PREANESTHETIC ASSESSMENT OF THE PATIENT WITH HEPATOCELLULAR CARCINOMA

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Introduction

Hepatocellular carcinoma (HCC) is a common cause of cancer-related death worldwide. The incidence of HCC in the United States has steadily increased over the last two decades. As such, a growing number of surgical candidates are afflicted with HCC. Advanced HCC causes destruction of normal functioning hepatic parenchyma eventually leading to a reduction in drug metabolism and clotting factor production, both of which can lead to anesthetic complications during surgery.

Primary hepatocellular carcinoma (HCC), the fourth leading cause of cancer-related death worldwide, is the most common primary malignancy of the liver. HCC is a progressive tumor of hepatic parenchyma that usually occurs secondary to chronic hepatic disease and cirrhosis. HCC is typically diagnosed late in the course of the disease leading to a median survival of 5-20 months following diagnosis. This carcinoma shows a propensity for invasion of the vascular channels within the liver, including the portal circulation and inferior vena cava, with hematogenous dissemination to other organs. HCC can range from well differentiated to highly undifferentiated tumors.

The development of hepatic cirrhosis is thought to be an important contributor to the emergence of HCC, but is by no means a perquisite to development of HCC. The main etiologic associations with HCC include viral infections, chronic alcoholism, food contaminants, tyrosinemia, and hereditary hemochromatosis. These diseases and food toxins cause repeated cycles of hepatocyte death and regeneration which is thought to be responsible for the development of HCC. The continuous cell division can lead to accumulation of DNA mutations. These mutations can eventually damage DNA repair genes allowing for uncontrolled growth of abnormal hepatocytes. Patients with HCC can present with a wide variety of signs and symptoms; none of which are pathopneumonic for HCC. Imaging modalities such as CT and MRI provide detailed information about hepatic nodules which aid in diagnosis of HCC. There are a variety of treatment options for HCC; the best of which is surgical resection of the tumor. Unfortunately, only a small fraction of patients are eligible for this treatment due to the aggressive nature of HCC.

Epidemiology

HCC accounts for approximately 5.4 percent of all cancers worldwide. Although it accounts for only a small percentage of cancers, HCC is the fourth leading cause of cancer-related death worldwide[1]. It is the third leading cause of cancer-related death in men. As these numbers suggest,

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HCC has a very high case fatality rate. The mean age for diagnosis of HCC is between 50-60 years old. The HCC incidence varies largely based on location, race, and gender.

In the United States, there are approximately 8500 new cases of liver cancer each year. The incidence of HCC in the U.S. was 4.1/100,000 from 1998-2000 according to the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute. The incidence has increased over the past two decades; possibly due to increased prevalence of Hepatitis C viral infection in the U.S between 1960 and 1990[2]. The incidence has nearly tripled since 1976 when the incidence was 1.4 cases per 100,000 people. This increase reflects the 20-30 year lag time between viral infection and development of viral induced cirrhosis and carcinoma.

The incidence of HCC varies widely by geographic location. This geographic difference in HCC incidence is likely due to regional variations in exposure to hepatitis viruses and environmental pathogens. Regions with higher HCV and HBV infection rates typically have a higher HCC incidence. More than 85 percent of HCC cases occur in countries with high rates of chronic HBV infection. In fact, over 75 percent of all cases of HCC are found in Asia due to the high incidence of HBV infection in these countries. The highest incidence rates are found in China, Hong Kong, Korea Taiwan, and sub-Saharan Africa, where the incidence approaches 36 cases per 100,000 people. Intermediate incidence rates (approximately 15/100,000) are found in eastern and Western Europe as well as New Zealand, Alaska, Jamaica, Haiti, and Thailand. The lowest incidence rates (4/100,000) are found in North and South America, Australia and many Middle Eastern countries.

Men are much more likely to develop HCC in comparison to women. The increased incidence in males is more pronounced in high incidence areas compared to lower incidence areas. In high incidence areas the male to female HCC ratio is 2.1-5.7:1, 2.4:1 in intermediate incidence areas, and even lower in low incidence regions[3]. This difference in gender distribution is likely due to increased viral hepatitis infection rates in males, increased exposure to environmental toxins, and possibly the trophic effects of androgens. Race also seems to play a role in the development of HCC. African Americans have HCC incidence rates that are about three times higher than Caucasians regardless of the geographic location.

Etiology

Screening surgical candidates for possible chronic hepatic conditions is important because the majority of HCC occurs in the setting of chronic liver disease or hepatic cirrhosis. A number of different risk factors have been implicated in the development of HCC including, but not limited to hepatitis B carrier state, chronic hepatitis C viral infection, hereditary hemochromatosis, environmental toxin exposure, and cirrhosis of any cause. While HCC can still occur in individuals without any known risk factors, these risk factors allow us to determine patients at greatest risk of developing HCC.

Numerous epidemiologic studies have linked chronic HBV and chronic HCV infections with HCC. As stated earlier, over 85 percent of HCC cases occur in countries with high incidence rates of chronic HBV infection. In Asia, where vertical transmission of HBV from an infected mother to infant is high, HBV carriers have a greater than 200-fold increase in the risk of developing HCC. In a study done on 22,707 male government employees in Taiwan, 15 percent of subjects were hepatitis B surface antigen positive. These patients were then followed over a three year period and the relative risk of developing HCC was 223 times higher in hepatitis B surface antigen positive patients compared to surface antigen negative patients[4]. Patients who are hepatitis B surface antigen (HBsAg) positive and HBeAg positive have a much higher risk of developing HCC compared to patients who are HBsAg positive but HBeAg negative. One large prospective study that followed hepatitis B infected patients for ten years showed that patients who were HBsAg and HBeAg positive had a relative risk of 60.2 for HCC while patients were HBsAg positive and HBeAg negative had a relative risk of 9.6[5]. Serum levels of HBV DNA seems to play a role in the development of HCC. Studies suggest that the incidence of HCC is directly related to the level of HBV DNA in infected patient's serum[6]. The HBV genome contains a regulatory region that encodes a protein known as

the X-protein which acts as a transcription activator for many of the HBV genes. Many experts believe that this X-protein disrupts normal hepatocyte growth control causing activation of proto-oncogenes which can lead to disruption of cell cycle controls leading to the development of HCC.

In the U.S., hepatitis C accounts for approximately one-third of HCC cases. Unlike HCC in patients with HBV which can develop without significant fibrosis or cirrhosis, HCC caused by HCV occurs almost exclusively in patients with cirrhosis or advanced stages of hepatic fibrosis[7]. The HCV causes a chronic inflammatory state in the liver caused by increased numbers of pro-inflammatory cytokines migrating to the liver leading to increased inflammation and cell turnover[8]. In fact, the degree of hepatic inflammation can be used to determine prognosis once HCC is discovered. Oxidative stress and inflammatory markers, including CD68+ cells, 8-hydroxydeoxyguanosine DNA adducts, and 4-hydroxynonenal adducts are elevated to higher levels in HCC patients with a worse prognosis[9]. Several other concomitant risk factors including alcoholism, diabetes mellitus, obesity, and co-infection with HBV increase the risk of HCC in HCV infected patients. The core protein of HCV also has potential oncogenic properties leading to the development of HCC similar to HBV's mechanism for causing HCC.

Hereditary hemochromatosis (HH) is an autosomal recessive genetic disorder associated with increased intestinal absorption of dietary iron leading to deposition of excessive amounts of iron into hepatic, pancreatic, and cardiac tissue, as well as other organs. HH is the most common inherited single-gene disorder in people of northern European descent. In fact, in the U.S. one in ten people are carriers of the mutation. The mutation is caused by a mutation in the HFE gene, most commonly the C282Y mutation[10]. Classically, patients with HH often present in their forties with diabetes mellitus, cutaneous hyperpigmentation, and hepatic cirrhosis; the latter of which contributes to the development of HCC. If HH is diagnosed early, and treatment with routine phlebotomy is initiated, cirrhosis can be prevented. However, once cirrhosis occurs; it effects are irreversible. In patients with HH, HCC usually only occurs after the liver becomes cirrhotic. Patients with HH and cirrhosis have a 200 times higher risk of developing HCC in comparison to the general population[10]. Therefore, if HH is diagnosed and treated early in its course, HCC can be avoided in most of these patients. As expected, studies have shown patients with HH and concomitant hepatitis B infection or alcohol abuse are at an even further increased risk of developing HCC. Hereditary tyrosinemia is also a genetic disease, although very rare, that is a risk factor for the development of HCC. Hereditary tyrosinemia is caused by a defect in the tyrosine degradation pathway, usually a deficiency of fumarylacetoacetate hydrolase, which leads to the accumulation of maleylacetoacetate, succinylacetone, and fumarylacetoacetate. The accumulation of these metabolites leads to the development of HCC in nearly 40 percent of patients with hereditary tyrosinemia despite attempts at restricted tyrosine diets.

Environmental toxins can also play a role in the development of HCC. The main toxins involved here are dietary aflatoxins and betel nuts. Aflatoxin is derived from the Aspergillus flavus toxin. It is a mycotoxin that commonly contaminates corn, soybeans and peanuts. Excessive exposure to aflatoxin usually occurs in Asia and South Africa. Chronic exposure to aflatoxin leads to HCC because the toxin can covalently bond to cellular DNA leading to mutations in the tumor suppressor gene, p53. The betel plant is most commonly found and cultivated in South and Southeast Asia. Chewing of the betel nut is usually seen in these same regions secondary to religious, ceremonial, and medicinal purposes as well as its known stimulatory effects. Unfortunately, this practice is associated with the development of cirrhosis, HCC, esophageal, and squamous cell carcinoma.

Chronic alcohol abuse is also linked to HCC. It is unclear whether alcohol has a direct relationship to HCC, or if the development of cirrhosis secondary to chronic alcohol abuse leads to the development of HCC. It is also worth noting that some but not all studies have linked cigarette smoking to the development of HCC. While there are several substances that increase the risk of HCC, a meta-analysis demonstrated consumption of two or more cups of coffee per day decreased the risk of HCC by 43 percent in both patients with and without liver disease[11].

Clinical Manifestations and Diagnosis

Clinical manifestations of HCC are seldom pathopneumonic, and are often masked by background cirrhosis or hepatitis preceding the development of HCC. The clinical manifestations of HCC are rarely present early in the course of the disease, leading to poorer outcomes due to advanced disease and often widespread metastasis on initial diagnosis of HCC. Extrahepatic metastases are seen in 10 percent of patients at the time of diagnosis. The most common sites of metastasis are the lungs, intrabdominal lymph nodes, bone, brain, and adrenal glands. Extrahepatic metastasis is seen much more commonly with intrahepatic tumors greater than 5 centimeters in diameter[12, 13]. Some of the more common signs and symptoms of HCC in patients without known liver disease can include, but are not limited to, mild to moderate ill-defined upper abdominal pain, early satiety, fatigue, weight loss, night sweats, fever, malaise, jaundice, hepatomegaly, splenomegaly, gastrointestinal or esophageal bleeding, and in more advanced cases a palpable abdominal mass. In patients with known chronic liver disease or cirrhosis, suspicion for HCC should be heightened when previously compensated cirrhotic patients develop signs of decompensation such as ascites, hepatic encephalopathy, obstructive jaundice, or variceal bleeding. These complications are often associated with extension of the tumor into the hepatic or portal veins or arteriovenous shunting caused by the tumor[14]. Some other less common signs and symptoms of HCC can be seen in both patients with and without a history of liver pathology. Diarrhea can occur in these patients. It is believed that some tumors may secrete increased levels of vasoactive intestinal peptide (VIP) and gastrin which causes increased intestinal secretion leading to watery diarrhea. Bone pain or dyspnea can be presenting symptoms due to metastasis to the bone and lung if the HCC is not diagnosed early.

There are also several cutaneous manifestations that have been associated with HCC, but are not specific to HCC. Dermatomyositis is sometimes seen in patients with HCC. Dermatomyositis is characterized by idiopathic inflammatory myopathies of varying muscle groups, erythema of the face, neck, trunk, knuckles, and edema of the eyelids and periorbital area[6]. Pityriasis rotunda, a rash characterized by multiple round sharply demarcated scaling patches. Finally, Porphyria cutanea tarda (PCT), a rash composed of hemorrhagic bullae and vesicles caused by sun exposure, is often seen in patients with HCC caused by chronic hepatitis C viral infection[15].

Several lab values may also be abnormal in HCC patients but are rarely conclusive alone for a diagnosis of HCC. Elevated levels of serum alpha-fetoprotein (AFP) are found in 50-75% of patients with HCC. AFP levels of greater than 500 mcg/L in patients with known hepatic disease is near diagnostic of HCC. Thrombocytopenia, hypoprothrombinemia, hypoalbuminemia, and hyperbilirubinemia can be seen due to decreased hepatic function secondary to cirrhosis, tumor invasion and replacement of normal hepatocytes. Serum aminotransferases, alkaline phosphatase, and gammaglutamly transpeptidase may be elevated as well. Mild hypoglycemia can be seen secondary to the increased metabolic needs of malignant tumor cells. Erythrocytosis is often seen in HCC. In fact, elevated levels of erythropoietin is seen in up to 23 percent of patients with HCC due to tumor secretion of EPO[16]. Less commonly, hypercalcemia may be seen because of either osteolytic metastasis or tumor secretion of parathyroid hormone-related peptide[17].

Diagnosis of HCC requires a multi-faceted approach including clinical suspicion, physical exam, laboratory values, imaging modalities, and biopsy. The American Association for the Study of Liver Diseases (AASLD) has issued guidelines for the diagnosis of HCC when a unknown hepatic nodule is discovered incidentally or while screening patients with known hepatic disease based on the size of the nodule. (see Table 1) The AASLD goes on to state that a hepatic mass found in a patient with known hepatitis B or cirrhosis is likely to be HCC[18].

In patients presenting with a combination of any symptoms mentioned above, a thorough history and physical exam must be the initial step preformed. Several laboratory values must also be examined as well including complete blood counts with differentials, electrolytes, direct and indirect bilirubin, albumen, alkaline phosphatase, AST, ALT, GGT, PT, PTT, bleeding time, and if suspicion is initially high for HCC, AFP levels. Imaging should be the next step

Table 1

AASLD Guidelines	
SIZE	RECOMMENDATION
<1 cm	Follow with ultrasound every 3-6 months. If no growth over a 2 yr. period, revert to routine surveillance.
1-2 cm	Further investigation of nodule using 2 dynamic imaging studies. If suggestive of HCC, treat as HCC. If findings not characteristic of HCC, biopsy lesion.
>2 cm	If typical features of HCC on dynamic imaging study, no biopsy necessary treat as HCC. If AFP >200 ng/ml, no biopsy necessary. If imaging is not characteristic of HCC or in non-cirrhotic liver, perform biopsy.
All sizes	If biopsy is negative for HCC, patients should be followed with ultrasound or CT imaging every 3-6 months until the nodule disappears, enlarges, or displays diagnostic characteristics of HCC. If the lesion enlarges but remains atypical for HCC, repeat biopsy is indicated.

to diagnosing HCC. Ultrasound can be used to evaluate the liver for lesions as a first line imaging study, but when clinical suspicion is high (ex: pts with chronic liver disease and elevated AFP) CT scan and/or MRI offers a more detailed view of the liver. Ultrasound has more of a role in screening patients with known chronic hepatic disease for nodules. CT scans have a sensitivity and specificity for HCC of 68 percent and 93 percent, respectively. Likewise MRI offers a sensitivity of 81 percent and a specificity of 85 percent[19]. Lesions that appear hypervascular, have increased signal intensity, or show venous invasion are highly suggestive of HCC. Percutaneous biopsy of hepatic nodules can be helpful when a definitive diagnosis is uncertain or when histopathology results will influence patient management. The use of percutaneous biopsy should be limited to the aforementioned situations because there is a risk of tumor spread along the needle track which can affect the possibility of surgical tumor resection.

Treatment

There are numerous treatment options available for HCC depending on the TNM staging at diagnosis including partial hepatectomy, liver transplantation, radiofrequency ablation, percutaneous ethanol/ acetic acid ablation, transarterial chemoembolization, cryoablation, radiation therapy, and systemic chemotherapy. The mainstay of treatment is surgical resection of HCC, but since diagnosis is usually made late in the course of the disease many patients are not candidates for surgical resection. Treatment options must be discussed with patients and tailored to fit their specific case. Below is a brief description of the above mentioned treatment options.

Partial Hepatectomy- A potentially curative procedure if the HCC is a small (<5 cm) solitary nodule without hepatic vascular invasion, metastasis, and well-maintained hepatic function. Few patients meet criteria for this treatment, but in eligible patients, five-year survival rates are approximately 90 percent[20].

Liver Transplantation: This treatment option is normally used in HCC patients with solitary lesion greater than 5 cm, no metastasis, no vascular invasion, and moderate to severe hepatic dysfunction. Also, patients with up to three separate hepatic nodules less than 3 cm each in size without vascular invasion or metastasis are good candidates for liver transplantation. In highly selective cases, five-year recurrence-free survival rates approach 92 percent[20].

Radiofrequency Ablation: This treatment uses high frequency lesion directed alternating current that causes ions in the lesion to attempt to align with the alternating current emanating from the electrode. As these ions move in concordance with the alternating current, frictional heating of the tissue occurs resulting in necrosis of the HCC nodule surrounding the electrode. This treatment option is used in patients who do not meet surgical resection criteria, but HCC is still confined only to hepatic tissue.

Percutaneous Ethanol or Acetic Acid Ablation: Used in patients with small HCCs who are not candidates for surgical resection due to hepatic functional reserve. Its use has been largely replaced by radiofrequency ablation, although the two treatments have similar outcome data.

Transarterial Chemoembolization: This treatment works on the premise that the majority of the blood supply to HCC is via the hepatic artery. It works to eliminate the tumors blood supply or more commonly to administer chemotherapeutic drugs directly to the tumor via the hepatic artery. This treatment option is used for large HCC nodules that are not amendable to

other treatments due to the nodules large size. However, this modality is absolutely contraindicated in patients with absent hepatoportal blood flow, encephalopathy, and biliary tract obstruction[20].

Cryoablation: This technique is often used intraoperatively. A cryoprobe is inserted into the nodule, and alternating cycles of freezing and thawing are used to kill the tumor cells. Like percutaneous ablation, this therapy has also been largely replaced by radiofrequency ablation.

Radiation Therapy: This treatment uses external beam radiation to destroy HCC. This technique is used in patients with diffuse HCC confined to the liver, numerous small hepatic nodules, or even metastatic disease. HCC is a very radiosensitive. Unfortunately, the liver is extremely radiosensitive as well, leading to hepatic parenchymal destruction.

Systemic Chemotherapy: This treatment is not routinely used in HCC patients. HCC is considered to be relatively chemotherapy refractive due to expression of drug resistance genes. It is not well tolerated in patients with advanced HCC. New data suggest that combination chemotherapy may offer modest benefits in some HCC patients[20].

Preanesthetic Considerations and Management

General preanesthetic considerations

Because patients with hepatocellular carcinoma and other advanced hepatic diseases have a wide range of pharmacodynamic and metabolic abnormalities, it is even more important to tailor the anesthetic and optimize the patient prior to surgery. A thorough history and physical examination is necessary in addition to blood tests. Previous blood transfusions, unusual bleeding, and prior anesthetic techniques should be noted in the history. The physical examination should detail the degree of jaundice, ascites, and encephalopathy. Laboratory tests should include a complete blood count, coagulation times, and a complete metabolic profile including serum electrolytes, BUN, creatinine, aminotransferases, alkaline phosphatase, lactate dehydrogenase, and hydroxybutyrate dehydrogenase[21].

After abnormalities are identified, the patient should be prepared accordingly prior to surgery. Particular attention should be directed toward correcting coagulation abnormalities. Patients with a prolonged prothrombin time or elevated INR should receive vitamin K for several days if time permits. They should receive fresh frozen plasma if surgery is emergent or vitamin K is ineffective. Cryoprecipitate should be considered if fresh frozen plasma is ineffective or a fibrinogen abnormality is present. Prothrombin time should be corrected to within 2 seconds of normal[22]. If coagulopathies are uncorrected, complications include severe surgical hemorrhage, encephalopathy, and renal failure. Hematomas can also occur as a result of spinal or epidural anesthesia. For patients with thrombocytopenia or platelet dysfunction, platelet infusions should be considered. Electrolyte and fluid imbalances should also be addressed, as ascites and fluid retention occur. Patients receiving aggressive diuresis will often need correction of serum sodium, potassium, and calcium levels. Patients who are volume overloaded will need diuretic therapy with furosemide, mannitol, spironolactone, or low dose dopamine[21]. Therapeutic paracentesis may also be used in the treatment of ascites. Aspiration precautions such as ranitidine or metoclopramide are recommended as ascites, active GI bleeding, or hepatic encephalopathy may result in delayed gastric emptying and intestinal motility. Additional monitoring is needed. Arterial blood pressure monitors, pulmonary artery catheters or central venous catheters are often necessary.

The Child-Pugh classification scheme can be used to correlate patient laboratory values and the incidence of perioperative complications and mortality in cirrhotic patients. Criteria used are albumin, prothrombin time, INR, bilirubin, and degree of ascites. See Table 2.

Table 2
Child-Pugh Score[22]

Factor and Score	1	2	3
Albumin (g/dl)	>3.5	3.0-3.5	<3.0
Prothrombin time prolongation	<4	4-6	>6
INR	<1.7	1.7-2.3	>2.3
Bilirubin (mg/dl)	<2	2-3	>3
Ascites	None	Easily controlled	Poorly controlled

Class A = 5-6 points, Class B = 7-9 points, Class C = 10-15 points

In patients undergoing open abdominal procedures, mortality rate is 10%, 30%, and 80% for Classes A, B, and C, respectively.

Changes in Drug Metabolism

Changes in pharmacokinetics and pharmacodynamics are often somewhat unpredictable, and medications must be titrated carefully. Portosystemic shunting of blood should be expected and will affect drugs with high hepatic extraction. Hypoalbuminemia will affect protein bound medications such as thiopental that requires a lower initial dose. Preoperative sedatives should be given in lower doses due to impaired drug metabolism and increased response. However, vasopressors and ionotropes should be expected to have a decreased effect. Medications with potential hepatotoxicity should be avoided. Examples include halothane, acetaminophen, sulfonamides, tetracycline, penicillins, and amiodarone[22]. The effect of succinylcholine will be mildly prolonged due to decreased cholinesterase activity. Nondepolarizing neuromuscular blocking agents such as cis-atracurium will require higher doses to achieve total relaxation because even though it undergoes Hofmann elimination independent of hepatic function, hypergammaglobulinemia creates a larger volume of distribution for these drugs[21]. Transcutaneous nerve stimulators can be used to facilitate titration of muscle relaxants. When selecting an inhalational anesthetic, older agents, including halothane and enflurane should be avoided because they decrease hepatic blood supply and are associated with postoperative hepatic dysfunction. Desflurane, the inhalational agent that is most minimally metabolized is an ideal and attractive choice. Sevoflurane or isoflurane, used in combination with low dose fentanyl, have also been utilized successfully[21].

Special Considerations in Hepatic Resection

In patients undergoing hepatic resection, there is risk for massive blood loss and there is often a need for transfusions. Fluid management must be carefully considered. Controversial schools of thought exist. Traditionally, the patient is kept slightly hypervolemic or euvolemic during the surgery. The reasoning behind this is that with risk of sudden blood loss, the patient can be more easily resuscitated from a starting point of euvolemia as opposed to hypovolemia. However, another view believes that the fluids should be minimized, as to keep central venous pressure low. If central venous pressures are low, hepatic venous pressures will be kept low, and bleeding from cut hepatic surfaces will be minimized. This approach has been supported in recent literature, and improved surgical conditions, decreased blood loss, and decreased need for transfusions has been reported[23].

Other recent studies have demonstrated the effectiveness of acute normovolemic hemodilution in patients undergoing elective liver resection. This procedure involves removing blood from the patient immediately before the operation and replacing it with the appropriate volume of crystalloid or colloid fluids. The removed blood is then reinfused as autologous whole blood after the procedure is completed. If bleeding occurs, more erythrocytes are preserved with this technique, and the need for allogenic blood transfusions is significantly reduced[24].

It has also been shown that administration of aprotinin after induction can significantly reduce intraoperative blood loss and the need for transfusions. Traditionally recommended for cardiac surgery with extracorporeal bypass and liver transplantation, aprotinin has also been shown to be effective in patients undergoing liver resection. The mechanism is unclear, but its effects have been attributed to inhibition of fibrinolytic activity and preservation of platelet membrane-binding functions[25].

Epidural catheters may be used for postoperative analgesia following liver resection; however, their use is also debatable. Postoperative incisional pain is severe and controlling it also provides benefits to the patients respiratory status. One study has shown that a single dose of epidural morphine (3.5-5 mg) with small-dose ketamine (20-30 mg) provides effective analgesia with Child-Pugh grade A patients[26]. However, the high risk of coagulopathy may make the placement and removal of an epidural catheter a risky procedure. Spinal hematomas can develop. Prothrombin time and platelet count must be monitored carefully before removal of the catheter, as they often do not return to preoperative levels until post-op day 5[27,28]. The anesthesiologist must assess and weigh the benefits of pain control versus the risk of the consequences of coagulopathy.

Special Considerations in Liver Transplantation

The specific details of the large spectrum of anesthesia involved in liver transplantation are beyond the scope of this article; however, many of the same

general concerns still apply in the preanesthetic evaluation. The patient's coagulation profile, metabolic profile, and volume status must be assessed and optimized. Some of these derangements will not be correctable until after transplantation. Cardiac reserve must be adequate to tolerate the high stress of transplantation. Often peripheral arteriovenous shunting occurs due to increases in the levels of endogenous vasodilators usually metabolized by the liver. Intrapulmonary shunting can also occur, worsening respiratory compromise caused by ascites and pleural effusions. Encephalopathy and renal dysfunction are also commonly seen.

Extra monitoring is necessary: Intra-arterial pressure monitors are placed in two sites, one with a heparin-free infusion for laboratory samples. Pulmonary artery catheters allow for rapid assessment of oxygen delivery and utilization. Transesophageal echocardiography is useful for monitoring cardiac function and fluid status, as well as portopulmonary syndrome, reperfusion crisis, and suspected tamponade. In addition, preparation must be made for potential rapid transfusions. At least two large bore peripheral IV catheters (radial and femoral) should be placed and a rapid infusion system should be considered. 10-20 units of packed red blood cells, fresh frozen plasma, and platelets should be readily available[22,29].

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