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EDITORIAL COMMENTARY

Young for young! Mandatory age-matched exchange of paediatric kidneys

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Abstract Some allocation systems include a mandatory donation of paediatric kidneys to children, others do not. Both approaches have medical and organisational advantages and disadvantages for adults and children. This article discusses why "young for young" is the best allocation system for children. Primary age-matched kidney allocation to children is one important factor leading to: (1) higher long-term glomerular filtration rates (GFRs) and graft survival and, thereby, to lesser need for dialysis; (2) better psychosocial rehabilitation, growth and development of children and, last but not least, (3) likely increase of the donor pool. As a consequence, health care costs will be reduced for children with end-stage renal failure. The chance of adults receiving an adequate kidney would be only minimally reduced by this policy. Therefore, we recommend an age-matched allocation programme giving children with end- stage kidney diseases a better prognosis.

Keywords Kidney transplantation · Children · Allocation · Age match · GFR · Graft survival

Organ allocation is an important focus of discussion in many countries, because, in most systems, there is a lack of suitable organs. Children are a minority on the waiting lists for a kidney transplant (1–4%). These numbers will further decrease, because the number of children with end-stage kidney disease remains almost stable, whereas the number of adults needing renal replacement therapy is increasing. Therefore, the chances of children receiving an adequate organ will deteriorate. There is evidence that children deserve special consideration, because early transplantation avoids damage to a child's further development. Better growth, regular school attendance, healthy family life and normal intellectual and psychological development are goals that are achievable by early transplantation and better graft survival. In many cases parents are willing to do a living donation (LD), which leads to better graft survival than grafts from cadaveric donors (CADs), even in infants [1]. Therefore transplantation of organs from LDs is the best option for children.

When no living donor is available, the child has to await the organ of a CAD. In Eurotransplant waiting times were often exceeding 2 years [2], whereas other allocation systems gave absolute priority to paediatric recipients, with shorter waiting times [3–5]. It has been shown that, in the long term, grafts from adult cadaveric donors adapt to the body size of the child directly after transplantation but are unable to parallel the growth thereafter, whereas kidneys from paediatric donors present with an increase in absolute glomerular filtration rate (GFR), leading to a long-lasting stable relative GFR [6]. These results have been confirmed by a matched-pairs analysis of adult and paediatric donors, where one kidney was allocated to an adult and the other to a child [7]. It was also shown that the advantage of graft function in children receiving paediatric organs was followed by better growth of the paediatric kidneys [8]. Unfortunately, the proportion of paediatric organs transplanted into children was only 1% in Europe (Eurotransplant, unpublished data). In the United States of America the percentage of the paediatric population on the kidney waiting list declined from 1.8% to 1.4% in the past decade, whereas the total number of patients on the waiting list doubled [3]. This led to a prolonged waiting time for children.

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Table 1 Mean GFR (millilitres per minute per 1.73 square metres body surface area) and survival (percent)] over 5 years in children receiving kidneys from paediatric or adult donors [8]

Parameter	Tx	1 year	2 years	3 years	4 years	5 years
Donor age<16 years (n=22)						
GFR	65 SD 22	67 SD 21	63 SD 21	69 SD 23	68 SD 28	65 SD 21
Graft survival	90	82	82	82	82	82
Donor age>16 years (n=48)						
GFR	81 SD 30	64 SD 18	58 SD 17	56 SD 16	53 SD 17	50 SD 16
Graft survival	90	84	84	84	84	84

Differences in GFR are significant in years 3–5 [analysis of variance (ANOVA), P<0.05]

There are three main medical reasons for the use of paediatric organs for children: (1) minimal size mismatches; (2) no hypoperfusion and reduction of initial non-graft function, and (3) lower cardiovascular risks. This is of special importance, because the proportion of children aged below 6 years who undergo renal transplantation is increasing. The size of an adult kidney ranges between 150 ml and 200 ml, fitting poorly into a small child with a body weight of 6–15 kg. Sometimes, it may not be possible to close the abdomen without an artificial net. With regard to the blood volume of a small child, with about 1 l in a 10 kg child, one-fifth will enter the adult graft at the time of reperfusion. Furthermore, the blood pressure of the child is lower than that to which the donor kidney was adapted. Therefore, large amounts of fluid and catecholamines may be necessary to sustain blood pressure and satisfactory graft perfusion.

We conclude that there should be a primary allocation of paediatric kidneys to paediatric recipients in all Eurotransplant countries. In 2005, the United States of America changed its allocation system because of the above arguments and in order to decrease the waiting time for children. Kidneys from donors less than 35 years old are now offered preferentially to paediatric candidates. Only patients with no human leukocyte antigen (HLA) mismatches, and those who are highly sensitized, have a higher priority. Paediatric candidates less than 11 years old are given additional point priority because of their age and the greater impact of kidney failure on development [3]. In the Eurotransplant allocation system [2] children less than 16 years old receive double points for the HLA matches, decreasing their average waiting time of 5 to 7 years by approximately 1 to 3 years. Available organs are first allocated to recipients of simultaneous pancreas and kidney transplantation and other combined transplants, and second to recipients with zero mismatches. Organs are then allocated by use of the point system, in which they compete within the pool of patients on high urgency or hyperimmunization. As there are (nearly) no children who require pancreas transplantations, it can be reasonably stated that children are, in fact, penalized, because paediatric organs are primarily allocated to adult pancreas–kidney recipients. Eurotransplant is planning a "young for young" programme. This decision includes a mandatory exchange of paediatric donor kidneys (donor age<10 years) to paediatric recipients (< 6 years) in order to reduce the medical risk factors in young children. Older children will not benefit from this new programme, because it was not the primary intention to decrease the waiting time for all children under 16 years. At Eurotransplant mandatory allocation will only take place with a match on HLA-DR locus.

In the past, two main arguments were used against primary allocation of paediatric kidneys to children. Firstly, graft survival was said to be worse when paediatric organs were used. Secondly, adults may be penalized by a young-to-young programme.

Historic data on graft survival of single renal transplants from donors <5 years were inferior to those of adult donors if transplanted into young or older children [9]. The main reasons were infections and technical problems, such as graft thrombosis [10–12]. Analysing data from 1988–1995, Bresnahan et al. [10] described decreased graft survival in children with paediatric donor grafts because of a high rate of complications with organs from paediatric donors below 5 years of age. Survival of paediatric (5–18 years) and adult grafts was comparable between paediatric and adult donors in this large United Network for Organ Sharing (UNOS) analysis. Reports from the 1990s showed disadvantages in graft survival when paediatric kidneys were transplanted into children in comparison with good success with kidneys from adult donors without tubular necrosis [11, 13]. In the past years improvements in surgical technique and immunosuppression dramatically improved the success of transplantation of paediatric kidneys into children: The North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) report 2005 demonstrated that the worse outcome of very young donors was completely based on donors aged 1–2 years. Unfortunately, differences in long term GFR, depending on donor age, were not evaluated in the annual NAPRTCS report [14]. In our centre, graft survival after 5 years was higher than 80% in children

receiving grafts from both paediatric and adult donors [8]. We could also show that transplantation of CAD kidneys from young donors could even reach survival rates equal to those from LDs when transplanted into children with a body weight of less than 11 kg [1]. In fact, only graft survival in the first year, but not long-term graft function, was the fundamental argument for deciding whether paediatric grafts should be primarily used in paediatric recipients or not. However, we could show that graft survival in the past 5 years was comparable in all ages and that GFR was better in recipients of paediatric grafts (Table 1).

Better GFR means longer graft survival, and longer organ survival means a better quality of life and lower costs. Better graft survival leads to a smaller number of expensive dialysis days and a lower number of re-transplantations. Children with better psychosocial rehabilitation also require less paramedical support and have a better chance of finding work, therefore not requiring social welfare in the future.

Children only represent 1% of the patients on the Eurotransplant waiting list, so that a primary allocation of paediatric kidneys to children would lead to only a statistically minimal change in waiting time or allocation chances for the individual adult on the waiting list. In the United States of America the OPTN Board of Directors showed that this change will have a minimal impact on the allocation system, because, in the USA, the total number of paediatric organ recipients (381) of kidneys from deceased paediatric donors is small compared with the 2,595 deceased kidney donors under 35 years of age in 2004. Also, taking into consideration that the economic and social future of the western world is based on children, who are not able to fight for their own interests themselves, a minimal additional disadvantage for adults has to be accepted by society.

In our opinion, all allocation systems should follow the guideline of young to young but avoid a limited offer of very young donors for paediatric recipients. At the actual time, organs from donors below 2 years of age should only be used depending of the experiences of each centre. For those children with no paediatric organ available, organs from adults below the age of 35 years should be allocated. Depending on the experiences of the next years, the new Eurotransplant programme may even be expanded to paediatric recipients older than 6 years. We are convinced that the number of advantages of these changes substantially outweighs any possible disadvantages. In summary, the goal for the future may be an age-matched (and thereby size-matched) organ allocation of all kidneys from donors to “young for young” and “old for old”. As the number of paediatric kidneys matches the number of waiting children per year in Eurotransplant, no extra priority for children on the waiting list will be necessary. This approach will give children with end-stage renal disease the best suitable organs in an acceptable waiting time and, thereby, the chance of a better future.

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