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A logical basis for age matching in organ transplantation: studies of recipient renal function in relation to donor age

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The ever rising demand for renal transplantation has led to an increased use of older (> 50 years) organ donors [9]. Previous studies have shown that donor-to-recipient age difference is an independent risk factor for allograft survival [3]. A recent multicentre study of 6397 first cadaver renal transplants showed that, where donors are more than 5 years older than the recipient, there is significantly impaired graft survival [11]. The mechanism of this effect is unclear, but it has been suggested that age-related donor factors may influence subsequent graft function.

Pathological studies have shown that native kidneys acquire specific histological (i.e. glomerulosclerosis, interstitial fibrosis) and functional defects in a linear fashion related to increasing age [1, 5]. Whilst graft loss may be seen as the worst outcome from using older donors, impaired function leading to shortened half-life may also occur. Recipients of kidneys from donors > 50 years of age also have a significantly higher creatinine than those from donors < 50 years of age [3]. A study was therefore undertaken to investigate in greater detail the effect of age on the function of donor kidneys in their respective recipients.

Key words: Renal transplantation – Donor age – Kidney function

Patients and methods

Cadaver kidneys were harvested from 48 donors of mean age 36.4 (range 13–67) years. All donors had normal serum creatinine at the time of harvesting. The kidneys were transplanted to 48 recipients of mean age 43.4 (range 19–72) years. Immunosuppressive therapy for all patients consisted of cyclosporin at a starting dose of 17 mg/kg and prednisolone 2.0 mg/kg both tailed as previously described [10]. The patients had been previously transfused and dialysed. All patients had attained a stable level of renal function (serum creatinine below 300 μmol/l) between 6 weeks and 2 years post-transplantation. Further assessment of renal function was made by measuring creatinine clearance and glomerular filtration rate (GFR). Serum and urea concentrations of creatinine were measured on automated laboratory analysers which utilized the Jaffe reaction. GFR was measured using a single-injection isotope technique using ethylene diamine tetra-acetic acid (EDTA) labelled with ^{51}Cr [4].

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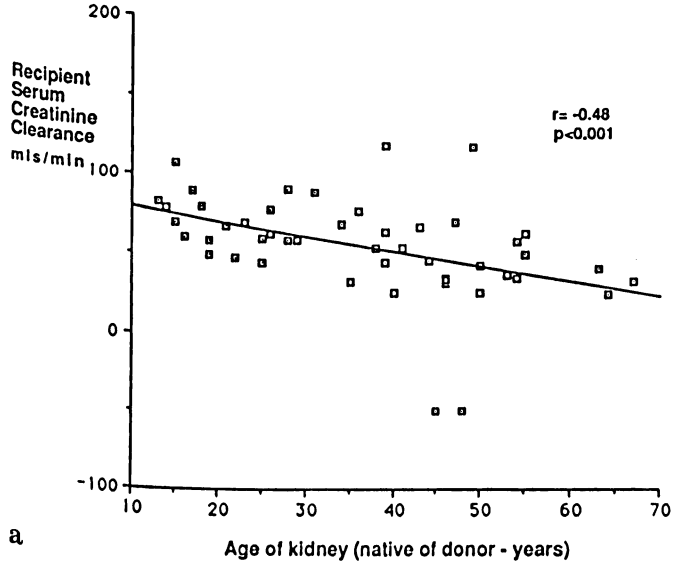
Results

Serum creatinine was found to be positively correlated ($r = 0.371$; $P < 0.01$) with donor age, whilst there was no correlation with recipient age or time post-transplantation. Creatinine clearance was significantly worse for kidneys taken from older donors ($r = -0.48$; $P < 0.001$) (Fig. 1 a) whilst there was no significant correlation with recipient age or time post-transplant. GFR was highly significant ($P = 0.0001$) and inversely correlated ($r = -0.527$) with donor age (Fig. 1 b). Recipient age was weakly correlated with GFR ($P < 0.05$) consistent with some matching of older donors to recipients (i.e. within 5 years of age for 13% of the recipients).

Discussion

Previous physiological studies have established that native kidneys show decreasing functional reserve with increasing age [1]. GFR has been shown to decrease linearly from 130 to 80 ml/min in the age range 30–80 years, equivalent to 13 ml/min per decade. Assuming both kidneys contribute equally to the GFR a single normal kidney (not allowing for hyperfiltration) would expect a loss of GFR of 6.5 ml/kidney per decade. The actual loss of GFR in the transplant kidneys was equivalent to 5.7 ml/kidney per decade. It would appear that the transplant kidney has less function for a particular age of donor than would be expected in the native kidney. For example, a 40-year-old patient with a single native kidney would on average expect a GFR of at least 60 ml/min whereas a transplant patient with a kidney from a 40-year-old donor would expect a GFR of only 45 ml/min.



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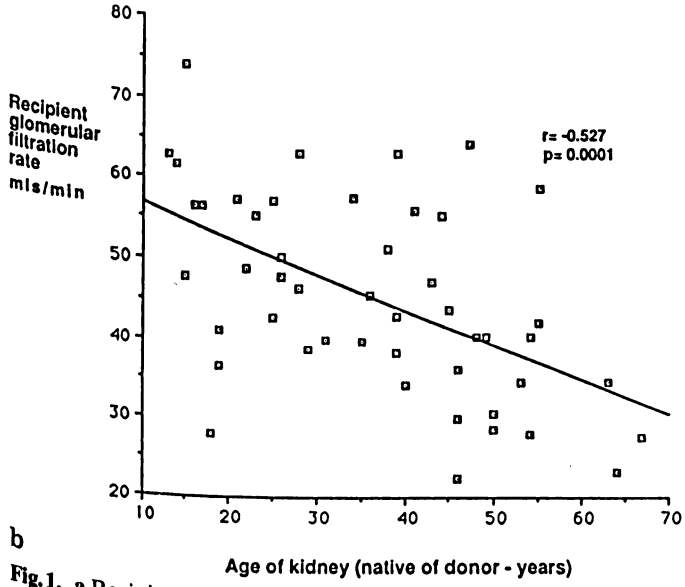

b

Fig. 1. a Recipient creatinine clearance and age of donor kidney. b Recipient glomerular filtration rate and age of donor kidney

At present kidneys are shared almost exclusively on the basis of 'ageless' HLA matching in which kidneys are assumed to be functionally equivalent provided serum creatinine is normal at the time of retrieval. This study confirms the view that if native kidneys conceal a significant age-related defect of function the same will apply to cadaveric organ recipients. The whole process of retrieval and transplantation seems to further reduce the reserve of the kidney [7]. Whilst the live donor situation provides an opportunity to select the donor organ on the basis of functional studies the same is not true of cadaver organs. Clearly the donor creatinine may mask significant defects and, although there is a large individual range of GFR results, the donor age would seem to be a reasonable predictor of functional reserve [8]. At present donor age is not implicated in long-term graft loss which is largely attributed to chronic rejection. This is despite the fact that the half-life of kidneys from donors of 55–69 years of age is only 4.7 years compared with 8 years for donors of 11–24 years of age [6]. Since the histological differentiation of the two processes is by no means precise it would seem wise not to transplant old donor organs to young patients [3, 9]. Multicentre data suggest that a recipient's immune response decreases with advancing age [12], and it would seem logical to take advantage of the favourable immune environment of an older recipient to place an older kidney, which would potentially require less toxic immunosuppressive therapy [2] and possibly be less prone to damaging rejection. Given the rising transplant waiting lists older donor organs should perhaps be offered more frequently to recipients of comparable age.

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