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A comparison of pedriatric and adult kidney donors for adult recipients

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Abstract The high demand for organs for transplantation has made it necessary to consider using even the oldest and youngest of potential donors in order to increase the organ supply. In this retrospective study, the outcome of kidney transplantation using cadaveric pediatric donors was compared with that of an adult control series. Graft procurement took place in two regions of Italy (Emilia-Romagna and Piemonte) over an 11-year period. A group of pediatric donors (< 15 years old, $n = 30$) was compared with an adult donor group ($n = 67$). All recipients were adults who received cyclosporin as immunosuppression. Actuarial patient and graft survival rates did not differ significantly between the two groups (patient survival 96 % and 96 % for pediatric donors versus 98 % and 92 % for adult donors at 1 and 5 years post-transplantation; graft survival 76 % and 68 % for pediatric donors versus 88 % and 74 % for adult donors 1 and 5 y post-transplantation). Complications were also evaluated, but no difference was found (the only exception being the creatinine level in the 5th year). Renal transplantation with cadaveric donors starting at 4 years of age gave results comparable to kidneys coming from adults. These data show that cadaveric pediatric donor kidneys may be used in adult recipients with good results. The ethical implications of the subject are extensively reviewed.

Key words Donor age · Pediatric donors · Pediatric kidneys · Renal transplantation

Introduction

Since 1902, when the first successful experimental kidney transplantation was performed by Emerich Ullmann [11], the improved quality of life achieved by patients has made this therapy the best solution for end-stage renal disease. This has also meant that the transplant waiting list has increased and produced an ever-widening gap between the supply and demand for organ donors. Consequently, the aim to expand the donor pool has pushed researchers to study different kind of donors, including the so-called "non-ideal" donor. The literature already includes trials with non-heart-beating donors [33], as well as donors with hepatitis C [22]. The very old have also been investigated [14], as have pediatric [6, 16, 30] and even anencephalic donors [8].

The impact of organ donation from the young on graft survival continues to be equivocal. A detrimental influence is found by some investigators [21, 22, 24] while others support the practice and claim a successful outcome [15, 23]. Children represent between 10 %–15 % of all cadaveric donors, and for this reason every effort to improve utilization of this source would be of great interest.

The aim of this study was to evaluate the graft outcome of kidneys harvested from pediatric donors and to compare it with the outcome of adult donor kidneys transplanted into adult recipients.

Table 1 Demographic characteristics of the groups studied

	Pediatric donors (group 1)[a]	*n*	Adult donors (group 2)[a]	*n*	*P*
Donor age (years)	11.16 ± 3.06	30	29.31 ± 13.29	66	0.001
Recipient age (years)	31.70 ± 10.77	30	31.89 ± 10.48	67	NS
Cold ischemia time (hours)	19.53 ± 9.16	30	17.23 ± 9.50	67	NS
Number HLA A/B/DR mismatches	4.43 ± 1.10	30	4.26 ± 1.20	67	NS
Recipient sex M/F	76% M	30	64% M	67	NS
Renal dialysis treatment (months)	39.43 ± 32.80	30	35.34 ± 32.54	67	NS
Waiting list (months)	25.86 ± 21.53	30	22.38 ± 17.54	67	NS
Polytransfused recipients	33%	30	36%	66	NS
Blood group 0/A/B/AB	13/12/3/0	28	30/29/5/0	64	NS
Multiorgan donor	71%	28	71%	62	NS
Follow-up (months post-transplantation)	57.46 ± 44.40	30	59.14 ± 40.13	67	NS

[a] mean + SD

Materials and methods

Population characteristics

Thirty cadaveric renal transplantations carried out at the Nephrology Unit of St. Orsola's Hospital, Bologna, Italy, were retrospectively studied. The kidneys came from pediatric donors below 15 years of age and were procured by two transplant reference centers, Emilia-Romagna and Piemonte, with a population of 8,000,000.

In this group (group 1), mean donor age was 11.16 years (range 4–14 years), mean recipient age 31.70 years (range 15–52 years), mean number of HLA A/B/DR mismatches 4.4 (range 2–6), mean cold ischemia time 19.53 hours (range 4–40 hours), and mean time of renal dialysis treatment 39.43 months (range 3–145 months). All of the patients underwent primary transplantation and they received cyclosporin as immunosuppression. There was no en-bloc kidney transplantation.

Control group

The control group consisted of 67 renal transplant recipients with kidneys coming from adult donors. The transplantations were performed at the same institution and in the same period of time. In this group (group 2), mean donor age was 29.31 years (range 15–62 years), mean recipient age 31.89 years (range 14–53 years), mean number of HLA A/B/DR mismatches 4.2 (range 1–6), mean cold ischemia time 17.23 hours (range 2–40 hours), and mean time in renal dialysis treatment 35.34 months (range 0–198 hours). They too all underwent primary transplantation and received a similar therapy.

Period of study

The study period began on 1 January 1985 and ended on 31 December 1996, after the introduction of cyclosporin. The mean period of follow-up in this study was 57.46 months (range 0.1–128 months) for group 1 and 59.14 months (range 0.1–129 months) for the control group.

Outcome variables

The outcome variables studied included:

1. primary graft nonfunction (delayed): passage of less than 1500 ml of urine in the first 24 h and/or need for dialysis in the first 6 days after transplantation;
2. pre-emptive graft: transplantation before dialysis is required;
3. graft loss: patient returned to dialysis or died with or without a functioning graft;
4. graft survival: calculated from the time of transplantation to return to dialysis, retransplantation, or patient death.

Statistical analysis

The SPSS program was employed for this analysis. Nonparametric data were compared using the chi-square test and Pearson's coefficients of correlation. All the other variables were compared with the Mann-Whitney U-Wilcoxon rank-sum W-test. To generate graft survival curves, we used the Kaplan-Meier method, while hypothesis tests on the differences of these curves were performed using the Wilcoxon (Gehan) test. Differences were considered statistically significant when P levels were less than 0.05.

Results

The demographic characteristics of the groups studied can be seen in Table 1. Of the patients who received organs from pediatric donors (group 1), nine returned to dialysis and one died of sepsis. The causes of graft loss were: chronic rejection ($n = 4$), hyperacute rejection ($n = 2$), primary nonfunction ($n = 1$), vascular thrombosis ($n = 1$), and unknown ($n = 1$). In the control group (group 2), 16 patients lost their grafts due to: chronic rejection ($n = 14$), hyperacute rejection ($n = 1$), and recurrence of primary renal disease ($n = 1$). Five patients died. The causes were: sepsis ($n = 2$), pancreatitis ($n = 1$), malignant tumor ($n = 1$) and accident ($n = 1$).

Patient survival is depicted in Fig. 1. In group 1 this was 96% and 96% versus 98% and 92% for group 2

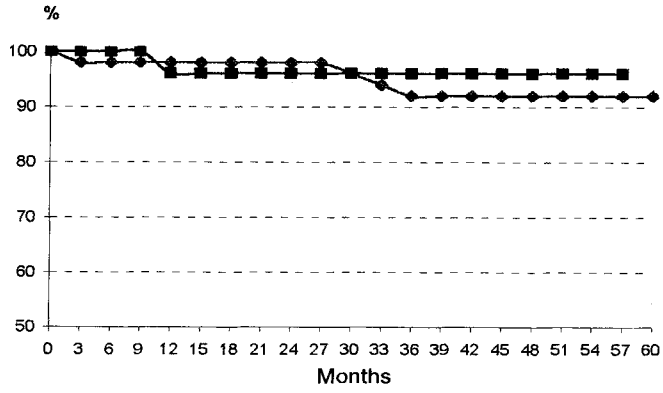

Fig. 1 Actuarial patient survival in the pediatric donor group and the adult control series 1985–1996. -◆-% adult, -■-% pediatric

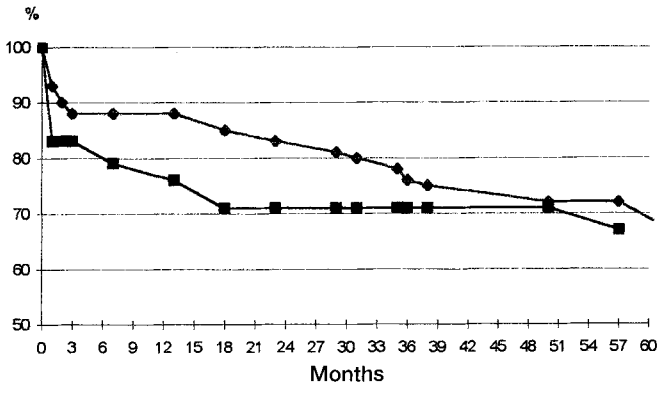

Fig. 2 Actuarial graft survival in the pediatric donor group and the adult control series 1985–1996. -◆-% adult, -■-% pediatric

for the 1st and 5th years past-transplantation, respectively. The difference is not significant.

The graft survival of the two groups is shown in Fig. 2. The 1- and 5-year post-transplant survival rates were 76% and 68% for group 1 versus 88% and 74% for group 2. This was not a significant difference ($P = 0.48$).

We also analysed the differences in life survival, delayed graft function, rejections during the first three months and first year post-transplant as well as the serum creatinine levels at 1 and 5 years (results can be seen in Table 2). From all these parameters the only significant difference found was in the creatinine at the fifth year ($P = 0.001$)

Discussion

Patient and graft survival rates were unaffected by donor age at our institution, where no differences were found throughout the period of follow-up (Figs. 1, 2). The values obtained are similar to those reported in other series [10, United Network for Organ Sharing]. The results suggest that not only organs from adults, but also those from pediatric donors may successfully be grafted onto adult recipients. Similar results were observed pre- [32] and post-cyclosporin administration [22]. Previously published studies [23, 29] showed that rapid, compensatory hypertrophy of the small pediatric kidneys occurred when transplanted into adults. Kidney size was enlarged by 50% in 3 months, resulting in a threefold increase in creatinine clearance by 6 months post-transplantation [2].

Table 2 Postoperative course and patient and graft survival rates

	Pediatric donors (group 1)	*n*	Adult donors (group 2)	*n*	*P*
Delayed function	40.0%	30	40.0%	67	NS
Rejection first 3 months	43.0%	30	39.0%	67	NS
Rejection months 3–12	17.0%	30	10.0%	60	NS
Rejection years 1–5	12.5%	24	15.7%	57	NS
Surgical complications	6.6%	30	7.4%	67	NS
Urological complications	10.0%	30	10.4%	67	NS
Renal complications	none	30	2.9%	67	NS
Vascular complications	3.3%	30	none	67	NS
Cardiac complications	none	30	2.9%	67	NS
Neoplastic complications	3.3%	30	1.4%	67	NS
Infectious complications	3.3%	30	1.4%	67	NS
Gastric complications	3.3%	30	4.4%	67	NS
Creatinine 1st year (mg/dl)	1.59 ± 0.90	22	1.46 ± 0.61	50	NS
Creatinine 5th year (mg/dl)	1.30 ± 0.48	13	2.21 ± 1.35	19	0.001
% Patient survival 1st year	96%	26	98%	59	NS
% Patient survival 5th year	96%	21	92%	42	NS
% Graft survival 1st year	76%	23	88%	57	NS
% Graft survival 5th year	68%	19	74%	38	NS

Reports have also been published showing that kidneys from younger donors have a worse graft outcome due to insufficient nephron mass [22, 31] and an increased number of vascular [27] postoperative [25] and urological complications [13]. These undersized kidneys are also alleged to have a higher incidence of hypertension [1] and immunological failure [34]. Analyzing the data from the Collaborative Transplant Study, Opelz in 1988 [24] concluded that kidneys from very young donors did poorly, with graft survival improving as donor age increased. Other authors also suggest that pediatric donors perform less well than those with a higher number of nephrons as a consequence of hyperfiltration damage. In such a situation, glomerular sclerosis is reported to be the long-term result. The first to note these detrimental changes were Chanutin and Ferris in 1932 [7]. This issue later received much attention in studies by Brenner et al. [4] who, in 1982, postulated the hyperfiltration hypothesis. This theory explained the inexorable progress towards hypertrophy and sclerosis of the overloaded nephron mass. Many researchers confirmed this theory [22, 34]. Terasaki et al. [31] showed that this effect could be predicted by an increase in serum creatinine at discharge from hospital, and that the latter had a strong correlation with the further outcome of the graft. All of these problems have been found with the youngest donors, especially those under 2 years of age. With these donors, en bloc transplantation has been demonstrated to improve the results of renal transplantation. En bloc kidneys have a greater renal function reserve and show a lesser risk of hyperfiltration [20].

In our study, we found no differences in either outcome or complications between the pediatric and control groups. Donor age was over 4 years, and for this reason it was not necessary to use en bloc transplantation. A vascular thrombosis was observed within the pediatric group; this complication, related to the small vessels of these kidneys, is frequently observed with pediatric donors [27], but rarely present in adult ones.

Assuming, however, that pediatric kidneys do have a good outcome and that complications will continue to decline thanks to medical (new immunosuppressive drugs) and surgical (percutaneous angioplasty for revascularization of occluded arteries [28], en bloc techniques [18]) advances, the next consideration must be that of allocation. A basis for age-matching kidneys is found in certain functional studies [5, 9], reporting the best outcome in situations where the age difference between donor and recipient is less than 5 years. There are also ethical reasons to consider: pediatric patients must be transplanted as soon as possible in order to offset the negative effects of renal disease in growth and development. Many investigators also advocate early transplantation to maximize growth potential [12, 17], while there are even countries where the use of pre-emptive grafts is being developed [19].

We support the allocation of pediatric donors to pediatric recipients. Pediatric donor grafts seem better able to increase their function with the growth of the pediatric recipient than adult grafts [3]. Moreover, results in pediatric patients are usually not so good as in adult patients [15, 19], leading in many cases to subsequent retransplantation. For this reason and to prevent further hypersensitivization, it is important to obtain the best possible match. With this purpose in mind, a national program for pediatric transplantation was started in Italy [26] to create an unique national pediatric waiting list and to allocate pediatric organs only to pediatric recipients.

In conclusion, the present study shows that cadaveric pediatric donor kidneys from children at least 4 years of age and adult donor kidneys give equivalent results when transplanted into adult recipients. We advocate pediatric transplantation and suggest that more adult kidneys could be directed to pediatric recipients in order to improve the speed at which pediatric patients receive transplants.

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References

1. Abouna GM, John P, Samhan M, Kumar MSA (1990) Transplantation of single paediatric cadaveric kidneys into adult recipients after prolonged preservation. Transplant Proc 22: 407
2. Abouna GM, Kumar MSA, Chvala R, Mc Sorley M, Samham M (1995) Transplantation of single pediatric kidneys into adult recipients – 12 years experience. Transplant Proc 27: 2564–2566
3. Berg UB, Bohlin AB, Tyden G (1997) Influence of donor and recipient ages and sex on graft function after pediatric renal transplantation. Transplantation 64: 1424–1428
4. Brenner BM, Meyer TW, Hostetter TH (1982) Dietary protein intake and the progressive nature of kidney disease: the role of hemodynamically mediated glomerular injury in the pathogenesis of progressive sclerosis in aging, renal ablation and intrinsic renal disease. N Engl J Med 307: 652–659

5. Brown MW, Akyol AM, Junor BJR, Macpherson SG (1987) Transplantation of cadaver kidneys from donors under 10 years of age. Transplant Proc 19: 1518–1520
6. Burrows L, Knight R, Polokoff E, Schanzer H, Panico M, Solomon M (1996) Expanding the donor pool with the use of en-bloc paediatric kidneys in adult recipients. Transplant Proc 28: 173–174
7. Chanutin A, Ferris EB (1932) Experimental·renal insufficiency produced by partial nephrectomy. I. Control diet. Arch Intern Med 49: 767–787
8. Díaz JH (1993) The anencephalic organ donor: a challenge to existing moral and statutory. Crit Care Med 21: 1787–1790
9. Donnelly PK, Mobb G, Simpson AR, Veitch PS, Bell PRF (1992) A logical basis for age matching in organ transplantation: studies of recipient renal function in relation to donor age. Transpl Int 5 [Suppl 1]: 38–39
10. Feduska NJ Jr, Cecka JM (1994) Donor factors. In: Terasaki PI (ed) Clinical transplants 1994. UCLA Tissue Typing Laboratory, Los Angeles, pp 381–394
11. Hamilton D (1994) Kidney transplantation: a history. In: Morris PJ (ed) Kidney transplantation. Saunders, Philadelphia, pp 1–6
12. Harmon WE (1993) Pediatric renal transplantation (letter). Transplantation & Immunology, Letter published by the National Medical Information Network 9: 3, 15, 16
13. Hayes JM, Novick AC, Streem SB, Hodge EE, Bretan PN, Graneto D, Steinmuller DR (1988) The use of single paediatric cadaver kidneys for transplantation. Transplantation 45: 106–110
14. Higgins RM, Sheriff R, Bittar AA, Richardson AJ, Ratcliffe PJ, Gray DWR, Morris PJ (1995) The quality of function of renal allografts is associated with donor age. Transpl Int 8: 221–225
15. Hirata M, Terasaki PI (1994) Pediatric renal transplantation In: Terasaki PI (ed) Clinical transplants 1994. UCLA Tissue Typing Laboratory, Los Angeles, pp 395–402
16. Hume DM, Lee HM, Williams GM, White HJO, Ferré J, Wolf JS, Prout GR Jr, Slapak M, O'Brien J, Kilpatrick SJ, Kauffman HM Jr, Claveland RJ (1966) Comparative results of cadaver and related donor renal homografts in man, and immunologic implications of the outcome of second and paired transplants. Ann Surg 164: 352–395
17. Inglefinger JR, Grupe WE, Harmon WE, Fernbach SK, Levey RH (1981) Growth acceleration following renal transplantation in children less than 7 years of age. Pediatrics 68: 255
18. Kirste G, Blümke M, Krumme B, Pisarski P, Hauenstein KK, Farthmann EH (1994) A new operative technique of paratopic positioning of paediatric en bloc kidneys for transplantation. Clin Transplant 8: 139–143
19. Loirat C, Ehrich JHH, Geerlings W, Jones EHP, Landais P, Mallick NP, Margreiter R, Raine AEG, Salmela K, Selwood NH, Tufveson G, Valderrabano F (1994) Report on management of renal failure in children in Europe, XXIII, 1992. Nephrol Dial Transplant 9 [Suppl 1]:26–40
20. Maranes A, Herrero JA, Marron B, Marques M, Cruceyra A, Portoles J, Prats D, Sanchez-Fructuoso AI, Barrientos A (1998) Functional glomerular reserve in recipients of en bloc pediatric transplant kidneys. Transplantation 65: 677–680
21. Miles AMV, Sumrani N, John S, Markell S, Distant DA, Maursk V, Hong JH, Friedman EA, Sommer BG (1996) The effect of kidney size on cadaveric renal allograft outcome. Transplantation 61: 894–897
22. Modlin C, Novick AC, Goormastic M, Hodge E, Mastroianni B, Myles J (1996) Long-term results with single paediatric donor kidney transplants in adult recipients. J Urol 156: 890–895
23. Nghiem DD, Hsia S, Carpenter BJ, Chao SH, Marcus RJ, Palumbi MA, Paul CL, Kijanka BA, Breckenridge MA, Meleason DF, Schlosser JD, Lucke JF, Vu PT (1994) Renal transplantation at Allegheny General Hospital with special reference to the use of extreme-age cadaveric donors. In: Terasaki PI (ed), Clinical transplants 1994. UCLA Tissue Typing Laboratory, Los Angeles, pp 213–218
24. Opelz G for the Collaborative Transplant Study (1988) Influence of recipient and donor age in paediatric renal transplantation. Transpl Int 1: 95–98
25. Ploeg RJ, Visser MJT, Stijnen Th, Persijn GG, Schilfgaarde R van (1987) Impact of donor age and quality of donor kidneys on graft survival. Transplant Proc 19: 1532–1534
26. Programma Nazionale di Trapianto Pediatrico (1996) Attività della Consulta Nazionale. In: Attività donazione e trapianto di organi, Centro Riferimento Trapianti Emilia-Romagna, Resoconto1996, pp 103–104
27. Ruder H (1996) Nierentransplantation im Kindes-und Jugendalter. Monatsschr Kinderheilkd 144: 951–964
28. Sankari BR, Geisinger M, Zelch M, Brouhard B, Cunningham R, Novick A (1996) Post-transplant renal artery stenosis: impact of therapy on long-term kidney function and blood pressure control. J Urol 155: 1860–1864
29. Spencer RP, Rosenberg RJ, Schweizer RT (1998) Analysis of growth rate of pediatric kidneys transplanted into juveniles or adults. Growth Dev Aging 61: 111–117
30. Speybroeck J van, Feduska N, Amend W, Vincenti F, Cochrum K, Salvatierra O (1979) The influence of donor age on graft survival. Am J Surg 137: 374–377
31. Terasaki PI, Koyama H, Cecka JM, Gjertson W (1994) The hyperfiltration hypothesis in human renal transplantation. Transplantation 57: 1450–1454
32. Vliet JA van der, Cohen B, Kootstra G (1982) Transplantation of pediatric cadaver kidneys. Transplant Proc 14: 74–76
33. Vromen MAM, Leunissen KML, Persijn GG, Kootstra G (1988) Short- and long-term results with adult non-heart-beating donor kidneys. Transplant Proc 20: 743–745
34. Wetzels JFM, Hoitsma AJ, Koene RAP (1986) Influence of cadaver donor age on renal graft survival. Clin Nephrol 25: 256–259