

ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Current Status of Liver Transplantation



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G&H Currently, what are the most common indications for liver transplantation in the United States?

RV The 3 most common indications for liver transplantation in cirrhotic patients are alcoholic liver disease (40%), nonalcoholic steatohepatitis (NASH; 30%), and hepatitis C virus (HCV; 20%). However, the order is different in patients with hepatocellular carcinoma (HCC). In this setting, HCV is the leading indication (40%) and then NASH (25%) and alcoholic liver disease (15%). HCV used to be the most common indication for liver transplantation in cirrhotic patients as well but is decreasing because of the highly effective medical treatments that are now available for HCV. NASH and alcoholic liver disease are climbing quickly as indications, and HCC continues to increase in patients with underlying liver disease.

G&H Currently, what are the typical outcomes following liver transplantation?

RV Most centers around the country now have a 1-year survival rate above 90%, which is very good. The 3-year survival rate is above 80%, and survival beyond 3 years remains steady, dropping only a few percent every year. HCV used to be difficult to manage because it could recur after transplantation. However, with highly effective medical treatments now available, I believe that 3- and

5-year survival rates will further improve. Of course, people may still die of other, nontransplant-related causes, such as heart attacks and strokes.

It should also be noted that, unlike other solid organs, the liver can regenerate. In addition, it is more tolerant to episodes of rejection than other solid organs, and it is more resistant to chronic damage by the immune system.

G&H What are the biggest challenges involving liver transplantation at the current time?

RV Organ distribution has been challenging. Allocation keeps changing, and some transplant candidates benefit while others do not. Despite many attempts to improve the allocation system, regional discrepancy remains an issue. Another challenge is expanding the donor pools. Across the country, there is a large discrepancy in the performances of the agencies that procure organs. Some are performing very well, which benefits local and regional centers. However, other agencies are performing badly, which is a hurdle that ends up causing discrepancies in the availability of organs.

In addition, patients waiting for combined liver/intestine transplants currently have a disadvantage, as organs are allocated through the liver waiting list. It is very challenging to find organs for these patients, in whom very complex operations are required. People who need only a liver have a much higher likelihood of being transplanted than if they need other organs as well.

G&H What have been the most recent changes in the allocation system, and what further adjustments should be considered?

RV Instead of geographic donor areas, nautical miles are now being used. Priority for receiving organs is given to the sickest patients within a radius of 150 nautical miles of the donor hospital and then 250 nautical miles and then 500 nautical miles. This system works well for centers surrounded by cities and populated areas. However, my institution in Miami is in the bottom of a peninsula. Thus, when drawing a 360-degree circle around us with nautical miles, there is population only on the coast; we are otherwise surrounded by the Everglades and the ocean. This is one of the flaws of the system.

In addition, access to livers should be improved. Many patients are still dying because they do not have access to hospitals or hepatologists, particularly in less-populated areas in the middle of the United States. Distribution of organs is complicated, but I think we should increase access for people with liver disease as well as improve the performance of centers and procurement agencies.

G&H Has the coronavirus disease 2019 pandemic affected liver transplantation?

RV It did, but only for a brief period of time. As soon as the coronavirus disease 2019 (COVID-19) pandemic hit, there was a decrease in the number of liver transplants performed, but transplantation never stopped. The Miami Transplant Institute (MTI) tied with the University of California, Los Angeles for performing the most transplants (overall, not just liver transplants) last year—721. The MTI actually performed more liver transplants in 2020 than in 2019, even with the COVID-19 pandemic. People with chronic disease have a higher likelihood of dying of COVID-19 than posttransplant patients who have renal or liver failure. Fortunately, the MTI and the hospital system understood the risk for patients with chronic liver disease and kept transplanting.

G&H Should HCV-positive patients be treated for HCV infection before or after liver transplantation?

RV This question is still being debated, but I think treatment should depend on the center's current practice and for how long the patient will most likely remain on the transplant waiting list. I think HCV-positive patients can be treated before liver transplantation if the procedure can be avoided. If a patient is treated for HCV infection and later receives an HCV-positive organ, the patient would

have to be retreated for HCV. Use of HCV-positive livers increases the donor pool and the chances of receiving a life-saving liver transplant.

G&H Could you further discuss the current status of using HCV-positive livers in patients who are not infected with HCV?

RV My institution and I think most centers are now using HCV-positive organs and then are treating patients for HCV infection afterward. These patients will be infected with HCV after transplantation, but HCV is now a curable disease in more than 99% of cases so patients will be infected only for a brief period of time. A patient should not miss out on a good organ because of HCV.

G&H Does the 6-month rule still have value for the transplantation of patients with alcoholic liver disease?

RV As HCV decreases as an indication, I am seeing many articles being written about which patients with alcoholic liver disease should be transplanted. Many centers have had policies that patients have to wait for 6 months of sobriety before they can be transplanted and that patients who are dying of liver failure caused by acute alcohol abuse should not be transplanted. The 6-month rule has been reevaluated because the time period was chosen arbitrarily. Researchers have looked at outcomes and have found that it is very important to know if patients keep drinking even if they are told to stop, how many times patients relapse, and if patients have social support. There are scores now that allow for liver transplantation in patients with alcoholic liver disease without making them wait 6 months.

G&H Have there been any recent trends involving living-donor liver transplantation in the United States?

RV There are a few centers that are performing it, but the number is still low. The United States has prioritized many patients who are sick, so patients with high Model for End-Stage Liver Disease (MELD) scores can be transplanted quickly. One gray area is if patients have low MELD scores that are not reflecting how sick they are, or if they have a tumor and fall off the criteria for transplantation. Those are the patients receiving livers from live donors. There are areas that are suboptimized in the United States (eg, donation after cardiac death). Only 10% to 15% of those organs are being used; that proportion could increase. In addition, there is some aversion for centers to start living-donor programs. I am very often able to find a

suitable liver for patients with lower MELD scores, which I think should always be the preferred option.

G&H What is the current status of liver transplantation in patients with HCC?

RV HCC represents 30% to 40% of liver transplants performed in the United States, depending on the center, and continues to increase as an indication. Even if a patient is treated for HCV cirrhosis and does not need a liver transplant at that point, that liver is still inflamed and has a greater likelihood of developing HCC. The same situation occurs in patients with cirrhosis caused by NASH. Currently, patients have to wait 6 months on the transplant waiting list to see how their tumor behaves. I believe that improvements are needed for liver allocation for patients with HCC. For example, a 75-year-old patient and a 35-year-old patient with a 5-cm tumor are given the same number of points for transplantation even though the younger patient likely has many more years of life left than the older patient.

G&H What are the priorities of research in liver transplantation?

RV There has been much research on developing immunosuppression with fewer side effects, but more research is still needed. Tacrolimus is the most-used drug and is

combined with others, but side effects can still occur. It is also crucial to improve research on how to use organs that are currently being discarded and deemed not suitable for transplantation.

The most meaningful research would involve ending the transplant waiting list, perhaps with regenerative medicine to improve liver function or to recreate a liver, or with xenotransplantation, which is the transplantation of an animal liver into humans. These advances would impact not just liver transplantation but transplantation of all organs.

Disclosures

Dr Vianna has no relevant conflicts of interest to disclose.

Suggested Reading

- Burton JR Jr, Terrault NA, Goldberg DS, et al. Liver and kidney recipient selection of hepatitis C virus viremic donors: Meeting Consensus Report from the 2019 Controversies in Transplantation. *Transplantation*. 2020;104(3):476-481.
- Chadha R, De Martin E, Kabacam G, et al. Proceedings of the 25th Annual Congress of the International Liver Transplantation Society. *Transplantation*. 2020;104(8):1560-1565.
- Crabb DW, Im GY, Szabo G, Mellinger JL, Lucey MR. Diagnosis and treatment of alcohol-associated liver diseases: 2019 practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2020;71(1):306-333.
- Hughes CB, Humar A. Liver transplantation: current and future [published online January 17, 2020]. *Abdom Radiol (NY)*. doi:10.1007/s00261-019-02357-w.
- Müller PC, Kabacam G, Vibert E, Germani G, Petrowsky H. Current status of liver transplantation in Europe. *Int J Surg*. 2020;82S:22-29.