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ORIGINAL ARTICLE

Split-liver transplantation in the high-MELD adult patient: are we being too cautious?

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Summary

The fear that patients with high-mathematical model for end stage liver disease (MELD) score may not be suitable candidates for segmental grafts because of their need for greater liver mass has continued to push the transplant community toward the use of whole LT (WLT) in preference to split LT (SLT). In order to define the outcome of segmental liver transplantation in a better manner in high-MELD patients (score ≥26), we queried the UNOS registry for graft and patient survival results according to MELD score in adult patients receiving WLT and SLT in the United States from the inception of MELD allocation (February 27, 2002) through March 9, 2007. A total of 316 adult patients received a SLT as compared with 20 778 WLTs. Patient and graft survival rates at 6 and 12 months were comparable for all MELD ranges, including the 'high-MELD' recipients (e.g. at MELD score 31–35, patients' and grafts' survival rates at 12 months was 87.5% in SLT group vs. 84.4% and 76.7% in WLT group respectively). The results even at higher MELD scores (i.e. >35) were more than acceptable. In conclusion, patient and graft survival rates for SLT in high-MELD adult patients are comparable to the same for WLT.

Introduction

Segmental liver transplant (LT) has been an essential tool in the field of transplantation for nearly 20 years. Common techniques and concepts have evolved in the overlapping areas of live donor and reduced size or split-liver transplantation, as surgeons have pushed to expand the available donor pool.

In this regard, many authors have noted that, in general, segmental and full-size grafts yield comparable results in both patient and graft survival rates [1–3], although the results from right split LT (SLT) are comparable to the ones obtained with whole LT (WLT) using marginal organs [4].

Since its introduction in 2000, the MELD-score has proven to be a useful tool in many aspects of chronic liver disease, including prognosis with transjugular intrahepatic porto-systemic shunts (TIPSS) [5]; as predictor of non transplant surgical mortality [6]; prognosis after hepatectomy for hepatocellular carcinoma (HCC) in cirrhotic patients [7]; and for guidance of perioperative management of LT with vasopressors and transfusions [8]. Still, its primary and most relevant application has been in foreseeing the 3-month mortality-risk for patients with end-stage chronic liver disease [9], thereby identifying the patients most in need of liver transplantation and making MELD the primary component of current organ allocation process [10–12].

Under MELD-based allocation, liver grafts are directed to the 'sickest first.' However, often the caveat is made that 'sicker' patients (i.e. the ones with high-MELD scores) [9,13] may not be suitable candidates for segmental grafts because of their need for greater liver mass and their tendency to not tolerate even minor postoperative complications as well [14]. As a consequence of this philosophy, in such patients, whole-liver transplantation

(WLT) has been promoted in preference to split-liver transplantation (SLT).

In practice, this means that the center with a patient with the highest MELD score has the choice of transplanting the full-size graft or splitting the liver [15]. Potentially, this type of allocation discourages split-liver transplantation, especially when the primary organ offer is to an adult recipient, because of the intrinsic ethical dilemma resulting from the obligation of the transplant center to the individual patient (who is potentially benefited more by a full-size graft) and the obligation to society (which favors the transplantation of two recipients from one donor liver) (UNOS Ethics Committee White Paper http://www.unos.org/resources/bioethics.asp). This dilemma, however, is predicated on the belief that segmental grafts yield more inferior results than whole grafts in sicker patients.

Aim

Concerned that the modification of any allocation policy would not alone provide enough incentive for split-liver transplantation, we set out to define the outcome of segmental liver transplantation in a better manner in patients with high-MELD scores (score ≥26). We queried the SRTR/OPTN registry for graft and patient survival results according to MELD score in patients receiving WLT and SLT in order to see if outcomes varied according to severity of recipient illness.

Patients and methods

The SRTR/OPTN database was queried for the results of all liver transplants performed in the United States from the inception of MELD allocation (February 27, 2002) through June 30, 2006. The data, as initially reported on October 5, 2005 (data request # 092805-2) and updated on March 9, 2007(data request # 030907-9), were analysed for available patient and graft survival at 6- and 12-months after transplant. The results were divided into adult recipients of split grafts and adult recipients of whole grafts and were initially stratified according to the wait-list-MELD score ('List MELD') of the recipient at the time of liver allocation. In order to avoid any bias resulting from higher MELD scores offered to exceptional cases (e.g. HCC), the data was then re-stratified according to the laboratory (i.e. calculated) MELD score ('Lab MELD') of the recipient at the time of liver allocation.

Results

Since the inception of MELD-based liver allocation, a total of 316 adult patients (1.5%) received a Split LT (SLT) from a deceased donor as compared with 20,778 whole liver transplants (WLT). Recipients in each group were then separated according to the MELD score at which the patient was listed at the time of transplantation ('List MELD') (<16, 16–20, 21–25, 26–30, 31–35 and 35+) and then according to the calculated MELD score ('Lab MELD') at the time of allocation (Table 1). It should be noted that the total number of patients transplanted with 'List MELD' is always less than number transplanted with 'Lab MELD' because of some of the patients being Status 1 and because some patients transplanted on first day of MELD having been allocated with old Status 2A the day before converting. Additionally, 'List MELD' would be higher than 'laboratory MELD' because of MELD exceptions (like for instance, HCC). This is important for us to be aware so that one is clear as to why the total numbers in the two groups are different.

Table 1. Total number of SLT and WLT recipients according to: Listed MELD-Score ('List MELD') at time of allocation; Laboratory MELD-Score ('lab MELD') at the time of allocation.

	SLT (*n*)	WLT (*n*)	SLT (%)	WLT (%)
'List MELD'				
<16	48	2788	15.2	13.4
16–20	66	4020	20.9	19.3
21–25	87	6335	27.5	30.5
26–30	62	3714	19.6	17.9
31–35	32	1873	10.1	9
>35	21	2048	6.7	9.9
Not Reported				
Total	316	20778	100	100
'Lab MELD'				
<16	131	7445	40.4	33.5
16–20	75	4874	23.1	21.9
21–25	58	3671	17.9	16.5
26–30	22	2278	6.8	10.2
31–35	16	1689	4.9	7.6
>35	22	2298	6.8	10.3
Not Reported				
Total	324	22255	99.9	100

SLT, split LT; WLT, whole LT.

For the purposes of this study, we defined 'high-MELD' patients as those with a score of 26 or greater. The percentage of high-MELD recipients of SLT and WLT were comparable (36.3% and 36.8% respectively).

Patient and graft survival rates at 6 and 12 months (Tables 2 and 3) were comparable for all MELD ranges, including the 'high-MELD' recipients and the results even at higher MELD scores (i.e. >35) were more than acceptable. Additionally, Patient and graft survival rates remained comparable when both WLT and SLT recipients were grouped according to 'List MELD' rather than 'Lab MELD' at the time of allocation.

Table 2. Survival rates according to *listed* MELD-Score ('List MELD') at time of allocation.

	'List MELD'	Time	SLT (*n*)	SLT Pt. Surv (%)	WLT (*n*)	WLT Pt. Surv (%)
Patients' survival	<16	6	48	91.57	2788	92.67
		12		86.62		89.36
	16–20	6	66	91.96	4020	92.53
		12		91.96		89.43
	21–25	6	87	93.90	6335	91.84
		12		89.47		87.28
	26–30	6	62	91.45	3714	90.98
		12		89.54		87.28
	31–35	6	32	87.50	1873	86.16
		12		87.50		80.91
	>35	6	21	84.45	2048	83.64
Grafts' survival	<16	6	48	85.42	2788	88.33
		12		80.80		84.14
	16–20	6	66	86.36	4020	88.30
		12		86.36		84.40
	21–25	6	87	85.00	6335	88.25
		12		79.52		83.09
	26–30	6	62	85.29	3714	88.25
		12		83.52		83.36
	31–35	6	32	87.50	1873	83.09
		12		84.26		77.33
	>35	6	21	76.19	2048	80.81
		12		n.r.		74.91

SLT, split LT; WLT, whole LT.

Table 3. Survival rates according to *laboratory* MELD-Score ('Lab MELD') at the time of allocation.

	'Lab MELD'	Time	SLT (*n*)	SLT Pt. Surv. (%)	WLT (*n*)	WLT Pt. Surv (%)
Patients' survival	<16	6	131	90.51	7445	93.12
		12		88.78		89.10
	16–20	6	75	94.33	4874	92.85
		12		92.70		89.19
	21–25	6	58	90.67	3671	89.38
		12		86.25		85.31
	26–30	6	22	95.45	2278	86.68
		12		90.15		82.48
	31–35	6	16	87.50	1689	84.40
		12		87.50		80.57
	> 35	6	22	81.82	2298	80.67
		12		70.91		75.95
	Not Reported	6				
Grafts' survival	<16	6	131	86.23	7445	89.39
		12		82.85		84.76
	16–20	6	75	86.48	4874	89.10
		12		84.99		84.77
	21–25	6	58	77.59	3671	85.40
		12		73.80		80.43
	26–30	6	22	90.91	2278	83.67
		12		85.86		78.72
	31–35	6	16	87.50	1689	81.14
		12		87.50		76.79
	>35	6	22	77.27	2298	77.39
		12		66.97		71.88
	Not Reported	6				

SLT, split LT; WLT, whole LT.

As this was data from a national registry, limited graft- and donor-specific information was available. The recipients of segmental grafts were reported according to the type of graft that they received. Left lateral segment (LLS) grafts accounted for 3.2% of the more than 330 segmental grafts transplanted into adult recipients; left lobe (LL) grafts, 17.1%; right lobe (RL) grafts, 22.7%; and right trisegment (RTS) grafts, 13.0%. However, the type of segmental graft was not specified 43.9% of the time. Of the LLS grafts, 27% were transplanted into high 'list-MELD' patients, while high 'lab-MELD' recipients received only 9% of the LLS grafts. High 'list-MELD' patients received 29.3% of the LL grafts while 24.1% of LL grafts went into high 'lab-MELD' patients. RL grafts were used 40.3% of the time in high 'list MELD' but only 15.6% of high 'lab-MELD' recipients received a RL graft. Some 36.4% of the RTS grafts were given to high 'list-MELD' recipients, but only 22.7% of the RTS recipients had high 'lab-MELD'. The largest group of segmental grafts was 'not specified' (43.9% of all segmental grafts). Of these, 40.5% went into high 'list-MELD' patients while only 18% went into high 'lab-MELD' recipients. Fifty-seven percent of grafts were procured *in vivo* while 43% were separated in the back table. Graft and patient outcomes according to specific graft type, procurement method and recipient MELD score were not available. Also unavailable through the registry were specific data regarding cold ischemic time for each graft, graft-to-recipient body-weight ratio and donor age and vasopressor use as they correlated with recipient and graft outcome.

Discussion

The fear that patients with high-MELD score (i.e. the 'sickest' ones) may not be suitable candidates for segmental grafts because of their need for greater liver mass has continued to push the transplant community toward the use of whole LT in preference to split LT. SLT accounted for only 1.5% of US liver transplants performed in the MELD era, and within the Eurotransplant area, the rate of SLT is steadily diminishing. In 2006, the rate of performed SLTs within Eurotransplant was only 6.4% of the total number of LTs [15]. Further emphasizing the point, only 2.5% of registered livers were used for split-liver transplantation, even though 15% of the donors met the criteria as acceptable candidates for use as split-livers

(Broering D., personal communication at Eurotransplant Meeting 2007).

The misperception that sicker patients are not good candidates for segmental grafts is being challenged by the data presented in this article and by other authors as well. In this regard, Schaubel and Biggins [16,17] recently reported that 'patients with high-MELD score still benefit from extended donor criteria (high donor risk index)' like in case of split procedures [18–21]. This concept may also be reinforced by the fact that even in case of acute liver failure, it seems that segmental liver transplantation may reach more than acceptable results. For example, Ikegami *et al.* [22] reported 1- and 10-year graft survival rates of 77.6% and 65.5% and patient survival rates 80.0% and 68.2% for patients who underwent a LDLT for acute liver failure. These data are similar to the ones for the allocation MELD > 35 in our study.

Among nine recent comparative studies of SLT and WLT showing similar results for both procedures [4,14,21,23–28] only Bonney *et al.* [21] from Leeds reported for the first time the outcomes of a matched pair analysis using the MELD score for matching extended right SLT ($n = 27$) and WLT ($n = 27$) recipients. Interestingly, the mean MELD score was 16 in both groups (i.e. very low score) and, although the scores ranged between 7 (!) and 36, nothing was reported about results in patients with high MELD scores.

Therefore, despite the potential flaws of a retrospective study from a national registry and the fact that data does not differentiate outcomes based upon different type of grafts such as right trisegment or right lobe or left lateral grafts (as noted, incomplete data are available on number of each graft type, but not correlated to graft and patient survival results), we show that patient's and graft's survival rates for SLT in high-MELD patients are comparable to WLT. Therefore, we believe that SLT in high-MELD patients is justified and should be more broadly applied to this candidate population.

Concern over using SLT in high-MELD patients, however, is not the only factor contributing to the underutilization of SLT. In the US, UNOS Liver allocation policy 3.6.11 clearly defines the livers of different categories of donors, which are felt to be potentially splittable (donor age less than 40 years, donor on a single vasopressor or less, transaminases no greater than three times normal and BMI of 28 or less). While the policy does not limit the application of split-liver to these donors, it does not require its use with these donors either. The same policy also states that 'the center getting the primary whole graft organ offer will determine the method of splitting and use of the vessels.' While this might seem appropriate, the varying preferences among transplant centers for method of splitting and what constitutes 'appropriate use of vessels' frequently conflict, resulting in yet another barrier to the use of SLT.

In this regard, relevant factors limiting the development of SLT like lack of trained surgeons for both *in situ* and *ex situ* splitting techniques, lack of national split teams, lack of share of split-livers (at least in Eurotransplant Area), as well as logistic difficulties related to the complexity of coordination and allocation have been recently discussed in detail by Sainz-Barriga *et al.* [25]

The transplant community must take steps either through practice or policy to overcome these and other obstacles if it wishes the use of SLT to reach its full potential.

In conclusion, we believe that SLT remains underutilized, particularly in high-MELD patients. In light of this data suggesting comparable results in appropriately selected high-MELD recipients, new allocation formats should continue to promote the use of split LT from suitable donors, regardless of whether allocated primarily to a pediatric or adult recipient [29].

The transplant community has an obligation to maximize the utilization of livers for transplantation. The splitting of livers from suitable donors offers yet another way for centers to collaborate in order to achieve this goal.

Other parts of the world that have recently adopted MELD allocation (see Eurotransplant) along with the US transplant community should take this US experience into account and consider the institution of policies that result in broader usage of SLT.

Authorship

SN: Designed the study, wrote and revised the paper. RS: Collected data, analysed data, edited and revised the paper. NF: Collected data, designed the study.

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