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An evaluation of the impact of donor BMI on survival and post-transplant obesity in pediatric liver transplant recipients

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Abstract

Introduction—In adult liver transplant recipients, donor BMI is associated with post-transplant obesity but not graft or patient survival. Given the U.S. obesity epidemic and already-limited supply of liver donors, clarifying whether donor BMI affects pediatric outcomes is important.

Methods—UNOS data on pediatric U.S. liver transplants 1990-2010 was evaluated. Data on transplants 2004-2010 (n=3788) was used for survival analysis with Kaplan-Meier and Cox proportional hazards models and for post-transplant obesity analysis with generalized estimating equations.

Results—For children receiving adult donor livers, donor BMI 25-35 kg/m^2 was not associated with graft or patient survival in univariate or multivariate analyses. Donor BMI>35 kg/m^2 increased the risk of graft loss (HR 2.54, 95%CI 1.29-5.01, p=0.007) and death (HR 3.56, 95%CI 1.64-7.72, p=0.001). For pediatric donors, donor BMI was not associated with graft loss or mortality in univariate or multivariate analysis. Donor overweight/obesity was not a risk factor for post-transplant obesity.

Conclusions—Overweight/obesity is common among liver transplant donors. This analysis suggests that for adult donors, BMI 25-35 should not by itself be a contraindication to liver donation. Severe obesity (BMI>35) in adult donors increased the risk of graft loss and mortality, even after adjustment for recipient, donor, and transplant risk factors. Post-transplant obesity was not associated with donor BMI in this analysis. Further research is needed to clarify the impact of donor obesity on pediatric liver transplant recipients.

Keywords

overweight; obesity; pediatrics; liver transplant; long-term complications

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Introduction

The prevalence of overweight and obesity in donors to adult liver transplant recipients has increased over the last two decades. (1) This trend has not been examined in the pediatric donor pool. However, overweight and obesity in the general U.S. pediatric population has risen in parallel with adults and now exceeds 30%. (2, 3)

Donor BMI (dBMI) is one criterion used in decisions about the acceptability of a donor. Overweight adult donors are more likely to have hepatic steatosis, which is a predictor of early graft loss. (4, 5). But dBMI, even above 35 kg/m^2, was not associated with graft or patient survival in adult liver transplant recipients in the UNOS database 1988-2001.(1) One analysis found dBMI above 25 kg/m^2 increased the odds of adult post-transplant obesity more than 3-fold, even after adjustment for recipient pre-transplant BMI. (6)

Since overweight and obesity is common in the U.S. donor pool—and the demand for donors exceeds supply—understanding how dBMI affects patient outcomes in pediatric liver transplant could help guide decision-making about donor acceptability. We hypothesized that donor obesity would increase over the study period, following trends in the U.S. population, but that dBMI would not affect graft or patient survival. We also hypothesized that post-transplant obesity would be associated with dBMI in recipients of adult donors but not pediatric donors, if association seen in adults is driven by hepatic insulin resistance or other metabolic disturbances that worsen with age of the liver. Analyzing the United Network for Organ Sharing (UNOS) database allowed us to explore these hypotheses, although missing variables of interest and data prevent definitive conclusions from this study.

Methods

After obtaining approval from the institutional review board at the University of California, San Francisco, we assembled a historical cohort of all U.S. patients who underwent primary liver transplant at age 6 months-20 years between 1990 and 2010 using the UNOS Standard Transplant Analysis and Research database. Data from 1990-2010 was used to examine changes in donor weight status over time. Data from 2004-2010 only was used for the remainder of the analysis.

Recipient and donor weight status was categorized using age-appropriate cutoffs. Following guidelines recommended by the Centers for Disease Control (CDC) and the American Academy of Pediatrics, children 6-24 months were classified as underweight if their weight-for-length was less than the 5^{th} percentile for age and gender, normal weight if it was 5^{th}-95^{th} percentile, and overweight if it was greater than the 95^{th} percentile. Children 2-18 years were categorized as underweight if their BMI percentile was less than the 5^{th} percentile for age and gender, normal weight if it was 5^{th}-85^{th} percentile, overweight if it was higher than 85^{th}- 95^{th} percentile, obese if it was 95^{th}-99^{th} percentile, and severely obese if it was 99^{th} percentile or higher. (7, 8) Weight-for-length percentiles and BMI percentiles were calculated, based on the 2000 CDC growth charts using SAS software programs published by the CDC. (9) Donors older than 18 years and recipients older than 18 years in

follow-up, were classified as underweight if their BMI was < 18, normal weight for BMI 18-25, overweight for BMI 25-30, obese for BMI 30-35, and severely obese for BMI>35. (10) All BMI values are reported in kg/m^2.

We classified diagnosis based on the categories defined by the Studies in Pediatric Liver Transplant (SPLIT) Research Group. (11) Instances of graft loss included graft failure requiring re-transplantation and recipient death.

Statistical analysis

In comparing groups by transplant year and weight status, categorical variables were assessed with chi-squared testing. Continuous variables were compared with Kruskal-Wallis one-way analysis of variance. Chi-squared and two-sample tests of proportions were used to compare causes of graft failure and mortality.

To analyze predictors of graft loss and mortality, Kaplan-Meier and Cox proportional hazards models were used. Generalized estimating equations (GEE) were used in the analysis of post-transplant obesity to accommodate repeated measures of post-transplant weight status.

In the Cox models of graft loss and mortality and the GEE models for post-transplant obesity, multiple imputation (MI) with iterative chained equations was used to account for missing data in predictors. MI is a statistical technique in which plausible values for missing datapoints are imputed based on the observed distribution of non-missing values in the dataset. MI accounts for uncertainty about these imputed values by (1) creating multiple datasets, each with slightly different values for the missing data points, (2) developing a model based on each imputed dataset, and then (3) averaging the estimates for effect size and confidence interval derived from each imputed dataset. (12) Donor weight status, recipient weight status, cold ischemia time, and MELD/PELD score at transplant were the variables of interest with more than 5% missing data. **(TABLE 1)** For dBMI and recipient weight status, MI was used to estimate missing values and replace those values calculated to be “biologically implausible values” (BIV) according to CDC guidelines. BIV are outliers considered representative of data entry errors or mismeasurement, not extremes of growth. (9)

Factors predictive of missing predictor values were deduced by comparing groups with dBMI available vs. missing/BIV (data not shown). Predictive factors were included in the MI modeling: patient outcome, time to outcome, interaction between outcome and time, year of transplant, type of transplant, recipient characteristics (age, gender, race/ethnicity, primary diagnosis, number of previous transplants, medical condition at transplant, listing status at transplant), donor characteristics (age, gender, race/ethnicity).(12) Ten imputed datasets were created. The inclusion of variables in the final reported survival and post-transplant obesity models were hypothesis-driven, with variables chosen based on previous literature about factors associated with graft and patient survival in pediatric (13) and adult (14) liver transplant recipients.

Sensitivity analyses demonstrated that modeling with complete case analysis (including only those recipients with plausible dBMI in original UNOS dataset) gave similar results with the same statistically significant predictors as models with MI (data not shown), but the latter are reported given their larger statistical power.

A p-value<0.05 was considered statistically significant in all analyses. The growth percentiles and BIV were calculated using SAS Version 9.2 (SAS Institute, Cary, NC). All other statistical analysis was done with Stata version 12.0 (StataCorp, College Station, TX).

Results

Prevalence of donor overweight and obesity

From 1990-2010, 9103 pediatric liver transplants had donor weight status information available. Compared to earlier time periods, in 2004-2010 the proportion of overweight and obese donors was higher for adult donors (p<0.0005). Among pediatric donors, the percentage of overweight and obese donors remained stable but underweight donors decreased (p<0.0005). **(FIGURE 1)** In 2004-2010, 30% of adults donating to children were overweight (dBMI 25-30), 8% obese (dBMI 30-35), and 2.2% severely obese (dBMI>35). Among pediatric donors 2004-2010, 17% were overweight, 7% were obese, and 3% were severely obese.

Between 2004 and 2010, 3,788 pediatric liver transplant recipients were reported in the UNOS database; 1,259 had adult donors and 2,529 had pediatric donors. For those with adult donors, overweight or obese donors were most likely older males. The majority of severely obese adult donors were female, younger, Caucasian, deceased donor, whole liver donors. Recipients of severely obese donors had higher median MELD/PELD scores at transplant (30 vs. 22-23 for other weight groups), but this difference was not statistically significant (p=0.205). (TABLE 1, see SUPPLEMENTAL TABLE for details by donor weight category) Obese pediatric donors were most likely to be whole liver transplants into older children with acute liver failure or metabolic liver disease. Severely obese pediatric donors were most commonly placed in children with biliary atresia (34%). Donors 2-9 years old were most likely to be obese (11%, vs. 7% of 11-18 year olds, p=0.005) and severely obese (7.4%, vs. 0.4% of 11-18 year olds, p<0.0005). (**TABLE 1, SUPPLEMENTAL TABLE)**

Of 1,259 recipients of adult donors, 65 were missing dBMI and 5 had implausible values (6%); 69 of 70 were from living donors. 14% were missing recipient pre-transplant weight status, 11% were missing MELD/PELD score at transplant, and 13% were missing cold ischemia time. Of 2,529 recipients of pediatric donors, 6 were missing dBMI and 86 had BIV (4%). Twelve percent were missing recipient pre-transplant weight status, 16% were missing MELD/PELD at transplant, and 12% were missing cold ischemia time. Pediatric donor weight status was most often missing from transplants with the youngest recipients and donors. **(TABLE 1)**

Weight status of adult donors

In the 2004-2010 cohort, there were 740 instances of graft loss—20% of children with adult donors and 20% with pediatric donors (p=0.98). There were 473 deaths; in 12% of those with adult donors and 13% of those with pediatric donors (p=0.66).

For children receiving adult donor livers, graft survival and patient survival differed by donor weight status in Kaplan-Meier analysis (**FIGURE 2**). Decreased survival in the recipients of severely obese donors accounted for this finding. Donor overweight and obesity were not associated with graft or patient survival in univariate or multivariate **(**Graft survival: overweight HR 1.00, 95% CI 0.73-1.36, p=0.98 and obesity HR 0.84, 95% CI 0.49-1.42, p=0.50; Patient survival: overweight HR 1.20, 95% CI 0.81-1.78, p=0.36 and obesity HR 0.95, 95% CI 0.48-1.89, p=0.89**)** Donor severe obesity was associated with increased risk of graft loss (multivariate analysis: HR 2.54, 95% CI 1.29-5.01, p=0.007) and death (multivariate analysis: HR 3.56, 95% CI 1.64-7.72, p=0.001). **(TABLE 2)** Other significant predictors are listed in **TABLE 2**.

Weight status of pediatric donors

For recipients of pediatric donors, graft survival and patient survival were the same across donor weight groups in Kaplan-Meier analysis (**FIGURE 3**). Donor weight status was not associated with graft failure in univariate (data not shown) or multivariate analysis. Overweight donors had an increased risk of mortality that did not reach statistical significance in univariate (HR 1.30, 95% CI 0.97-1.73, p=0.075) or multivariate analysis (HR 1.31, 95% CI 0.98-1.77, p=0.068). However, obese and severely obese pediatric donors were not associated with mortality in univariate (data not shown) or multivariate (obese: HR 0.93, 95% CI 0.54-1.62, p=0.81; severely obese HR 1.14, 95% CI 0.56-2.33, p=0.71) analyses. Significant predictors are listed in **TABLE 3**.

Being in the ICU immediately prior to transplant and primary diagnosis of tumor were the most consistent risk factors for poor outcomes. **(TABLE 2, TABLE 3)**

Causes of graft failure and death

The database had inadequate information on causes of graft loss and death to allow full analysis of differences by donor weight category. Of those who died, 81% had cause of death listed. For those with available data, the causes of death did not differ by donor weight status (data not shown, p=0.540 for those with adult donors, p=0.587 for those with pediatric donors). Eight of the 26 children with severely obese adult donors died during follow-up, of multi-organ system failure (n=2), cardiac or cerebrovascular causes (n=2), chronic rejection and biliary complications (n=1), unspecified graft failure (n=2), and complications of acute rejection and recurrent hepatitis (n=1).

Of those with graft loss, only 39% had data available on contributing causes; this included 4 of 10 with severely obese adult donors (n=1 acute rejection, n=1 vascular thrombosis, n=1 chronic rejection, n=1 recurrent hepatitis) and 88 of 228 other adult donors.

Donor steatosis

The UNOS database contains very limited information on graft steatosis for pediatric recipients, starting in 2004 in a minority of patients (n=224 of 3788). No living donors had biopsy information. For adult donors, older age and a history of obesity, diabetes, or hypertension increased the likelihood of biopsy. Eighteen percent of obese donors and 37% of severely obese donors were biopsied, compared to 8% of normal weight donors ($p<0.0005$). For pediatric donors, weight status was not associated with biopsy likelihood (n=98, p=0.265 compared to weight status of un-biopsied). Of all those with biopsy data, 76% had <5% steatosis, 19% had 5-30% steatosis, and 5% had >30% steatosis. For those with data available, donor steatosis was not associated with recipient graft survival in Kaplan-Meier analysis (p=0.2892, graph not shown).

Donor BMI and post-transplant obesity

Multivariate analysis of post-transplant obesity included adjustment for recipient characteristics (gender, age, race/ethnicity, primary diagnosis, overweight/obesity at transplant), living-related vs. cadaveric transplant, donor demographics (gender, age, race/ethnicity) and testing for interactions with follow-up time.

In recipients of adult donors, donor weight status was not a statistically significant predictor of post-transplant obesity in univariate (n=342, data not shown) or multivariate analysis (n=290). In multivariate analysis, the odds of post-transplant obesity did not differ by donor weight status, compared to those with normal weight donors: underweight OR 1.11 (95% CI 0.23-5.15), p=0.89; overweight OR 0.83 (95% CI 0.45-1.56), p=0.57; obese OR 2.73 (95% CI 0.63-11.96), p=0.18; severely obese OR 0.47 (95% CI 0.13-2.80), p=0.52).

In recipients of pediatric donors, donor severe obesity actually reduced the risk of post-transplant obesity in univariate analysis (OR 0.27, 95% CI 0.09-0.80, p=0.018); other weight categories were not associated with post-transplant obesity (n=635, data not shown). In multivariate analysis (n=501), the odds of post-transplant obesity did not differ by donor weight status, compared to those with normal weight donors: underweight OR 1.26 (95% CI 0.68-2.34), p=0.467; overweight OR 0.86 (95% CI 0.46-1.60), p=0.637; obese OR 1.07 (95% CI 0.44-2.59), p=0.874), severely obese OR 0.59 (95% CI 0.19-1.85), p=0.366.

As has been previously described, (15) recipient overweight/obesity at transplant was the strongest predictor of post-transplant obesity (adult donors: OR 4.43, 95% CI 1.65-11.92, p=0.003; pediatric donors: OR 5.73, 95% CI 3.65-9.00, $p<0.0005$ compared to normal weight recipients at transplant) in multivariate analysis. For those with pediatric donors, months from transplant (OR 1.04, 95% CI 1.02-1.06, p=0.001), and donor age 5-14 years (OR 2.14, 95% CI 1.35-3.42, p=0.002) or 15-18 years (OR 2.35. 95% CI 1.22-4.51, p=0.010) compared to 0-4 years also increased risk of post-transplant overweight/obesity in multivariate analysis.

Discussion

Our study is the first to evaluate the impact of donor BMI on pediatric liver transplant recipients. The proportion of overweight and obese adult and pediatric liver donors in the

U.S. has increased over time, mirroring trends in the general U.S. population. For pediatric donors, weight status was not associated with graft or patient survival.

For adult donors, our analysis suggests that dBMI 25-35 should not be an absolute contraindication to liver donation, as it did not affect patient outcomes for deceased donor or living-related transplants. For living-donor transplants, obesity does carry a surgical risk to the donor that our analysis does not account for.(16) Assessment of dBMI should not replace workup for hepatic steatosis, particularly given recent research showing that donor macrosteatosis is an independent risk factor for early graft failure.(4, 5) Though protocols for acceptance of overweight donors are not standardized, our analysis suggests that criteria currently being used have been successful in making recipient risk with overweight adult donors equal to that with non-overweight donors.

In this analysis, severe obesity (dBMI>35) in adult donors was an independent risk factor for graft loss and mortality, even after adjustment for other risk factors known to be associated with poor outcomes. Although donors with dBMI>35 represented <1% of all donors, the percentage of severely obese donors per 5-year period actually increased slightly between 1990 and 2010; the vast majority were deceased donors (87%).

Severely obese adult donors did not seem to be used preferentially in sicker or higher-risk recipients—which would be an alternative explanation for the poor outcomes observed in this group. Recipient status at transplant—as measured by listing status, MELD/PELD, and hospitalization or ICU care—was not associated with getting a severely obese donor. We cannot rule out the possibility that other unmeasured factors made those with severely obese donors high-risk, but the available variables are the most commonly used measures to evaluate recipient status and make decisions about donor acceptability.

Lack of donor biopsy information prevented analysis of whether hepatic steatosis might explain the poor outcomes seen with severely obese donors. Obese donors are more likely to have steatosis. (5, 17) In our cohort, severely obese adult donors were more likely to have donor biopsy information available, suggesting increased vigilance for steatosis in this group. But the vast majority of donors had no biopsy information available. Interestingly, severe obesity in pediatric donors was not associated with graft loss or mortality; one explanation for this inconsistency is that the negative impact of donor obesity on the liver accumulates as donors age—for example, in the form of hepatic insulin resistance or fatty liver disease.

The incidence of primary graft non-function and biliary complications are higher in steatotic grafts. (5, 18, 19) We did not find an increased prevalence of primary graft non-function or biliary complications in our patients with severely obese donors compared to other adult donors who had graft failure, but small sample size limited comparisons and further analysis of causes of graft failure and mortality.

Our analysis surprisingly suggested that severe donor obesity reduced the risk of post-transplant obesity in recipients—in contrast with previous findings in adults. The link between dBMI and post-transplant obesity comes from one widely-cited study in adults.(6) In their cohort of 744 adults who underwent transplant 1990-1994, the incidence of post-

transplant obesity in previously normal weight recipients was 22.2% with dBMI 20-25, 26.6% in those with dBMI 25-29.9, and 30.4% in those with dBMI 30 or higher (p=0.03). This raised the possibility that the donor liver might affect the recipient's metabolism or insulin resistance, increasing the risk of post-transplant obesity. Our study did not support this theory for pediatric patients. It also does not, however, provide strong support for an inverse relationship between dBMI and recipient post-transplant obesity; the association was not significant in multivariate analysis.

The limitations of this study stem from its retrospective nature and reliance on an existing dataset. Although the UNOS database is the largest and most comprehensive record of pediatric liver transplants available, we were limited to the available variables and data. There may be unmeasured recipient factors which put children at high-risk for poor outcomes and explain why severely obese donors were accepted for them.

There was a considerable amount of data missing or biologically implausible from our predictors of interest, although we were able to account for this using multiple imputation—a powerful statistical method to reduce bias and increase precision in large datasets. (12) Height and weight measurements were not collected in a standardized fashion. We could not control for other factors that might influence weight status—like ascites in recipients or edema in deceased donors. In considering post-transplant obesity, we could not consider important variables like recipient pubertal status or immunosuppression.

In summary, this analysis suggests that adults with dBMI 25-35 may be acceptable candidates as living or deceased donors. Severely obese adults (dBMI>35) should be considered very high-risk donors. Limitations of the dataset prevent us from drawing conclusions about the impact of donor obesity on pediatric liver transplant recipients from this analysis—and highlight areas for future research. Substantial missing data on causes of graft loss, causes of death, and donor steatosis prevented us from exploring mechanisms of the risk associated with severely obese donors. The relationship between donor obesity and recipient post-transplant obesity requires further investigation. Given the increasing prevalence of overweight donors, further research on the impact of donor obesity and graft steatosis in pediatric liver transplant, as well as the role of obesity in decision-making about donor acceptability, is needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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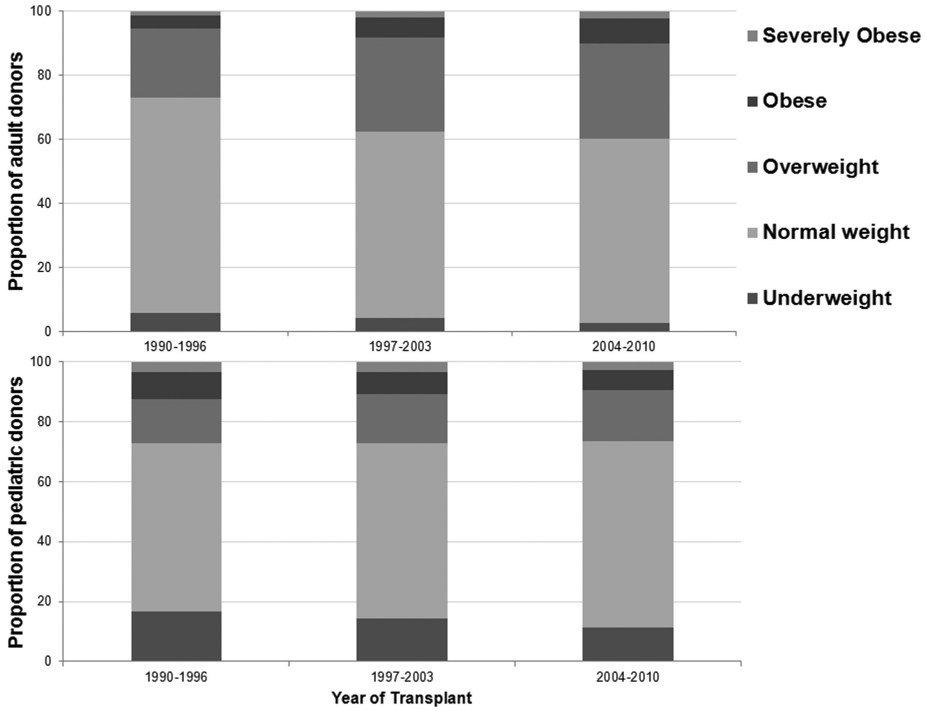

Figure 1. Weight status of adult and pediatric liver transplant donors to pediatric liver transplant recipients, 1990-2010

Based on UNOS/OPTN database. For adult donors, underweight includes those with BMI<18 kg/m^2, normal weight BMI 18-25 kg/m^2, overweight BMI 25-30 kg/m^2, obese BMI 30-35 kg/m^2, severely obese BMI>35 kg/m^2. For pediatric donors, weight status is based on weight-for-length percentile for donors < 2 years of age and BMI percentile for donors 2-18 years of age. Underweight includes those <5th percentile, normal weight 5-85th percentile, overweight 85th-95th percentile, obese 95th-99th percentile and ≥2 years old, and severe obesity >99th percentile and ≥2 years old. p<0.0005 for both adult and pediatric liver transplant donors.

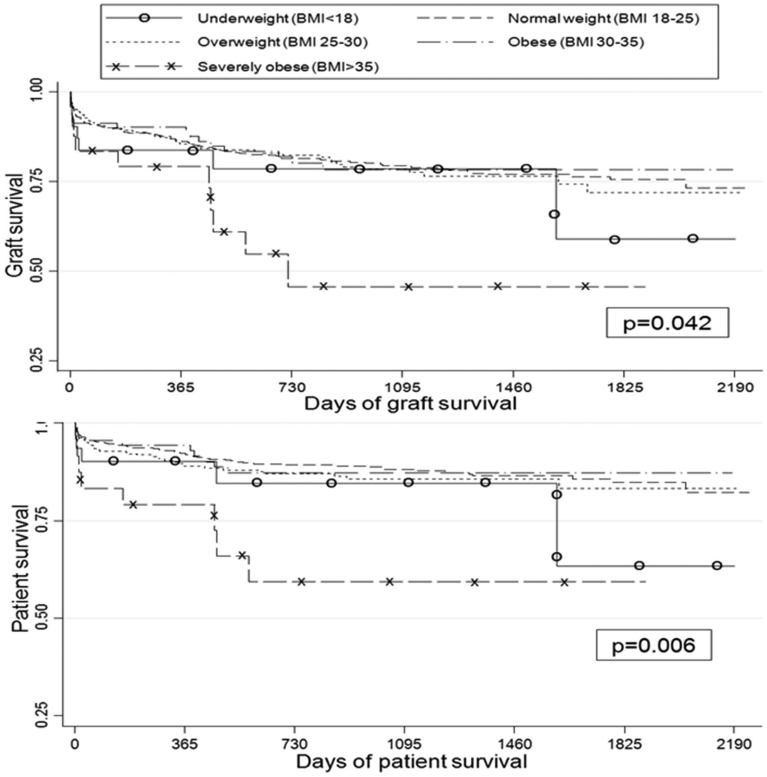

Figure 2. Pediatric recipients of adult donor livers, graft failure and patient mortality by donor weight status

In children who receive adult donor livers, donor weight status is associated with cumulative incidence of graft failure (p=0.042) and with patient mortality (p=0.006) by Kaplan-Meier analysis. Graphs reflect outcomes recorded through May 2010. Analysis includes n=1189 transplant recipients with non-missing donor weight status data.

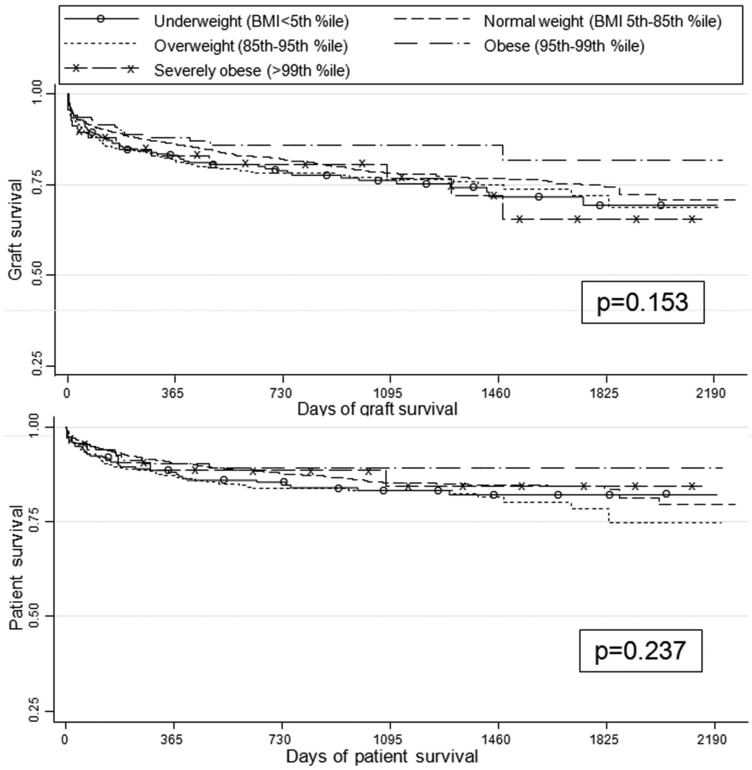

Figure 3. Pediatric recipients of pediatric donor livers, graft failure and patient mortality by donor weight status

In children who receive pediatric donor livers, donor weight status is not associated with graft failure (p=0.153) or patient mortality (p=0.237), by Kaplan-Meier analysis. Graphs reflect outcomes recorded through May 2010. Analysis includes n=2439 transplant recipients with non-missing donor weight status data.

Table 1

Recipient and donor characteristics, by donor age category

	Adult donors (n=1259)		Pediatric donors (n=2529)	
	Total (% of total)	**Missing Donor BMI (% of total)**	**Total (% of total)**	**Missing Donor BMI (% of total)**
Recipient gender				
Male	627 (50%)	39 (3%)	1229 (49%)	52 (2%)
Female	632 (50%)	31 (2%)	1300 (51%)	40 (2%)
Recipient age (years)				
0-1	401 (32%)	39 (3%)	1245 (49%)	68 (3%)
2-5	148 (12%)	14 (1%)	503 (20%)	14 (1%)
6-11	175 (14%)	7 (1%)	398 (16%)	6 (<1%)
12-18	535 (42%)	10 (1%)	383 (15%)	4 (<1%)
Recipient race/ethnicity				
White	692 (55%)	38 (3%)	1320 (52%)	51 (2%)
Black	215 (17%)	8 (1%)	435 (17%)	12 (<1%)
Hispanic	254 (20%)	17 (1%)	552 (22%)	18 (1%)
Asian	67 (5%)	5 (<1%)	123 (5%)	4 (<1%)
Other‡	31 (2%)	2 (<1%)	99 (4%)	7 (<1%)
Recipient primary diagnosis				
Acute Liver Failure	296 (24%)	13 (1%)	197 (8%)	3 (<1%)
Biliary Atresia	285 (23%)	23 (2%)	804 (32%)	23 (1%)
Metabolic Liver Disease§	168 (13%)	11 (1%)	300 (12%)	8 (<1%)
Other cholestatic‖	154 (12%)	10 (1%)	650 (26%)	39 (2%)
Tumor	108 (9%)	4 (<1%)	174 (7%)	7 (<1%)
Other¶	248 (20%)	9 (1%)	404 (16%)	12 (<1%)
Recipient pre-transplant weight status*				
Underweight	125 (10%)	31 (2%)	287 (11%)	13 (1%)
Normal weight	697 (55%)	9 (1%)	1388 (55%)	45 (2%)
Overweight/ obese	280 (22%)	9 (1%)	578 (23%)	20 (1%)
Missing data	157 (12%)	21 (2%)	276 (11%)	14 (1%)
Recipient status at transplant				
Status 1	555 (44%)	22 (2%)	548 (22%)	20 (1%)
Other	692 (55%)	47 (4%)	1981 (78%)	72 (3%)
Missing	12 (<1%)	1 (<1%)	0	0
MELD/PELD prior to transplant (median, IQR)				
	23 (14-31)	21 (15-29)	17 (10-24)	17 (9-23)
n with available data	*1056*	*59*	*2040*	*78*
Medical condition prior to transplant				
Not hospitalized	537 (43%)	32 (3%)	1603 (63%)	56 (2%)
Hospitalized, not ICU	207 (16%)	10 (1%)	417 (16%)	17 (1%)
ICU	495 (39%)	19 (2%)	467 (18%)	15 (1%)

	Adult donors (n=1259)		Pediatric donors (n=2529)	
	Total (% of total)	**Missing Donor BMI (% of total)**	**Total (% of total)**	**Missing Donor BMI (% of total)**
Missing	20 (2%)	9 (1%)	42 (02%)	4 (<1%)
Type of transplant				
Living donor	377 (30%)	69 (5%)	0	0
Deceased donor, whole	628 (50%)	1 (<1%)	2267 (90%)	92 (4%)
Deceased donor, split	254 (20%)	0	262 (10%)	0
Donor gender				
Female	612 (49%)	43 (3%)	1082 (43%)	32 (1%)
Male	647 (51%)	27 (2%)	1447 (57%)	60 (2%)
Donor age (years)				
0-1			853 (34%)	53 (2%)
2-5			597 (24%)	31 (1%)
6-9			320 (13%)	5 (<1%)
10-13			247 (10%)	2 (<1%)
14-18			512 (20%)	1 (<1%)
19-24	420 (33%)	16 (1%)		
25-34	364 (29%)	29 (2%)		
35-44	243 (19%)	19 (2%)		
45-54	171 (14%)	3 (<1%)		
55-64	47 (4%)	2 (<1%)		
65-74	7 (<1%)	0		
>75	6 (<1%)	0		
Missing	1 (<1%)	1 (<1%)		
Donor ethnicity				
Caucasian	800 (64%)	38 (3%)	1406 (56%)	43 (2%)
African-American	165 (13%)	11 (1%)	507 (20%)	28 (1%)
Hispanic	236 (19%)	17 (1%)	542 (21%)	20 (1%)
Asian/other‡	58 (5%)	4 (<1%)	74 (3%)	1 (<1%)
Donor weight status*				
Underweight	32 (3%)	NA	276 (11%)	NA
Normal weight	684 (54%)	NA	1516 (60%)	NA
Overweight	354 (28%)	NA	414 (16%)	NA
Obese	93 (7%)	NA	160 (6%)	NA
Severe Obesity	27 (2%)	NA	71 (3%)	NA
Donor cause of death**				
Anoxia	107 (12%)	1 (<1%)	775 (31%)	38 (2%)
CVA/Stroke	280 (32%)	0	163 (6%)	3 (<1%)
Head trauma	468 (53%)	0	1445 (57%)	48 (2%)
CNS tumor	7 (1%)	0	16 (01%)	0
Other	20 (2%)	0	128 (05%)	3 (<1%)

	Adult donors (n=1259)		Pediatric donors (n=2529)	
	Total (% of total)	**Missing Donor BMI (% of total)**	**Total (% of total)**	**Missing Donor BMI (% of total)**
Non-heart beating donor**				
Yes	6 (1%)	0	25 (1%)	0
No	876 (99%)	1 (<1%)	2502 (99%)	92 (4%)
Missing	0	0	2 (<1%)	0
Location of donor liver				
Local	900 (71%)	69 (5%)	787 (31%)	21 (1%)
Regional	340 (27%)	1 (<1%)	1038 (41%)	25 (1%)
National	19 (2%)	0	700 (28%)	46 (2%)
Foreign	7 (1%)	4 (<1%)	4 (<1%)	0
Distance (miles from donor hospital to transplant center; median, IQR)				
	87 (14-206)	254	223 (75-526)	403 (114-747)
n with available data	*881*	*1*	*2437*	*92*
Cold ischemia time (hours; median, IQR)				
	6 (4-8.2)	1.5 (1-3)	7.1 (5.9-9)	7.3 (6.1-9)
n with available data	*1048*	*49*	*2150*	*76*

*Weight status for recipients and donors classified by weight-for-height percentiles for those less than 2 years of age, by BMI percentiles for 2-18 year olds, and by BMI for those older than 18 years. All percentiles calculated based on age and gender.

‡Other race includes: Native American/Alaskan, Pacific Islander/Hawaiian, Multiracial, Unknown

§Metabolic disease includes: alpha-1-antitrypsin deficiency, Crigler-Najjar syndrome, cystic fibrosis, glycogen storage disease, inborn errors in bile acid metabolism, neonatal hemochromatosis, primary hyperoxaluria, tyrosinemia, urea cycle defects, and Wilson's disease.

//Other cholestatic conditions includes: Alagille syndrome, Byler disease, progressive intrahepatic cholestatic syndromes, total parenteral nutrition cholestasis, sclerosing cholangitis, and idiopathic cholestasis.

¶Other diagnosis includes: congenital hepatic fibrosis, Budd-Chiari syndrome, autoimmune hepatitis cirrhosis, drug toxicity, hepatitis C cirrhosis, and unknown cirrhosis.

**Data on adult donors includes 882 cadaveric donors.

Table 2

Recipients of adult donors, significant predictors of graft loss and mortality in multivariate analysis *

	Reference group	Risk of graft loss		Risk of death	
		HR (95% CI)	p†	HR (95% CI)	p†
Recipient primary diagnosis‡					
Other	Acute liver failure	1.49 (0.99-2.25)	0.053	1.47 (0.88-2.43)	0.139
Tumor	Acute liver failure	2.55 (1.45-4.48)	0.001	3.53 (1.78-6.98)	<0.0005
Medical condition prior to transplant					
ICU	Not hospitalized	1.38 (0.96-2)	0.083	1.62 (1.00-2.6)	0.049
Type of transplant					
Cadaveric, whole liver	Living donor	1.76 (0.98-3.16)	0.058	1.83 (0.88-3.81)	0.104
Cadaveric, split liver	Living donor	2.85 (1.59-5.09)	<0.0005	3.1 (1.51-6.34)	0.002
Donor weight status					
Morbidly obese (BMI>35)	Normal (BMI 20-25)	2.54 (1.29-5.01)	0.007	3.56 (1.64-7.72)	0.001
Donor cause of death					
CVA/Stroke	Anoxia	0.6 (0.37-0.96)	0.034	0.54 (0.31-0.97)	0.040
Head trauma	Anoxia	0.57 (0.37-0.87)	0.01	0.43 (0.26-0.72)	0.001

* All hazard ratios adjusted for effects of transplant year, recipient characteristics (age, race/ethnicity, primary diagnosis, medical condition at transplant), donor characteristics (age, race/ethnicity, weight status, cause of death) and transplant characteristics (type of transplant, share type, cold ischemia time). Variables listed only if $p<0.06$ in multivariate models.

† p-values based on multivariate Cox proportional hazards models.

‡ See definitions of primary diagnosis categories in Table 1.

Table 3

Recipients of Pediatric Donor Organs: Significant Predictors of Graft Loss and Mortality in a Multivariate Analysis

		Risk of Graft Loss		Risk of Death	
	Reference Group	**HR (95% CI)**	***P* Value***	**HR (95% CI)**	***P* Value***
Recipient age: 6-11 years	0-<2 years	0.71 (0.51-1.01)	0.06	0.72 (0.47-1.10)	0.14
Recipient primary diagnosis†					
Other cholestatic	Acute liver failure	1.80 (1.22-2.66)	0.003	2.15 (1.37-3.38)	0.001
Biliary atresia	Acute liver failure	1.05 (0.70-1.60)	0.80	0.59 (0.35-1.00)	0.049
Tumor	Acute liver failure	1.72 (1.04-2.83)	0.03	1.65 (0.91-3.00)	0.10
Medical condition before transplantation					
Hospitalized, not ICU	Not hospitalized	1.36 (1.06-1.74)	0.01	1.55 (1.15-2.11)	0.004
ICU	Not hospitalized	2.09 (1.64-2.68)	<0.001	2.42 (1.78-3.28)	<0.001
Donor age					
6-13 years	0-5 years	0.73 (0.55-0.96)	0.02	0.75 (0.53-1.08)	0.12
14-18 years	0-5 years	0.55 (0.36-0.84)	0.005	0.58 (0.35-0.98)	0.04

All HRs have been adjusted for the effects of the transplant year, recipient characteristics (age, race/ethnicity, primary diagnosis, and medical condition at the time of transplantation), donor characteristics (age, race/ethnicity, weight status, and cause of death), and transplant characteristics (type of transplant, share type, and cold ischemia time). Only variables with $P \leq 0.06$ in multivariate models are listed.

*The *P* values are based on multivariate Cox proportional hazards models.

†See Table 1 for the definitions of the primary diagnosis categories.