The Safety of Continuous Hepatic Inflow Occlusion During Major Liver Resection

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To evaluate the safety of temporary hepatic inflow occlusion during major liver resection, we reviewed 71 consecutive noncirrhotic patients who underwent elective liver resection using this technique. There were 27 males and 44 females (mean age, 54.4 years), the majority of whom had hepatic malignancies. There were 31 right hepatectomies, 21 left hepatectomies, and 19 extended right hepatectomies. Ischemic injury of the liver was assessed using changes in postoperative liver function tests and patient outcome was assessed using morbidity and mortality rates. After preliminary ligation of the blood supply to the lobe to be removed, global hepatic ischemia was produced by temporary occlusion of the main portal vein and hepatic artery proper while the liver parenchyma was divided. The average duration of inflow occlusion was 59 minutes (range, 25 to 90 minutes). There was no operative mortality, and no patient developed liver failure. The liver enzymes reached their peak on the first postoperative day (mean aspartate aminotransferase [AST] level, 283 ± 227 IU/L; mean alanine aminotransferase [ALT] level, 269 ± 238 IU/L) and they returned to normal by 7 days. The most common postoperative complications were related to the chest, wound, and urinary tract. The mean intraoperative transfusion was 3.4 ± 2.6 U of packed red blood cells, and 0.94 ± 2.13 U of fresh frozen plasma. We conclude that continuous hepatic inflow occlusion for periods of 1 hour during major liver resection is safe and well-tolerated when there is no underlying parenchymal liver disease.

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 Patients and Methods

Seventy-one consecutive major liver resections using continuous inflow occlusion performed on a single surgical service in patients with noncirrhotic livers between 1984 and 1993 were reviewed. There were 44 females and 27 males ranging in age from 23 years to 76 years (mean age, 54.4 ± 14.2 years). The indications for liver resection are listed in Table 1. Metastatic colon cancer was the most common indication, accounting for 35 of 50 resections for malignancy. There were 21 resections for benign disease. The types of liver resection were as follows: 31 right hepatectomies, 21 left hepatectomies, and 19 extended right hepatectomies (right lobe plus medial segment of left lobe). Patients who had fibrotic or cirrhotic livers or who had significant gross fatty change in the liver were not considered as candidates for inflow occlusion.

During the surgery the patients had monitoring of arterial pressure, central venous pressure, and urine output. Blood was transfused intraoperatively on the basis of measured losses and hemodynamics.

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The operative technique was the same in all cases. Bilateral subcostal incisions were used with an occasional upper midline extension to the xiphoid process. After complete mobilization of the lobe of the liver to be removed, the corresponding branch of the portal vein, hepatic artery, and bile duct in the porta hepatis was ligated and divided. The venous drainage of the lobe to be resected was then similarly ligated for either right or left hepatectomies. For extended right hepatectomies the right hepatic vein was ligated but ligation of the middle hepatic vein was left until the hepatic parenchyma had been divided. The main portal vein and hepatic artery proper were temporarily occluded while the liver parenchyma was transected. The artery was occluded with a Drake aneurysm clip and the portal vein was occluded by a tourniquet tape. The resections were performed along anatomic planes, according to the description by Bismuth et al of partial hepatectomy. For right or left hepatectomies, the line of parenchymal division was approximately 2 cm to the right of the falciform ligament. Preliminary hilar ligation of the vessels to the right lobe was performed and the feeding vessels to the medial segment of the left lobe were taken within the liver parenchyma when the liver was transected. The gallbladder was removed in all cases. The Cavitron ultrasonic dissector (Valley Lab, Richmond Hill, Canada) was used to divide the liver. Vascular and biliary tributaries encountered during the parenchymal division were ligated with hemoclips or chronic catgut ligatures.

Arterial and portal inflow was restored after completion of the resection. Bleeding from the raw edge of the liver after restoration of blood flow was controlled with chromic catgut sutures or topical hemostatic agents (gelatin soaked in topical thrombin). Liver enzymes (aspartate aminotransferase [AST], alanine aminotransferase [ALT] and alkaline phosphatase [ALP]), and serum bilirubin levels and prothrombin time (PT) were monitored during the first postoperative week. It was part of the routine postoperative management to give 1 or 2 U of 25% albumin daily for the first 5 days after surgery. Drains were removed between 5 and 7 days if no bile was evident in the drainage. The patients were kept on intravenous fluids that included 5% glucose until they were able to eat.

Statistical analysis was carried out using Student’s t-test, χ² test, analysis of variance, and linear regression using Statview II/SuperANOVA (Abacus Concepts Inc, Berkeley, CA). Values are expressed as mean ± SD unless otherwise indicated.

Results

The 30-day operative mortality rate was zero, and all patients were discharged from hospital. Overall, 15 patients (21%) experienced 16 postoperative complications (Table 2). More than half of the complications were infections related to the chest, wound, or urinary tract. One patient developed a subphrenic abscess after a right hepatectomy that was successfully treated with percutaneous drainage. One patient had a bile leak that was controlled by the drain placed at the time of surgery. The bile leak closed spontaneously after 9 days of drainage. One patient developed an inhibitor to factor V postoperatively, which was thought to be caused by an idiosyncratic reaction to topical thrombin placed on the raw liver edge during the surgery. Postoperative morbidity was not significantly associated with age, gender or diagnosis (benign versus malignant; P > .05).

The average postoperative hospitalization stay was 14.2 ± 8.0 days (range, 7 to 49 days; median, 12 days). Two patients had prolonged postoperative stays of 48 and 49 days. The first patient required a prostatectomy for urinary retention after the liver surgery, and he subsequently developed a pulmonary embolism. The second patient developed pulmonary insufficiency and the adult respiratory distress syndrome and needed assisted ventilation for 1 week after the hepatic resection. She made a slow but complete recovery.

The mean duration of inflow occlusion was 59 ±
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15 minutes (median, 60 minutes; range, 25 to 90 minutes). The mean intraoperative blood transfusion was $3.4 \pm 2.6$ U of packed red blood cells (median, 3 U; range, 0 to 19 U). Three patients required no transfusion. Only one patient required more than eight U of blood. This patient had a large angiosarcoma that was intimate with the retrohepatic vena cava, and when the tumor and the liver were being mobilized, an opening was inadvertently made into the inferior vena cava that resulted in sudden, massive blood loss. Duration of inflow occlusion did not correlate with the amount of transfusion ($r^2 = 0.001$). The mean intraoperative transfusion of fresh frozen plasma was $0.94 \pm 2.13$ U.

Transient elevation occurred in the AST and ALT levels during the first 7 postoperative days. The enzymes reached their peak on the first postoperative day and then decreased to preoperative levels by 7 days (Figs 1 and 2). The alkaline phosphatase decreased slightly during the first 3 days after surgery and began to increase by the fourth day (Fig 3). The level of enzymes did not significantly correlate with the duration of inflow occlusion ($r^2 = 0.079$ and 0.090 for AST and ALT, respectively) nor did they correlate with the postoperative complications listed in Table 2. The same was true for the serum bilirubin. Hyperbilirubinemia was common in the immediate postoperative period and the average serum bilirubin level was still approximately three times normal by the end of the first postoperative week (Fig 4). However, no cases of prolonged jaundice were observed.

The mean preoperative PT was 10.2 seconds. It was slightly prolonged on the first and second postoperative days (12.5 seconds and 12.6 seconds, respectively), but the difference was not statistically significant.

Discussion

The safety and success of liver resection depends upon effective control of bleeding during surgery and the ability of the nonresected lobe to sustain life in the immediate postoperative period and regenerate to a normal volume within a few months from surgery. In this study of major liver resections, continuous vascular inflow occlusion resulted in modest blood loss, and the changes in liver function tests after surgery did not suggest that it caused any significant ischemic injury to the liver. There were no manifesta-
tions of liver insufficiency, and although the rate of liver regeneration after surgery was not documented, the clinical course of the patients did not suggest that there was any impairment of the regenerative response. Neither ascites nor prolonged jaundice were observed in the postoperative period. Inflow occlusion did not seem to have caused any adverse effects in this series of patients. The complications that occurred were typical of those that are commonly reported after liver or other major abdominal surgery and there was no evidence that inflow occlusion was causally related to any of them.

The concept of an exquisite sensitivity of the liver to ischemia originated in experiments in dogs more than 4 decades ago. The canine model of liver ischemia does not directly reflect human physiology because of the unique hepatic vein sphincters in dogs and the presence of bacteria in their portal blood that resulted in hepatic gangrene after ligation of the hepatic artery. It was erroneously assumed that the human liver was similar, and the warning was given that the liver should not be subjected to warm ischemia for periods of more than 15 or 20 minutes.

In 1978, Huguet et al reported 9 patients who had both portal and caval occlusion for an average of 38 minutes without mortality. Stimulated by that report, we studied experimental hepatic ischemia in a pig model. Those experiments and data from Nordlinger et al showed that the porcine liver could tolerate periods of normothermic inflow occlusion (with simultaneous portal decompression) for 90 to 120 minutes. Extension of the ischemic period to 180 minutes resulted in greater physiological and clinical abnormalities, and some of the animals did not survive. Based on those experiments and the handful of reported clinical cases until that time, we began using inflow occlusion during major liver resections. Over the past 10 years there have been sporadic reports, mainly from the same centers, that have shown that the human liver has considerable tolerance for ischemia at normal body temperature. Reported experiences indicate that it is safe to use inflow occlusion for 60 minutes, and our results show that it is possible to use inflow occlusion for as long as 90 minutes without producing serious liver injury.

Significant bleeding may occur at any of three stages during liver resection. The first is during the initial mobilization of the lobe to be resected. Problematic bleeding may occur at this stage if a vascular tumor is present that is adherent to adjacent structures, i.e., diaphragm, retrohepatic cava, retroperitoneal tissues, etc. The second is when the liver is divided and intrahepatic vessels are secured. Bleeding at this stage is most likely to be reduced by inflow occlusion. The third stage of bleeding occurs from the raw edge of the liver after completion of the resection, when blood flow is restored. The technical advantage of a relatively bloodless field during the second stage has permitted accurate and secure control of vascular tributaries such that significant bleeding from the raw edge, after inflow is restored, is minimal. Thus, we have not found it necessary to reinstitute inflow occlusion during the third stage.

There are several variations on the theme of inflow occlusion, and the modifications include intermittent inflow occlusion, total vascular exclusion, and hypothermic vascular exclusion. Intermittent as opposed to continuous inflow occlusion has been recommended by some to give the liver a periodic "drink" with the intention of reducing the possibility of ischemic injury. Intermittent release at 5- to 20-minute intervals has been reported with good results. Our results suggest that this approach is unnecessary. Indeed, there is evidence suggesting that intermittent reperfusion may be harmful. Reperfusion injury has been shown to be an important component of tissue damage from ischemia, and it may be that subjecting the liver to several reperfusion episodes could cause more harm than a single, prolonged period of continuous ischemia. Complete hepatic vascular exclusion was described as early as 1966 by Heaney et al for the resection of difficult tumors. In a series of 51 patients (38 had major liver resections) who underwent total hepatic vascular

![Figure 4. Mean (± SD) serum bilirubin levels (normal, less than 17 umol/L).](image-url)
occlusion, Bismuth et al. reported a low transfusion rate of 1.4 U of packed red blood cells and mortality and morbidity rates that are similar to our results. Recently Habib et al. reported good results with total hepatic vascular exclusion for a mean period of 37 minutes in 47 patients. There was no 30-day mortality, and the average transfusion was 930 mL of blood. Total vascular exclusion achieves the best possible vascular control, because the vena cava is isolated above and below the liver in addition to occlusion of the portal vein and hepatic artery. That approach may be most suited to the unusually large tumors that lie in close proximity to the vena cava, during which there is the risk of producing a tear or hole in the vena cava. Total hepatic vascular exclusion may cause significant hemodynamic effects with a decrease in the mean arterial blood pressure and a reduced cardiac index. Changes that do not occur with portal triad occlusion alone. The most extreme approach is that of cooling the liver as part of vascular exclusion, as described by Fortner et al. That technique would only seem necessary if several hours of liver ischemia were required.

The increase in liver enzymes during the first few days after the resections in our series was moderate and it may be explained by local tissue injury at the line of the liver transection plus the effect of the transient ischemia on the nonresected lobe of the liver. The brief increase and subsequent decrease of the aminotransferases observed in the patients in our study are similar to what has been documented after major liver resection without inflow occlusion. This suggests that tissue trauma at the line of resection is primarily responsible for the acute change in the liver enzymes. One study by Makuuchi et al. showed no significant difference in the aminotransferase level between two groups of patients with and without intermittent inflow occlusion during liver resection with a mean occlusion time of 30 minutes.

We have been reluctant to apply continuous inflow occlusion to patients in whom the liver was found to be grossly fatty at the time of surgery because of the experience with fatty livers in transplantation. Fatty livers do not tolerate cold preservation well, and there is recent experimental evidence showing that livers laden with fat do not tolerate warm ischemia. We also did not use this technique in patients who had cirrhotic livers. Nonetheless, two clinical reports have shown that inflow occlusion appears to be safe even in cirrhotic livers for periods of 30 to 57 minutes. In those studies, most of the patients were Child’s class A which may be relevant to the results.

We doubt that absolute hepatic ischemia was created by the technique that we have used. Some collateral arterial supply to the nonresected lobe of liver exists in the undivided ligamentous attachments of that lobe, and there is likely some supply via small collateral channels within the connective tissue of the porta hepatis. As opposed to methods in which a clamp is applied across the entire portal triad, we isolated and occluded the hepatic artery proper and the portal vein leaving other vascular tributaries in the hepatoduodenal ligament undisturbed. When this technique was used in pigs, we found there was a residual flow of approximately 10% of the preocclusion flow as measured by Xenon washout. Whether that residual flow has any clinical significance in preventing ischemic injury to the remainder of the liver is unknown.

In conclusion, continuous hepatic inflow occlusion is a safe technique and was not harmful to the liver for periods of 1 hour. It offers technical advantages without compromise to the liver in the immediate postoperative period.

References
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