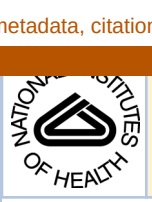

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IMPROVEMENT IN SURVIVAL ASSOCIATED WITH ADULT-TO-ADULT LIVING DONOR LIVER TRANSPLANTATION,[1,2]

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CONFLICTS OF INTEREST
No Conflicts of Interest exist.

the A2ALL Study Group

Abstract

Background and Aims—More than 2000 adult-to-adult living donor liver transplants (LDLT) have been performed in the U.S., yet the potential benefit to liver transplant candidates of undergoing LDLT compared to waiting for deceased donor liver transplant (DDLT) is unknown. The aim of this study was to determine if there is a survival benefit of adult LDLT

Methods—Adults with chronic liver disease who had a potential living donor evaluated from 1/98 to 2/03 at nine university-based hospitals were analyzed. Starting at the time of a potential donor's evaluation, we compared mortality after LDLT to mortality among those who remained on the waitlist or received DDLT. Median follow-up was 4.4 years. Comparisons were made by hazard ratios (HR) adjusted for LDLT candidate characteristics at the time of donor evaluation.

Results—Among 807 potential living donor recipients, 389 received LDLT, 249 received DDLT, 99 died without transplant, and 70 were awaiting transplant at last follow-up. Receipt of LDLT was associated with an adjusted mortality HR of 0.56 (95% confidence interval [CI] 0.42–0.74; P<0.001) relative to candidates who did not receive LDLT. As centers gained greater experience (> 20 LDLT), LDLT benefit was magnified, with a mortality HR of 0.35 (CI 0.23–0.53; P<0.001).

Conclusions—Adult LDLT was associated with lower mortality than the alternative of waiting for DDLT. This reduction in mortality was magnified as centers gained experience with living donor liver transplantation. This reduction in transplant candidate mortality must be balanced against the risks undertaken by the living donors themselves.

INTRODUCTION

Demand for liver transplantation in the United States has grown faster than the availability of deceased donor organs. Consequently, waiting time for liver transplantation has increased more than four-fold, and death on the waitlist is common. Despite efforts to increase organ donation and changes to the organ allocation system that have reduced candidate mortality, about 2000 adults die yearly while awaiting liver transplantation in the U.S.1 An attractive but controversial approach to increasing availability of livers for transplantation is the use of live donors. First developed for pediatric recipients, utilizing the left lateral segment from adult living donors, the technique was later modified to use the larger right lobe from adult donors for transplantation into adult recipients.2 The challenge associated with living donor liver transplantation (LDLT) in adults is that almost 60% of the liver mass of the donor must be transplanted, and rapid liver regeneration is required in both donor and recipient.

Over 2000 LDLT have been performed in the U.S., but the benefits and risks to the recipients relative to deceased donor liver transplantation (DDLT) have not been fully assessed. LDLT permits more timely transplantation, eliminating the mortality associated with continued residence on the waitlist.3 In addition, elective receipt of a living donor allograft might permit the recipient to be healthier at the time of transplantation, and thus diminish post-transplant mortality. These theoretical benefits could be negated by the use of a partial liver and the increased surgical complexity of LDLT.4

A single report found a 50% reduction in waitlist mortality among liver transplant candidates who had a potential living donor compared to candidates who did not have a potential living donor. The overall rate of transplantation was markedly higher for candidates with a potential living donor.5 Markov models suggested a benefit of LDLT in comparison to waiting for DDLT, particularly for patients with hepatocellular carcinoma (HCC).6,7 However, reports of recipient outcomes following LDLT 8–13 and comparisons

of outcomes after LDLT versus DDLT, starting from the date of transplant surgery, 14,15 have demonstrated higher allograft failure rates and trends toward lower patient survival in LDLT recipients.

Previous reports provide little guidance for patient decision-making as none specifically addressed whether the benefit of shortening the time until transplantation with LDLT outweighs the potential for poorer post-transplant outcome. In order to counsel patients regarding the potential benefits of LDLT, we analyzed the mortality experience for a large cohort of LDLT candidates from the time of evaluation of their first potential living donor. This design allowed comparison of LDLT recipients to the transplant candidates who remained on the waitlist without transplant or received DDLT.

METHODS

The primary objective of the Adult-to-Adult Living Donor Liver Transplantation (A2ALL) Retrospective Cohort Study was to determine the survival benefit, if any, of adult LDLT. Patient entry occurred at the date that each potential LDLT candidate's first potential living donor presented for their initial donor history and physical examination.

Data sources

Candidate and donor data were provided by the nine participating A2ALL transplant centers based on a common protocol. Chart reviews were supplemented by additional ascertainment of deaths and transplants through October 2005 under a data use agreement with the Scientific Registry of Transplant Recipients.16 The A2ALL study included 819 patients who had at least one potential living donor evaluated between 1/1/98 and 2/28/03. Transplant candidates with fulminant hepatic failure (n=12) were excluded from the analyses. For the remaining 807 candidates, median follow-up time was 4.4 years.

Statistical methods

The cumulative incidence function was calculated using the SAS® macro "comprisk".3 The Model for End-stage Liver Disease score (MELD) was calculated based on laboratory data only,17 and ignored exception MELD scores used in allocation. LDLT recipients were classified as having received their transplant when the center was less experienced (had performed ≤ 20 LDLT) or more experienced (had performed >20 LDLT).4 Eight centers each performed >20 LDLT during the study and one performed 20.

Survival analyses, starting at the time of evaluation of each subject's first potential donor, were used to compare mortality following LDLT versus the standard strategy of continued waiting for possible DDLT. The non-LDLT group included those who received DDLT or domino liver transplant, those who remained on the waitlist at study end, and those who died without receiving a transplant. LDLT or DDLT procedures that were aborted intraoperatively due to recipient reasons were considered to be transplants.

We used two Cox regression methods to compare the effect of LDLT with not receiving an LDLT. Both methods address the following question: "Does the patient who undergoes an LDLT have lower mortality than a comparable patient who waits for a DDLT?" Modeling LDLT as a conventional time-dependent variable compared mortality following a given LDLT with mortality for all other patients alive at that point who had not yet received LDLT, including those who had already received a DDLT.18 These latter patients, although uncommon, are no longer truly LDLT candidates and thus should not be in the comparison group. The second approach, sequential stratification,19 provides a similar comparison but correctly excludes any recipients who have already received DDLT from the comparison group for a given LDLT. Specifically, for one or more LDLTs performed at a given number

of days since first donor evaluation, a separate comparison group (stratum) was created that included all patients alive and without any transplant (either LDLT or DDLT) prior to the time of the index LDLT(s). The survival of the index LDLT patient(s) was compared to that of all other eligible patients in that stratum. Within each stratum, patients were censored at the earliest of the date of later receipt of an LDLT, the date of last known follow-up, or end of study (October 2005). The results across all LDLT strata were pooled in a stratified Cox regression. Because portions of the time at risk for a patient may appear in multiple strata, the standard errors of the hazard ratios were corrected with robust (sandwich estimator) variance estimates. Both time-dependent and sequentially stratified Cox models were adjusted for baseline covariates of age, HCC, and MELD score, all determined at the time of first donor evaluation. Multiplicative interactions (effect modification) between LDLT and the other variables in the final model were evaluated. An additional Cox regression model examined the risk of mortality by transplant type, starting from the time of transplant, adjusted for age, HCC, and MELD score at transplant.

For graphical representation, survival probabilities were calculated as follows. Survival without any transplant was estimated from a Cox regression censored at LDLT or DDLT. Survival following LDLT or DDLT was estimated based on a Cox model stratified by transplant type. Both models were adjusted for age, HCC, and MELD score. Probabilities of survival through the waitlist period followed by transplant were estimated by multiplying the waitlist survival probability at the respective median transplant time by the post-transplant (LDLT or DDLT) survival probability. All analyses were carried out using SAS 9.1 software (SAS Publishing, Cary, NC: SAS Institute Inc., 2004).

Human subjects protection

The Institutional Review Boards and Privacy Boards of the Data Coordinating Center and the nine participating transplant centers approved the study.

RESULTS

The 807 non-fulminant liver transplant candidates for whom at least one potential living donor was evaluated represented 9.9% of 8,176 liver transplant candidates listed for DDLT at the nine A2ALL centers during the study period. Compared with patients evaluated for LDLT (whose characteristics are shown in Table 1), this much larger group had higher mean body mass index (28.5 kg/m^2; $p<0.001$), were less likely ($p<0.05$) to be female (39%), white (84%), have a diagnosis of hepatitis C (42%) or hepatocellular carcinoma (5%), or a history of variceal bleeding (5%).

Eighty-two percent of the potential living donor recipients had one potential donor evaluated, 15% had two donors evaluated, and 3% had at least three donors evaluated (maximum of seven). Nearly one-half of the living donor recipient candidates (48% or 389) actually underwent LDLT (Figure 1). The LDLT recipients were similar to the other patients in regard to most features such as sex, body weight, diagnosis and various co-morbidities (Table 1). There were small but statistically significant differences between the two groups in mean age, race, MELD score, presence of ascites, encephalopathy, functional status, employment status, year of evaluation, and time from listing to evaluation. Among the 389 LDLT recipients, the median time from donor evaluation to LDLT was 1.8 months (range 4 days to 4.3 years); eight (1%) occurred beyond one year. The median number of LDLT cases performed at each center was 31 (range 20 to 71). For the 249 DDLT recipients, the median time from donor evaluation to transplant was 4.6 months (range 2 days to 5.0 years). The probability of receiving an LDLT, receiving a DDLT, or dying on the waitlist starting from the time of initial donor evaluation is shown in Figure 2. By one year after donor evaluation, 47.2% of patients had received a LDLT, 22.7% had received a DDLT, and 7.7%

had died without a transplant. By 3.5 years after donor evaluation, 30.8%, of patients had received a DDLT and 12.1% had died without a transplant.

In an unadjusted sequential stratification analysis of time from initial donor evaluation to death, patients who underwent LDLT had a hazard ratio [HR] of 0.62 (95% confidence interval [CI] 0.47 – 0.82; P<0.001), compared to patients who did not receive an LDLT. In the adjusted analyses that controlled for differences at donor evaluation, patients who received LDLT had a HR of 0.56 (95% CI 0.42 – 0.74; P<0.001) relative to patients who did not receive LDLT (Figure 3). Recipients of LDLT during the early experience at a center (≤20 cases) had marginally lower mortality (HR=0.83; P=0.27) than non-LDLT patients (Table 2). In contrast, once a center had performed 20 LDLT, the relative mortality risk for LDLT was only 35% of the risk for candidates who did not receive LDLT (P<0.001). There was a significant difference in the relative mortality risk of LDLT between the less experienced and the more experienced periods (P<0.001). Older recipient age, higher MELD score, and diagnosis of hepatocellular carcinoma were also associated with death. No effect modifications were identified by multiplicative interaction between LDLT and these other features. Neither the year of donor evaluation nor the introduction of MELD-based DDLT allocation was a significant predictor of death.

In models designed to look for a possible center effect, we did not find a significant association either as a main effect (p=0.51) or as an interaction with the LDLT effect (p=0.10). The addition of center variables also did not alter the LDLT effect in the main effects model compared to the original model without the center variables (LDLT less experienced HR 0.82 vs. 0.83; LDLT more experienced HR 0.37 vs. 0.35, respectively). In addition, no significant association was found between waiting time for DDLT (dividing the centers into three groups based on the 25th percentile of each center's OPO's waiting time) and LDLT survival benefit.

Waiting time as a main effect was not significant (p=0.52), and the effect of LDLT in this model remained virtually identical to the original model without the waiting time variables (less experienced 0.81 vs. 0.83; more experienced 0.35 vs. 0.35, respectively). We also looked for an interaction between the LDLT survival benefit and waiting time (i.e., does the relative risk of death with LDLT vs. without LDLT vary by waiting time). This interaction test was also not significant (p=0.35). However, as expected, the direction of the interaction did indicate that LDLT at centers with longer waiting times were associated with greater benefit.

A separate Cox regression analysis that modeled LDLT as a conventional time-varying covariate showed results similar to that of the adjusted sequential stratification method (LDLT more experience: HR=0.47; 95% CI 0.32 – 0.69; P<0.001; LDLT less experience: HR=1.08; 95% CI 0.79 – 1.49; P=0.62).

Figure 4 shows the cumulative probability of mortality from the time of initial living donor evaluation for patients remaining on the waitlist, for patients received DDLT at the median time to DDLT (4.6 months), and for patients who had LDLT at the median time to LDLT when centers had less experience (1.7 months) or more experience (2.0 months). Long-term transplant candidate mortality on the waitlist was higher than the mortality after either LDLT or DDLT. The survival advantage of LDLT appeared to be a result of removal from continued exposure to the risk of death on the waitlist.

An analysis restricted to the 198 patients who had an initial living donor evaluation following the institution of the MELD liver allocation score (February 2002) had similar results as those of the entire cohort (Table 2). After introduction of MELD, mortality risk was 70% lower with LDLT overall (HR=0.30; 95% CI 0.14–0.67; P=0.0033), by which time

all but four LDLT cases were performed after centers had performed more than 20 LDLT cases. The more favorable liver allocation for patients with higher MELD scores or hepatocellular cancer substantially decreased the mortality hazard ratios for each. An additional analysis of those with MELD score <15 at study entry (54%) showed an LDLT adjusted mortality hazard ratio of 0.94 (95% CI 0.59–1.52; p=0.81) during earlier center experience and 0.41 (95% CI 0.24–0.68; p<0.0001) with greater experience.

While not the primary focus of the study, analyses of survival were also performed beginning at the time of transplant (rather than at time of first donor evaluation) to compare mortality following the two different transplant procedures. In adjusted analyses, survival probabilities for DDLT recipients (with mean covariate values of age=50 years, MELD=15, and no HCC) were 92.1% at one year and 86.3% at three years. Corresponding post-transplant survival probabilities for LDLT recipients were 92.0% at one year and 84.8% at three years (P=0.36 compared with DDLT). Adjusted survival probabilities for LDLT performed while centers were less experienced were 89.4% at one year and 78.3% at three years (P=0.01 vs. DDLT). Post-LDLT survival increased after centers gained greater experience (94.0% at one year and 89.7% at three years; P=0.29 vs. DDLT; P<0.001 vs. LDLT with less experience). Early re-transplantation (<3 weeks) was performed in 1.1% of DDLT recipients, and 7.8% and 3.6% of LDLT recipients while centers were less and more experienced, respectively.

DISCUSSION

Adult-to-adult LDLT affords selected liver transplant candidates an alternative to waiting for a liver from a deceased donor. While the technique is practiced at numerous transplant centers around the world, analyses have not adequately assessed the potential benefits or risks of receipt of a living donor graft.20 The few published analyses that examined the outcomes of LDLT at individual U.S. liver transplant centers, or included the entire U.S. LDLT experience, have shown that LDLT is associated with higher mortality rates than DDLT. These analyses, however, were limited to the experience of candidates who survived to transplantation. Not considered by most of these reports was mortality while awaiting transplantation. As practiced in the U.S., pursuit of LDLT, which is initiated by the evaluation of a potential living donor, often results in a LDLT months or even years before DDLT would occur. We utilized a novel study design that accounted for the contribution of waitlist mortality in assessing the survival experience of individuals who did not receive an LDLT despite evaluation of a potential living donor. Results from this study are thus directly applicable to the counseling of liver transplant candidates who are contemplating pursuit of LDLT as an alternative to DDLT.

An advantage of the study design was that entry required evaluation of a potential donor without preconception of whether the recipient would actually receive an LDLT. As a result, LDLT recipients were drawn from the same pool of candidates as those who did not receive LDLT, reducing differences at time of study entry. Adjustment for any measurable differences between the two groups that might have affected survival had little effect on the estimated survival advantage of LDLT. It is possible that unmeasured confounders may have influenced the survival advantage of LDLT, despite the care taken to establish an appropriate comparison group and the apparent comparability of LDLT and non-LDLT patients in the study. However, given the substantial survival advantage of LDLT, the influence of unknown confounders would have had to have been large to eliminate this advantage.

Liver transplant candidates who received their LDLT after centers had gained considerable experience with the technique had markedly lower mortality than that of the candidates who

were considered for, but did not receive, an LDLT. Conversely, the analysis did not find significantly better survival for LDLT recipients during the centers' early LDLT experiences, when LDLT was associated with higher post-transplant mortality than either the later LDLT experience or DDLT. The benefit of greater experience resulted from lower post-transplant mortality, as was shown in our secondary analysis (Figure 4). Prior reports that described worse outcomes following LDLT compared to DDLT may have been heavily influenced by the early experiences of LDLT programs.14, 15 Our results suggest that even if waiting time for DDLT was only slightly longer than for LDLT, there would still be a survival benefit to choosing LDLT once centers are experienced. The benefit of LDLT is enhanced as waiting time for DDLT and its associated mortality increase.

The institution of deceased donor liver allocation using the MELD scoring system in 2002 has decreased the overall death rate on the waitlist by assigning priority to patients most likely to die in the short term. Thus, it is an important and relevant finding that an analysis restricted to patients eva luated for LDLT after the introduction of MELD demonstrated an LDLT survival advantage similar to that of the entire cohort. (Table 2). Furthermore, LDLT was even found to be beneficial for those with MELD <15, a group that was recently shown not to benefit from DDLT,21 and may reflect unmeasured differences between LDLT and DDLT candidates. Thus, the survival benefits observed in this study are directly applicable to the current MELD-based allocation environment.

Only 10% of liver transplant candidates at A2ALL centers had a donor evaluated for LDLT. As outlined, those who did not have a living donor evaluated were quite different from those who did. It cannot be assumed that the results would be similar to the current analysis if LDLT was available for a broader pool of transplant candidates with much higher MELD scores or comorbidities beyond those in our cohort. Rather, this study provides previously unavailable survival information to patients who are considering the possibility of LDLT and have characteristics similar to our study population. There is also the potential for selection bias on the recipient side within our study cohort. However, we have reported that progression to unsuitability as a living donor recipient after the initial donor history and physical examination accounted for only 21% of cases that did not result in completed living donor transplants.22 This supports the presumption of comparability between recipients of LDLT and those who did not receive LDLT in the current study.

LDLT poses significant ethical tension. It has the potential to substantially increase the number of livers available for transplantation and therefore decrease overall mortality for candidates awaiting transplantation. But this benefit must be weighed against the risks of morbidity and mortality borne by the healthy volunteer donor.23 The A2ALL group has reported on psychiatric morbidity after living liver donation24 and an overall rate of donor complications of 38% using a comprehensive inventory.25 This ethical issue can be informed by empirical information on whether the decision to perform LDLT improves survival for the recipient. Our results indicate that LDLT did reduce candidate mortality, and the observed benefit was greater after centers developed experience with the procedure. In fact, the magnitude of mortality reduction was among the largest observed with any form of transplant intervention.20 These findings should be useful for liver transplant candidates and potential donors as they attempt to balance the risks and benefits of the various routes to liver transplantation, as well as for transplant centers as they evaluate patients for LDLT or consider establishment of new LDLT programs.

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Dr. Berg and Dr. Gillespie had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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ABBREVIATIONS

A2ALL	Adult-to-Adult Living Donor Liver Transplantation
ASTS	American Society of Transplant Surgeons
DDLT	deceased donor liver transplant
HCC	hepatocellular carcinoma
HR	hazard ratio
HRSA	Health Resources and Services Administration
LDLT	adult living donor liver transplants

MELD	Model for End-stage Liver Disease score
NIDDK	National Institute of Diabetes & Digestive & Kidney Diseases
SRTR	Scientific Registry of Transplant Recipients

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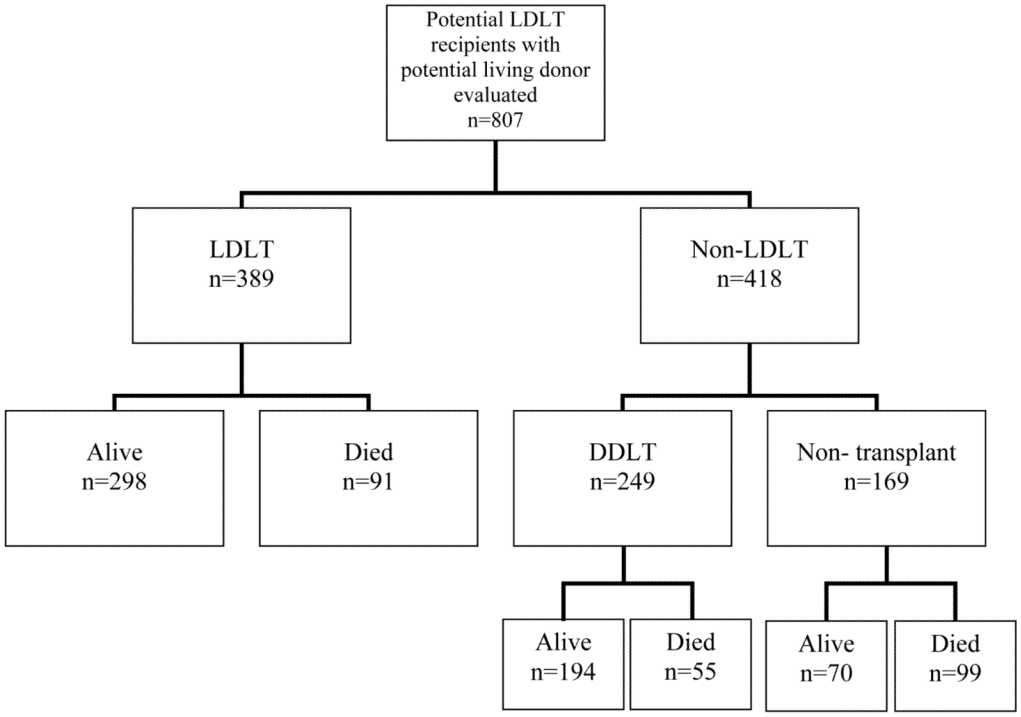

Figure 1.
Flow diagram of the cohort of A2ALL liver transplant candidates from the time of first living donor evaluation.

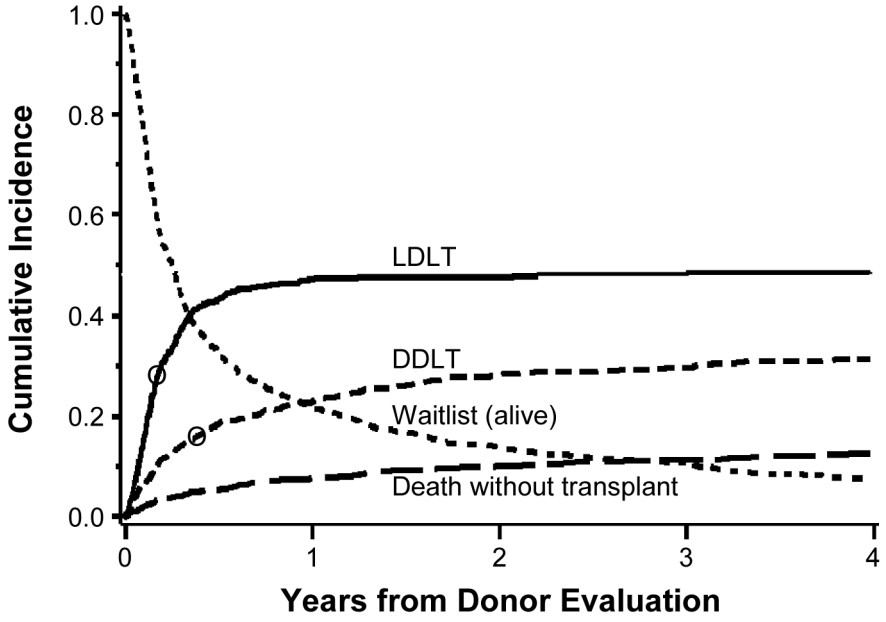

Figure 2. Cumulative probability of receiving a LDLT or DDLT or dying while awaiting transplantation among 807 liver transplant candidates

The small circles mark the time of performance of the median number of LDLT (1.8 months) and DDLT (4.6 months). The probability of remaining alive while still awaiting transplantation is also shown.

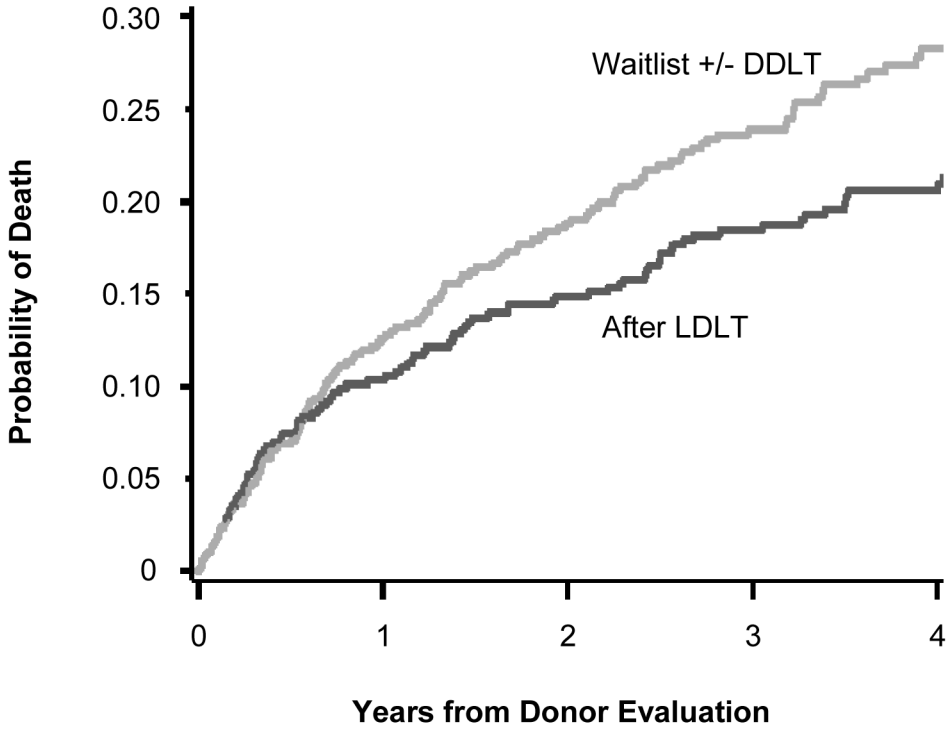

Figure 3. Cumulative risk of death after initial living donor evaluation for patients receiving LDLT versus not receiving LDLT

Risk of death following LDLT diverges beginning at median time of LDLT following donor evaluation (1.8 months) (green line). Estimates are adjusted for age, MELD score, and HCC status, and apply to a patient with age=50, MELD=15, and no HCC.

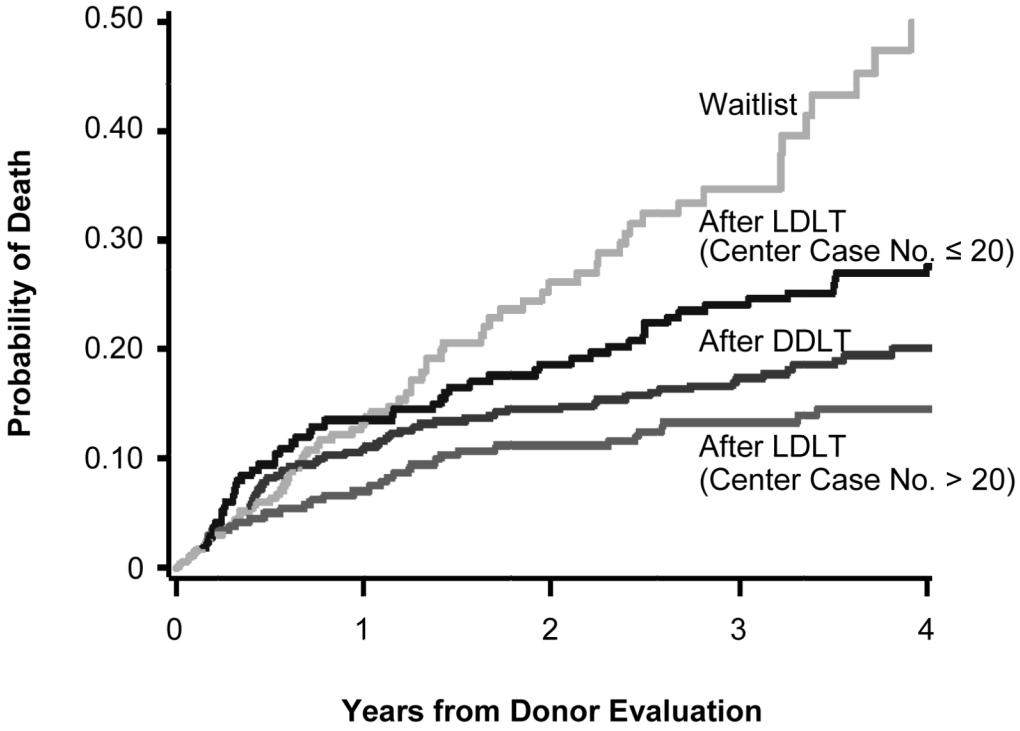

Figure 4. Cumulative risk of death after initial living donor evaluation for patients not transplanted (yellow), patients receiving DDLT (red), and patients receiving LDLT during earlier (blue) and later center experience (green)

Estimates are adjusted for age, MELD score, and HCC status, and apply to a patient with age=50, MELD=15, and no HCC. Risks of death following transplant diverge beginning at the median times for each type: LDLT case ≤20 (1.7 months); LDLT case >20 (2.0 months); and DDLT (4.6 months).

Table 1

Characteristics of potential LDLT recipients at time of donor evaluation

Characteristic	Overall (n=807) * Mean±SD or Percent	LDLT (n=389) Mean±SD or Percent	Non-LDLT (n=418) † Mean ±SD or Percent	LDLT vs. Non-LDLT P-Value
Age (years)	50.3±10.1	49.3±10.7	51.3±9.5	0.006
Sex				0.55
Male	57%	58%	56%	
Female	43%	42%	44%	
Race				0.03
White	90%	91%	89%	
African-American	5%	3%	7%	
Other	5%	6%	4%	
Height (cm)	171.1±10.3	171.4±10.8	170.8±9.8	0.45
Weight (kg)	79.6±18.0	78.6±18.0	80.5±18.0	0.15
Body Mass Index (kg/m^2)	27.1±5.2	26.7±5.2	27.4±5.2	0.04
Previous Transplant Diagnosis‡	2%	3%	1%	0.25
Hepatitis C	47%	48%	47%	0.79
Hepatocellular Carcinoma (HCC)	13%	15%	11%	0.10
Alcoholic liver disease	14%	14%	15%	0.62
Cholestatic liver disease	19%	19%	19%	0.97
Other non-cholestatic cirrhosis	20%	21%	20%	0.87
Metabolic disease	3%	3%	3%	0.81
Biliary atresia	0.4%	1%	0%	0.11
Non-HCC malignancy	2%	3%	2%	0.29
Other	3%	3%	4%	0.31
Ascites	65%	61%	68%	0.01
Encephalopathy	48%	40%	55%	<0.001
Variceal Bleed	18%	17%	19%	0.34
Upper Abdominal Surgery	20%	20%	19%	0.51
Spontaneous Bacterial Peritonitis	7%	8%	6%	0.27
TIPSS§	11%	8%	12%	0.14
MELD¶	15.6±6.8	14.8±6.4	16.4±7.2	0.002
MELD (categories)				0.003
6–10	22%	26%	19%	
11–20	56%	56%	55%	
21–30	15%	11%	18%	
31–40	5%	3%	6%	
Missing	3%	4%	2%	
Recipient Medical Condition				0.22
ICU	2%	1%	3%	
Hospitalization, no ICU	7%	6%	8%	

Characteristic	Overall (n=807) * Mean±SD or Percent	LDLT (n=389) Mean±SD or Percent	Non-LDLT (n=418) † Mean ±SD or Percent	LDLT vs. Non-LDLT P-Value
Not hospitalized	90%	92%	89%	
Diabetes Mellitus	20%	19%	21%	0.14
Angina/Coronary Artery Disease	4%	3%	5%	0.50
Drug Treated Systemic Hypertension	13%	12%	13%	0.19
Functional Status				0.003
No activity limitations	46%	54%	40%	
Activities of daily living with some assistance	40%	34%	45%	
Activities of daily living with total assistance	1%	1%	1%	
Hospitalized	7%	6%	8%	
Unknown	5%	4%	5%	
Employment Status				0.03
Working full time	24%	29%	19%	
Working part time	11%	9%	12%	
Not working	50%	48%	53%	
Retired	8%	7%	8%	
Unknown	8%	7%	8%	
Year of Evaluation				<0.001
1998	4%	6%	3%	
1999	14%	17%	10%	
2000	22%	23%	21%	
2001 to 2/27/2002	35%	35%	36%	
2/28/2002 to 2003 (MELD era)	25%	19%	30%	
Time from Candidate Listing to Donor Evaluation (days)	225±344	192±319	256±362	0.009

*Percent of values missing is less than 3% for each variable.

†Non-LDLT group includes deceased donor transplant recipients and those who are still waitlisted.

‡Patients may have more than one diagnosis.

§TIPSS: transjugular intrahepatic portosystemic shunt.

¶MELD: Model for End-stage Liver Disease score.

Table 2

Risk factors for death among transplant candidates following evaluation of a potential living donor. Results are based on a Cox regression model using sequential stratification

	Overall (n=807) (Donor evaluation 1/1/1998 to 2/28/2003)			MELD era (n=198) (Donor evaluation 2/28/2002 to 2/28/2003)		
Variable	**Mortality Hazard Ratio**	**95% Confidence Interval**	**P-Value**	**Mortality Hazard Ratio**	**95% Confidence Interval**	**P-Value**
Recipient age at enrollment (per 10 years)	1.25	(1.04, 1.50)	0.02	1.39	(0.97, 1.99)	0.07
MELD at enrollment (per unit MELD)	1.08	(1.04, 1.11)	<.001	1.05	(0.99, 1.11)	0.13
Diagnosis of hepatocellular carcinoma	2.20	(1.40, 3.48)	<.001	1.46	(0.54, 3.91)	0.45
LDLT when center had done ≤20 cases (vs. no LDLT)	0.83	(0.59, 1.16)	0.27	--*	--	--
LDLT when center had done >20 cases (vs. no LDLT)	0.35	(0.23, 0.53)	<.001	0.32	(0.14, 0.71)	0.005

*All but 4 LDLT transplants in the MELD era occurred when the center had done >20 cases. There were no deaths among these 4 LDLT transplants.

LDLT = Living donor liver transplantation

MELD = Model for End-Stage Liver Disease