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Combined Heart-Liver Transplantation; Implications for Liver alone wait List Mortality

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Combined heart-liver (HL) transplants are increasingly performed as the definitive treatment for patients with dually failing organs (1). The scarcity of organs however, raises ethical concern about allocating two life-saving organs to a single patient (2,3). The principle of

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equitable distribution is further challenged by the current rules governing multi-organ allocation, which permit the primary organ, allocated based upon the recipient's wait list priority, to automatically sequester a second organ from the same donor, regardless of wait list priority specific to the second organ (4). This rule applies to all solid organs, with the exception that kidneys are always allocated secondarily (5). Latent wait list attrition resulting from multiple organ allocation to one recipient has not been quantified, but is of concern to the transplant community.

We hypothesize that the current scheme for allocating a second organ may bypass more highly ranked wait list candidates, who subsequently incur excessive mortality and morbidity. To address this hypothesis, we studied HL transplants performed at a single medical center and retrospectively evaluated the survival of liver transplant candidates concurrently appearing in the same match runs with HL recipients. We focused our study specifically on liver transplant candidates occupying the first five wait list positions in these match runs. The survival rate of this cohort of wait list candidates was compared to a control set of candidates from match runs that resulted in representative liver-alone (LA) transplants. The aims of this study are to determine if livers allocated to HL candidates bypass higher ranked transplant candidates, and subsequently, whether bypassed liver candidates experience increased wait list drop out and mortality.

In all HL transplants (n=16), the heart was the organ that received allocation priority, while the liver was acquired secondarily from the same donor. Cardiogenic cirrhosis was the cause of liver failure for 15 HL recipients, while hepatitis C was the etiology of disease in 1 patient. None of the HL recipients were among the first five candidates on the liver match run at the time of allocation. In contrast, 24 of 32 (67%) of the LA recipients in the control group were among the first five positions of their respective match-runs. The mean calculated laboratory MELD score at transplant was significantly less for HL than for LA recipients (15 (8.3) vs. 29 (8.2), $p = 0.001$). Of the HL recipients, 14 were anticoagulated with warfarin while awaiting transplant, thus artificially elevating the MELD scores.

To assess the impact of allocating livers to HL recipients on liver alone candidates, we compared the wait list survival of the first five patients bypassed on the waiting list by HL recipients (n=80) to that of candidates in the first five positions in LA match runs (n=160). Both cohorts of top ranking wait list candidates were found to be close in age (51 (16.2) vs. 54 (14.7) years, $p=0.20$) and had similar match MELD scores at the time of the match run (31 (5.7) vs. 31 (3.9), $p=0.97$, Table 1). There was a similar proportion of liver candidates in concurrent HL match runs who died or were removed from the waiting list due to illness (17 of 80 candidates, 21%) when compared to candidates in LA match runs (32 of 160 candidates, 20%, $p=0.84$; Table 1). These results indicate no significant effect to wait list mortality among the first five liver wait list candidates concurrently in HL match runs.

In this study, we found that allocation for HL transplantation regularly bypassed more highly ranked liver wait list candidates but is not associated with a greater risk of wait list mortality compared to patients from control match runs. To our knowledge, this is the first study that has attempted to quantify the impact of dual organ transplant on the survival of candidates awaiting a single organ. The results of this study suggest that distributing organs

to select candidates in need of two organs does not have a readily measureable negative impact to other critically ill candidates on the liver waitlist. The national HL experience has grown significantly during the last decade (6); at the time of this report, 52 of the 132 reported HL transplants within the United States have taken place in the last 3 years. As HL transplantation increases, it is critical to consider the effects of HL allocation on LA candidates.

Whether bypassing single organ candidates in order to facilitate dual organ transplants is ethically acceptable within the current framework of organ allocation remains an open question, and one that requires careful consideration by the transplant community. According to “the Final Rule,” priority for organ allocation should be determined by relative medical urgency, balancing the principles of utility and equity (7). Our data support that allocation practices are not exposing patients to increased risk at the current frequency of heart-liver transplants.

This study has several limitations inherent to any observational cohort study, including a small sample size representing HL practice at a single center, potentiating the risk of a type 2 error. In this study, the heart was the primary organ for allocation in all HL recipients, which may not be representative of the national HL experience (8). The effects of bypassing candidates on the wait list are most likely pertinent at the first few match run positions, which we believe justifies our inclusion of only the first five candidates. Confirmation of the findings from this study awaits analysis of national data.

In summary, this analysis suggests that liver candidates bypassed by HL dual transplants do not incur a survival disadvantage. Our intention is to highlight the previously unstudied consequences of dual organ transplantation and spur further inquiries into the indications and allocation practices for dual organ transplantation. Guidelines for dual-organ transplantation will ultimately need to be established which provide equipoise to single as well as dual organ candidates.

Methods

This is a single center retrospective cohort study of candidates who were ranked in the first five positions in liver transplant match runs that generated HL transplants (n=16) performed between 2001 and 2011 at the Hospital of the University of Pennsylvania. A control cohort was identified by matching each HL match run to two match runs that resulted in LA transplants. Donor characteristics, including: year of transplant, donation after neurological determination of death, ABO blood type, donor age (+/- 5 years), gender, and race were used to identify control match runs. As with HL match runs, the control cohort included the first five liver waiting list candidates at the time of a liver match. Wait list survival was categorized into the following groups: active on list at time of study, survival to transplant, removal from waiting list due to death or illness, and removal from list for other reasons. National figures of HL transplantation were obtained from the UNOS database (1987 through 2013).

Comparisons of baseline characteristics between cohorts were calculated by student's t-test for normally-distributed continuous variables and Chi-square for categorical data. All statistical analyses were performed with SPSS version 20 software.

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Abbreviations

HL	combined heart-liver
LA	liver-alone
MELD	Model for End-Stage Liver Disease
UNOS	United Network for Organ Sharing

Table 1

Baseline characteristics and wait list survival of top five wait list candidates concurrent with HL and LA transplants. HL = combined heart-liver, LA = liver-alone.

	Position on liver list at time of HL matching					Total
	1	2	3	4	5	
<i>n</i>	16	16	16	16	16	80
Age (SD)	49 (20.4)	48 (17.3)	54 (12.3)	61 (7.5)	55 (10.0)	54 (14.7)
MELD	35 (4.5)	32 (3.8)	31 (3.1)	30 (2.8)	29 (2.6)	31 (3.9)
Transplanted (% of total)	11 (69%)	10 (62%)	12 (75%)	10 (62%)	13 (81%)	56 (70%)
Not transplanted						
Deceased/Delisted	4 (25%)	5 (31%)	3 (19%)	3 (19%)	2 (11%)	17 (21%)
Other	1 (6%)	1 (6%)	1 (6%)	3 (19%)	1 (6%)	7 (9%)
	Position on liver list at time of liver-alone control					Total
	1	2	3	4	5	
<i>n</i>	32	32	32	32	32	160
Age (SD)	47 (19)	48 (16)	54 (12)	51 (13)	52 (16)	51 (16.2)
MELD	34 (8)	32 (6)	32 (5)	30 (4)	29 (4)	31 (5.7)
Transplanted (% of total)	24 (75%)	24 (75%)	23 (72%)	24 (75%)	25 (78%)	120 (75%)
Not transplanted						
Deceased/Delisted	6 (19%)	7 (22%)	7 (22%)	6 (19%)	6 (19%)	32 (20%)
Other	2 (6%)	1 (3%)	2 (6%)	2 (6%)	1 (3%)	8 (5%)