative Blood Transfusion (units of PRBC)	3.3 ± 0.4	7.0 ± 0.7‡
Ischemia duration (minutes)	24.7 ± 1.5	38.2 ± 1.5‡
Length of ICU stay (days)	5.1 ± 0.7	7.1 ± 0.8
Length of hospital stay (days)	15.7 ± 1.0	19.0 ± 1.2†
Patients with complication	9 (16%)	37 (44%)‡
Hepatic failure	3 (5%)	6 (7%)
Mortality	2 (3.5%)	6 (7.1%)

* Plus-minus values are mean ± SEM.
† $p < 0.05$.
‡ $p < 0.001$ *versus* minor liver resections.

transfused was greater for patients who died (11.6 ± 2.9 units of PRBC) than for patients who survived after surgery (5.2 ± 0.5 units, $p < 0.01$), and was likewise greater for patients with a complicated postoperative course (8.2 ± 1.2 units of PRBC) than for patients without complication (4.3 ± 0.4 units, $p < 0.001$). Lengths of ICU stay and hospital stay correlated with the amount of PRBC units transfused during operation ($r = 0.675$, $p < 0.001$, and $r = 0.485$, $p < 0.001$, respectively). The 15 patients who received more than 10 units of PRBC during surgery were compared with those who had received less than 10 units (Table 6). The first group demonstrated increased mortality, morbidity, and length of ICU and hospital stays.

Duration of liver ischemia. Two groups of patients were compared: patients in whom the duration of liver ischemia was less than 45 minutes (28.3 minutes ± 0.8 minutes; range of 8–44 minutes) and patients in whom the duration of ischemia exceeded 45 minutes (55.9 minutes ± 2.9 minutes; range of 45–90 minutes) (Table 7). Major liver resections were more frequent in this latter group. However, no other difference between the two groups was observed concerning mortality rate, incidence of liver failure or other complications, and length of ICU and hospital stays.

In this population, there was no correlation between the durations of liver ischemia, the length of ICU and hospital stays, and the serum levels of transaminases after surgery.

Type of hepatic vascular arrest. We have compared the 35 patients who underwent major liver resection using HVE with the 50 patients undergoing major liver resection using PTC only (Table 8). The size of liver resection was greater in patients undergoing liver resection using HVE than those undergoing liver resection using PTC. None of the other criteria differed significantly between the two groups.

Discussion

Temporary inflow occlusion of the liver is an easy way to obviate the risk of arterial and portal venous bleeding during liver resections. However, although the method was described in 1908 by Pringle,[1] because of fear of deleterious consequences, it has received little clinical application for more than 70 years.

PTC results in general hemodynamic effects on one hand and liver ischemia on the other. For many years it has been studied only in laboratory animals. Acute occlusion of the portal vein is poorly tolerated in dogs.[7,8] It results in a rapid cardiovascular collapse and death within 1 hour. The main factor is the reduction of the circulating blood volume due to the sequestration of blood in the splanchnic bed.[8,9] Most laboratory animals have very few spontaneous portosystemic collateral veins. As a consequence, they survive portal occlusion only if provision is made for escape of blood from the portal to the systemic circulation. This can be achieved by progressive ligation

TABLE 6. *Influence of Blood Transfusion: Comparison of Patients Who Received More or Less than 10 Units of PRBC During Surgery**

Variables	Intraoperative Blood Transfusion ≤ 10 units of PRBC	Intraoperative Blood Transfusion > 10 units of PRBC
Number of patients	127	15
Cirrhosis	12 (9%)	3 (20%)
Major liver resection	72 (57%)	13 (87%)†
Intraoperative Blood Transfusion (units of PRBC)	4.0 ± 0.2	18.3 ± 2.3‡
Ischemia duration (minutes)	32.0 ± 1.1	39.4 ± 5.7
Length of ICU stay (days)	5.2 ± 0.4	17.9 ± 4.2‡
Length of hospital stay (days)	16.7 ± 0.7	28.7 ± 5.3‡
Patients with complication	37 (29%)	9 (60%)†
Liver failure	7 (6%)	1 (7%)
Mortality	4 (3.1%)	4 (26.7%)‡

* Plus-minus values are mean ± SEM.
† $p < 0.05$.
‡ $p < 0.001$ *versus* patients who received less than 10 units of PRBC.

TABLE 7. *Influence of Liver Ischemia: Comparison of Patients in Whom Ischemia Lasted More or Less than 45 Minutes**

Variables	Duration of Liver Ischemia < 45 Minutes	Duration of Liver Ischemia ≥ 45 Minutes
Number of patients	119	23
Cirrhosis	11 (9%)	4 (17%)
Major liver resection	66 (55%)	19 (83%)†
Intraoperative blood Transfusion (units of PRBC)	5.2 ± 0.5	7.4 ± 0.8
Ischemia duration (minutes)	28.3 ± 0.8	55.9 ± 2.9‡
Length of ICU stay (days)	6.0 ± 0.7	7.5 ± 0.8
Length of hospital stay (days)	17.3 ± 0.9	19.7 ± 1.8
Patients with complication	37 (31%)	9 (39%)
Liver failure	7 (6%)	2 (9%)
Mortality	7 (5.9%)	1 (4.3%)

* Plus-minus values are mean ± SEM.
† $p < 0.05$.
‡ $p < 0.001$ *versus* patients with hepatic ischemia duration below 45 minutes.

of the portal vein[7] or by an external shunt.[10] In humans and primates, clamping the portal vein is better tolerated because of a more efficient portosystemic collateral network through which splanchnic blood can return to the heart.[11] In dogs, occlusion of the whole portal triad produces the same dramatic cardiovascular consequences as portal occlusion.[12] In humans, the hemodynamic response is clearly different;[13] PTC induces a small decrease in cardiac output, whereas arterial pressure increases.

In patients with large or posterior tumors, the main risk is related to massive hemorrhage or air embolism if a hepatic vein or the inferior vena cava is accidently torn during the liver transection.[14] In these patients, PTC can be associated with occlusion of the inferior vena cava below and above the liver to achieve complete HVE.[2-4] HVE performed for partial liver resections includes the same vascular occlusions as the anhepatic period of liver transplantation. Their hemodynamic effects are now well-known;[4,15,16] arterial pressure is maintained despite a 50% decrease in cardiac output. The duration of HVE for partial liver resections is shorter than for liver transplantations and is usually well-tolerated. There is no need for the administration of vasopressors or the insertion of a venovenous bypass. Moreover, aortic cross-clamping—which, in combination with HVE, was used in patients treated early in order to improve its hemodynamic tolerance[2,3]—is necessary only when a good complete exclusion of the liver cannot be obtained by the venous occlusions of HVE. Intraoperative metabolic consequences of hepatic vascular isolation are also mild, transient, and spontaneously reversible.[4]

TABLE 8. *Influence of the Type of Vascular Occlusion in Patients Undergoing Major Liver Resections: Comparison of Portal Triad Clamping with Hepatic Vascular Exclusion**

Variables	Portal Triad Clamping Group	Hepatic Vascular Exclusion Group
Number of patients	50	35
Specimen weight (g)	730 ± 56	1271 ± 108†
Ischemia duration (minutes)	36.8 ± 2.0	40.0 ± 2.2
Intraoperative blood transfusion (units of PRBC)	6.3 ± 0.7	8.0 ± 1.4
Length of ICU stay (days)	6.4 ± 0.5	8.3 ± 1.9
Length of hospital stay (days)	19.3 ± 1.2	18.6 ± 2.2
Patients with complication	22 (44%)	15 (43%)
Liver failure	4 (8%)	2 (5.7%)
Mortality	3 (6.0%)	3 (8.9%)

* Plus-minus values are means ± SEM
† $p < 0.001$ *versus* PTC group.

The classical belief that human liver cannot tolerate normothermic ischemia for longer than 15–20 minutes had led many surgeons to restrict the use of PTC to critical hemorrhagic circumstances, or to release the clamps at fixed time intervals. In 1978, Huguet et al.[5] showed in patients undergoing elective liver resections that the human liver could withstand a much longer period of normothermic ischemia. This was confirmed later by trauma surgeons.[6,17] This study shows that normothermic ischemia of the liver is well-tolerated for periods as long as 90 minutes. Operative mortality and morbidity after liver resections are not modified by the duration of hepatic vascular inflow occlusion within these limits. The longest periods of ischemia required for either the resection of large lesions or when surgical difficulties occurred were not associated with an increased mortality or with higher rates of postoperative complications, liver failure, or prolonged postoperative hospital stays.

The overall mortality rate of 5.7% is in the same range as that published in other recent series of patients who underwent operation in specialized institutions.[18-23] After minor liver resections, the mortality rate was nil when the remnant liver parenchyma was normal; two deaths due to postoperative liver failure have occurred in patients with cirrhosis.

We have considered as major liver resections only right, extended right, and left lobectomies, excluding left lateral segmentectomies. Thirty-five of these major hepatic resections have been performed with HVE because the tumors had previously been considered as either entirely nonresectable or safely nonresectable without the use of this method. The mortality rate was 7.1% in all patients with major liver resections, 6% in those in whom only the liver pedicle had been clamped, and 8.9% in the group with complete HVE. Thus HVE has allowed the ability to perform the most extended and hazardous liver resections with the same mortality rate as that of standard major liver resections.

Intraoperative bleeding can be reduced by vascular occlusions during the phase of liver transection. In 127 patients, 72 of whom have undergone a major liver resection, the mean amount of blood transfusion was only four units of PRBC. However, vascular occlusions are of no help during the period of dissection and mobilization of the liver. Bleeding at that time is related mainly to the large size of the lesions, their hypervascularization, local extension, or adhesions due to previous liver surgery; eleven of the 15 patients who received more than 10 units of PRBC during surgery bled during preliminary dissection of the liver.

This study confirms the relation between amounts of blood lost and replaced and the rate of perioperative complications in major liver surgery.[21-23] Of course, it is obvious that the patients who received the larger amounts of blood and had a complicated postoperative course were usually those who had undergone the most extensive or difficult procedures. Extensive surgical dissections and large hepatic raw surfaces may result in imperfect local hemostasis that is associated with an increased risk of subphrenic fluid collections or abcesses and secondary pleural effusions. In liver surgery, bleeding can lead to hemorrhagic shock and its consequences. Moreover, blood transfusion itself behaves as an independent factor contributing to multiple organ failure.[24] This contribution cannot be attributed to the underlying conditions that required blood transfusion. Thus it appears preferable to take the necessary time to obtain a good local hemostasis, even if it requires an increased duration of vascular occlusions, rather than lose more blood with an imperfect hemostasis.

Blood transfusion may worsen the coagulation disorders observed in liver surgery.[25] Our transfusion regimen associated FFP with red blood cells. The policy of blood replacement recently advocated that suggests the restriction of FFP administration[26] and its replacement by crystalloid or colloid solutions may be dangerous during major liver resections that are frequently associated with a reduction of coagulation factors and an increased fibrinolysis.[27,28] In this series, we have observed significant blood coagulation disorders with nonmechanical bleeding only in the two patients who suffered hemorrhage at removal of the clamp.

Liver failure is a postoperative complication specifically related to liver resection. It was responsible for three of eight deaths that occurred in-hospital and for most of the prolonged hospital stays. Its occurrence is related to the quantity and the quality of the remnant liver parenchyma. When the remnant liver is normal, hepatic failure hardly ever occurs, except when an extensive resection of normally functioning parenchyma is required for the removal of a poorly located small lesion, particularly in the case of an extended right lobectomy. On the other hand, hepatic failure occurs frequently after resection in the presence of liver cirrhosis. The proportion of liver resections carried out in patients with cirrhosis in different series published in the literature[18-23,29-31] accounts for the many discrepancies in mortality rates observed among them. In patients with cirrhosis, large liver resections are usually associated with an increased risk of operative mortality. In recent series, most of which are from Asia, an improved prognosis seems to be related to a better selection of patients with cirrhosis[29] and an increased proportion of limited liver resections.[30,31] In our series, a 13.3% mortality rate was observed in the 15 patients with cirrhosis, although seven patients underwent major liver resection. Vascular occlusions were used in all of these patients in order to reduce blood loss during surgery and were well-tolerated for up to 60 minutes. A similar experience was reported by Nagasue et al.[32] for segmental liver resections in patients with cirrhosis; postoperative mortality and morbidity was reduced by minimizing blood loss with the help of hepatic vascular arrest, which lasted for up to 47 minutes. Thus, patients with liver cirrhosis appear to behave similarly to those with a normal hepatic parenchyma during liver resections and tolerate liver ischemia within certain limits better than they do the consequences of massive bleeding and blood transfusion.

Because operative blood loss is the main factor of early prognosis after liver resections, the first operative priority should be to reduce bleeding. Vascular occlusions aim at achieving this goal and allow 90% of liver resections with blood transfusions of less than 10 units of PRBC to be performed. Most liver resections may be carried out with PTC alone. PTC can also be associated with the occlusion of the inferior vena cava in order to obtain a complete HVE. This method reduces the risks of massive hemorrhage or air embolism if the vena cava or a hepatic vein is accidently torn during resection. It should therefore be reserved to large or posterior tumors that can thereby be removed with low mortality and morbidity rates. This study demonstrates that the human liver can tolerate normothermic ischemia for up to 90 minutes. Thus it seems preferable to take the time necessary for obtaining a good local hemostasis under vascular occlusions, even if this requires increasing the duration of liver ischemia, rather than hurry and lose more blood.

References

1. Pringle JH. Notes on the arrest of hepatic hemorrhage due to trauma. Ann Surg 1908; 48:541–549.
2. Heaney JP, Stanton WK, Halbert DS, et al. An improved technic for vascular isolation of the liver. Ann Surg 1966; 163:237–241.

3. Huguet C, Nordlinger B, Galopin JJ, et al. Normothermic hepatic vascular exclusion for extensive hepatectomy. Surg Gynecol Obstet 1978; 147:689–693.
4. Delva E, Barberousse JP, Nordlinger B, et al. Hemodynamic and biochemical monitoring during major liver resection with use of hepatic vascular exclusion. Surgery 1984; 95:309–318.
5. Huguet C, Nordlinger B, Bloch P, Conrad J. Tolerance of human liver to prolonged normothermic ischemia. Arch Surg 1978; 113: 1448–1451.
6. Pachter HL, Spencer FC, Hofstetter SR, Coppa GF. Experience with the finger fracture technique to achieve intrahepatic hemostasis in 75 patients with severe injuries of the liver. Ann Surg 1983; 197:771–778.
7. Bernard C. Lecons Sur les Propritéés Physiologiques et les Altérations Pathologiques des Liquides de L'organisme. Paris: JB Baillière et Fils, 1859; 190–195.
8. Johnstone FRC. Acute ligation of the portal vein. Surgery 1957; 41: 958–971.
9. Bernard C. Lecons Sur le Diabéte et la Glycogenèse Animale. Paris: JB Baillière et Fils, 1877; 316–317.
10. Nordlinger B, Douvin D, Javaudin L, et al. An experimental study of survival after two hours of normothermic hepatic ischemia. Surg Gynecol Obstet 1980; 150:859–864.
11. Child CG, Milnes RF, Holswade GR, Gore AL. Sudden and complete occlusion of the portal vein in the macaca mulatta monkey. Ann Surg 1950; 132:475–494.
12. Raffucci FL. The effects of temporary occlusion of the afferent hepatic circulation in dogs. Surgery 1953; 33:342–351.
13. Delva E, Camus Y, Paugam C, et al. Hemodynamic effects of portal triad clamping in humans. Anesth Analg 1987; 66:864–868.
14. Iwatsuki S, Geis WP. Hepatic complications. Surg Clin North Am 1977; 57:1335–1356.
15. Carmichael FJ, Lindop MJ, Farman JV. Anesthesia for hepatic transplantation: cardiovascular and metabolic alterations and their management. Anesth Analg 1985; 64:108–116.
16. Delva E, Huguet C, Camus Y, et al. Hemodynamic effects of suprahepatic inferior vena cava clamping with hepatic vascular exclusion. Anesthesiology 1986; 65:A409.
17. Feliciano DV, Jordan GL, Bitondo CG, et al. Management of 1000 consecutive cases of hepatic trauma (1979–1984). Ann Surg 1986; 204:438–445.
18. Iwatsuki S, Shaw BW, Starzl TE. Experience with 150 liver resections. Ann Surg 1983; 197:247–253.
19. Thompson HH, Tompkins RK, Longmire WP. Major hepatic resection. Ann Surg 1983; 197:375–388.
20. Tsuzuki T, Ogata Y, Iida S, Shimazu M. Hepatic resection in 125 patients. Arch Surg 1984; 119:1025–1032.
21. Nagao T, Inoue S, Mizuta T, et al. One hundred hepatic resections. Ann Surg 1985; 202:42–49.
22. Ekberg H, Tranberg K-G, Andersson R, et al. Major liver resection: perioperative course and management. Surgery 1986; 100: 1–7.
23. Gennari L, Doci R, Bozzetti F, Bignami P. Surgical treatment of hepatic metastases from colorectal cancer. Ann Surg 1986; 203: 49–54.
24. Maetani S, Nishikawa T, Hirakawa A, Tobe T. Role of blood transfusion in organ system failure following major abdominal surgery. Ann Surg 1986; 203:275–281.
25. Clagett GP, Olsen WR. Non-mechanical hemorrhage in severe liver injury. Ann Surg 1978; 187:369–374.
26. Fresh-frozen plasma: indications and risks. Consensus Conference, NIH. JAMA 1985; 253:551–553.
27. Nilehn JE, Nilsson IM, Aronsen KF, Ericsson B. Studies on blood clotting factors in man after massive liver resection. Acta Chir Scand 1967; 133: 189–195.
28. Conard J, Moérisot P, Huguet C. Les troubles de l'hémostase au cours des hpatectomies partielles. Nouv Presse Med 1976; 5: 2519–2523.
29. Nagasu N, Yukaya H, Ogawa Y, et al. Clinical experience with 118 hepatic resections for hepatocellular carcinoma. Surgery 1986; 99:694–701.
30. Kanematsu T, Takenaka K, Matsumata T, et al. Limited hepatic resection effective for selected cirrhotic patients with primary liver cancer. Ann Surg 1984; 199:51–56.
31. Lee CS, Sung JL, Hwang LY, et al. Surgical treatment of 109 patients with symptomatic and asymptomatic hepatocellular carcinoma. Surgery 1986; 99:481–490.
32. 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; 72:565–568.