

Anesthetic considerations during liver surgery

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Recent advances in surgical and anesthetic management have reduced the operative risk of major hepatectomies significantly. Although these advances have been multifactorial, anesthetic approaches derived from liver transplantation have had a major impact in our own practice and given us greater capacity to perform complex resections safely. We have been liberal in the use of vascular isolation techniques to prevent hemorrhage in our approach to liver surgery, a modification that mandates a high level of anesthetic expertise to manage complex liver cases [1].

Understanding the underlying pathological conditions of liver disease and the physiology of vascular exclusion and surgical resection has significantly contributed to goal-oriented anesthetic management. The recognition of the importance of expert anesthetic management for liver surgery has led to the formation of anesthesiology teams dedicated to liver surgery and transplantation in most major institutions.

Preoperative considerations

Our experience with hepatectomy over nearly 2 decades has spanned a broad range of clinical scenarios, ranging from the healthy living donor to the patient with advanced cirrhosis undergoing local excision of a malignancy. The preoperative assessment is tailored to accommodate the clinical

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needs of the patient, estimating the need for invasive monitoring based on the extent of resection and the general health of the patient. Otherwise healthy individuals presenting for even extensive liver surgery need no additional work-up other than routine preoperative laboratories, which include a complete blood count, serum chemistries, and plasma coagulation studies. Increasingly, patients with significant comorbidities are scheduled for major liver resections. Assessing the functional status of these patients is often a significant challenge, as very few tests are available to assess with adequate predictive power the hemodynamic, respiratory, and hepatic reserve in this population.

Cardiac evaluation

Routine liver resections without major vascular exclusion represent a mild-to-moderate hemodynamic challenge, and should be well tolerated by all but those with marginal or unstable cardiac status. Major vascular exclusion is always a possibility when extensive liver resection is planned, however, and the hemodynamic consequences can only be handled with unrestricted cardiac function and pulmonary circulation. We prefer exercise or pharmacologic stress echocardiography for the preoperative assessment of the cardiac status of our patients. This test informs us about the contractile reserve of the myocardium, the mechanics of flow through the cardiac valves and chambers, and the status of the pulmonary circulation at rest and under duress. When limitations in cardiac function or reserve are found, adjustments in surgical approach and anesthetic management can be planned before surgery. In these cases, it is extremely important that the surgical and anesthetic teams discuss and agree on an intraoperative plan.

Pulmonary evaluation

Room air-oxygen saturation measured using pulse oximetry may give early indication of impaired pulmonary gas exchange or inadequate ventilatory reserve [2]. Using cutoff values of 97% and 94% identifies patients with an arterial pO_2 below 70 mmHg and 60 mmHg, respectively. Should an abnormal value be found during preoperative assessment, detailed arterial blood gas analysis and pulmonary function tests may become warranted. Approximately one third of patients with cirrhosis or noncirrhotic portal hypertension present with varying degrees of hepatopulmonary syndrome. The mild hypoxemia in these patients is due to ventilation/perfusion mismatching, characterized by an increase in pulmonary perfusion secondary to capillary distension, impaired hypoxic pulmonary vasoconstriction, and accelerated transpulmonary blood flow with unchanged alveolar ventilation [3]. Increasing cardiac output with the progression of cirrhosis worsens the diffusion impairment and hypoxia. Although hypoxemia in hepatopulmonary syndrome is initially responsive to supplemental oxygen, as the disease advances major intrapulmonary

shunting develops that is refractory to oxygen therapy. Clinical signs like platypnea (dyspnea induced by the upright position), finger clubbing, and spider nevi are characteristic, and strongly suggestive of the presence of hepatopulmonary syndrome. Contrast-enhanced echocardiography was found to be the most sensitive noninvasive diagnostic tool for demonstrating the presence of intrapulmonary vascular dilatations [4]; however, it does not quantify the extent of shunting, nor does it differentiate between vascular dilations and direct arteriovenous anastomoses.

Hepatic reserve

Hepatic cirrhosis limits the ability of the liver to regenerate. Fortunately, it appears that all but the most advanced cirrhotic livers can tolerate even major resections, and the presence of cirrhosis should not preclude potentially curative or life-prolonging surgery [5]. These patients may be more vulnerable to perioperative insults secondary to ischemia and hypoperfusion, which is reflected in the increased perioperative morbidity and mortality of this population [6]. Patients presenting with obstructive jaundice or for emergency liver resection, whether traumatic or infectious in origin, have the highest perioperative morbidity and mortality [6].

Intraoperative management

Induction and monitoring

Liver resections are performed under general anesthesia with endotracheal intubation and controlled ventilation. Patients presenting with significant ascites or other risk factors for regurgitation of stomach contents undergo rapid sequence induction to secure the airway; otherwise the anesthetic induction is adapted to the general condition of the patient. Maintenance of anesthesia is achieved using a halogenated volatile agent (most commonly isoflurane, which is a potent peripheral vasodilator with relatively mild cardiodepressive effects) in an air-oxygen mixture, supplemented with an intravenous narcotic. At least two large-bore intravenous cannulas are inserted, usually following induction of anesthesia. Although rapid infusion devices are seldom needed, they are available and primed in the operating room area at all times. The large operative field exposure necessary for liver resections is associated with significant heat losses. Hypothermia inhibits the enzymes of the coagulation cascade [7] and contributes to intraoperative blood loss. To counteract these losses, anesthetic gases are passed through a large-capacity heat-moisture exchanger, all fluids administered to the patient are warmed, and forced warm-air devices are applied to the upper and lower parts of the body.

Intraoperative monitoring is adapted to the preoperative condition of the patient, the extent of the liver resection, and the anticipated amount of

blood loss. For healthy patients with expected blood loss below 1000 mL one can use routine monitoring only: EKG, pulse oximetry, noninvasive blood pressure, and capnometry. An arterial line is inserted when repeat blood sampling is anticipated, or as part of extended hemodynamic monitoring. A large-bore central venous line is used for prolonged procedures with the potential for significant blood loss. Pulmonary artery catheterization is reserved for patients with known preoperative left-ventricular dysfunction, anticipated prolonged major vascular exclusion (eg, vena cava resection and reconstruction), or preoperative sepsis. We use point-of-care blood gas, chemistry, and coagulation analysis to detect and correct intraoperative anemia, acid-base, electrolyte, and coagulation disturbances.

Fluid management

In our practice colloids—5% albumin and hetastarch in a balanced salt solution—are used as maintenance and replacement fluid, and intraoperative use of crystalloid solutions is limited to a minimum. The use of colloid rather than crystalloid as maintenance fluid reduces extravascular translocation of fluids, which results in less bowel edema, improved mesenteric perfusion, and more rapid restoration of postoperative gut function. Fresh-frozen plasma is used as maintenance fluid in patients who are coagulopathic and require correction of their coagulopathy. Red cells are not transfused unless the hematocrit falls below 25%, except in patients with known coronary or cerebrovascular disease. Adequate volume status almost always results in satisfactory systemic blood pressure. In some cirrhotic patients, however, the vasculature acts as a fluid sump, and vasodilation and reduced sympathetic drive secondary to general anesthesia may result in inadequate peripheral perfusion pressures. Judicious use of vasopressin (2–5 U/hour) or a combination of vasopressin and norepinephrine is used to restore peripheral vascular resistance and systemic blood pressure in these patients, always keeping in mind the primary importance of avoiding undesired hypovolemia.

Blood transfusion and conservation

Major liver resections may result in significant blood loss, necessitating transfusion of red blood cells in about 25% to 30% of patients [8]. For example, healthy donors undergoing right hepatectomies are expected to lose about 600 mL to 900 mL of blood on average [9]. In our own series of living donor hepatectomies, blood loss has ranged from 294 ± 145 mL for left lateral hepatectomy to 583 ± 277 mL for right hepatectomy [10]. The presence of a preoperative coagulopathy, malignancy, and the extent of resection were the only predictors consistently found to correlate with the need for intraoperative blood transfusion. Transfusion requirements for

liver resections are quite unpredictable, however, and when blood transfusion is required, the mean volume of packed red blood cells is relatively high [11]. This makes, at least in our opinion, preoperative autologous blood donation ineffective and costly. Chronically ill patients are often already anemic and are poor candidates for autologous blood donation, whereas healthier patients, who are good candidates for autologous blood donation, tolerate blood loss well. The use of intraoperative blood recovery systems further reduces the need for autologous blood donation. In liver resections for malignancy, blood recovery systems are usually avoided, due to the concern of hematogenous spread [12].

The use of antifibrinolytic agents has been promoted in operations with major blood loss. In a randomized, controlled trial “full-dose” aprotinin (2×10^6 KIU load followed by 5×10^5 KIU/hour infusion) was found to reduce intraoperative blood loss by about 25% and transfusion requirements by half, without any thrombotic or thromboembolic complications [13]; however, the average blood loss, even in the aprotinin group in this study, was two times the prestudy estimate, based on average blood loss for the same operation in the same institution (1200 mL versus 600 mL). Aminocaproic acid and tranexamic acid have not been studied in the context of liver resection surgery. Limited experience with their use in liver transplantation has yielded equivocal results so far [14]. In our practice, we often use intraoperative “half-dose” aprotinin (10^6 KIU load followed by 2.5×10^5 KIU/hour infusion) during hepatic transplantation in patients who have a significant coagulopathy or portal hypertension, as well as in those who have had previous abdominal surgery.

Hemodynamic manipulation

Intraoperative hemodynamic management is dictated by the surgical approach. Keeping the central venous pressure (CVP) low, that is between 2 mmHg and 5 mmHg, limits the distention of hepatic veins and sinusoids and was shown repeatedly to reduce blood loss during liver surgery [15,16]. This approach necessitates the placement of a central venous line, and restricts fluid administration during induction of anesthesia and hepatic resection to a minimum. Intravenous nitroglycerine is used to reduce the CVP to the target range if fluid restriction alone is ineffective [17]. Once the resection is completed and hemostasis is achieved, euvolemia is restored by fluid expansion, using crystalloid or colloid. The low-CVP approach exposes the patient to the risks of intraoperative hypovolemia, with potentially inadequate organ perfusion, and insufficient volume reserves, should a sudden unexpected intraoperative hemorrhage occur. Although there is no prospective, randomized trial to date addressing the relative risks and benefits of low-CVP anesthesia during liver resection, the incidence of perioperative renal failure has not been found to increase significantly when compared with historical controls [15].

As we seldom monitor central venous pressure during routine liver resection at our institution, fluid therapy is adjusted to maintain urine output at 0.5-1cc/kg/hr and to the extent of blood loss. When the resection is planned without vascular occlusion or with occlusion of the vessels of the portal triad only, we limit intravenous fluid administration prior to and during the resection, while maintaining hemodynamic stability and adequate (>0.5 mL/kg/hr) urine output. The use of nitroglycerine is limited to the resection phase, when distension of the liver or excessive oozing of the resection surface is observed. Using this approach, our blood loss and intraoperative blood transfusion rate is comparable to or less than those reported for low CVP anesthesia. In patients undergoing extensive liver resections, where there is a high likelihood of vascular exclusion, a large-bore CVP line is placed from which a CVP can be monitored. If the anesthesia/surgical team feels that the information gained by measuring the CVP is necessary to guide fluid management, one should be placed to aid in fluid and hemodynamic manipulation.

When a major hepatectomy using total vascular exclusion is planned, anesthetic management is adjusted to anticipate the reduction in venous return, sudden decrease in cardiac output, and increase in afterload associated with cross-clamping of the inferior vena cava and portal vein [1]. Although pulmonary artery pressure monitoring is perhaps not necessary for successful management of routine cases with major vascular occlusion, it is often performed for the benefit of a more detailed assessment of intravascular volume status and cardiovascular response to cross-clamping. Furthermore, should a catastrophic hemorrhage from injury to the inferior vena cava occur, a pulmonary artery catheter will allow administration of a vasopressor agent beyond the site of the injury, to maintain adequate organ perfusion until control over the site of the injury is achieved. Volume expansion to a CVP of at least 14 mmHg allows cross-clamping of the inferior vena cava in most patients, while maintaining adequate circulation and blood pressure. Should the patient not tolerate cross-clamping after volume loading alone, pressors (vasopressin or norepinephrine) are added. If hypotension persists, veno-venous bypass using axillary or right atrial cannulation can be established to improve hemodynamics, or, if possible, the surgical plan is modified to avoid total vascular occlusion. Augmentation of renal function with an infusion of furosemide, dopamine, or mannitol is decided on an individual basis and is not used routinely.

Vascular exclusion

Temporary occlusion of hilar vessels is commonly used to reduce blood loss. For more extended resections, intra- or extrahepatic control of hepatic veins may also be necessary. Cross-clamping of the hepatic artery and the portal vein results in hepatic ischemia. It is believed that a healthy human

liver can tolerate ischemia for up to 90 minutes. This time is reduced to about 30 minutes when significant cirrhosis is present [18]. Our own experience indicates that carefully selected patients with cirrhosis can tolerate planned hepatic clamping to ensure safe hepatectomy [19].

Portal triad clamping increases systemic vascular resistance by up to 40% and reduces cardiac output by 10%. The net effect on mean arterial blood pressure is an increase of about 15% (Fig. 1) [20]. Plasma vasopressin, epinephrine, and norepinephrine levels are significantly increased, whereas plasma renin activity remains unchanged following portal triad clamping [20]. Afferent discharges of sympathetic nerve fibers originating in the hepatic pedicle are responsible for these changes, as these hemodynamic and neurohumoral responses are prevented by infiltration of the hepatic pedicle with local anesthetics before clamping [21]. Following the release of the clamp, systemic vascular resistance, cardiac index, and heart rate increase, whereas mean arterial pressure and central venous pressure remain unchanged [22]. Indocyanine green clearance, an indicator of hepatic metabolic function, decreases following portal triad clamping, but returns close to the preoperative value toward the end of surgery [23]. Hepatic vascular exclusion combines portal vessel clamping with occlusion of the supra- and infrahepatic inferior vena cava. This intervention produces more profound hemodynamic changes than portal clamping alone. Although systemic vascular resistance and heart rate increase, the cardiac index is

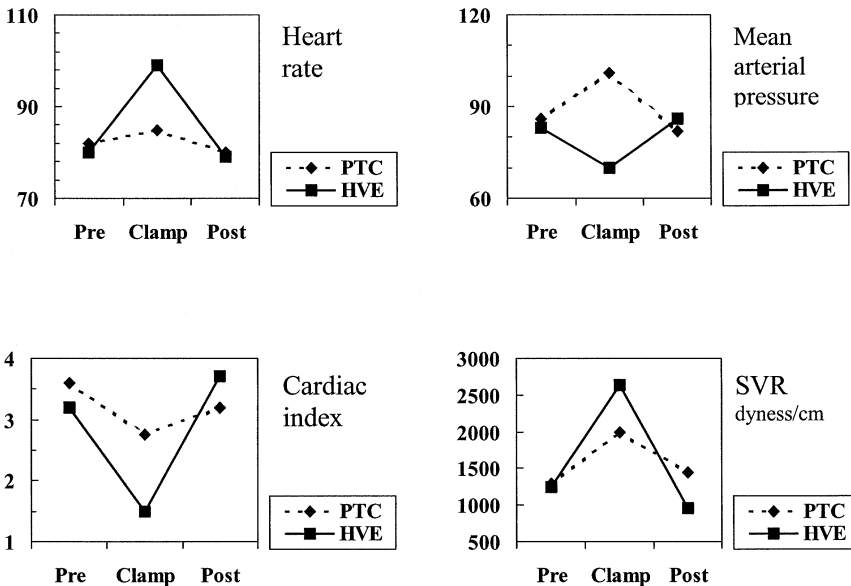


Fig. 1. Characteristic changes in heart rate, mean arterial blood pressure, cardiac index, and systemic vascular resistance following portal triad clamping (PTC) or hepatic vascular exclusion (HVE).

reduced by half secondary to a steep reduction in preload (see Fig. 1) [24]. In our experience, it is characteristic for the CVP and pulmonary artery diastolic pressure to decrease from the mid teens to low single-digit numbers. As with portal triad clamping, serum vasopressin, epinephrine, and norepinephrine levels increase after hepatic vascular exclusion, but serum renin activity remains unchanged [24]. The elevated blood hormonal concentrations rapidly return to baseline following unclamping. Unclamping is also followed by an increase in cardiac index, normalization of cardiac filling pressures, and a significant reduction in systemic vascular resistance.

In preparation for total vascular occlusion, we often volume load with 500 mL colloid; that is, 5% albumin, hetastarch, or fresh frozen plasmas (FFP) if indicated. Some patients require blood pressure support with pressors if volume loading alone is inadequate. Most patients tolerate hepatic vascular occlusion with a mild-to-moderate reduction in the mean arterial pressure. Should the mean arterial pressure drop precipitously following clamping and show no tendency of recovery with rapid fluid loading and pressor support, the clamps should be released, and an alternate mode of circulatory support such as veno-venous or veno-atrial bypass must be considered.

Renal preservation

Understanding renal physiology and alterations in renal blood flow and function caused by liver disease, general anesthesia, and major liver surgery are necessary to maintain adequate renal function throughout the perioperative period. Renal autoregulation effectively ceases below renal perfusion pressures of 70 mmHg to 75 mmHg, below which flow becomes pressure dependent. In cirrhotic patients, the concomitant sympathetic activation results in a rightward shift of the autoregulation curve; thus these patients have even less tolerance of reductions in renal perfusion pressure [25]. Anesthetic agents reduce cardiac output and often cause vasodilation, resulting in a further reduction of renal blood flow. Redistribution, sequestration, and loss of extracellular and intravascular fluids are commonly associated with major surgery. The anesthesiologist has to maintain both adequate renal perfusion pressure and flow throughout the entire case to prevent renal impairment. It is no easy task: 3% of patients experience permanent and 10% transient renal dysfunction following major liver surgery [15].

Postoperative care

Approximately 20% of otherwise healthy patients may experience postoperative complications after elective liver resections [6]. The most frequent of these are pulmonary infection and abdominal abscesses, both usually responsive to antibiotic therapy. Less frequent but more significant complications include postoperative hemorrhage necessitating

re-exploration, hepatic, and renal failure. Preoperative American Society of Anesthesiologists (ASA) classification, presence of steatosis, extent of resection, simultaneous extrahepatic resection [6], and perioperative blood transfusion [26] have been found to be independent predictors for the development of postoperative complications. In-hospital mortality following liver resection has been associated with perioperative myocardial infarction, sepsis with multiple organ failure, pulmonary embolism, and duodenal ulcer perforation [6,26]. Extravascular lung-water accumulation, indicating mild-to-moderate pulmonary edema following liver resection, has been reported; however, this does not appear to affect oxygenation significantly in the postoperative period [23]. Postoperative hepatic failure remains a significant challenge. Although low residual liver volume was found to be associated with postoperative liver failure, the regenerative ability of the liver is remarkable, and the residual, otherwise healthy liver is expected to double in size within the first week following the resection. A hyperdynamic state with increased cardiac index and augmented splanchnic blood flow persists for at least 3 days postoperatively [23]. This increased blood supply to the residual liver parenchyma ensures rapid growth. Increase in hepatic parenchymal mass does not necessarily result in full restoration of functional ability. Even when clinical parameters such as the coagulation profile return to normal, more sensitive tests such as indocyanine green clearance may remain below the baseline value 5 days after major hepatic resections [22]. Pre-existing cirrhosis or positive virus carrier status limits liver regeneration, and these patients are more susceptible to developing postoperative hepatic failure. The ability of the liver to regenerate is also reduced in diabetic patients, who have an increased incidence of postoperative hepatic failure following extensive resections [27].

Transient renal dysfunction is common in the postoperative period. Maintaining normovolemia and adequate renal perfusion pressure minimizes this risk. There is little, if any, benefit from routine use of low-dose dopamine and diuretic infusions to support renal function. Dopexamine, a dopamine-2 receptor agonist, is gaining popularity as a selective renal vasodilator; however, its renoprotective role remains to be proven. In cases of acute oliguric renal failure, continuous hemofiltration or intermittent hemodialysis may be necessary until renal function improves [25].

Postoperative pain following liver surgery is significant, and adequate analgesia remains a challenge for the caregivers. Neuraxial anesthesia has severe limitations in liver surgery. Many patients presenting for hepatic surgery have a coagulopathy or thrombocytopenia that makes them ineligible for an epidural or intrathecal therapy. Epidural catheter placement has been studied in a group of patients undergoing liver surgery, and the postoperative prolongation in prothrombin time delayed catheter removal in 9% of patients who had three or more segments resected [28]. Although we have no knowledge of any reports of spinal hematoma following epidural catheter placement in patients after liver surgery, the prolongation of prothrombin time potentially predisposes these patients to spinal hematoma

formation and cord compression. Thus we use epidural catheters only in selected patients, undergoing limited resections with normal coagulation status and good hepatic function. Intrathecal morphine in doses of 0.5 mg to 0.7 mg is used as an alternative in almost all patients who have no underlying coagulopathy or thrombocytopenia. This significantly reduces systemic morphine requirements postoperatively, without increasing the risk of neurological complications. Patients who do not qualify for intrathecal morphine administration receive preoperative coaching in the use of a patient-controlled analgesia device.

Summary

This article demonstrates the broad range of considerations that affect the outcome of patients undergoing hepatectomy. The progressive improvements in survival, despite the increasing complexity of the surgery, are a testament to advances in both surgery and anesthesia. The key elements include careful patient selection, appropriate monitoring, and mechanical and pharmacologic protection of the liver and other vital organs.

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