Innovative Approaches to Improving Organ Availability for Small Bowel Transplant Candidates

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Small bowel transplant candidates have unique features that create special challenges for providing them with organs in a timely manner. More than half of intestinal transplant candidates also need livers. Because there is a greater overall demand for livers than for small bowels, organ allocation in this candidate subset is dictated by the liver allocation policies. However, the extremely high mortality rate associated with patients on the waiting list for combined liver-intestinal transplantation (LIT) attests to the inadequacies of the liver allocation system in recognizing the unique risk factors in patients with intestinal failure who develop end-stage liver disease (ESLD). This report addresses some of the organ allocation issues underlying the discrepancies in waiting list outcomes seen in LIT candidates and discusses possible contributory factors and potential solutions to this problem. The use of living donor and segmental grafts from deceased donors are discussed specifically as potential surgical solutions to the problem, and the potential utility, limitations, and ethical concerns associated with these innovative strategies are discussed.

The Impact of Liver Disease on Organ Allocation for Intestinal Transplantation

Medicare recognizes the specific complications that define total parenteral nutrition (TPN) failure and warrant proceeding to intestinal transplantation.[1] Of these, liver disease may have the most devastating consequences. ESLD can develop in up to 50% of patients with irreversible intestinal failure,[2] and these patients have essentially 100% mortality within 5 years.[3] Therefore, in short-bowel syndrome (SBS) patients with ESLD, combined LIT becomes the only option for survival. Patient survival following combined LIT is 60% at 1 year.[4] If ESLD has not developed, the intestine is transplanted alone and 1-year patient survival is significantly better (79.1%).[5] This survival discrepancy is partially due to the fact that with isolated intestinal transplants, many life-threatening complications can be overcome by removing the graft; with LIT, this is not an option. For these reasons, it is preferable to perform isolated intestinal transplantation before ESLD develops. Unfortunately, however, most patients are not referred to an intestinal transplant center until irreversible liver disease has already developed. Since 1995, 75% of patients listed for intestine transplants have also been listed for livers (United Network for Organ Sharing [UNOS], unpublished data, April 2005).

UNOS data have shown that mortality on the waiting list for intestinal transplant candidates has greatly exceeded that for all other organ transplant candidates since 1994.[6] Of these waiting list deaths, more than 90% occurred in candidates also needing a liver. Only 6% of waiting list deaths occurred in candidates needing intestine grafts only. Since 1993, $<1\%$ of the overall liver transplant waiting list consisted of candidates listed for both liver and intestine transplants.[7] During this period, there has been a small but steady decrease in the mortality rate of candidates on the overall liver transplant waiting list, while the mortality rate has increased in candidates awaiting LIT and has consistently exceeded that of the overall liver transplant waiting list.[7]

LIT candidates had higher mortality than the overall liver candidate population in all age categories. Before the 1998 UNOS status modifications, the highest mortality rates occurred in neonates; after the UNOS modifications, the highest mortality rates were seen in adult candidates. For the overall period, 82% of deaths (ie, 136) occurred in candidates younger than 18 years. This age group accounted for 90% of the deaths between 1993 and 1997 (ie, 80 deaths) and 74% of the deaths (ie, 56 deaths) between 1998 and 1999.[7]

Part of the explanation for this discrepancy may be that many of the parameters used in the Child–Turcotte–

Abbreviations used in this paper: ESLD, end-stage liver disease; LIT, liver-intestinal transplantation; MELD, Model for End-Stage Liver Disease; PELD, Pediatric End-Stage Liver Disease; SBS, short-bowel syndrome; UNOS, United Network for Organ Sharing.

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Pugh–based UNOS score create a disadvantage for the LIT candidates. First, because all LIT candidates are on TPN, they may have a better overall nutritional status than the liver-only candidates. This may contribute to higher serum albumin levels and less ascites. Regular administration of vitamin K in their TPN may contribute to lower prothrombin times and/or international normalized ratios. The absence of significant portions of their abdominal viscera contributes to less portal blood flow and less potential for portal hypertension–related complications, including ascites. Finally, the diarrhea associated with a short gut may be protective for hepatic encephalopathy.

Although it is conceivable that these factors may contribute to lower UNOS scores in LIT candidates, they should not directly contribute to their higher mortality. The most important factor contributing to high mortality in LIT candidates is sepsis. While all patients with ESLD are at risk for fatal episodes of sepsis,[8] patients with SBS on TPN are particularly susceptible.[9,10] Several factors may contribute to this. First, unlike most patients with ESLD, LIT candidates need long-term central venous catheters. Because of constant diarrhea and/or the need to maintain stomas and/or enteral tubes, patients with SBS must be especially meticulous in their technique to avoid contamination of their central venous catheters with enteral organisms. While their central venous catheters are susceptible to infection in the best of circumstances,[11] they are even more likely to become infected as their clinical status deteriorates and their ability to provide meticulous central venous catheter maintenance deteriorates. For the same reasons, the risk of urinary tract infections due to contamination with enteral organisms is increased. Another factor that may contribute to increased sepsis in LIT candidates is bacterial overgrowth and translocation.[12,13]

Regardless of the reasons for it, the great discrepancy in mortality between LIT candidates and other liver transplant candidates reflects a flaw in the liver allocation system. Clearly, the old Child–Turcotte–Pugh score–based UNOS system failed to appropriately prioritize LIT candidates on the liver transplant waiting list. The basic premise for implementing the Model for End-Stage Liver Disease (MELD)/Pediatric End-Stage Liver Disease (PELD) system was to better direct organs to the candidates that were most likely to die waiting.[14] Unfortunately, the MELD/PELD scoring system does not specifically address the disproportionate risk of mortality in LIT candidates compared with other candidates on the liver waiting list, and not unexpectedly waiting list mortalities have not improved for adult or pediatric LIT candidates since its implementation (UNOS, unpublished data, April 2005). UNOS has recently implemented additional policies to increase the priority of LIT candidates by automatically augmenting their MELD/PELD scores and by giving individual organ procurement organizations the option of prioritizing liver allocation to LIT candidates provided no status 1 liver transplant candidates are on the list. Furthermore, additional MELD points are now automatically allotted to LIT candidates on the liver transplant waiting list. Although these policy changes hold great promise, their impact on LIT candidate outcomes has yet to be seen.

While graft and patient survival results after LIT are currently inferior to the results seen after isolated liver transplantation, they have steadily improved with increased experience,[4,5] and the early progress of LIT is comparable to that encountered with other solid organ transplants.[15,16] Furthermore, before implementation of the MELD/PELD system, LIT candidates prioritized as status 2B made up the majority of the waiting list deaths. However, the status 2B candidates who did undergo LIT had significantly better posttransplant outcomes than those with higher priority status. These data support the premise that earlier transplantation of LIT candidates not only reduces waiting list mortality but also improves posttransplant outcomes. Following implementation of the MELD/PELD system, there have been no apparent changes in the number of LITs performed or in posttransplant outcomes (UNOS, unpublished data, April 2005). However, because there seems to be some center-to-center variability in the criteria used for discriminating LIT from multivisceral transplantation, accurate analysis of these posttransplant data must be interpreted with some caution.

LIT candidates are a small subset of liver transplant candidates that have a high mortality on the waiting list. Several modifications to current practices are needed to better address this problem. First, high-risk patients with intestinal failure must be referred early to centers using aggressive strategies to reduce TPN dependency and prevent development of ESLD in the first place. Second, patients who are unable to be weaned from TPN should be considered for intestinal transplantation early, before ESLD develops. Finally, patients who develop ESLD must be given high priority on the liver transplant waiting list.

Living Donor Intestinal Transplantation

One strategy that has increased access to organ transplants has been the use of living donors. Although this practice has been controversial with all organs, it