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Defining Long-term Outcomes with Living Donor Liver Transplantation in North America

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Abstract

Objective—To compare long-term survival of living donor liver transplant (LDLT) at experienced transplant centers to outcomes of deceased donor liver transplant (DDLT) and identify key variables impacting patient and graft survival.

Summary Background Data—The Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL) is a prospective multicenter NIH study comparing outcomes of LDLT and DDLT and associated risks.

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Methods—Mortality and graft failure for 1427 liver recipients (963 LDLT) enrolled in A2ALL transplanted between 1/1/1998 and 1/31/2014 at 12 North American centers with median follow-up 6.7 years were analyzed using Kaplan-Meier and multivariable Cox models.

Results—Survival probability at 10 years was 70% for LDLT and 64% for DDLT. Unadjusted survival was higher with LDLT (HR=0.76, p=0.02) but attenuated after adjustment (HR=0.98, p=0.90) as LDLT recipients had lower mean MELD (15.5 vs 20.4) and fewer were transplanted from ICU, inpatient, on dialysis, ventilated, or with ascites. Post-transplant ICU days were less for LDLT. For all recipients female gender and primary sclerosing cholangitis were associated with improved survival, while dialysis and older recipient/donor age were associated with worse survival. Higher MELD score was associated with increased graft failure. Era of transplantation and type of donated lobe did not impact survival in LDLT.

Conclusions—LDLT provides significant long-term transplant benefit resulting in transplantation at a lower MELD score, decreased death on waitlist, and excellent post-transplant outcomes. Recipient diagnosis, disease severity, renal failure, and ages of recipient and donor should be considered in decision-making regarding timing of transplant and donor options.

Clinical Trials ID—NCT00096733.

Introduction

The first report of adult-to-adult living donor liver transplantation (LDLT) in the United States (US) was in 1998 (1), followed by rapid expansion to numerous centers in the US and Canada as a potential solution to the organ shortage and to decrease death on the waitlist. However, while LDLT has grown exponentially in countries where deceased donor liver transplantation (DDLT) is limited or non-existent (2, 3), it remains a very small percentage of total transplants in the US (4). Early reports demonstrating inferior outcomes in LDLT compared to DDLT (5), and donor morbidity and mortality may have contributed to the limited growth in North America (6, 7). As experience increased, early post-transplant outcomes improved and single center reports demonstrated similar or even better outcomes of LDLT compared to DDLT (8–11), and recent registry studies have demonstrated comparable outcomes between LDLT and DDLT across many indications (12–14). Analyses from large unfunded registries, however, provide less detailed information than is possible from a federally supported multicenter observational cohort study.

The Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL) was established by the US National Institutes of Health (NIH) in 2002 as the first multicenter study of donor and recipient LDLT outcomes. Recipient outcomes starting from the time a potential donor was evaluated, demonstrated the survival benefit of choosing LDLT as opposed to waiting for DDLT. Recipient survival with LDLT was superior to DDLT due mainly to decreased death on the waitlist (15, 16). An important early finding was the impact of the learning curve, with significant improvement in outcomes of LDLT once a center gains experience (17). A2ALL demonstrated similar early post-transplant outcomes between LDLT and DDLT overall, and in subgroups of patients with hepatocellular carcinoma (HCC) or cirrhosis due to hepatitis C virus (HCV) (18–20).

The purpose of the current study was to compare outcomes after LDLT and DDLT in the A2ALL cohorts with follow-up to 10 years post-transplant and to identify factors associated with long-term patient and graft survival.

Methods

Study Design

A2ALL is an observational cohort study designed to investigate outcomes in donors and recipients of adult-to-adult LDLT. A2ALL-1 enrolled potential liver recipients evaluated for living donation between 1/1/1998 and 8/31/2009. Starting in 2011, A2ALL-2 enrolled LDLT recipients who were transplanted between 9/1/2009 and 1/31/2014 or previously enrolled in A2ALL-1. Subjects were enrolled pre- or post-transplant, but those enrolled post-transplant in A2ALL-2 had to be alive with their original graft at the time of enrollment. Patients were followed in A2ALL-1 through 8/31/2010 and in A2ALL-2 through 5/31/14. Median follow-up time was 6.7 years (range 0–15 years). Twelve North American centers (11 US, one Canadian) were involved, nine in each phase, with six centers participating in both phases. Additional ascertainment of death and graft failure was available for patients transplanted at US centers in the Scientific Registry of Transplant Recipients (SRTR) through 9/30/14.

This study considers 1600 recipients whose transplants occurred between January 1, 1998 and January 31, 2014. All recipients had a living donor evaluated for donation; some ultimately received a DDLT. LDLT recipients from the 9 centers in A2ALL-1 whose transplant was among the first 20 LDLTs at their center were excluded (n=173) to minimize the learning-curve effect. All three centers that joined A2ALL-2 had performed more than 20 cases by their study entry on 9/1/2009. Clinical and laboratory data, patient and graft survival, and intraoperative information were collected. Missing center data were supplemented with data from the SRTR. The SRTR data includes data on all donors, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere (21). The Health Resources and Services Administration (HRSA), US Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. Each clinical center and the Data Coordinating Center had the study protocols and consent forms approved by the respective Institutional Review Boards prior to enrolling patients.

Statistical Methods

Descriptive statistics (means, standard deviations, frequencies, and percentages) were calculated for demographic and clinical variables. Comparisons between LDLT and DDLT recipients were made using t-tests for continuous variables and chi-square or Fisher's exact tests for categorical variables.

Subjects who enrolled in A2ALL-2 after transplant and were not previously enrolled in A2ALL-1 (n=122) had their follow-up time left truncated at the time of enrollment to avoid giving credit for time at risk when any graft failure or death would not have been observed.

Subjects who enrolled during A2ALL-1 and subsequently enrolled in A2ALL-2 had continuous follow-up available through SRTR. Unadjusted patient and graft survival curves were estimated using left-truncated Kaplan-Meier (implemented using software for Cox regression) and are shown graphically for LDLT and DDLT.

Multivariable Cox regression was used to test for differences in patient and graft survival between LDLT and DDLT (transplant type). Covariates tested included recipient age, gender, race, ethnicity, body mass index (BMI), diagnosis, medical severity at transplant (on ventilator or on dialysis), model for end-stage liver disease (MELD) score at the time of transplant, cold ischemia time, age of donor, and time on waitlist (US centers only). Calendar year of transplant and lobe donated were tested among LDLTs. The method of best subsets was used to guide model selection (22). Potential interactions between transplant type and other covariates were explored after fitting separate models for LDLT and DDLT recipients by formally testing the interactions in models that included both transplant types. Forest plots were created to visually compare covariate effects between LDLT and DDLT. Adjusted survival curves for patient and graft survival by transplant type were also generated. The proportional hazards assumption was tested in all models.

Competing risks methods were used to compare causes of death and graft failure between LDLT and DDLT recipients. Cumulative incidence functions were plotted for each cause using the comprisk macro (mayoresearch.mayo.edu/mayo/research/biostat, modified to account for left-truncation) and a generalized linear rank test was used to compare the cumulative incidence functions between LDLT and DDLT (compCIF macro, http://www.uhnres.utoronto.ca/labs/hill/datasets/Pintilie/SASmacros/compcif.txt, *modified to account for left-truncation*). All analyses were completed using SAS 9.3 (SAS Institute Inc., Cary, NC).

Results

Characteristics of LDLT and DDLT Recipients

After excluding 173 LDLTs that occurred during the first 20 cases at each of the 9 A2ALL-1 centers, 963 LDLTs and 464 DDLTs whose recipients had at least one living donor evaluated from 1/1/1998 to 8/31/2010 (9 centers) were enrolled in the A2ALL studies (Table 1). Of the 963 LDLT recipients, 834 were transplanted at a US center, representing 86% of living donor transplants at these US A2ALL centers during the study enrollment periods, and129 were performed at a Canadian center. LDLT recipients enrolled in A2ALL did not differ by age (p=0.07), gender (p=0.70), or ethnicity (p=0.58) from the 138 LDLT recipients who did not enroll, but a higher proportion of LDLT recipients who enrolled in A2ALL vs. did not enroll were white (92% vs. 88%, p=0.02).

Compared to the DDLT recipients, LDLT recipients enrolled in A2ALL had a higher prevalence of white race (91% vs 84%, p<0.001) and lower incidence of Hispanic ethnicity (13% vs 19%, p=0.005) (Table 1). A smaller proportion of LDLT recipients had HCV (35% vs 45%, p<0.001) and HCC (16% vs 21%, p=0.02), and a higher proportion had primary biliary cirrhosis (PBC) (8% vs 3%, p<0.001). There were no significant differences in age, gender, or BMI between LDLT and DDLT recipients.

The DDLT recipients enrolled in A2ALL had more severe liver disease. MELD at evaluation and at transplant were significantly lower in the LDLT group (p<0.001 for each); 16% had a MELD >20 at the time of transplant compared to 43% of DDLT recipients (Table 1). More DDLT recipients were transplanted from the intensive care unit (ICU) (11%) and 15% were hospitalized but not in the ICU at the time of transplant compared to 2% and 6% of LDLT recipients, respectively (p<0.001). Significantly more DDLT than LDLT recipients were on a ventilator (6% vs 1%, p<0.001), were on dialysis (5% vs 1%, p<0.001), and had ascites (62% vs 46%, p<0.001) at the time of transplant.

Among the 963 living donor recipients in A2ALL, there were 866 corresponding A2ALL donors who agreed to participate in the study. Mean donor age was 37 (range 18–63). Most were female (52%) and white (89%); 13% were Hispanic. The mean BMI was 26 (range 16 – 42). The majority were biologically related (65%).

Many perioperative characteristics were different between LDLT and DDLT. LDLT recipients had longer total operative time (median 7.6 hours vs 5.8 hours, p<0.001) and shorter total ischemia time (median 98 minutes vs 487 minutes, p<0.001) than DDLT recipients. Intraoperative blood transfusion requirements were lower in LDLT compared to DDLT (median 4 vs 6 units, p<0.001). Recipients of LDLT generally stayed in the ICU for a shorter period of time (p=0.05) after the operation, but overall hospital length of stay did not differ significantly between the two groups (p=0.65).

Post-transplant mortality and graft failure

Unadjusted long-term mortality was significantly lower after LDLT compared to DDLT (hazard ratio (HR) = 0.76, p = 0.02); however, after adjustment for recipient gender, age, diagnosis, dialysis, MELD, and donor age, the mortality risk was similar (HR = 0.98, p = 0.90) (Figure 1(a) and (b)). Unadjusted long-term graft failure risk was marginally lower after LDLT compared to DDLT, although did not reach statistical significance, and similar when adjusted for recipient age, diagnosis, MELD, dialysis, and donor age (Figure 1(c) and (d)).

Causes of death after LDLT and DDLT were similar (Figure 2). In unadjusted competing risk analyses, DDLT recipients had a marginally higher cumulative incidence of death due to infection or sepsis (p=0.06), and death due to graft failure (p=0.09). The cumulative incidences of death due to other causes were not significantly different between LDLT and DDLT.

The unadjusted cumulative incidence of re-transplant was similar in both DDLT and LDLT (p=0.19), but there was a higher cumulative incidence of death without re-transplant among DDLT recipients (p=0.01, Figure 3). Among the specific causes of graft failure prior to re-transplant, LDLT recipients had a higher cumulative incidence of graft failure due to vascular thrombosis than DDLT recipients (p=0.05).

Predictors of Mortality and Graft Failure

Adjusted models of patient death and graft failure over 10 years of follow-up showed no significant differences between recipients of a LDLT vs. a DDLT. Female gender and

diagnosis of primary sclerosing cholangitis (PSC) were associated with lower mortality risks (HR = 0.74, p=0.01 and HR = 0.45, p<0.001, respectively, Table 2[a]). Dialysis at transplant was the strongest predictor of mortality (HR 3.59, p<0.0001). Older recipient age and donor age > 50 also had a negative impact on recipient survival. Similar to the patient survival model, PSC was also associated with a reduced risk of graft failure (HR = 0.66, p=0.02), as was a diagnosis of autoimmune hepatitis (HR = 0.44, p=0.009, Table 2[b]). Dialysis at the time of transplant, and older recipient and donor age were associated with increased risk of graft failure, similar to the patient survival models. Unlike patient survival, an increase in MELD score at the time of transplant was associated with a significant increase in the risk of graft failure in the combined model (p=0.04).

Predictors of patient death and graft failure in separate LDLT and DDLT models were largely overlapping, and no significant interactions between transplant type and other predictors were found for either patient death or graft failure (Figure 4). Within the LDLT group, variables that had significant adverse impact on the risk of patient death included a diagnosis of HCC, dialysis at transplant, recipient age over 55, and older donor age. Higher risk of graft failure risk was associated with HCC and older donor age, and female gender and diagnosis of PSC were associated with lower risk (Supplementary Table 1[a] and [b]). Within the DDLT group, malignancy other than HCC (i.e. cholangiocarcinoma), dialysis at transplant, and older recipient age resulted in decreased patient survival, and dialysis, older recipient and donor age resulted in higher graft failure.

Additional variables were tested in the LDLT group alone (Supplementary Table 2 [a] and [b]) including era of transplant by A2ALL cohort, year of transplant, or right versus left lobe. None of these variables were found to be significant with regard to patient or graft survival. Time on waitlist was also analyzed for both DDLT and LDLT, and this did not influence adjusted survival in those patients receiving transplants.

Discussion

Living donor liver transplantation has emerged as an important source of organs when there is a critical scarcity of deceased donor grafts. While early outcomes with LDLT were thought to be inferior to DDLT, this comprehensive report from A2ALL demonstrates the durability and success of the LDLT procedure, with prolonged (5–12 years) follow-up of a well-characterized cohort, in a carefully documented, multicenter study. We provide evidence that LDLT can have equal long-term outcomes to DDLT when risk-adjusted. Given the longer wait-times and higher MELD needed for DDLT, LDLT provides superior transplant outcomes over DDLT as nearly all the risk adjustment variables reflect the greater severity of disease in DDLT that is prevented if the candidate chooses LDLT at an earlier stage.

The findings in this report represent a culmination of 16 years of LDLT research performed within the A2ALL consortium. A2ALL was the first multicenter study to investigate, in meticulous detail, the outcomes of both recipients and donors who consider and undergo living donor transplantation. One of the first important findings of A2ALL was the existence of a significant and steep learning curve (17). Because of the complexity of the operation,

the initial LDLT recipients had more vascular and biliary complications than seen in DDLT, and more graft and patient loss (17, 20). Fortunately, the early graft failure and patient mortality experienced by centers starting LDLT programs markedly improved after the first 15–20 procedures, true for both A2ALL and non-A2ALL centers (23). Dysfunction of the segmental graft, or "small-for-size syndrome", remains a significant concern (24), and the biliary reconstruction and post-operative complications continue to be the Achilles heel of LDLT (25, 26), but even these were less frequent after experience is gained (20, 27, 28).

Because A2ALL followed potential recipients from the time a possible donor was identified, we were able to carefully assess waitlist mortality. Two landmark studies from A2ALL demonstrated that LDLT provides significant transplant benefit to candidates, even at low MELD scores, primarily because of less death on the waitlist (15, 16). In this report, the A2ALL consortium demonstrates that the post-transplant experience also adds to the benefit of LDLT. Risk-adjusted post-transplant patient and graft survival was not significantly different between DDLT and LDLT, confirming previous reports from the A2ALL retrospective cohort which have also shown similar post-transplant risk-adjusted survival overall, and in specific patient cohorts such as HCC and HCV (18–20). Furthermore, the findings presented show a post-transplant benefit for LDLT when not adjusted for the "healthier" case mix of LDLT. This benefit can add to the substantial pre-transplant benefit gained from earlier transplantation.

Several recent large registry reports have compared LDLT to DDLT with similar findings to those in this report. Hoehn et al. used a linkage between the University Health System Consortium and SRTR databases to compare 14,282 patients at 62 centers who underwent DDLT from 2007 to 2012 and 715 patients at 35 centers who underwent LDLT, performing a 1:1 propensity score matching approach using age, MELD, and pre-transplant status. They found no difference in length of stay, costs, patient survival, or graft survival, but higher readmissions for LDLT (13). More recently, Goldberg et al. analyzed graft and patient survival using the national OPTN/United Network for Organ Sharing (OPTN/UNOS) data from 2002–2012 and found unadjusted graft survival to be significantly higher after LDLT (after the first 15 LDLT), and equivalent to DDLT overall when adjusted for recipient characteristics. There was substantial improvement over time, and superior outcomes of LDLT in autoimmune hepatitis and cholestatic liver disease at experienced centers (12). Kashyap et al. performed a retrospective analysis of US national data for patients transplanted between February 2002 and October 2006, and demonstrated higher unadjusted survival after LDLT compared to DDLT; for patients with autoimmune hepatitis, PSC, and PBC, they found similar outcomes for the two graft types after adjusting for covariates (14).

When a deceased donor is not available, even Status 1 and high MELD patients likely benefit from LDLT. However, because the allocation system in North America prioritizes the sickest patients, these candidates have a greater chance to receive a deceased donor offer. In this report, we did not find disease severity by MELD to be a significant predictor of post-transplant patient survival for LDLT or DDLT. However, LDLT recipients were transplanted within a lower range of MELD scores compared to those generally needed to access a deceased donor organ. A higher MELD was associated with reduced graft survival, but this was true for both LDLT and DDLT. Urrunga et al analyzed OPTN data for adults

with acute liver failure (ALF) who were listed for liver transplantation as Status 1 or 1A and underwent LDLT (N = 21) or DDLT (N = 2316) between October 1987 and April 2011. They found no strong evidence that the unadjusted survival probabilities for adults with ALF who underwent LDLT were inferior to those who underwent DDLT (29), and recent reports from Japan and Korea demonstrate patient survival exceeding 70% for ALF (30, 31). Several reports from large centers have also shown acceptable outcomes in selected patients with higher MELD scores or renal insufficiency (32–35).

These results strongly support the concept that after 15–20 cases LDLT centers have reached a "steady state" following their initial learning curve, and can confidently contend that post-transplant outcomes for LDLT are essentially equivalent to DDLT, and better if pre-transplant morbidity and mortality is considered. This is extremely important when one considers that some of the risk factors contributing to poor outcome, such as renal failure, can be avoided if LDLT can be performed in a more timely fashion than DDLT. Both improved pre- and post-transplant survival in experienced centers suggests that in a patient with a suitable living donor, LDLT should be considered the preferred procedure performed prior to the progressive deterioration of liver disease, similar to the benefits offered to kidney patients when transplantation is performed prior to the initiation of dialysis (36, 37). We also know that the MELD score, while an excellent tool to risk stratify candidates on the waitlist, has its limitations and many patients with lower MELD scores with decompensated cirrhosis have an elevated risk of death as well (38–41). Waiting too long for a deceased donor offer at a higher MELD score often results in death on the waitlist and potentially a higher risk of graft failure and/or death after transplant. If LDLT is a viable option with an appropriate donor, patients with symptomatic or decompensated liver disease can be transplanted earlier, with lower MELD scores, less renal failure, and better nutritional status, resulting in less death on the waitlist and better post-operative outcomes.

Our findings regarding clinical variables impacting post-transplant outcome, as well as other results reported in recent publications, delineate which recipient and donor characteristics can result in optimal results. In addition, they provide important information and potential recommendations for recipients when discussing the LDLT option. An important finding is that donor age has significant impact on both patient and graft survival in the LDLT group, and this may influence which donor is chosen if the recipient has multiple choices.

When discussing LDLT, the donor must always be taken into consideration. While this report focuses on recipient outcomes, A2ALL has comprehensively reported on donor recovery and outcomes, providing information that can contribute to the increased safety of donation. In both the retrospective study and the prospective cohort, A2ALL has shown that approximately 40% of donors experience some sort of complication following donation (42, 43). While most complications were minor (Clavien grade I and II) and 95% resolved within the first year, there were significant events and even donor deaths reported at A2ALL centers (44). It is critical that we strive to decrease these risks if we are to increase the number of LDLT performed in North America. The A2ALL consortium has detailed data on liver regeneration and recovery in the donor, and found variables associated with better outcomes, and identified issues in the donor including liver function, laboratory tests, psychosocial concerns and quality of life that will require long-term follow-up and merit

further study (45–49). We should continue to be aware of potential long-term effects of donation, both physical and psychosocial. Having identified and characterized the most common reasons for donor morbidity, it is then possible to address the issues and decrease their incidence.

There are some limitations to this study. First, it includes both retrospective and prospectively collected data, and was an observational study, not a randomized trial between LDLT and DDLT. It does, however, reflect the actual practice at experienced LDLT centers. In addition, the timing of placing a patient on the waitlist reflects actual center specific practice patterns and was not by protocol.

In summary, the A2ALL multicenter prospective study in LDLT has demonstrated that there is a significant and sustained benefit to liver transplant candidates with LDLT compared to DDLT. This benefit occurs not only during the waitlist period, but also by providing real benefit after transplantation by offering transplantation at a lower MELD, before disease progression associated with renal dysfunction and other life support requirements ensue. Our results provide evidence that when a deceased donor organ is not immediately available, as is usually the case, LDLT should be considered a primary liver transplant option early in the course of transplant evaluation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Appendix

Requests for Reprints – Reprints will not be available from authors.

This study was presented in part at the 135th annual meeting of the American Surgical Association, San Diego, California.

This is publication number 31 of the Adult-to-Adult Living Donor Liver Transplantation Cohort Study.

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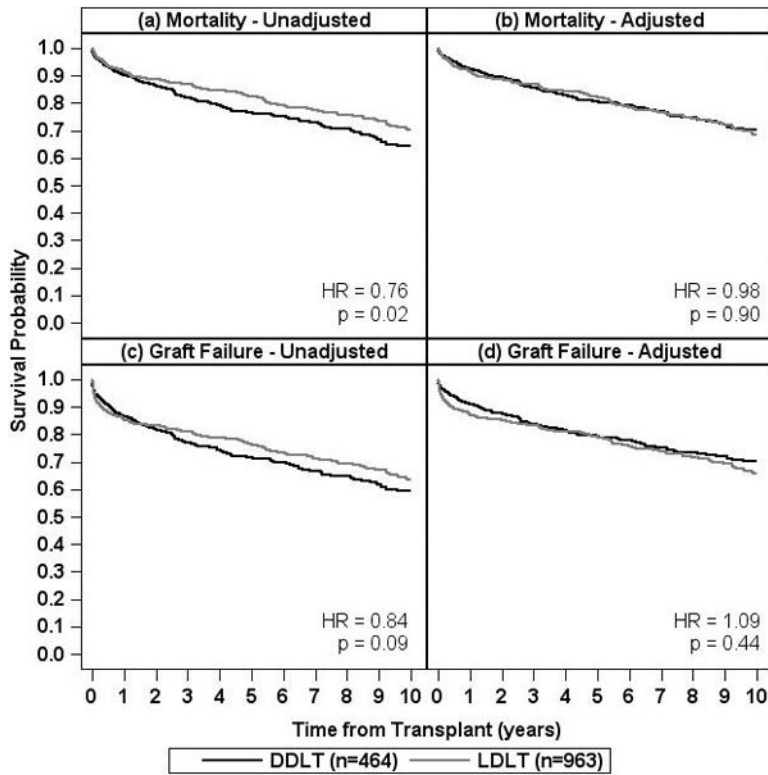
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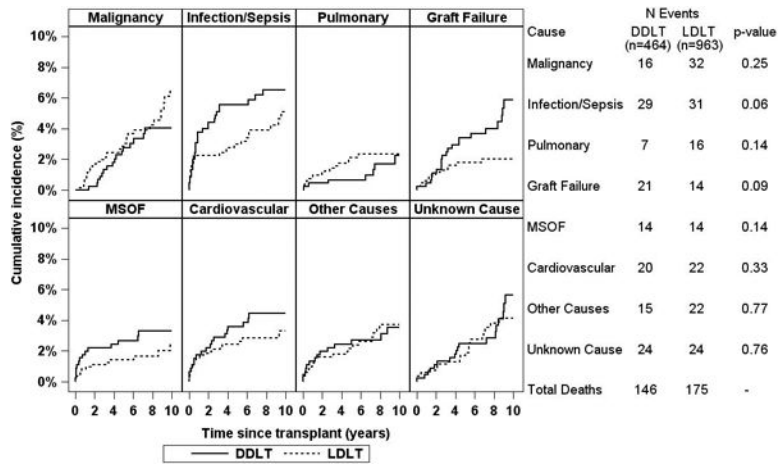
Figure 1.
Survival plots of mortality and graft failure by transplant type. Panels (a) and (b) show unadjusted and adjusted probability of freedom from death. Panels (c) and (d) show unadjusted and adjusted probability of graft survival. Adjusted survival probabilities are presented for a 53 year old male patient without non-HCC malignancy or PSC, not dialysis at transplant, MELD of 16, and received a liver from a donor under 50 years old. Adjusted graft survival probabilities are presented for a 53 year old patient without autoimmune hepatitis, HCC, or PSC, a MELD of 16 at transplant, and not on dialysis at transplant, and received a liver from a donor under 50 years old. HCC=hepatocellular carcinoma, PSC=primary sclerosing cholangitis, MELD=model for end-stage liver disease.

Figure 2.
Unadjusted cumulative incidence for specific causes of death by transplant type. The number of deaths in each group due to each specific cause and p-values from tests of differences between unadjusted cumulative incidence functions for LDLT vs. DDLT are shown on the right. MSOF=multiple system organ failure.
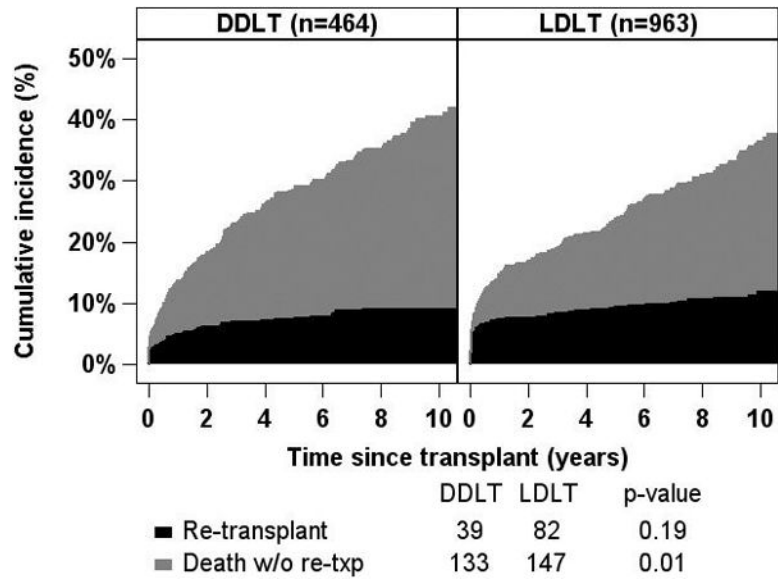
Figure 3.
Unadjusted cumulative incidence for causes of graft failure (summarized as re-transplant or death without re-transplant) by transplant type.
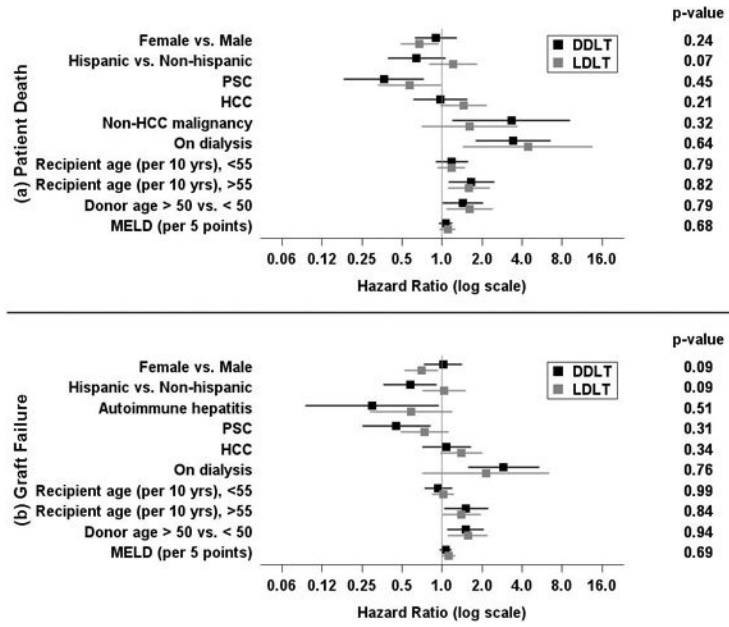
Figure 4.
Forest plots showing estimated hazard ratios on the log scale for covariate effects associated with (a) patient mortality and (b) graft failure from separate Cox models for LDLT (grey boxes) and DDLT (black boxes) recipients; whiskers show 95% confidence intervals for true log hazard ratios. P-values are from tests of interaction between each covariate and LDLT/ DDLT in a combined model. Note all p-values >0.05 imply no significant differences in log hazard ratios between LDLT and DDLT.

Table 1

Recipient Characteristics at Transplant

	DDLT (n=464)			LDLT (n=963)*			
	N	Mean (SD) or Frequency	Range or %	N	Mean (SD) or Frequency	Range or %	p-value
Age	463	52.08 (10.49)	18–74	963	51.37 (11.48)	18–76	0.25
Female	464	182	39%	963	408	42%	0.26
Hispanic	463	87	19%	963	126	13%	0.005
Race	464			963			<0.001
White		390	84%		877	91%	
Black		33	7%		29	3%	
Asian		17	4%		31	3%	
Other Race		24	5%		26	3%	
Body mass index	412	26.78 (5.01)	13–50	919	26.54 (5.26)	15–55	0.42
Diagnosis (multiple diagnoses possible)	464			963			
Acute liver failure		19	4%		24	2%	0.10
Alcohol-related cirrhosis		86	19%		155	16%	0.25
Autoimmune hepatitis		20	4%		63	7%	0.09
Cryptogenic cirrhosis		53	11%		80	8%	0.06
HBV		12	3%		28	3%	0.73
HCC		98	21%		154	16%	0.02
HCV		210	45%		339	35%	<0.001
Hemochromatosis		3	1%		10	1%	0.47
Other metabolic liver disease		16	3%		21	2%	0.16
Malignancy other than HCC		7	2%		26	3%	0.16
PBC		12	3%		81	8%	<0.001
PSC		61	13%		162	17%	0.07
Other diagnosis		21	5%		90	9%	0.001
MELD at evaluation	452	16.77 (6.61)	6–40	538	14.55 (6.00)	6–40	<0.001
6–10		67	15%		130	24%	
11–10		267	59%		348	65%	
21–30		97	21%		44	8%	

	DDLT (n=464)			LDLT (n=963)*			
	N	Mean (SD) or Frequency	Range or %	N	Mean (SD) or Frequency	Range or %	p-value
31–40		21	5%		16	3%	
MELD at transplant	440	20.42 (8.92)	6–40	935	15.47 (5.90)	6–40	<0.001
6–10		52	12%		169	18%	
11–10		201	46%		614	66%	
21–30		118	27%		132	14%	
31–40		69	16%		20	2%	
Medical condition at transplant	462			567			<0.001
Intensive care unit (ICU)		51	11%		9	2%	
Hospitalized not in ICU		70	15%		35	6%	
Not hospitalized		341	74%		523	92%	
Comorbidities							
Ventilator	461	28	6%	959	12	1%	<0.001
Ascites	455	284	62%	567	260	46%	<0.001
Dialysis	457	25	5%	957	7	1%	<0.001

Perioperative Characteristics	N	Median	IQR	N	Median	IQR	p-value
Duration of recipient surgery (h)	421	5.78	5–7	533	7.57	7–9	<0.001
Total ischemia time (min)	442	486.50	364–600	847	98.00	71–140	<0.001
PRBCs$^\delta$	439	6.00	3–11	557	4.00	2–8	<0.001
Recipient ICU LOS (days)	370	2.00	1–5	915	2.00	1–3	0.05
Recipient Total LOS (days)	407	10.00	7–17	945	10.00	7–15	0.65

*
Excludes LDLT cases 20.

δ
Collected in A2ALL-1 only.

DDLT=deceased donor liver transplant; LDLT=living donor liver transplant; SD=standard deviation; HBV=hepatitis B virus; HCC=hepatocellular carcinoma; HCV=hepatitis C virus; PBC=primary biliary cirrhosis; PSC=primary sclerosing cholangitis; MELD=model for end-stage liver disease; IQR = interquartile range; PRBC = packed red blood cells; LOS = length of stay.

Table 2

(a): Multivariable Cox Model: Mortality

Parameter	Hazard Ratio	95% Lower Confidence Limit for Hazard Ratio	95% Upper Confidence Limit for Hazard Ratio	p-value
LDLT vs. DDLT	0.98	0.77	1.27	0.90
Female vs. male	0.74	0.58	0.94	0.01
Recipient diagnosis: malignancy other than HCC	2.16	1.13	4.11	0.02
Recipient diagnosis: PSC	0.45	0.30	0.69	<.001
On dialysis at transplant	3.59	2.05	6.28	<.001
Recipient age at transplant (per 10 years), < 55	1.20	1.00	1.44	0.05
Recipient age at transplant (per 10 years), > 55	1.65	1.27	2.15	<.001
Donor age > 50 vs. < 50	1.49	1.14	1.94	0.003
MELD at transplant (per 5 points)	1.06	0.98	1.16	0.15

(b): Multivariable Cox Model: Graft Failure

Parameter	Hazard Ratio	95% Lower Confidence Limit for Hazard Ratio	95% Upper Confidence Limit for Hazard Ratio	p-value
LDLT vs. DDLT	1.09	0.87	1.37	0.44
Recipient diagnosis: autoimmune hepatitis	0.44	0.24	0.82	0.009
Recipient diagnosis: HCC	1.32	1.01	1.73	0.05
Recipient diagnosis: PSC	0.66	0.47	0.93	0.02
On dialysis at transplant	2.54	1.50	4.31	<.001
Recipient age at transplant (per 10 years), < 55	1.03	0.89	1.19	0.71
Recipient age at transplant (per 10 years), > 55	1.39	1.08	1.78	0.009
Donor age > 50 vs. < 50	1.52	1.20	1.93	<.001
MELD at transplant (per 5 points)	1.09	1.00	1.17	0.04

DDLT=deceased donor liver transplant; LDLT=living donor liver transplant; HCC=hepatocellular carcinoma; HCV=hepatitis C virus; PSC=primary sclerosing cholangitis; MELD=model for end-stage liver disease;