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Outcome of machine-perfused non-heart-beating donor kidneys, not allocated within the Eurotransplant area

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Abstract Eleven non-heart-beating (NHB) donor kidneys considered vital during machine perfusion (MP), could not be allocated inside Eurotransplant (ET). With the help of ET, five kidneys were transplanted in Karachi and six in Basel. Our goal was to prove that NHB kidneys successfully passing MP viability tests can be transplanted safely. *Methods*: Donor age, serum creatinine (some post-mortem) and warm ischaemic time were, respectively, (mean and range): 44 (14–70) years, 137 μmol/l, and 44 (9–80) min. Reasons for refusal were: bold ureter (one), suboptimal flush (one), relatively long hypotensive phase (seven), and donor age of 70 years (two). After 8 h of MP, mean lactate dehydrogenase, intrarenal resistance and alpha glutathione S-transferase were (including range): 556 U/l (range 366–819 U/l), 0.86 mmHg/ml per min (0.41–1.15 mmHg/ml per min) and 1188 μg/l (575–2677 μg/l), respectively. Mean cold ischaemic time was 45 (range 28–72) h. *Results*: Two kidneys showed immediate function, and nine showed delayed function. Mean creatinine levels after 1, 3 and 6 months were 295, 200 and 206 μmol/l, respectively. Four patients died for reasons not related to their kidney transplantation. *Conclusions*: We claim that MP can successfully assess viability of NHB donor kidneys. The reluctance to accept MP, and judged vital, NHB donor kidneys is no longer justified.

Key words Non-heart-beating · Donor kidney · Machine perfusion · Viability assessment · Kidney transplantation · αGST

Introduction

For most patients with end-stage renal disease a kidney transplant is the ultimate treatment. Owing to the limited number of brain-dead donors available, the waiting list for a kidney transplant is still increasing rapidly [1].

For this reason our centre has now been focusing on non-heart-beating (NHB) donors for over a decade. The use of NHB donors can easily increase the total number of transplants by over 30% on a yearly basis [2–4]. Kidneys of NHB donors inevitably sustain warm ischaemic damage (WIT) to a certain extent. Consequently pretransplant viability assessment is crucial to prevent nonviable transplants [5, 6]. For this reason we reintroduced a machine perfusion (MP) programme for NHB kidneys in 1993. Besides being a superior method of preserving ischaemic-damaged kidneys, it offers the opportunity of viability assessment.

New viability tests are currently being developed and implemented rapidly in MP programmes. For instance alpha glutathione S-transferase (αGST), an enzyme specific for proximal tubular cells within the kidney, has been shown to be able to separate viable from nonviable kidneys retrospectively [7, 8].

The goal of this study was to prove that the reluctance to accept NHB kidneys, judged vital during MP, is no longer justified.

Materials and methods

Four categories of NHB donors have been recognized [9]. Most kidneys are procured from category II (unsuccessful resuscitation) and category III (awaiting cardiac arrest) NHB donors. Because the quality of kidneys from NHB donors is often compromised, strict donor criteria have been defined. The most important criteria in our centre are a maximum donor age of 65 years and a maximum WIT of 30 min. If professional cardiac massage and artificial ventilation are applied another 2 h of WIT is accepted.

After declaration of death and consent of the donor family has been obtained, an in-situ preservation (ISP) procedure is performed instantly in order to minimize the WIT [10]. However, before the ISP is started a period of 10 min of "no-touch" is respected in order to comply with the dead donor rule [11]. Heparin and phentolamine are administered at doses of 25000 IU and 0.1 mg/kg, respectively, in order to prevent thrombosis and vasoconstriction. The ISP procedure is performed with a double balloon triple lumen (DBTL) catheter (AJ 6516 Porges, France) inserted into the aorta. The kidneys are flushed and cooled with at least 15 l of histidine tryptophan ketoglutarate.

After donor nephrectomy, every NHB kidney is put in a Gambro PF-3B pulsatile perfusion machine which has been slightly modified and is primed with 0.5 l Belzer's UW solution (based on hydroxyethyl starch) [12]. The kidney is continuously perfused at 4 °C with an initial systolic pressure of 60 mmHg, set by flow regulation. Intrarenal resistance (IRR) is calculated from the pressure, flow and kidney weight at 0, 1, 2, 4, 6 and 8 h after the start of MP. At the same times samples of perfusate are collected to measure pH and concentration of the enzymes lactate dehydrogenase (LDH) and αGST.

During 1995 and 1996, 66 out of 90 NHB kidneys tested during MP were considered vital. Of these kidneys, 11 (16.6%) could not be allocated within the Eurotransplant (ET) area. Four kidneys were procured from category II donors and seven from category III donors. The mean donor age was 44 years (range 14–70 years) and the mean first WIT was 44 min (range 9–80 min). Mean serum creatinine was 137 μmol/l, but blood was predominantly collected post-mortem through the DBTL catheter. All kidneys showed excellent MP test results. The mean IRR, LDH and αGST 8 h after the start of MP were, respectively, (including range): 0.86 mmHg/ml per min (0.41–1.15 mmHg/ml per min), 556 U/l (366–819 U/l) and 1188 μg/l (575–2677 μg/l). (All results are expressed per 100 g kidney weight.)

Donors of six kidneys had a blood group relatively uncommon within the ET area: ABpos (three) and Bpos (three). Reasons for nonallocation within the ET area were: long hypotensive period (seven), macroscopic suboptimal flush (one), bald ureter (one) and donor age of 70 years (two). With the help of ET, six kidneys were allocated to Basel, Switzerland, and five to Karachi, Pakistan. The mean age of the 11 recipients was 46 years (range 20–66 years). All except one received a first graft. The immunosuppressive protocol was similar for all recipients: cyclosporin A, azathioprine, steroids and antithymocyte globulin. Mean cold ischaemic time (CIT) was 45 h (range 28–72 h).

Results

Two kidneys gave immediate life-sustaining function, and nine showed delayed function (DF). An average of 9 (range 1–15) dialysis sessions was needed during 24 (range 3–50) days. Nonfunction was not observed. The mean serum creatinine levels 1, 3 and 6 months post-transplant were, respectively, (including range): 295 (94–606), 200 (61–325) and 206 (76–332) μmol/l.

Four patients died for reasons not directly related to their kidney transplant at an average of 103 days after operation from pneumonia (two), multiorgan failure due to sepsis (one) and pulmonary embolism (one).

Discussion

Different approaches towards solving the shortage of donor kidneys have been tried. Living-related and -unrelated donation provide excellent transplant results as a result of limited CIT and optimal preparation of the donor and recipient [13, 14], However, not all patients on dialysis have a spouse or relative willing or able to part with a kidney. Also, there is an increasing tendency towards using kidneys from so-called "nonideal donors". Because of improved immunosuppressive agents, transplant results using kidneys from paediatric and hypertensive donors are good [15]. Studies of the outcome of transplantation using kidneys from donors over 60 years of age show contradictory results [15, 16]. Transplantation of both renal grafts of an older donor into one recipient may provide a solution to this problem [17]. Although important, these attempts can only make a minor contribution to decreasing the organ shortage.

For two reasons, centres both within and outside Europe are considering reintroducing an MP programme, or have already started such a programme. Besides allowing viability assessment of NHB kidneys, reducing DF in "heartbeating" donor kidneys is another important advantage of MP [18, 19]. DF is known to have a deleterious effect on graft survival, at least partly owing to a higher percentage of acute rejection episodes, which are moreover difficult to diagnose [20].

A high percentage of DF in NHB kidneys has until now been almost inevitable [21]. Given the tremendous organ shortage, we have little choice but to accept this. Continuous careful evaluation of donor acceptance criteria, however, remains important. Since the number of functional glomeruli is known to diminish with age and older donors often suffer from arteriosclerosis and hypertension, it is reasonable to be critical in accepting older NHB donors with a long WIT. Another reason is that viability testing, although fairly accurate in assessing ischaemic damage, cannot properly analyse damage related to ageing. The high percentage (82%) of DF in the small group described in this study might have been less with a reduced CIT. Because DF is known to increase significantly with CIT [20], it may be especially useful for a NHB kidney to be transplanted locally, even though machine perfused. Serum creatinine levels

were still raised 6 months posttransplant in our study. However, it is possible that creatinine levels improve for over a year after transplant, especially with younger donor kidneys [22].

The use of new immunosuppressive agents, such as FK506 which has resulted in 15% fewer acute rejection episodes, will possibly have beneficial effects on NHB kidney transplant results [23]. Giving the first dose of immunosuppressive drugs known to be nephrotoxic, such as cyclosporin A and FK506, a few days after transplantation instead of on day 1, may prove to have a beneficial effect on graft survival, immediate function and initial diuresis [24].

The decision to accept or refuse a deceased patient as a suitable NHB donor should always be based on multiple parameters. In particular, donor age, WIT and previous medical history are of great importance. The decision to transplant or discard MP NHB kidneys is also a multifactorial process. MP test results are clearly of great importance, but also the macro- and microscopic appearance of the kidney should not be disregarded. An NHB donor kidney considered suitable for transplantation based on all these parameters should not be withheld from a dialysis patient. This would be an unwarranted and expensive mistake, denying the patient a better quality of life.

References

1. DeMeester J (1995) Kidney: donation, waiting lists and transplants. In: Cohen B, Persijn GG, DeMeester J (eds) Eurotransplant International Foundation, Annual Report 1995. Eurotransplant Foundation, Leiden, pp 25–30
2. Daemen JH, Wit RJ de, Bronkhorst MW, et al (1996) Non-heart-beating donor program contributes 40% of kidneys for transplantation. Transplant Proc 28: 105–106
3. Varty K, Veitch PS, Morgan JD, et al (1994) Kidney retrieval from asystolic donors: a valuable and viable source of additional organs. Br J Surg 81: 1459–1460
4. Daemen JHC, Oomen APA, Kelders WPA, et al (1997) The potential pool of non-heart-beating kidney donors. Clin Transplant 11: 149–154
5. Kootstra G (1997) The asystolic, or NHB, donor. Transplantation 63: 917–921
6. Daemen JH, Heineman E, Kootstra G (1995) Viability assessment of non-heart-beating donor kidneys during machine preservation. Transplant Proc 27: 2906–2907
7. Daemen JW, Oomen AP, Janssen MA, et al (1997) Glutathione S-transferase as predictor of functional outcome in transplantation of machine-preserved non-heart-beating donor kidneys. Transplantation 63: 89–93
8. Kievit JK, Oomen APA, Janssen MA, et al (1997) Viability assessment of non-heart-beating donor kidneys by alpha glutathione S-transferase in the machine perfusate. Transplant Proc 29: 1381–1383
9. Kootstra G, Daemen JH, Oomen AP (1995) Categories of non-heart-beating donors. Transplant Proc 27: 2893–2894
10. Heineman E, Daemen JH, Kootstra G (1995) Non-heart-beating donors: methods and techniques. Transplant Proc 27: 2895–2896
11. Arnold RM, Youngner SJ (1995) The dead donor rule: should we stretch it, bend it, or abandon it? In: Arnold RM, Youngner SJ, Shapiro R (eds) Procuring organs for transplant. The debate over non-heart-beating cadaver protocols. Johns Hopkins Press, Baltimore, pp 219–234
12. Hoffmann RM, Stratta RJ, D'Alessandro AM, et al (1989) Combined cold storage-perfusion preservation with a new synthetic perfusate. Transplantation 47: 32–37
13. Lowell JA, Brennan DC, Shenoy S, et al (1996) Living-unrelated renal transplantation provides comparable results to living-related renal transplantation: a 12-year single-center experience. Surgery 119: 538–543
14. D'Alessandro AM, Sollinger HW, Knechtle SJ, et al (1995) Living related and unrelated donors for kidney transplantation. A 28-year experience. Ann Surg 222: 353–362
15. Shapiro R, Vivas C, Scantlebury VP, et al (1996) "Suboptimal" kidney donors: the experience with tacrolimus-based immunosuppression. Transplantation 62: 1242–1246
16. Frutos MA, Cardona JG, Gonzalez Molina M, et al (1996) Renal transplantation from nonideal donors. Transplant Proc 28: 3406–3407
17. Johnson LB, Kuo PC, Schweitzer EJ, et al (1996) Double renal allografts successfully increase utilization of kidneys from older donors within a single organ procurement organization. Transplantation 62: 1581–1583
18. Koning OHJ, Ploeg RJ, Bockel H van, et al (1997) Risk factors for delayed graft function in cadaveric kidney transplantation. Transplantation 63: 1620–1628
19. Light JA, Gage F, Kowalski AE, et al (1996) Immediate function and cost comparison between static and pulsatile preservation in kidney recipients. Clin Transplant 10: 233–236
20. Ojo AO, Wolfe RA, Held PJ, et al (1997) Delayed graft function: risk factors and implications for renal allograft survival. Transplantation 63: 968–974
21. Daemen JHC, Vries B de, Oomen APA, et al (1997) Effect of machine perfusion preservation on delayed graft function in non-heart-beating donor kidneys – early results. Transplant Int 10: 317–322
22. Wijnen RM, Booster MH, Stubenitsky BM, et al (1995) Outcome of transplantation of non-heart-beating donor kidneys. Lancet 345: 1067–1070
23. Pirsch JD, Miller J, Deierhoi MH, et al (1997) A comparison of tacrolimus (FK506) and cyclosporine for immunosuppression after cadaveric renal transplantation. FK506 Kidney Transplant Study Group. Transplantation 63: 977–983
24. Barber WH, Hudson SL, Deierhoi MH, et al (1990) Pulsatile perfusion preservation: early posttransplant dialysis requirement predicts rapid graft loss. Transplant Proc 22: 446–447