LETTER TO THE EDITORS

Liver transplantation with geriatric liver allograft in the US: a matter of epidemiology or outcome requirements?

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Dear Editors,

We read with interest the letter "Liver transplantation with geriatric liver allografts: the current situation in Eurotransplant" by De Boer *et al.* [1] as it analyzes important aspects in the utilization of "older" donor allografts. In this communication, we would like to discuss how the utilization of elderly donors (≥70 years old) in the United States differs from that of Europe, offer potential explanations for these different utilization pattern and suggest a potential intervention which could function to systematically enhance older liver donor transplantation in the United States.

In 2015 in the USA, 14 046 candidates were registered on the waiting list of which 11 699 were in active status. Of those on the waiting list, 1673 patients died (12%) and 1227 (8.7%) were removed due to being too sick to undergo transplantation [2]. Therefore, there is an obvious need in the USA to increase the current pool of potential deceased donors and the conversion of those donors into transplantation.

Although it has been difficult to quantify the exact number of potential brain dead organ donors (DBD) in the USA, one study gathering data from 36 Organ Procurement Organizations (OPOs) over a 3-year period identified 18 524 potential DBD donors younger than 70 years of age. Fifty-four percent of families agreed to donation, and 42% of potential donors converted into actual donors. Consent for donation was not obtained in 39% of potential donors, and 16% of families were not asked to participate in organ donation [3]. Another US study found that increasing the age limit from 65 to 75 years added 61 396 potential donors accounting for

62% of the total number of potential donors but only to 4.4% of actual donors [4].

The utilization rate of older donors in Eurotransplant increased by more than 10% in the past two decades. However in the Unites States, only 3.4% of all liver transplants are performed with allografts from donors 70 years and older (Fig. 1). Elderly donor allografts are associated with primary nonfunction (PNF) and poor early graft function but they have been used with good results [1,5,6]. Therefore, it is not yet clear how to best balance the potential risks associated with utilization of older donor organs with the need to maximize the rate of transplantation. It should be noted that liver function is more important than chronological age. As already stated by Lai et al. [7], "if a liver can withstand the stressors of 80+ years of life then it may be successfully transplanted with acceptable long-term outcomes". In this sense, an age limit ought not to be strictly necessary.

It has been suggested that the high rates of chronic disease and lifestyle factors (e.g., obesity, diabetes, and tobacco use) in the USA influence the quality of older grafts, potentially contributing to historically low usage rates. We believe there are three additional salient factors specific to the United States that continues to significantly impede transplantation of older liver donors.

The first is related to the increase in quality oversight of transplant centers where government (e.g., Centers for Medicare and Medicaid Services) and private payers utilize quality metrics to determine reimbursement levels. While there are many potential benefits of quality oversight, imperfect risk adjustment may induce risk adverse behaviors, resulting in the reluctance to treat patients who are perceived to potentially threaten a center's measured outcomes. For example, a transplantation using a young donor with a low Donor Risk Index (DRI) theoretically has less potential to negatively impact measured outcomes than an 80 years old graft and therefore, decreasing the likelihood that older donor grafts will be utilized.

decade	40-49		50-59		60-69		70-79		>80		Total	
	Total	Tx (% of	Total (%)	Tx (%of	Total (%)	Tx (%of	Total (%)	Tx (%of	Total	Tx (%of	Total	Tx (%)
	(%)	total Tx)		total Tx)		total Tx)		total Tx)	(%)	total Tx)		
1987-	1163	407	849	143	253	7	9	2	0	0	8465	3811
1989	(13,7)	(10.7)	(10)	(3.8)	(3)	(0.2)	(0.1)	(0.05)	(0)	(0)		
1990-	8636	5515	7165	4321	4202	2284	998	585	71	48	50518	35303
1999	(17)	(15.6)	(14.2)	(12.3)	(8.3)	(6.5)	(2)	(1.6)	(0.15)	(0.13)		
2000-	13989	10200	13770	9523	7655	5353	2989	2163	434	320	70529	54038
2009	(19.9)	(18.9)	(19.5)	(17.6)	(10.8)	(9.9)	(4.2)	(4)	(0.61)	(0.6)		
2010-	9519	6537	10580	6923	5284	3734	1453	1112	170	131	49370	36307
2015	(19.3)	(18)	(21.5)	(19)	(10.7)	(10.3)	(3)	(3)	(0.35)	(0.36)		

Figure 1 Number of donors and transplants in the USA divided for decades (Tx: transplant).

A second factor is that OPOs are evaluated by donor yield, the number of organs transplanted per donor. Based on this performance metric published by the Scientific Registry of Transplant Recipients, procurement of donors likely to only yield a single organ is disincentivized. As older potential donors are less likely to have multiple organs viable for transplantation, OPOs may be less aggressive consenting this population for donation.

Finally, donor age significantly varies across geographic regions. In European countries such as Italy, the median donor age is over 60 years old and it is predicted that the donor age will reach 80 within a decade [8]. Liver transplant activity is mainly supported by these older donors and out of necessity, transplant surgeons have been "pushed" to learn how to successfully utilize them. In the USA, the median/mean donor age is significantly lower and therefore just centers that really wants to push the limits and increase the number of transplants consider old donors as a resource.

Two factors are crucial for the successful utilization of old donors in transplantation: strategic recipient selection and minimizing ischemia/reperfusion injury. Strategic recipient selection of these grafts ought to take into consideration that implanting a graft with less functional reserve in a severe sick recipient with high MELD can led to worse outcome [9]. I/R injuries plays an important role as these graft have less tolerance to stress accounting for their higher rate of primary nonfunction and delayed graft function. Machine perfusion technology has been used with old donors with promising results [10,11]. NMP allows a reduction in I/R injuries and, moreover, an evaluation of graft function before implantation; these are two key factors that could significantly increase the transplant rate of these organs.

We strongly believe that efforts to enhance the number of transplants ought to include all extended criteria donors. Boundaries related to performances may be more inhibitory than beneficial to recipients.

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