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Living Donor Liver Transplantation: Balancing Donor Risk with Recipient Need

Michael R. Lucey

In the past few years in the United States, while transplant waiting lists have burgeoned, especially with relatively stable patients, the absolute number of patients dying awaiting liver transplantation has grown every year. This fact is the principal stimulus to the growth of live donor liver transplantation. Living donor liver transplantation removes the mandatory and uncertain interval between selection for transplantation and receiving the operation. Living donor liver transplantation reunites selection and transplantation. The pressure for living donor liver transplantation arises from patients and families faced with an uncertain interval to receive a cadaveric allograft.

The number of donor deaths after liver donation from living adult donor to adult recipient is in dispute. My non-scientific informal survey at the recent NIH-sponsored workshop suggested that there have been two such deaths in Germany, one in France, and at least one in the United States. The denominator of transplants from which this experience arose is uncertain also, but a rough estimate would suggest 500 procedures. Therefore the mortality risk to the donor might be as high as 1%. I was struck by the notion, put forward at the NIH workshop by Mark Siegler, that this risk is inherent to the procedure, and is unlikely to be reduced by improvements in technical ability and clinical management consequent upon greater experience within the individual programs. In addition, there is the risk of morbidity, loss of time from work, and immediate financial losses. The psychological risks should be considered, including the need for the donor to accept allograft

failure after live donation. Finally, there is the potential for late financial risk which might occur if the donor were to be penalized by health and/or life insurance providers on account of some consequence of becoming a living liver donor. The complexity of these risks makes getting informed consent from the donor and the recipient more difficult.

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An important question concerns whether the rules governing selection of patients with serious liver disease for cadaveric donor livers are appropriate for living donor liver transplantation. This is illustrated by the following example. In our program, we have adopted an arbitrary rule that a potential recipient for live liver donation must first qualify for a cadaveric organ. In other words, we require the

patient to meet the accepted minimal criteria first, broad though they may be. The minimal criteria rules include directions to exclude patients with large liver cancers, even when the tumor is confined within the hepatic capsule, without evidence of spread. The rationale of this rule for allocation of cadaveric allografts is based on the impaired survival in patients transplanted for bulky HCC, and the notion of proper stewardship of the scarce donor organ resource. The utilization of a live liver donor would appear to obviate the second of these concerns. It should be noted that live donor transplantation might still affect the cadaveric pool of donor organs in the following way. Whenever a partial allograft from the healthy living donor exhibits primary graft non-function, the recipient may have to undergo emergency retransplantation with a donor organ from the cadaveric pool. Nevertheless, when discussing balancing risk to the donor with benefit to the recipient in the context of living donor liver transplantation we should keep in mind that the rules formulated for transplanting cadaveric organs may not apply, and new rules will have to be developed.

I am going to discuss balancing donor risk with recipient need in the context of four separate groups of recipients.

Fulminant Hepatic Failure

Patients with fulminant hepatic failure represent the most urgent patients likely to need liver transplantation. Once it has been decided that liver transplantation is the best therapy, there is no advantage to the recipient to delay the procedure. Questions regarding the best way to determine the prognosis in fulminant failure, and therefore, when to choose transplantation rather than supportive care are beyond the scope of this brief overview, as are considerations of alternatives to orthotopic transplantation such as auxiliary transplantation. Most programs would accept a cadaveric donor if one were forthcoming in the interim while preparing for living donor liver transplantation. The dilemma in this case concerns the consent of the donor and of the recipient. Regarding the donor, the rapid deterioration of the candidate recipient

puts added pressure on the potential donors. We should ask what are the appropriate checks and balances to protect the donor from coercion, harassment or simply an excessively hasty decision? At the same time, this circumstance of the potential recipient differs from the more typical patient with cirrhosis, in that he or she may not be capable of participation in the decision-making process. It is a common experience among cirrhotic candidates that the patient will decline to accept an organ from a family member or friend. In my experience this is particularly the case in donation from child to parent. The encephalopathic fulminant patient on assisted ventilation is shut off from the discussion on their willingness to put their family member/friend at risk.

Decompensated Chronic Liver Failure

This patient group corresponds to the fulminant group in urgency, but differs in that the recipients often have significant chronic multi-organ dysfunction and malnutrition. For these reasons, the potential for a poor outcome after liver transplantation is greater. More specifically, it is at least theoretically possible that cirrhotic patients with decompensated liver disease may be less able to regenerate the partial liver graft than recipients who are better conditioned prior to surgery. In other words, it may be preferable to wait for very ill patients to recover pulmonary or renal function, or gain nourishment before undertaking liver transplantation with a partial graft. Conversely, it has not been established whether patients with multi-organ system failure or malnutrition should be prevented from receiving a living donor graft. More data on outcomes are needed after living donor liver transplantation in this population. The pressure on the transplant team from family members may be great, especially if the patient has already waited a long time on the list, enduring a slow decline. The capacity of the potential recipient to participate in the discussion may be compromised by encephalopathy or assisted ventilation (as discussed in relation to fulminant hepatic failure).

Well-Compensated Liver Disease

This group corresponds to the UNOS status 3 patients. As mentioned above, this population includes many people unlikely to need a transplant in the next 2 years. Most of these patients would have been excluded from the waiting list had more stringent minimal criteria been adopted. There is a danger that these patients will become the substrate for growing living donor transplant programs. Among this population are patients with severe impairment of "quality of life" due to pruritus, ascites, sleep disturbance or muscle cramps. Here the question of balancing risk to the donor with benefit to the patient turns on the impact of transplantation on symptoms rather than quantity of life. I would advise withholding living donor liver transplantation from this population unless there is an exceptional symptomatic reason.

Liver Tumors

It goes without saying that primary resection is the treatment of choice of hepatoma whenever feasible. Similarly, any evidence of extra-hepatic spread of a hepatoma or cholangiocarcinoma precludes transplantation irrespective of the nature of the allograft donor. Patients with small tumors (<5 cm) or few tumors (<3) who meet UNOS listing criteria require transplantation without delay. Living donor liver transplantation offers a mechanism to provide transplantation quickly. In our area, any patient in blood group O or A who has a hepatoma should be considered for living donor transplantation. Even after the patient has been placed on the waiting list for a cadaveric donor organ, he/she will wait such a long time that they risk death from their tumor before their name rises up to the top of the UNOS allocation list. Therefore, these patients make good candidates for living donor liver transplantation.

Living donor liver transplantation for patients with hepatic tumors which would be considered untransplantable is an area of great controversy. The crux of the dilemma concerns the patient who is outside the UNOS guidelines for a cadaveric graft, but for whom the prospects for long-term survival without transplantation are poor. It will be

very difficult to get good comparative data on the relative merits of living donor liver transplantation compared to other types of treatment in this population. The goals of therapy need to be addressed: cure of the tumor, correction of liver failure, palliation of a tumor. These are issues of suitability for transplantation when the risks to the donor remain real, and the benefits to the recipient are, in all probability, palliative rather than curative.

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