Outcomes of Donor Evaluation in Adult-to-Adult Living Donor Liver Transplantation

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The purpose of donor evaluation for adult-to-adult living donor liver transplantation (LDLT) is to discover medical conditions that could increase the donor postoperative risk of complications and to determine whether the donor can yield a suitable graft for the recipient. We report the outcomes of LDLT donor candidates evaluated in a large multicenter study of LDLT. The records of all donor candidates and their respective recipients between 1998 and 2003 were reviewed as part of the Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL). The outcomes of the evaluation were recorded along with demographic data on the donors and recipients. Of the 1011 donor candidates evaluated, 405 (40%) were accepted for donation. The donor characteristics associated with acceptance ($P < 0.05$) were younger age, lower body mass index, and biological or spousal relationship to the recipient. Recipient characteristics associated with donor acceptance were younger age, lower Model for End-stage Liver Disease score, and shorter time from listing to first donor evaluation. Other predictors of donor acceptance included earlier year of evaluation and transplant center. *Conclusion:* Both donor and recipient features appear to affect acceptance for LDLT. These findings may aid the donor evaluation process and allow an objective assessment of the likelihood of donor candidate acceptance. (HEPATOLOGY 2007;46:1476-1484.)

Donor evaluation is one of the most important aspects of adult-to-adult living donor liver transplantation (LDLT).[1-3] The evaluation process is designed to reveal any condition that may increase the risk of complications for the donor. In addition, the transplant team should determine whether the donor will yield a suitable graft for the recipient. The evaluation process typically proceeds in a stepwise fashion so that unsuitable donors can be identified as early as possible. Acceptance of donors by the evaluating team implies that they have met all relevant medical, surgical, psychosocial, and informed consent criteria necessary to proceed with donor right hepatic lobectomy.

The Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL) is a multicenter project

Abbreviations: A2ALL, Adult-to-Adult Living Donor Liver Transplantation Cohort Study; BMI; body mass index; DDLT, deceased donor liver transplant; LDLT, living donor liver transplantation; MELD, Model for End-stage Liver Disease score; SRTR, Scientific Registry of Transplant Recipients.

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funded by the National Institutes of Health to evaluate the outcomes of donors and recipients evaluated for and undergoing this procedure. Although designed with both retrospective and prospective phases, the data presented in this report are derived from the retrospective phase of A2ALL. There were three major goals of the analysis: (1) to describe the characteristics and acceptance rate of donor candidates; (2) to examine the evolution of donor selection over time; and (3) to identify factors that predict donor candidate acceptance.

Patients and Methods

Study Subjects. A2ALL includes nine US liver transplantation centers.[4] Between January 1, 1998 and February 28, 2003, these centers evaluated 819 potential LDLT recipients, for whom 1011 donor candidates were evaluated. Two subsets of these potential donors have been previously reported in single-center evaluations of this topic.[5,6] The donor evaluation is typically performed in a stepwise fashion beginning with basic laboratory tests, blood type confirmation, and, at many centers, a basic medical screening questionnaire. Study subject entry was defined as the date the donor candidate underwent a history and physical examination as part of the donor evaluation. Thereafter, the donor candidate was either accepted or not accepted for donation. Data were retrospectively collected on all donor and LDLT recipient candidates using standardized forms. For 389 of the potential recipients, an LDLT was performed.

Donor Evaluation Outcomes. The primary reason for not accepting donor candidates was categorized as donor or recipient related. Donor reasons included: (1) medical contraindication (diagnosis of medical condition that could increase the risk of short-term or long-term complications in the donor candidate, such as hypertension, abnormal blood chemistries, or chest radiograph); (2) anatomic considerations (findings on hepatic cross-sectional imaging that either increase the risk of hepatectomy in the donor candidate, for example, large hemangioma, or preclude the donor candidate from yielding a suitable graft, for example, significantly abnormal hepatic vasculature, or both); (3) donor candidate declined to donate; (4) hepatic histology showing steatosis greater than 10%; or (5) psychosocial contraindications, such as active substance abuse. Recipient reasons included: (1) recipients who declined the donor's offer or (2) recipients who had a change in condition precluding the feasibility of or need for LDLT [improvement, deterioration, receipt of a deceased donor liver transplant (DDLT), or death].

To compare candidates wait-listed for liver transplantation who had a potential living donor with those who did not at the 9 A2ALL centers, we compared potential LDLT recipients with the complement of DDLT-listed candidates in the Scientific Registry of Transplant Recipients (SRTR) database, under a data use agreement. DDLT transplant candidates included those listed for transplantation between the date of their center's LDLT program initiation and February 28, 2003 at each A2ALL center, but who did not have a living donor evaluated. In addition, SRTR data were used to supplement A2ALL data where available.

The time from a candidate's listing to the date of his/her first potential donor's evaluation was calculated in days and categorized by quartiles. We found no significant difference in donor acceptance probabilities between the second through fourth quartiles, so this variable was dichotomized (before day 23 versus day 23 or after) for further analyses. Calendar time effects on donor acceptance were tested using 1998 to 2000 versus 2001 to 2003.

The Model for End-stage Liver Disease score (MELD) was calculated for the LDLT candidates at the time of donor evaluation as previously described.[7,8] Laboratory-based MELD was calculated for DDLT candidates listed after September 2001, when MELD component reporting became a requirement. For statistical comparisons of MELD scores between LDLT and DDLT candidates, those of LDLT candidates were restricted to the MELD era.

Body mass index (BMI) of recipient and donor candidates was calculated as weight in kilograms divided by height in meters squared (kg/m^2) at the time of evaluation and categorized as low ($<18.5\ kg/m^2$), normal (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), or obese ($\geq 30\ kg/m^2$).[9] In the logistic regression analysis, the combined group of underweight and normal weight served as the reference group.

A history of adverse events or diseases in potential recipients that had the potential to confound the likelihood of donor acceptance, such as coronary artery disease, diabetes mellitus, the need for mechanical ventilation, and renal failure, were collected for the recipient candidates at the time of donor evaluation.

The study was approved by the institutional review boards and privacy boards of the University of Michigan Data Coordinating Center and each of the 9 participating transplant centers.

Statistical Analysis. Demographic characteristics of potential donors were tabulated by donor acceptance status. Demographic and medical characteristics of potential recipients were tabulated by donor acceptance status and

Table 1. Characteristics of A2ALL Potential Donors (Evaluation Years 1998-2003)

Characteristic	Overall (n = 1,011)	Donors Who Were Accepted (n = 405)	Donors Who Were Not Accepted (n = 606)	*P* Value
	Mean (SD; range) or N (%)	Mean (SD; range) or N (%)	Mean (SD; range) or N (%)	
Age	37 (10.1; 18-59)	37 (9.6; 18-59)	38 (10.3; 18-59)	0.0846
Age (categories)				0.1676
Age 18-39	577 (57%)	244 (60%)	333 (55%)	
Age 40-49	301 (30%)	116 (29%)	185 (31%)	
Age ≥ 50	130 (13%)	44 (11%)	86 (14%)	
Sex				0.3430
Female	446 (44%)	186 (46%)	260 (43%)	
Male	565 (56%)	219 (54%)	346 (57%)	
Ethnicity*				0.7923
Hispanic/Latino	171 (17%)	68 (17%)	103 (18%)	
Non-Hispanic/Non-Latino	820 (83%)	335 (83%)	485 (82%)	
Race*				0.1129
White	894 (90%)	366 (91%)	528 (89%)	
African-American	53 (5%)	15 (4%)	38 (6%)	
Other	46 (5%)	22 (5%)	24 (4%)	
Height (cm)	173 (10.1; 145-211)	173 (10.0; 150-203)	173 (10.1; 145-211)	0.9234
Weight (kg)	81 (16.7; 41-146)	78 (15.3; 43-146)	83 (17.4; 41-146)	<0.0001
Body mass index (kg/m^2)	27 (4.6; 16-57)	26 (4.2; 17-57)	28 (4.8; 16-50)	<0.0001
Body mass index (categories)				<0.0001
BMI < 18.5	11 (1%)	6 (1%)	5 (1%)	
BMI 18.5-24.9	296 (29%)	148 (37%)	148 (24%)	
BMI 25.0-29.9	408 (40%)	182 (45%)	226 (37%)	
BMI ≥ 30	208 (21%)	61 (15%)	147 (24%)	
Missing	88 (9%)	8 (2%)	80 (13%)	
Relatedness to recipient				<0.0001
Biologically related				
Parent	27 (3%)	9 (2%)	18 (3%)	
Offspring	317 (31%)	139 (34%)	178 (29%)	
Sibling	210 (21%)	92 (23%)	118 (19%)	
Other biological	95 (9%)	35 (9%)	60 (10%)	
Not biologically related				
Spouse	86 (9%)	51 (13%)	35 (6%)	
Other nonbiological	223 (22%)	78 (19%)	145 (24%)	
Unknown/Missing	53 (5%)	1 (<1%)	52 (9%)	
Order of donor evaluated for their recipient candidate*				0.1589
1st donor evaluated	819 (81%)	339 (84%)	480 (79%)	
2nd donor evaluated	147 (15%)	52 (13%)	95 (16%)	
3rd-7th donor evaluated	43 (4%)	13 (3%)	30 (5%)	

*Missing at most 2%.

were compared with DDLT candidates not considered for LDLT at the 9 A2ALL centers during the same time period. Donor-related and recipient-related reasons for donors not being accepted, as well as information on aborted transplant procedures, were tabulated.

Logistic regression analysis was used to model the probability of donor acceptance as a function of donor and recipient characteristics. Robust (sandwich estimator) variances were used to adjust for possible correlation among potential donors of the same recipient. Two-way interactions were tested and not found to be significant. The strength of overall covariate prediction was assessed by the c-statistic (based on the area under the receiver operating characteristic curve), with a value of 0.70 or greater considered to provide acceptable discrimination.[10] Relative covariate predictive ability was assessed by the change in the c-statistic value (Δc-statistic) when a covariate was removed from the model. All analyses were performed using SAS version 9.1.

Role of the Funding Sources. The National Institutes of Health project scientist participated in study design and analysis and interpretation of data. The Health Resources and Services Administration and American Society of Transplant Surgeons had no direct involvement in the study.

Results

The characteristics of living donor candidates who were accepted and not accepted are depicted in Table 1. The overall proportion accepted (accepted donor candidates

Table 2. Characteristics of A2ALL Potential LDLT Recipients by Donor Acceptance Status Compared With DDLT Waitlist Candidates Not Considered for LDLT at A2ALL Centers

Characteristic	Potential Recipients With at Least One Donor Accepted (n = 401)	Potential Recipients With No Donors Accepted (n = 418)	*P* Value†	DDLT Waitlist Candidates Not Considered for LDLT (n = 7,358)	*P* Value‡
	Mean (SD) or Percent	Mean (SD) or Percent		Mean (SD) or Percent	
Age	49.0 (10.9)	51.1 (9.7)	0.0033	50.7 (10.3)	0.0635
Age (categories)			0.0290		0.2271
Age 18-29	7%	4%		4%	
Age 30-49	42%	37%		41%	
Age ≥ 50	51%	59%		54%	
Sex			0.4905		0.0230
Female	41%	44%		39%	
Male	59%	56%		61%	
Ethnicity*			0.6390		0.0708
Hispanic/Latino	20%	19%		17%	
Non-Hispanic/Non-Latino	80%	81%		83%	
Race*			0.0834		0.0005
White	90%	89%		84%	
African-American	3%	7%		7%	
Asian	4%	2%		6%	
Other	3%	2%		3%	
Height (cm)	171.3 (10.8)	170.9 (9.8)	0.6143	171.0 (11.0)	0.7865
Weight (kg)	78.5 (18.2)	80.4 (17.8)	0.1296	82.7 (20.4)	<0.0001
Body mass index (kg/m^2)	26.7 (5.3)	27.4 (5.2)	0.0526	28.5 (11.6)	0.0005
Body mass index (categories)			0.0898		<0.0001
BMI < 18.5	3%	2%		2%	
BMI 18.5-24.9	38%	35%		28%	
BMI 25.0-29.9	38%	34%		31%	
BMI ≥ 30	20%	28%		29%	
Missing	1%	1%		11%	
Education level*			0.2362		0.0003
None	<1%	0%		1%	
Grade/High School (0-12)	35%	41%		44%	
Tech/Bachelor/Graduate	49%	45%		40%	
Unknown	16%	14%		14%	
Diagnosis at enrollment and listing (more than one diagnosis per patient possible)					
HCV	47%	46%	0.7831	42%	0.0073
HCC	14%	11%	0.2040	5%	<0.0001
Alcohol	13%	15%	0.3862	16%	0.2699
Cholestatic liver disease	18%	19%	0.7275	10%	<0.0001
Noncholestatic cirrhosis other than HCV/alcohol	21%	20%	0.8327	21%	0.5761
Metabolic disease	3%	3%	0.7556	2%	0.0995
Biliary atresia	1%	0%	0.0765	<1%	0.2941
Malignancy other than HCC	3%	2%	0.3174	<1%	<0.0001
Fulminant	2%	1%	0.1124	6%	<0.0001
Other	3%	4%	0.4903	6%	<0.0017
Ascites*	61%	68%	0.0297	65%	0.4920
Variceal bleed*	17%	19%	0.5211	5%	<0.0001
Upper abdominal surgery*	19%	20%	0.9234	27%	<0.0001
Spontaneous bacterial peritonitis*	8%	5%	0.1509	6%	0.4725
Transjugular intrahepatic portosystemic shunt*	9%	12%	0.0711	5%	<0.0001
MELD			0.0388		
Pre-MELD period	15.5 (7.1)	16.0 (7.2)		N/A	N/A
Post-MELD period	14.5 (5.4)	17.1 (7.2)		15.8 (8.3)	0.6249
MELD categories§			0.0558		
6-10	25%	20%		26%	
11-20	58%	56%		54%	
21-30	13%	18%		10%	
31-40	4%	6%		9%	
Recipient medical condition*			0.9274		0.0094
ICU	4%	3%		5%	
Hospitalization, no ICU	7%	8%		6%	
Not hospitalized	89%	89%		89%	

Table 2. *Continued*

Characteristic	Potential Recipients With at Least One Donor Accepted (n = 401) Mean (SD) or Percent	Potential Recipients With No Donors Accepted (n = 418) Mean (SD) or Percent	*P* Value†	DDLT Waitlist Candidates Not Considered for LDLT (n = 7,358) Mean (SD) or Percent	*P* Value‡
Mechanical ventilation*	2%	2%	0.7359	3%	0.2044
Renal failure requiring dialysis*	4%	3%	0.7744	2%	0.0581
Diabetes mellitus*	19%	21%	0.4247	19%	0.5736
Angina/coronary artery disease*	3%	5%	0.2503	2%	0.0192
Drug treated systemic hypertension*	12%	13%	0.7686	13%	0.8236
Days from listing to first donor evaluation	194.9 (303.3)	258.5 (352.3)	0.0059	N/A	N/A
Number of evaluated donors per recipient*			0.5662		N/A
1	83%	81%		N/A	
2	14%	15%		N/A	
3-7	3%	4%		N/A	

*Missing at most 3%. †Recipients with at least 1 donor accepted versus recipients with no accepted donor. ‡All potential LDLT recipients versus DDLT waitlist candidates not considered for LDLT. §No significant difference found between MELD scores from the pre-MELD and post-MELD periods in A2ALL Potential LDLT Recipients ($P = 0.60$). Therefore, the MELD categories exhibited above incorporate MELD scores from both periods.

divided by all donor candidates) was 405 of 1011 (40%). There were no significant differences in the age, sex, ethnicity or race of accepted donor candidates compared with those who were not accepted. Accepted donors had significantly lower body weight (by 5 kg) and BMI (26 ± 4.2 versus 28 ± 4.8; both $P < 0.0001$) than candidates who were not accepted. Accepted donor candidates were significantly more likely to be an offspring, sibling, or spouse of the recipient ($P < 0.0001$). The most common donor candidate was an offspring of the recipient (31% of all donor candidates; 34% of accepted donor candidates). For some recipients, several potential donors were evaluated. The probability of donor acceptance was higher for the first donor evaluated (41%) than for the second (35%) or subsequent (30%), but these differences were not statistically significant ($P = 0.16$). The overall rate of donor acceptance was significantly higher during the early experience (47% from 1998-2000) compared with later experience (35% from 2001-2003; $P = 0.0002$).

Demographics of the 819 LDLT recipient candidates, by donor acceptance status, and 7358 waitlisted DDLT candidates not considered for LDLT from the 9 A2ALL centers are shown in Table 2. Among the LDLT recipient candidates, those who had at least 1 donor accepted for donation were younger, had a lower BMI, a lower prevalence of ascites, lower MELD scores, and significantly shorter times from listing to first donor evaluation. The number of donors evaluated for each recipient was similar between the LDLT candidates who did and did not have a donor accepted.

Differences between LDLT candidates with or without a donor accepted were substantially less than differences between all LDLT candidates and DDLT candidates (Table 2). Compared with all DDLT candidates, LDLT candidates were significantly more likely to be women and white, and to weigh less and have lower BMI. Potential LDLT recipients were significantly more likely to have cirrhosis caused by hepatitis C virus, hepatocellular carcinoma, other primary hepatic malignancies, and cholestatic disorders and less likely to have fulminant hepatic failure. LDLT candidates were no less likely to have alcoholic liver disease than DDLT candidates. After February 2002, potential LDLT recipients had similar MELD scores at the time of first donor evaluation compared with those among DDLT candidates at the time of listing (16.0 ± 6.7 versus 15.8 ± 8.3; $P = 0.62$). However, LDLT candidates were significantly more likely to have had a history of variceal hemorrhage, or treatment with a transjugular intrahepatic portosystemic shunt. LDLT candidates were significantly less likely to have had a history of prior upper abdominal surgery or to have been in an intensive care unit at the time of donor evaluation compared with DDLT candidates at the time of listing.

Table 3 shows the disposition of donor candidate evaluations. Sixty percent of evaluated donors were not accepted, a medical contraindication being the most common reason (n = 173). The most common recipient-related reason that donors were not accepted was availability of a DDLT before LDLT donation. There were no significant differences in the distributions of donor-related or recipient-related reasons for rejection of donor candidates in 2001 to 2003 compared with 1998 to 2000 ($P = 0.48$).

Twelve accepted donor candidates were taken to the operating room with the intent of donation, but the procedure was not completed ("aborted donation"). One additional accepted donor underwent right hepatic lobectomy, but the graft was not transplanted into the intended recipient. Nine of the "aborted donation" cases

Table 3. Disposition of A2ALL Potential Donors (n = 1011)

Characteristic	n (%)
Potential Donors Who Were Not Accepted	**606 (60%)**
Donor-related reasons	
Medical contraindictions	173 (17%)
Anatomical contraindications	115 (11%)
Donor liver steatosis	65 (6%)
Declined to donate	68 (7%)
Psychosocial contraindications	55 (5%)
Recipient-related reasons	
Recipient received DDLT	65 (6%)
Recipient died	24 (2%)
Recipient too sick/removed from transplant consideration	19 (2%)
Recipient improved	8 (1%)
Recipient declined/refused organ	5 (<1%)
Other/unknown	9 (1%)
Potential donors who were accepted	**405 (40%)**
Successful donation	392 (39%)
Went to operating room but procedure aborted	12 (1%)
Graft resected but not transplanted	1 (<1%)

occurred later in the LDLT experience between 2001 and 2003.

A logistic regression model was fitted to estimate the adjusted odds of donor acceptance associated with putative predictive factors (Table 4). With regard to donor age, candidates between 18 and 40 years were the most likely to be accepted. Accepted donors were less likely to be overweight (BMI, 25.0-29.9 kg/m^2) or obese (BMI $\geq$30.0 kg/m^2) and were more likely to be family members (biological or spousal relationship). Potential donors evaluated earlier in a center's LDLT experience were twice as likely to be accepted for donation ($P < 0.0001$). Younger potential recipients and those with lower MELD scores were significantly more likely to have their donor candidates accepted. Donor candidates were also more likely to be accepted if the recipient had been listed for DDLT less than 23 days before first donor evaluation. The medical center of evaluation was also a significant predictor of acceptance, with a 10-fold range of odds ratios (OR 0.26 to 2.4 versus the average donor acceptance over the A2ALL centers, $P < 0.0001$).

The overall c-statistic (area under the receiver operating characteristic curve) for the model predicting donor acceptance was 0.731. The strongest predictors of donor acceptance included (in descending order): medical center of evaluation (Δc-statistic = 0.060), donor BMI (Δc-statistic = 0.022), year of donor evaluation (Δc-statistic = 0.012), recipient MELD score (Δc-statistic =

Table 4. Logistic Regression Model of Donor Acceptance

Variable*	Adjusted Odds Ratio	95% Confidence Limits		*P* Value
Donor age				
18 $\leq$ donor age <40	1.00			Reference
40 $\leq$ donor age <50	0.81	0.57	1.14	0.2256
50 $\leq$ donor age <60	0.61	0.38	0.96	0.0332
Donor BMI				
BMI $\leq$ 24.9	1.00			Reference
25.0 $\leq$ BMI $\leq$ 29.9	0.77	0.55	1.06	0.1118
BMI $\geq$ 30	0.31	0.20	0.47	<0.0001
Relatedness to recipient				
Biologically related/Spouse	1.51	1.05	2.16	0.0258
Nonbiological (excluding spouse)	1.00			Reference
Era of donor evaluation				
1998-2000	2.03	1.48	2.79	<0.0001
2001-2003	1.00			Reference
Recipient age				
18 $\leq$ recipient age < 30	2.08	1.17	3.72	0.0132
30 $\leq$ recipient age < 50	1.37	1.01	1.87	0.0446
50 $\leq$ recipient age < 76	1.00			Reference
Recipient MELD				
6 $\leq$ MELD $\leq$ 10	1.85	1.17	2.93	0.0081
11 $\leq$ MELD $\leq$ 20	1.77	1.18	2.67	0.0063
21 $\leq$ MELD $\leq$ 40	1.00			Reference
Days from recipient listing to first donor evaluation				
< 23 Days	1.66	1.16	2.36	0.0052
$\geq$ 23 Days	1.00			Reference
A2ALL center				
Range of ORs among 9 centers	0.26-2.44			<0.0001
Average over all A2ALL centers	1.00			Reference

*Variables tested and excluded from the model included: donor gender, donor ethnicity, donor race, donor alkaline phosphatase, donor bilirubin, donor case number, number of evaluated donors per recipient, order of donors evaluated per recipient, recipient gender, recipient ethnicity, recipient race, recipient diagnosis, recipient BMI, donor-recipient ethnicity match, and estimated graft weight-recipient weight ratio.

0.010), time from recipient listing to first donor evaluation (Δc-statistic = 0.009), recipient age (Δc-statistic = 0.006), donor–recipient relatedness (Δc-statistic = 0.005), and donor age (Δc-statistic = 0.003).

Discussion

This analysis provides perhaps the largest collective experience documenting the outcomes of donor evaluation for LDLT among adults. Several of the results deserve comment. Although it was anticipated that donor acceptance might have increased with greater experience in donor evaluations, in fact the donor acceptance rate declined with greater center experience. There are several likely explanations for the decreased rate of acceptance over time. First, when LDLT was initially offered at each center, hundreds of patients were already listed for deceased donor transplantation, some of whom were ideal candidates for LDLT. Early in the experience of LDLT, a proportionally higher number of the recipients with ideal donors may have been identified and were likely accepted for LDLT at a higher rate. Once these ideal recipient-donor pairs were transplanted, the remaining donor candidates were rejected at a higher rate during the evaluation. Second, transplant centers may have become more conservative in their approach toward LDLT after the highly publicized death of a living donor in 2001 in the United States. After this catastrophic event, some centers may have become more conservative in their selection of donors in an attempt to minimize the risk of unfavorable donor outcomes. The overall reduction in the number of LDLT in the United States after 2001 by approximately 50% may reflect a more restrained approach toward the procedure.[11] Third, the institution of the MELD score as the basis for deceased donor liver allocation may have impacted LDLT. After February 2002, when MELD was introduced, fewer patients died on the waiting list, likely because of expedited DDLT. Between 2001 and 2003, we noted a higher proportion of LDLT candidates who had DDLT during the course of the donor's evaluation.

As expected, donor candidates with higher BMI were much less likely to be accepted as donors. Overweight and obese patients are higher-risk living liver donors because of greater likelihood of hepatic steatosis and medical problems (diabetes, hypertension, and heart disease), which could increase the postoperative complications.[12,13] However, recent data have shown that selected obese candidates may successfully undergo donation without evidence of increased complications.[14] Accepted donor candidates were more likely to be related to the recipient (including spouses) than rejected candidates. The most obvious explanation is that the related candidates may have demonstrated a greater interest and understanding of the donation procedure and therefore presented themselves as better candidates.

Changes in the recipient's condition were an important determinant of whether donor candidates were accepted for operation. Thirteen percent of donor candidates were not accepted because of a change in the recipient's condition, the most common of which was receipt of a DDLT. In these cases, the DDLT occurred before completion of the donor evaluation. Acceptance as a living donor did not ensure that the patient would undergo the operation. Thirteen approved donor candidates were taken to the operating room, but a donor hepatectomy was not completed because of intraoperative recipient death or unexpected findings in the donor or recipient. Each of these cases represents a failure of the donor or recipient evaluation process.

The logistic regression analysis identified important predictors of donor acceptance. Interestingly, several of the strongest predictors of donor acceptance were not related to any specific donor factors: medical center of evaluation, year of evaluation, recipient age, and recipient MELD. Perhaps younger, less sick recipient candidates evaluated early in the experience at specific centers had more favorable donor candidates. Alternatively, donor candidates may not have been evaluated independently of the recipient characteristics. That is, donor candidates may have been viewed more favorably if their recipient was deemed a better candidate. This issue requires further evaluation. Accepted donors were primarily the first donors evaluated for a given recipient because of the fact that these donors made up the majority of the subject population. However, the percentage of first donors accepted was only slightly higher than that of second and subsequent donors.

We were somewhat surprised at the large variation in the likelihood of donor acceptance based on the center of evaluation, and the explanation for this finding is not entirely clear. These variations in acceptance rates may be attributable to subtle and unmeasured differences in how transplant centers evaluate donors. That is, there may be important differences in how donor candidates were prescreened before the formal donor evaluation, which was the entry point for the A2ALL study. In addition, some of the difference may have been attributable to the small number of donor evaluations performed at some of the centers.

LDLT candidates differed substantially from DDLT candidates by demographic factors, disease cause, and severity of illness. This difference was much greater than differences between LDLT candidates with or without successful donor evaluation. This is not surprising, given

the effect of recipient characteristics on the likelihood of a potential LDLT donor being accepted. Importantly, the differences between DDLT and LDLT candidates point to potential problems in comparisons of transplant outcomes between groups of patients who may differ in fundamental ways.

There are several notable weaknesses of our analysis. Most important, the retrospective nature of this study precluded complete collection of data on all candidates. This was most apparent in the proportion with missing demographic data among donor candidates who were not accepted. Because the study was conducted up to 5 years after their evaluation, many of the donor candidates were no longer in contact with the transplant center. Therefore, there was no opportunity to obtain missing data values in these candidates. In contrast, the accepted living donor candidates, almost all of whom proceeded to donor hepatectomy, often had ongoing relationships with the transplant center, which facilitated data collection. Identification of the precise reason for rejecting donor candidates may have been imperfect when determined in retrospect. For example, a donor may have had extensive hepatic steatosis identified retrospectively as the indication for nonacceptance, but elected not to donate independently of the biopsy findings. Another significant weakness of this study is that we may not have captured the complexities of the donor evaluation process. Our analysis allowed the selection of only 1 of a limited number of reasons for donor nonacceptance when in some cases the reasons may have been multifactorial. For example, a donor candidate may have had a large hepatic hemangioma and abnormal electrocardiogram (either of which would preclude donation), but only a single reason was recorded for this study. Finally, although the evaluation process at each center is similar, there are likely subtle differences in the identification and selection of donors and recipients that could lead to differences in outcomes of the donation process. Because of the nature of our analysis we were not able to capture the effect of these differences on donor candidate outcomes.

One of the weaknesses of this study is that there are likely important differences in the subtle details in each center's approach to LDLT. Specifically, some centers may have been more or less aggressive in recruiting patients for the procedure. In addition, the specific approach to the donor evaluation, type of cross-sectional imaging used in assessment of donor anatomy, and use of the liver biopsy in donor evaluation likely varied slightly between the centers. We acknowledge that these subtle differences may not have been accounted for in our analysis and could result in slight differences in the donor acceptance rate between the 9 participating centers.

In summary, we have described the outcomes in a large group of donor candidates for LDLT. We found that (1) the overall rate of acceptance for donor candidates was 40%; (2) the acceptance rate has dropped over time; and (3) the strongest predictors of donor acceptance, in decreasing order of importance, were center of evaluation, donor BMI, year of evaluation, recipient MELD score, days from listing to first donor evaluation, recipient age, donor–recipient relatedness, and donor age. These findings may aid the donor evaluation process and allow an objective assessment of the likelihood of donor candidate acceptance.

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