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INVITED COMMENTARY

Allograft utilization for pediatric heart transplantation: what are we doing wrong?

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From way back on December 6, 1967, when Kantrowitz [1] performed the first human-to-human pediatric heart transplant, until today we accumulated remarkable experience in this field. More than 12 000 pediatric heart transplants have been performed in more than 418 centers worldwide [2]. The first transplant on the 18-day-old male infant was technically successful, regardless of the fact that the patient died 6½ h after surgery with severe metabolic and respiratory acidosis (surgery was performed under hypothermia, without cardiopulmonary bypass) [1].

Can we conclude today that we are satisfied with this therapy and that we are exploiting all the resources offered, and that the high mortality rate, especially in newborns and infants on waiting lists, is only due to the lack of donors?

First, we can confidently argue that pediatric heart transplantation remains the standard of care for children with end-stage heart failure caused by cardiomyopathy or complex congenital heart disease (CHD) that cannot be repaired and when primary reconstructive procedures or staged long-term palliative procedures have failed [3,4]. Complex CHD is the main indication for heart transplantation in infants, whereas end-stage cardiomyopathy is the main indication after the first year of life [3,5].

Second, we found out that the number of pediatric donors is stagnant for decades, so something has to be done to raise public awareness. Untapped potential in the use of hearts originating from pediatric donation after circulatory determination of death (DCDD) (as the first 2-day-old anencephalic male donor was) is waiting for the removal of all legal and ethical barriers.

Third, death rates on the pediatric heart transplant waiting lists have decreased over the years, as in Eurotransplant (ET) from 25% in 1997 to 18% in 2011 [6], and in Australian National Paediatric HT Programme from 27% in 1988–1995 era to 18% in 2006–2015 era [7], and in United Network for Organ Sharing (UNOS) waitlist mortality continues to decrease, to 9.3% in 2010 [8]. Latest percentages are promising, but still unacceptably high especially for candidates aged younger than 1 year, with 32% mortality in ET [6] and 42 deaths per 100 waitlist years in 2012–2013, almost 2.5 times higher than the rate for candidates aged 1–5 years [8]. We must be aware that the results in older children recipient subgroup could be somewhat misleading because in this group approximately a quarter of recipients received a heart from adult donors [2].

Forth, vigorous effect on the number of patients on waiting lists has improved mechanical support for the heart and circulation, offering extended survival to

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patients who would have died while waiting and due to that nowadays almost 34% of transplanted pediatric patients were bridged to transplant on mechanical support [2,3].

Fifth, new successful surgical approaches to neonates and infants with high-risk complex congenital heart diseases improve survival and also enable additional staging and palliative procedures [3], but also frequently increase the waiting list with highly sensitized patients.

Sixth, it was expected more from ABO-incompatible transplantation, the essential advantage, that the newborn and infant recipients have, compared to adults. The delay in the development of natural antibodies to ABO antigens in infants allows successful ABO-incompatible transplants with equivalent survival.

In this issue of Transplant International, Khan and coauthors in the article "Donor Predictors of Allograft Utilization for Pediatric Heart Transplantation" provide a detailed analysis of the donor risk factors that might affect graft use for transplantation by examination of the UNOS database from end of April 2006 until end of March 2014 [9].

Crucial and painful fact for everybody who is involved in this field of medicine is that the pediatric graft utilization rate was only 56.2% in UNOS [9] which is even slightly lower than 61.8% in ET [6].

The presented results show us that outdated and too restrictive adult donor criteria were used to determine suitability of pediatric donor hearts for transplantation.

How otherwise to explain such a strong influence of factors such as donor gender, inotropic support and depressed (<50%) left ventricular ejection fraction (LVEF) on donor heart utilization.

Pediatric heart donor gender has no effect on the outcome of the recipient [10], and this factor is transferred from adult donor criteria protocols.

Considering the large number of donor hospitals and relatively minor experience in pediatric donor management compared to adult donors, difficulties could be expected. A loss of sympathetic tone and peripheral vasodilatation with the resulting hypotension and echocardiographic evidence of myocardial dysfunction, which can be seen in half of brain-dead donors, could make pediatric donor management a true challenge for majority of pediatric intensivists.

The authors found that the non-O blood type was significantly associated with graft nonutilization which is difficult to accept after ABO-incompatible transplants were expanded in 2010. The percentage of ABO-incompatible transplants in 2011–2013 was 3.6% and that was a remarkable increase from 1.3% a decade earlier [8]. This is encouraging, but far from the expected rise.

This article has shown us that we need immediate change in the approach for assessing the appropriateness of pediatric hearts for transplantation. It is necessary to create new pediatric donor criteria on the basis of pediatric studies that associate donor factors to post-transplant outcome.

Despite the fact that better graft utilization should reduce mortality on the waiting lists, I believe that this will not solve the extremely negative disparity between the stagnant number of available donors and increasing number of desperate children needing cardiac transplantation. If, in the future, there will be no additional biological solutions, improved mechanical support or replacement could be the best answer.

The most appropriate and child-friendly device should be completely implantable, wireless, with implanted physiologic controller, durable for years, should enable free-range energy transmission, and should not require anticoagulation.

Am I unrealistic?

We are planning to send people to Mars, but we are not able to produce such a device?

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