ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Hepatic Complications and Liver Transplant in Congenital Cardiac Disease

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G&H What is the current understanding of the relationship between the liver and the heart?

KB The liver is the hub for several metabolic activities. In a normal anatomic setting, nutrients, medications, and toxins are absorbed from the gastrointestinal tract and reach the liver via the portal vein to undergo further metabolism. Processed blood from the liver reaches the heart via the inferior vena cava, which then gets circulated to the rest of the body. Thus, the heart and the liver are closely interconnected, and pathology in one organ can affect the other organ during the course of the disease.

G&H What liver complications may occur in patients who have congenital cardiac disease?

KB That depends on the type and severity of the congenital cardiac disease and how well the condition was managed. Congenital cardiac disease is usually found at birth, and patients require several cardiothoracic surgeries, which are scheduled sequentially in a stepwise fashion as the infant grows. Some surgeries for congenital cardiac disease require the heart, lungs, pulmonary arteries, and other parts of the body to mature. Patients with congenital cardiac disease can develop progressive heart and liver disease if the surgeries do not correct the underlying disorder or if the patient is noncompliant with the medico-surgical management.

In the past, not many infants with congenital cardiac disease reached adulthood, but with advances in medicine, the current epidemiologic data show that there are more adults than children with congenital cardiac disease. Many of these adults are now doing fairly well but still require close monitoring by their cardiology care team. Liver dysfunction can occur due to systolic heart failure (pumping of the blood) or due to diastolic heart failure (receiving of the blood). In systolic heart failure or circulatory failure, the liver and bile ducts can experience ischemic injury, but it occurs less frequently. A more common type of liver injury occurs due to diastolic heart failure, in which blood backflows from the heart into the liver, resulting in passive congestion also called congestive hepatopathy. Over time, the passive liver congestion can cause inflammation and also scar formation within the liver, which can result in cardiac cirrhosis. Similar to other causes of cirrhosis, once cardiac cirrhosis develops, the patient can develop hepatosplenomegaly, ascites, variceal bleeding, hepatic encephalopathy, end-stage liver disease, or hepatocellular carcinoma.

G&H Can congenital cardiac disease cause any other effects on the liver?

KB Congenital cardiac disease can cause a spectrum of liver disorders. The extreme end is cirrhosis and its related complications, as previously discussed, but many patients can have other manifestations. Patients with congenital cardiac disease can experience circulatory insults during the perioperative period of their cardiac surgery resulting from anesthesia, antibiotics, and cardiac medications. There are times when management needs to be tailored, especially when liver enzyme elevations are significant.

Infectious viral hepatitis, autoimmune hepatitis, drug-induced liver injury, alcoholic liver disease, metabolic liver disease, and fatty liver can also coexist in patients with congenital cardiac disease. Once the exact cause or causes are determined, specific therapies need to be administered, and strategies to avoid ongoing insults are necessary to prevent progression to cirrhosis.

Approximately 40% of patients with congenital cardiac disease can have clinical evidence of cirrhosis, but not every patient with cirrhosis has to undergo combined heart and liver transplant.

G&H When should a patient with congenital cardiac disease be evaluated for transplant, and what determines the requirement for heart or liver or combined organ transplant?

KB Transplant candidacy in a patient with congenital cardiac disease depends on the severity of cardiac or liver failure. In the absence of liver dysfunction, a congenital cardiac disease patient with severe cardiac failure can safely proceed with isolated heart transplant. Approximately 40% of patients with congenital cardiac disease can have clinical evidence of cirrhosis, but not every patient with cirrhosis has to undergo combined heart and liver transplant. Although rare, a congenital cardiac disease patient with normal cardiac function who develops end-stage liver disease due to a noncardiac cause can undergo isolated liver transplant. However, a more common scenario is when a patient with congenital cardiac disease develops both cardiac and liver dysfunction. In this scenario, there is no strict scientific consensus, but most congenital cardiac disease patients with non-severe liver dysfunction can safely undergo isolated heart transplant and infrequently require combined heart and liver transplant. In patients with early cirrhosis, there is evidence that the liver with its high regenerative capacity can experience reversal of cirrhosis if the heart transplant occurs in time. Patients with congenital cardiac disease who have complications of cirrhosis would require combined heart and liver transplant. In general, if a pre–heart transplant patient develops any of the following 4 complications from cirrhosis—ascites, variceal bleeding, hepatic encephalopathy, or hepatocellular carcinoma—he or she should undergo evaluation for combined heart and liver transplant. Such patients have poor outcomes if they undergo isolated heart or liver transplant or sequential heart and liver transplant (ie, they receive organs from different donors at different times). However, there is debate about the patients in the intermediate zone, and ongoing research is needed to establish cutoff criteria at which point patients with congenital cardiac disease would definitively require combined heart and liver transplant. A personalized approach is necessary to evaluate a patient with compensated cirrhosis (ie, there is excess scarring in the liver but the cirrhosis is not associated with complications) to determine if the patient can undergo isolated heart transplant, and if the liver would improve. Evidence has shown that if such a patient receives a heart transplant, although cirrhosis is present, it can reverse because it is secondary to heart failure.

It should be noted that the volume of patients who have undergone isolated heart transplant far exceeds the volume of patients who have undergone combined heart and liver transplant. However, although cirrhosis is found in many patients with congenital cardiac disease, the presence of cirrhosis alone does not warrant combined heart and liver transplant.

G&H Have other parameters for transplant in these patients been studied?

KB The trigger for combined heart and liver transplant is complications from cirrhosis. Most of the time, clinical parameters such as platelet count, liver function test results, international normalized ratio, and albumin level will indicate whether the patient will do well. Another indicator, especially in patients with cirrhosis, is the thickness of the scar seen in liver biopsy. Patients with thinner scars will be able to tolerate an isolated heart transplant, and if the insult to the liver is taken away (in this case, congenital cardiac disease), the liver will regenerate and the cirrhosis will reverse.

Other parameters, such as Model for End-Stage Liver Disease (MELD) score and hepatocellular carcinoma or other MELD exceptions as per United Network for Organ Sharing/Organ Procurement and Transplantation Network policies, are also taken into account when determining candidacy for liver transplant. In a study that analyzed patients who underwent combined heart and liver transplant vs isolated heart transplant, the only difference was an elevated international normalized ratio in

the combined heart and liver transplant group. This likely shows that these patients had significant hepatic dysfunction compared to patients who underwent isolated heart or liver transplant.

G&H Are there any other advantages to combined heart and liver transplant?

KB One of the advantages of combined heart and liver transplant is that the patient receives a heart and a liver from the same donor at the same time. Thus, there is not as much antigen overload as compared to when a patient receives a heart from one donor and a liver from another donor, as could occur in a sequential transplant.

Another advantage is that the liver, being an immune-tolerant organ, somehow protects the heart from acute rejection. Comparing patients who underwent isolated heart transplant and patients who underwent combined heart and liver transplant, episodes of rejection occurred less frequently in the latter group. The exact mechanism is unclear, but the evidence certainly points to the beneficial role of the liver to prevent rejection in recipients of combined heart and liver transplant compared to recipients of isolated heart transplant. However, that alone should not be the reason to consider combined heart and liver transplant, as the long-term outcomes at 3, 5, and 10 years are similar in recipients of isolated transplant and recipients of combined transplant. Thus, an individualized approach should be used to determine the candidacy for isolated or combined organ transplant.

G&H What are the next steps in research in this area?

KB There are clear-cut indications of when a patient requires a combined heart and liver transplant if there are overt signs of heart and liver failure. However, in a congenital cardiac disease patient with compensated cirrhosis, the current approach is still an individualized, case-by-case evaluation. Cutoff criteria and long-term outcomes in congenital cardiac disease patients with cirrhosis who undergo isolated heart or liver transplant vs combined heart and liver transplant are needed to endorse a uniform strategy. However, such research could be difficult because of the heterogeneous patient population. Congenital cardiac disease can range from one to multiple disorders, and can require few to many surgeries. The cumulative volume of combined heart and liver transplant has been relatively low over the years, and transplantable organs are a scarce resource, posing additional limitations for prospective trials with large sample sizes.

Disclosures

Dr Bhamidimarri has no relevant conflicts of interest to disclose.

Suggested Reading

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