Challenges in Living Donor Liver Transplantation

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KEYWORDS

- Living donor liver transplantation • Hepatocellular carcinoma
- ABO-incompatible transplant • Living donor

KEY POINTS

- Living donor liver transplantation (LDLT) is a procedure that accounts for approximately 3% of adult liver transplants in the United States. The enthusiasm toward this operation has waned in recent years.
- Although there is no apparent survival advantage for LDLT recipients with hepatocellular carcinoma, properly selected candidates may benefit from the shorter waiting time compared with deceased donor liver transplantation (DDLT).
- The publication of recent protocols with ABO-incompatible LDLT suggests that this barrier may be successfully overcome to expand the potential living donor pool.

INTRODUCTION

Adult-to-adult LDLT is a procedure that has evolved over the past 2 decades. First introduced in the United States in the 1990s, LDLT was primarily relegated to pediatric recipients until late in the decade. Then, a combination of factors contributed to a proliferation of cases. Waiting times for liver transplant increased in the late 1990s as the number of patients listed for transplant far exceeded the modest gain in deceased donors. In addition, important changes in the operative technique improved LDLT recipient outcomes. The initial experience with LDLT used the smaller left hepatic lobe. Although this small graft was adequate for diminutive (pediatric) recipients, initial results in adults were poor. In the late 1990s, selected centers demonstrated favorable recipient outcomes by transplanting the larger right hepatic lobe.[1,2] As the advantage of right hepatic lobe LDLT became apparent, the popularity of the procedure increased and the annual number of LDLTs increased from fewer than 100 to more than 500 in 2002, accounting for approximately 10% of adult liver transplants in the United States.[3] The application of LDLT over the past decade, however, has dropped substantially to fewer than 200 adult cases per year, representing only approximately

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3% of all liver transplants. The reasons for the decline of LDLT are not entirely understood but are likely due to a combination of forces.[4] As with any novel procedure, there is initial enthusiasm leading to rapid growth followed by a more measured approach as the full spectrum of risks and complications becomes apparent over time. Such is the case with LDLT. Over the past decade, there have been several publications highlighting complications in donors and recipients (discussed later), which has tempered interest in the procedure. The most important complication of LDLT, donor death, has received widespread media attention, although its occurrence is rare, at just over 1/500. Finally, federal regulators have placed transplant centers under increasing scrutiny for favorable outcomes. Consequently, transplant centers have become more risk averse and this may have had an impact on their decision to offer LDLT to their patients. The trend toward limited application of LDLT in the United States is largely reflective of the European experience, where living liver donor rates are approximately 1 donor per million (dpm) population. In some parts of the world, however, the procedure is thriving; most notable is South Korea, with 17 dpm, the highest rate worldwide, followed by Turkey (8 dpm), Egypt (5 dpm), and Japan (4 dpm). The Asan Medical Center in Seoul, South Korea, performs approximately 300 LDLTs per year surpassing the entire US volume by approximately 2-fold. This review focuses on 3 of the most important developments in LDLT in recent years: hepatocellular carcinoma (HCC), ABO-incompatible transplant, and donor risk and its management.

LDLT FOR HEPATOCELLULAR CARCINOMA

Compared with DDLT, LDLT offers the potential advantages of speed and timing, which can be particularly important for patients with HCC. The average living donor evaluation takes approximately 6 to 8 weeks; so, LDLT can often be performed faster than DDLT, where waiting times are months to a few years for HCC patients. Prolonged pretransplant waiting times increase the risk of tumor progression, which, in turn, increases the risk of removal from the DDLT list and posttransplant recurrence. Up to 20% of HCC patients are removed from the list due to disease progression while awaiting a transplant.[5–7] Therefore, rapid procession to transplantation potentially offers a therapeutic advantage in the treatment of HCC. Despite the theoretic advantage of LDLT for HCC patients, however, 3 separate reports have each concluded that there is no survival advantage for LDLT patients. A study from Toronto, which has a robust LDLT program, reported no survival advantage with LDLT.[8] It compared survival and HCC recurrence rates for 345 transplant recipients after LDLT, 58 (17%), and DDLT, 287 (83%), over a 16-year period. As expected, the LDLT recipients had significantly shorter waiting times compared with DDLT (3.1 vs 5.3 months; P = .003). There was no difference in 5-year HCC recurrence rates for LDLT (15%) and DDLT (17%) for the DDLT group (P = not significant [NS]). There was also no difference in 5-year survival rates for LDLT (75%) and DDLT (75%) (P = NS). Similar results were reported from a French group in 183 patients with HCC, with LDLT (n = 36) and DDLT (n = 147).[9] At listing, patient and tumor characteristics were comparable in the 2 groups, whereas the mean waiting time was shorter with LDLT (2.6 months) compared with DDLT (7.9 months) (P = .001). All of the 27 (18%) of patients who dropped off the list, primarily for tumor progression, prior to transplant were listed for DDLT. There was no difference in posttransplant recurrence rates, however, between the 2 groups, at 13% each (P = NS). More important, there was no difference in survival on an intention-to-treat basis. Finally, the Adult-to-Adult Living Donor Liver Transplantation Cohort Study Group (A2ALL) has published a large (n = 229) intention-to-treat analysis evaluating LDLT and DDLT in HCC patients who had at least 1 potential donor