

# Living Donor Liver Transplantation for Hepatorenal Syndrome: To Do or Not to Do? That Is the Question

Mitra K. Nadim<sup>1</sup> and Randall S. Sung<sup>2</sup>

<sup>1</sup>Division of Nephrology, Department of Medicine, University of Southern California, Los Angeles, CA; and

<sup>2</sup>Section of Transplantation Surgery, Department of Surgery, University of Michigan, Ann Arbor, MI

Received June 21, 2012; accepted June 21, 2012.

See Article on Page 1237

Acute kidney injury (AKI) is common in patients with end-stage liver disease with an estimated prevalence of 20% at the time of liver transplantation (LT).<sup>1-4</sup> The evolution of renal dysfunction in the context of liver failure ranges from insidious to rapid and from mild to severe. For patients who do not undergo LT, AKI is associated with a 90% in-hospital mortality rate.<sup>5</sup> Therefore, the development of AKI adds an element of urgency for the patient and strategic complexity for the transplant program in making appropriate and timely decisions.

Unfortunately, the utility of the current evidence is incomplete for defining appropriate management algorithms for this patient population. Studies in the published literature have usually been retrospective and single-center, and they have suffered from small sample sizes, reporting bias, and varying definitions of AKI; this makes study comparisons very difficult. The majority have demonstrated pretransplant AKI to be an independent predictor of post-LT mortality.<sup>1,4,6,7</sup> However, these studies have failed to categorize patients according to the etiology of AKI. In a recent single-center, retrospective study,<sup>8</sup> the etiology of AKI was shown to affect posttransplant outcomes: patients with hepatorenal syndrome (HRS) at the time of transplantation achieved survival outcomes similar to those of patients who had no AKI, regardless of the

dialysis duration, the Model for End-Stage Liver Disease (MELD) score, or the Sequential Organ Failure Assessment score.

The prognosis of patients with HRS and especially patients who develop type 1 HRS is extremely poor, and HRS is a terminal event for patients with advanced cirrhosis with a median survival of approximately 2 weeks.<sup>9</sup> Therapies such as terlipressin and albumin dialysis provide only a modest survival benefit (if any), and the only chance for survival is LT.<sup>10</sup> However, because of concerns about outcomes and ethical issues related to coercion and donor risk, many transplant centers have been reluctant to offer living donor liver transplantation (LDLT) to patients with high MELD scores, including patients with type 1 HRS.

In this issue of *Liver Transplantation*, Chok et al.<sup>11</sup> report the outcomes of patients with HRS who underwent LDLT or deceased donor liver transplantation (DDLT) at their institution. Seventy-one of 726 adult patients who underwent LT at a single center in Korea were considered to have had HRS at the time of transplantation, and 48 of these patients underwent LDLT. Although overall survival was lower for patients with HRS versus patients without HRS, the survival of LDLT recipients with HRS was better than or at least no worse than the survival of DDLT recipients with HRS. A subgroup analysis of patients with high MELD scores ( $\geq 30$ ) and patients with type 1 HRS also demonstrated similar survival

**Abbreviations:** AKI, acute kidney injury; DDLT, deceased donor liver transplantation; HRS, hepatorenal syndrome; LDLT, living donor liver transplantation; LT, liver transplantation; MELD, Model for End-Stage Liver Disease.

Address reprint requests to Mitra K. Nadim, M.D., Division of Nephrology, Department of Medicine, University of Southern California, 1520 San Pablo Street, 4th Floor, Suite 4300, Los Angeles, CA 90033. E-mail: nadim@usc.edu

DOI 10.1002/lt.23498

View this article online at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).

LIVER TRANSPLANTATION.DOI 10.1002/lt. Published on behalf of the American Association for the Study of Liver Diseases

rates for the LDLT and DDLT cohorts. Although the inferences that can be drawn are constrained by the limitations mentioned previously, the results suggest that LDLT is a viable alternative to DDLT for candidates with HRS. Although the better survival of the LDLT group was likely related to factors inherent to the transplant process (donor age and ischemic times) as well as other confounders (center experience and recipient selection), LDLT recipients had better posttransplant renal function, fewer infectious complications, and a lower rate of early mortality than DDLT recipients. This opens up the possibility that the enhanced quality of the graft or other favorable factors inherent to the LDLT process have a positive impact on postoperative renal function, and this outweighs or at least mitigates the risks associated with the increased surgical complexity and a smaller graft.

The success of LT has resulted in an increased demand for LT and thus a dramatic shortage of deceased donor organs. In a recent analysis of LT candidates on the United Network for Organ Sharing wait list as of January 2006, the median transplant time was 981 days.<sup>12</sup> Approximately 20% of patients with a MELD score > 30 died within 30 days without receiving a transplant, and only 50% underwent transplantation. Patients removed from the list because they were too sick for transplantation were not included; therefore, the true number of high-MELD score patients dying on the wait list may have been higher. Because of these high rates of wait-list mortality, LDLT should be considered as an alternative to increase the chance of survival. However, deciding which recipients will benefit from LDLT is a realistic problem that is of concern not only to transplant surgeons but also to donors and the families of recipients. The broad applicability of the experience of Chok et al.<sup>11</sup> to other transplant programs is uncertain because of the even greater shortage of DDLT organs and the extensive living donor experience at their center. In this context, the decision to perform LDLT in this population should be made carefully with consideration of the local availability of deceased donors and the experience of the transplant team with LDLT.

## REFERENCES

1. Gonwa TA, McBride MA, Anderson K, Mai ML, Wadei H, Ahsan N. Continued influence of preoperative renal function on outcome of orthotopic liver transplant (OLT) in the US: where will MELD lead us? *Am J Transplant* 2006;6:2651-2659.
2. Hampel H, Bynum GD, Zamora E, El-Serag HB. Risk factors for the development of renal dysfunction in hospitalized patients with cirrhosis. *Am J Gastroenterol* 2001;96:2206-2210.
3. Wu CC, Yeung LK, Tsai WS, Tseng CF, Chu P, Huang TY, et al. Incidence and factors predictive of acute renal failure in patients with advanced liver cirrhosis. *Clin Nephrol* 2006;65:28-33.
4. Nair S, Verma S, Thuluvath PJ. Pretransplant renal function predicts survival in patients undergoing orthotopic liver transplantation. *Hepatology* 2002;35:1179-1185.
5. Fraley DS, Burr R, Bernardini J, Angus D, Kramer DJ, Johnson JP. Impact of acute renal failure on mortality in end-stage liver disease with or without transplantation. *Kidney Int* 1998;54:518-524.
6. Markmann JF, Markmann JW, Markmann DA, Bacquerizo A, Singer J, Holt CD, et al. Preoperative factors associated with outcome and their impact on resource use in 1148 consecutive primary liver transplants. *Transplantation* 2001;72:1113-1122.
7. Brown RS Jr, Lombardero M, Lake JR. Outcome of patients with renal insufficiency undergoing liver or liver-kidney transplantation. *Transplantation* 1996;62:1788-1793.
8. Nadim MK, Genyk YS, Tokin C, Fieber J, Ananthapanyasut W, Ye W, Selby R. Impact of the etiology of acute kidney injury on outcomes following liver transplantation: acute tubular necrosis versus hepatorenal syndrome. *Liver Transpl* 2012;18:539-548.
9. Ginès A, Escorsell A, Ginès P, Saló J, Jiménez W, Inglada L, et al. Incidence, predictive factors, and prognosis of the hepatorenal syndrome in cirrhosis with ascites. *Gastroenterology* 1993;105:229-236.
10. Nadim MK, Kellum JA, Davenport A, Wong F, Davis C, Pannu N, et al.; for ADQI Workgroup. Hepatorenal syndrome: the 8th International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 2012;16:R23.
11. Chok KS, Fung JY, Chan SC, Cheung TT, Sharr WW, Chan AC, et al. Outcomes of living donor liver transplantation in patients with preoperative type 1 hepatorenal syndrome and acute hepatic decompensation. *Liver Transpl* 2012;18:1237-1244.
12. Freeman RB Jr, Steffick DE, Guidinger MK, Farmer DG, Berg CL, Merion RM. Liver and intestine transplantation in the United States, 1997-2006. *Am J Transplant* 2008;8(pt 2):958-976.