



The Ethics of Living Related Liver Transplantation When Deceased Donation Is Not an Option

Thomas D. Schiano, M.D.* and Rosamond Rhodes, Ph.D.†

Introduction

Organ transplantation raises numerous ethical issues, and over the past three decades, the transplant community has discussed many of them. A measure of consensus has been achieved on many issues, such as the acceptability of the brain death standard, the use of deceased donor organs, allocation of organs based on urgency and need rather than social factors, and the acceptability of living donor transplantation.¹

Donor safety is given the utmost priority in live donor liver transplantation (LDLT).² It requires comprehensive informed consent and judicious medical assessment for both donor and recipient.^{3,4} When a liver transplant (LT) candidate is declined for listing to receive a deceased donor organ, sometimes a loved one comes forward and offers to be a living donor. This rare occasion raises the ethical question of whether a patient who is not eligible for a deceased donor transplant should be eligible for LDLT. In other words, should the same standards that are used to decline listing a patient on the United Network for Organ Sharing (UNOS) waitlist also be used for determining whether a LDLT should be performed. The following two cases illustrate this vexing problem, followed by a discussion of the ethical justification for proceeding with LDLT.

Case 1

JJ is a 17-year-old adolescent with decompensated liver disease from extrahepatic biliary atresia. He has ascites, protein-calorie malnutrition, and recently had a hospitalization for esophageal variceal bleeding. His MELD (Model for End-Stage Liver Disease) score is 19. Over the last several years, JJ has had issues with nonadherence with follow-up in the Hepatology office and in taking his medications. He

is currently in school, but has displayed rebellious behavior. For a while, he had moved out of his parents' home and was living with a girlfriend, but that relationship has ended and he is now back at home with his family.

JJ was evaluated by the social worker and psychiatrist; no substance abuse issue or psychiatric problem was identified. Despite this, the LT team had mixed feelings about placing JJ on the waiting list, being concerned about potential non-compliance with posttransplant protocols and medications. Although the patient expressed interest in LT and had understanding of the severity of his liver disease, he seemed to lack insight regarding the detriments of his behavior.

Ultimately, JJ was declined as a LT candidate, because there were concerns about adherence with post-LT care. It was recommended to the patient and his parents that they seek an opinion from another LT center. His parents, however, came forward the next day, both volunteering to be living donors for their son. They strongly believed that their involvement in the LT process in this manner would strengthen their bond with JJ, promote his posttransplant adherence, and give him a new lease on life.

Case 2

RC is a 47-year-old woman with hepatitis C virus cirrhosis and hepatocellular carcinoma (HCC) and a natural MELD score of 15. She has a 3-cm tumor that has undergone several courses of locoregional therapy. With exception points related to her HCC, her current MELD score is 31, and she has made it to the top of the center's waiting list. A recent scan shows residual active tumor and a new 1.4-cm HCC. The imaging also showed a right breast mass. RC is worked up and found to have Stage 2 breast cancer after lumpectomy and sentinel node sampling. RC tolerates the

Abbreviations: HCC, hepatocellular carcinoma; LDLT, live donor liver transplantation; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; PNF, primary nonfunction; UNOS, United Network for Organ Sharing.

From the *Division of Liver Diseases, The Mount Sinai School of Medicine, New York, NY, and †Department of Medical Education, The Mount Sinai School of Medicine, New York, NY.

Potential conflict of interest: Nothing to report.

View this article online at wileyonlinelibrary.com

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doi: 10.1002/cld.508



procedures well, but her MELD rises to 20 with new-onset ascites. The team concludes that she is now unable to tolerate further treatment for her HCC or any adjuvant therapy for the breast cancer.

The LT team is split as to whether to proceed with imminent LT or de-list RC because of her recently diagnosed breast cancer, despite the potential excellent 5-year survival. The consensus opinion was to not proceed with LT. The next day, the patient, her husband, and their three children came in for a meeting in which they were given the committee's decision. It was recommended they seek a second opinion at another center. Her husband volunteered to be a live donor, and both he and his wife strongly expressed the desire to proceed with LDLT despite the potential risks associated with the breast cancer and the need for RC to undergo posttransplant cancer therapy.

Discussion

Both of these cases illustrate a problem that transplant centers infrequently confront, namely whether to proceed with LDLT for a patient who would not be listed for a transplant with a deceased donor organ. There has been no clear and convincing answer to the question of what to do when a living donor is available and the patient is eager to have a living donor transplant in this scenario. Should the transplant center evaluate the recipient by the same standards that are used for deceased donor transplantation or should the criteria be more rigorous or less demanding? Noting that none of these options is currently regarded as off the table suggests that the issue requires further exploration.

LT is markedly different from kidney transplantation, because kidney patients who are not listed for an allograft have the life-preserving option of dialysis. There is no alternative life-preserving treatment for patients with liver disease. Unlike the situation with kidney transplantation, a patient who is turned down for deceased donor listing and for LDLT will die.

All solid organ living donor transplantation involves the harms of scarring, the loss of an organ, as well as the physical and psychological risks and burdens associated with the organ procurement surgery and the physically and emotionally complicated aftermath for both donor and recipient. Subjecting a healthy person to such risks and burdens for the sake of another individual is remarkably unusual for medical practice in which the focus has traditionally been on "do no harm." That said, living donor transplantation has been accepted in our society because of the dire circumstances that the procedure addresses and because the transplant community has shown that it can be trusted in making the difficult decisions involved.

In any living donor situation, the harms and burdens to the donor are justified by the significant benefit to the recipient.²⁻⁴ Because there is an alternative to living donor transplantation in the kidney transplant situation, kidney transplant programs often require that the recipient of a living donor kidney have an equal or better prospect of long-term survival than the recipient of a deceased donor organ would. In other words, if a patient listed for kidney transplantation is required to have at least a 90% chance for a 5-year graft and patient survival, a patient who is to receive a living donor organ should have a similarly good prospect or an even a better chance of success. The comparison between LDLT and kidney transplantation is further complicated by the fact that LDLT involves significantly greater risks than living donor kidney transplantation does. In the United States, approximately 1 in 1000 liver donors may die, whereas death associated with kidney donation is extraordinarily rare.⁵

In LT, a 50% to 70% chance of 5-year survival is often a benchmark for listing patients for transplantation.⁶ Should the standard be higher or lower when a living donor is involved? What is at stake in these decisions is the life of the recipient, the reputation of the transplant community, and the standing of the transplant program.

Justice

The formal principle of justice requires that similar circumstances be treated similarly and different circumstances be treated differently. This principle applies to allocations of specific resources among all claimants who have standing relative to the distribution. UNOS and the transplant community demonstrate their appreciation of this basic requirement of morality in adopting allocation rules such as the MELD system, in which transplant programs show nonjudgmental regard in their treatment of every patient regardless of why the patient comes to need an organ transplant.

When it comes to allocation from the pool of deceased donor organs, we expect every LT candidate to be treated fairly, that is, they all should be assessed by the same standards. Because there are not enough deceased donor organs to meet the needs of every candidate who could benefit from an LT, we accept that those who are not expected to receive a significant benefit from LT should be denied an organ so that others who are more likely to derive a significant benefit can have the chance to receive the gift of life.⁷ For the most part, those who receive a LDLT will not be taking an organ from the pool. The organ would only be donated to that specific recipient largely because of some special feature of a personal relationship. No one else who needs an organ would be in line for that organ. In that way,



living donor transplantation does not involve any injustice to the other candidates on the transplant list.

The remaining issue of justice involves a comparison of those who receive LDLT with the treatment of people who have other medical needs. In our society, patients are typically provided with essential medical care regardless of how small the benefit they will derive. Treatments that are expected to extend life by 2 years or even 1 year are typically considered worthwhile and provided to patients who want them. Patients are even provided with costly treatments that are only expected to extend life by months or weeks or days. Considering LDLT in comparison with other medical needs suggests that justice requires that similarly effective interventions be made available to those with liver failure. So long as LDLT is likely to be effective it should be provided, as long as the recipient who was declined for listing may survive as long as the other LT patients who are listed for deceased donor organs.

Setting the Limits: The Not “Unreasonable” Standard

Our society is reluctant to ration health care and draw a line that limits access to medical interventions that are not likely to provide a significant benefit. Living donor transplantation may be an exception that actually requires setting limits. The important difference between living donor transplantation and other medical interventions is the risks and harms that are imposed on another person. Because of this unique feature of LDLT, we have to consider the amount of benefit to the potential recipient in relation to the risks incurred by the donor.²

In any decision involving the use of a living donor, the likely benefits to the recipient have to be assessed and weighed against the risks to the donor. Although it is hard to be precise, it may be enough to draw the line for LDLT a bit below the line for listing, but not far below that standard. This leniency could allow LDLT for example, when a patient had a 40% chance of 5-year survival, but not for a patient with a 40% chance of 2-year survival. Roughly speaking, the transplant community should accept living donor transplants when the risk/benefit ratio is reasonable, and not when it is unreasonable. This is the rigid stance that LT programs should hold when potential live donors come forward when LDLT might extend life for the recipient only for a very short time, as in the case of significant metastatic cancer to the liver.

Two reasons justify setting limits on living donor transplantation. First, is the medical duty to act in the interest of each patient. Whereas the living donor may see redeeming value in risk-taking, medical professionals have a fiduciary responsibility to advocate for their donor patient and

protect the donor from harm. From the point of view of the medical team, they must independently assess the benefits and burdens and conclude that the promised benefits are worth the risks involved.

Second, although, from the point of view of an eager potential donor, any amount of life extension may be worth the risk, a brief life extension (eg, six months) is likely to appear trifling to the society that is trusting the transplant community to make reasonable decisions. For society to continue to allow the transplant community to perform living donor transplants, it needs to be confident that decisions are being made carefully and thoughtfully, and with a due degree of caution. It is hard to imagine that our society would tolerate a practice that jeopardized the life of a healthy donor for the sake of a trivial benefit to another individual. Each individual transplant team is responsible for making its own decisions about when to go forward with LDLT. The eagerness of the live donor cannot be a factor in that decision.⁴ To maintain the trust that has contributed to the acceptance of living donor transplantation, programs have to be able to justify their decisions in a way that society will regard as being trustworthy. This consideration requires programmatic decisions to reflect the kinds of judgment that others will see as appropriate, rather than foolhardy, reckless, or self-serving.

Today's transplant programs tend to be vigilant and attentive in excluding living donors whose pretransplant workup indicates any medically identifiable additional risk that could make the overall risk to their lives greater than what could otherwise be expected. Numerous medical tests are performed in the evaluation of living donors; for medical reasons, a good program will rule out as many as 80% to 90% of those who come forward as potential donors.⁴ Caution is the well-accepted benchmark in donor evaluation.

At the same time, because likely benefit is the only justification for imposing risks on healthy live organ donors, the likelihood of the benefit also has to be considered. Whereas parents and other loved ones may be willing to take significant risks to prolong the life of their beloved for even a short period, they do not have the right to demand inappropriate medical interventions.^{1,8} As a society, we allow physicians the authority to make these decisions and we hold transplant physicians accountable for the decisions they make. In sum, as the Ethics Committee of the Transplantation Society noted in the 2004 Amsterdam Forum on the Care of the Live Kidney Donor, the use of organs from living donors must “be performed in a manner that will minimize the physical, psychological, and social risk to the individual donor and does not jeopardize the public trust of the healthcare community.”⁹

The transplant community would like to be able to use LDLT to help patients in the future, including some patients



who would be declined for deceased donor organ listing. In order to maintain their ability to do so, they must demonstrate that they behave responsibly in their decisions to undertake LDLT. As much as some members might want to deny it, the continued privileges of the transplant community depend on the public's confidence. Like Caesar's wife, whose actions must not only be good but also look good ("must be above suspicion"), the actions of the transplant community must always appear reasonable and measured. For all of these reasons, transplant programs must avoid performing living donor transplants when the risks involved are unreasonable and limit their agreement only to those cases where the risks are not unreasonable.

The Confounding Prospect of Primary Nonfunction

Primary nonfunction (PNF) is a rare complication of LT. The real possibility of PNF complicates our approach to LDLT and the issue of not impacting the deceased donor pool with LDLT, and requires some discussion.

Patients who are declined for listing and then accepted for LDLT are required to be placed on the UNOS list until they receive their LDLT. If PNF should ensue shortly after the LDLT, should these patients be eligible for a LT that would then involve taking an organ from the common pool? We have previously argued against listing patients for LT whose chance of success was below the preset standard. Nevertheless, we see reasons to support the position that LDLT patients who had been declined for listing but allowed a LDLT should be relisted and offered another transplant organ for PNF, so long as the patient still had a reasonably good chance for a successful outcome.

One reason to support this reflects the nature of human psychology. It is hard to imagine that the surgeons who explanted the patient's native organ would not feel tremendous guilt in the face of PNF and would have difficulty in allowing the patient to die when timely retransplantation would be life-saving. The anticipation of that reaction is likely to make the transplant team reluctant to undertake LDLT without having the retransplant option at their disposal. The psychological impact of anticipated guilt has made the option of retransplantation a critical component of LT practice. The potential benefits of LDLT to the psychological and emotional well-being of the donor would also be dashed if retransplantation was not pursued, and might even compromise them due to guilt surrounding the nonfunction of their donated organ.

An additional reason for supporting the need to retransplant in the setting of PNF is the reality of transplant program viability. Transplant outcomes are reported and monitored, and graft failures and patient deaths negatively

impact a program and can have a number of serious repercussions. It is hard to imagine that programs would be willing to offer LDLT if they were denied the option of relisting patients who still had a reasonable overall chance of success even after PNF. The same principles should also apply to other causes of graft failure, ie, ischemic cholangiopathy as well as other biliary complications and hepatic artery thrombosis, even if these occur sometime after the transplants. As long as the etiology of the graft failure is in no way related to nonadherence, re-LT should be considered. If the patient demonstrates compliance and the ability to take care of the organ, retransplantation is consistent with the initial decision of proceeding with LDLT.

Applying the Standard

In light of the above discussion, how do we reconcile the consideration and ultimate approval of LDLT in the two cases presented? In case 1, JJ's parents feel that their life-saving gesture of being a donor will further demonstrate their love and commitment to him, and that it will help him to better comply with post-LT care. Having their son die without being allowed the opportunity to help save his life might leave them with long-term guilt and psychological scars. If the issue of post-LT adherence and follow-up was mitigated, JJ's survival would be expected to be as good as if he was transplanted off the list. As long as JJ's parents complete the same rigorous evaluation as any potential donor candidate and are accepted as candidates by the independent donor advocacy team, including by social work and psychiatry, LDLT is reasonable in this case. We do not believe, however, that the reasoning for LDLT in JJ's case is applicable to every patient who abuses substances or demonstrates noncompliance. The consensus opinion of the LT team and JJ's parents was that this patient's behavior would be altered for the better by his parent's LDLT and with maturity. The same expectation might not hold true for adults having ingrained behaviors that would require more structured behavioral modifications or more significant support.

In case 2, the husband of RC would be expected to meet the same requirements and derive the same benefits as other living donors. He would know that he had done everything he could to save the life of his wife. The comprehensive informed consent process he would undergo would also include the prospect that the survival of his wife might be impacted by her recent cancer. However, with the typical long-term survival for stage 2 breast cancer, it could be expected that RC's long-term survival would still be excellent. Uncertainties would abound, however, regarding the additional risks of chemotherapy on allograft function, and the effects of immunosuppression on the natural history of



the cancer. The dissention of the transplant committee to delist RC reflected the view that it would not be fair to allocate an organ to her when it was likely that another patient on the waiting list would derive a significantly greater benefit from it. They did not find that the length of her survival would be very short. Non-utilization of the donor pool, and the potential psychological benefits to the husband of RC if accepted as a candidate, are the reasons why LDLT is reasonable in this scenario. In neither case are there concerns about coercion of the family since the LDLT option was independently broached by them, and because they would be required to undergo the same comprehensive donor evaluation as all others.

Conclusions

It is critically important to carefully consider the prospect of producing a reasonably good outcome before any LDLT is undertaken for patients who would otherwise be declined for listing. Because each case in which living donor trans-

plant for a patient who would otherwise be ineligible for a deceased donor transplant is likely to be heart-wrenching and involve its own idiosyncrasies, it is important to develop a programmatic policy in advance to guide these difficult decisions and carefully consider the prospect of LDLT. Criteria for declaring that the use of a living donor is not unreasonable should be clear. Ideally, they should be endorsed by a consensus of the team when there is no particular case at issue that could color the team's judgment. In addition to the well-accepted standards that focus on minimizing donor risks by excluding donors for medical reasons, the criteria for the acceptability of living donor transplantation should focus on the likelihood of both long-term and intact short-term recipient survival.

CORRESPONDENCE

Thomas D. Schiano, MD, Division of Liver Diseases/Recanati/Miller Transplant Institute, The Mount Sinai Medical Center, One Gustave L. Levy Place, Box 1104, New York, NY 10029. E-mail: thomas.schiano@mountsinai.org

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