

Assessment of donors with sub-optimal kidney function/structure

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GUIDELINES

No recommendations possible based on Level I or II evidence

SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

- Procurement of renal allografts from extended criteria donors should continue to be actively pursued.
- Assessment of such potential renal allografts should take into account donor factors, issues at the time of procurement, plus the result of a pre-implantation renal allograft biopsy.
- Use of extended criteria donors' renal allografts should only be in the setting of recipient informed consent, weighing up the risks versus benefits.
- The decision to accept a deceased donor as suitable for renal donation is the responsibility of both nephrologists and renal surgeons experienced in renal transplantation.
- The approach to a deceased organ donor should be to consider age, renal function and renal structure, other co-morbidities, to categorise the kidneys into optimal or marginal.
- Extended criteria donor (ECD) kidneys are those which after transplantation, lead to a significantly worse outcome as defined by poor graft survival or inferior renal function.
- The predominant features of ECD kidneys are reduced donor renal function and/or structural abnormality.
- These kidneys are usually procured from donors with cumulative effects of the following characteristics: age > 55 years, pre-existing hypertension, diabetes mellitus, history of vascular disease, elevated or rising serum creatinine, history of systemic disease or medications known to affect the kidneys, and non-heart-beating donor.

- **Assessment of ECD kidneys should include surgical assessment at procurement with particular note of renal size, presence of scars/masses, vasculature, and organ perfusion.**
- **Assessment of renal function is by estimated creatinine clearance using the best admission serum creatinine.**
- **Histological assessment of procurement needle biopsy is by taking particular note of percentage glomerulosclerosis, arteriolar disease and interstitial fibrosis. Any identified lesion should also be biopsied.**
- **Assessment of ECD kidneys should determine whether the kidney is acceptable for single transplantation. If not, a decision should be made to determine whether the kidneys are suitable for double transplantation. Double transplantation should not be considered unless the donor creatinine clearance is < 80 mL/min, and the percentage glomerulosclerosis is 20%–40%, or severe vascular disease is present. Organs not transplanted should be managed according to the wishes of the family and or the requirements of the coroner.**

Allocation Issues

- **Attention should be made to minimising the cold ischaemic time of ECD kidneys.**
- **Non-heart–beating donor kidneys and dual transplants should be allocated within the state of donation.**
- **There is conflicting evidence on the value of allocating ECD kidneys to either younger or older recipients.**
- **Education regarding the possibility of transplantation with an ECD or dual transplant including the risks and benefits of the procedure should be a prerequisite of entry onto the transplant waiting list. Recipients of ECD or dual kidneys must give specific informed consent prior to transplantation.**
- **Kidneys from paediatric donors < 15 kg and/or < 5 years should be considered for en-bloc transplantation.**
- **Beware of inotropes and either microscopic haematuria (dysmorphic red cells) or proteinuria in the donor.**
- **Radiological means of assessing donor kidneys prior to procurement may be of limited benefit.**
- **Backtable biopsy preferably involves a needle biopsy (not wedge biopsy) through the upper pole cortex.**

Background

There remains an imbalance between the number of deceased donor kidneys available on a per annum basis for transplantation versus the number of potential recipients on the renal transplant waiting list (ANZDATA 27th Annual Report 2004).

To help deal with this imbalance, transplantation of renal allografts from deceased donors (who have factors that have been identified as being associated with an increased risk for graft failure) has been pursued both within Australia and internationally.

Despite the increased risk of graft failure, data has emerged more recently showing that transplantation of renal allografts from extended criteria donors (ECD), if successful, may confer a survival advantage over that of the potential recipients remaining on dialysis (Ojo et al 2001).

Search strategy

Databases searched: MeSH terms and text words for kidney transplantation and cadaveric organs were combined with MeSH terms and text words for diabetes, hypertension, viruses, bacterial infections, non-heart beating, marginal donor, paediatric donor, aged donor, and donor with prior cancer. These were then combined with the Cochrane highly sensitive search strategy for randomised controlled trials and search filters for identifying prognosis and aetiology studies. The search was carried out in Medline (1966 – November Week 2 2003). The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline.

Date of searches: 12 December 2003.

What is the evidence?

There are no randomised controlled trials reported in the literature for this topic. All the evidence comes from individual centre reports and registry reports (Level III/IV). This remains essentially unchanged from the last review, however, increasing interest in this area particularly in the US, should see more information come through over the next 2–3 years.

Summary of the evidence

Outcome with ECD renal allografts

All of this evidence comes from Registry reports along with some centre reports. The recent evidence is summarised in Table 1. It is clear that donor age > 55 years of age impacts on allograft survival, along with a history of prolonged donor hypertension, history of prolonged donor diabetes mellitus, and a prolonged cold ischaemic time (> 36 hours) (Matas & Delmonico 2001). Older recipient age may also impact on allograft outcome. Oliguria (< 20 mL/hour) in the donor without hypotension, may impact on primary renal allograft survival (ANZDATA 21st Annual Report 1998). The

results for paediatric donors supports the use of en-bloc transplantation from deceased donors aged 0–5 years and body weight < 15 kg). The results for deceased donor DUAL kidneys remain mixed, with varying donor criteria being used to decide on proceeding to DUAL transplantation.

Use of allograft biopsy

Evidence comes from centre reports, all of which are retrospective analyses. There is marked variation in what parameters (both donor and recipient) have been looked at and analysed, between the reports, hence making it difficult to come up with firm recommendations. However, there is increasing evidence that not only the presence of glomerulosclerosis (GS), but also evidence of interstitial fibrosis, tubular atrophy, and arteriosclerosis may impact on allograft outcome. There is marked variation between centres with respect to the use of allografts versus discardment if > 20% GS is present (Table 2). In two reports, an attempt has been made to limit cold ischaemic time in allografts with > 20% GS, in order to help influence outcome (Lu et al 2000; Di Paolo et al 2002). Further long-term follow-up studies are required with respect to this issue.

Discardment

It is important not only to know what the outcome is with the use of ECD renal allografts but also to know what the precise factors are leading to the discardment of renal allografts. Australia has a relatively low rate of discardment of deceased donor organs (including for biopsy abnormality) (Table 3). Discardment data are not always well documented in published reports.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative: No recommendation.

British Transplant Authority: No specific guidelines with respect to extended criteria deceased donors. The BTA has published ‘Standards for Solid Organ Transplantation in the United Kingdom (2003)’. Available at: <http://www.bts.org.uk/standards%20document%20edition%202%20-%20final.pdf>

Canadian Society of Nephrology: No recommendation.

Transplant Society of Australia & New Zealand: There is a section on ‘marginal donors’ in its Australian National Organ Allocation Protocols which are available at: <http://www.racp.edu.au/tsanz>. The National Organ Allocation Protocols are revisited on a regular basis.

The United Network for Organ Sharing: This group has a policy outlining the definition of expanded criteria organ donors (ECD) versus ideal donors (policy 3.5.1) available via the UNOS web site at: www.unos.org/policiesandbylaws/policies/pdfs/policy_70.pdf

The Expanded Kidney Donor: the decision matrix using the relative risk of graft failure > 1.7 for donors older than 50 years of age, as shown, are now the UNOS

approved expanded criteria by which kidney donors are defined as expanded and placed in the expedited system.

Donor condition	Donor age categories (yr)				
	< 10	10–39	40–49	50–59	≥ 60
CVA + HTN + Creat > 1.5				X	X
CVA + HTN				X	X
CVA + Creat > 1.5				X	X
HTN + Creat > 1.5				X	X
CVA					X
HTN					X
Creatinine > 1.5					X
None of the above					X

X = Expanded Criteria Donor, CVA = CVA was cause of death, HTN = history of hypertension at any time, Creat > 1.5 = creatinine > 1.5 mg/dL

The background to how this policy was developed and adopted is outlined in a report by Rosengard et al (2002).

All patients who have agreed to receive an expanded criteria donor kidney, have an ABO blood type that is compatible with the donor, and who are listed as active on the UNOS Patient Waiting List, will be assigned points and priority according to UNOS policy 3.5.12.

UNOS also has a Double Kidney Allocation policy (3.5.7).

Eurotransplant International Foundation: Donors with vascular disease, diabetes and malignancies are excluded. Available at: www.transplant.org/?id=kidney

European Renal Association–European Dialysis and Transplant Association Guidelines:

D. Relative contra-indications against organ donation are based on the quality of the potential graft and include suboptimal to non-acceptable renal function or presence of risk factors. It is recommended that each procurement centre formulates its standards and follow up on the effects of their implementation. (Evidence level C)

E. The aim of the procurement team should be to increase the acceptance rate of potential donors without risking unacceptably poor graft function and survival. (Evidence level C)

F. At this time and in the absence of a 'gold standard' it is recommended that donors be evaluated on the basis of renal function (calculated creatinine clearance, CrCl),

age and vascular disease. Limits may be set as CrCl > 60 ml/min as acceptable, 50–60 ml/min as marginal and < 50 ml/min as non-acceptable for single kidney transplantation. Non-acceptable kidneys may be considered for dual transplantation. High donor age (70+) and vascular risk factors such as long-term history of hypertension, severe vascular disease, long-term diabetes or proteinuria, or findings of vascular changes or extensive glomerular sclerosis on procurement biopsy may add negatively to the evaluation. (Evidence level B)

G. Recipients of sub-optimal kidneys or dual kidneys should have given their informed consent prior to transplantation. (Evidence level C)

Available at: http://ndt.oxfordjournals.org/cgi/reprint/15/suppl_7/39

Implementation and audit

- 1 All State/Territory & New Zealand Organ Procurement Agencies need to be aware of the CARI Deceased Kidney Donor Suitability guidelines.
- 2 All State/Territory & New Zealand Organ Procurement Agencies should consider developing and implementing protocols for procurement biopsy of ECD kidneys.
- 3 Consideration should be given by all State/Territory & New Zealand Organ Procurement Agencies to performing an annual audit of the number of ECD kidneys procured on a per annum basis, versus the number of ECD kidneys not procured or discarded. Results of such audits should be compared to published international benchmarks.

Suggestions for future research

- 1 Prospective data collection by State/Territory Organ Procurement Agencies to include data from pre-implantation/donor procurement biopsy results. This data could be provided to ANZODR for future audit/data analysis.
- 2 Assessment of NIDDM deceased donors could be conducted.
- 3 Outcome data on non-heart-beating donors could be specifically analysed by ANZDATA.
- 4 Ongoing analysis of renal allograft recipient outcome (ANZDATA) for known ECD factors impacting on renal allograft outcome could be conducted.

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Appendices

Table 1. Outcome of marginal renal allografts

Allograft Survival	Authors/Registry	Number	Time Period
5 yr allograft survival 53% (vs 67% ideal)	Ojo (USRDS/SRTR)	7454*	1992–1998
Actuarial allograft survival donors aged < 55 yrs higher at 1,2,3 yrs vs for donors 55+ (p < 0.0001) Older donors with hypertension > 10 yrs had lower allograft survivals -graft survival less if donor > 55 yrs + estimated creatinine clearance < 80 mL/min (NB: mean CI [†] = 22 hrs)	Carter (UNOS)	4732/33,595	1994–1998
Recipient of 0 HLA mismatch allografts & > 36 hrs CI, had no allograft survival advantage at 5 yrs vs recipients of 1 or more HLA mismatched allografts	Lee (SRTR)	63,688	1/1990–7/1998
Donor age > 60 yrs, older recipient age associated with inferior renal allograft outcome at 3 yrs	Morris (UKTSSA)	6363 (> 50% exclusion)	1986–1993
Only independently significant findings in Cox Regression Analysis – high donor/ recipient age ratio > 1.10 impacted on graft survival	Swanson (USRDS)	20,306 Adult donors	7/1994–6/1998

The CARI Guidelines – Caring for Australians with Renal Impairment

<p>3-yr allograft survivals 71% in affected donor organs vs 75% in controls</p> <p>Duration donor hypertension (> 10 yrs) is independent factor for graft survival</p>	<p>Ojo (USRDS)</p>	<p>25,039</p>	<p>7/1994–6/1997</p>
<p>Mean glomerulosclerosis on procurement was 16 ± 13%</p> <p>Mean CI 29 hr in recipients with DGF[‡] vs 22 hr in recipients without DGF (DGF impacted on 1 & 5 yr graft survival)</p> <p>1-yr graft survival 86%, 5-yr graft survival 69%</p>	<p>Alfrey (DUAL)</p>	<p>287</p>	<p>1994–2001</p>
<p>Renal allograft survival better for en-bloc kidneys (751) vs single kidney donors (n = 1447) aged 0-5 yrs</p>	<p>Bresnahan (UNOS)</p>	<p>12,838 Paediatric donors</p>	<p>1988–1995</p>

* Donor age > 55 yrs, non-heart-beating donor, CI > 36 hr, donor hypertension or donor diabetes mellitus > 10 yr duration; [†] CI = cold ischaemia time; [‡] DGF = delayed graft function

Table 2. Summary of the literature – biopsy of renal allografts

Results	Source	Donors	Year	Other
<p>Increased donor age associated with increased GS*/tubular atrophy/arteriosclerosis</p> <p>Interstitial fibrosis associated with worse outcome at 6 months</p> <p>Relationship between histological parameters imperfect</p>	Rhandawa et al	Deceased (n=78)	Not known	<p>Discard if > 30% GS</p> <p>Do not transplant if > 20% GS</p> <p>Mean CI = 30.6 hr</p> <p>Did not analyse for DGF[†]</p>
<p>Donor vessel score 3/3 associated with 100% incidence</p> <p>DGF and mean serum creatinine at 1 yr = 275 µmol/L</p>	Karpinski et al	Deceased (n=34)	1994–97	<p>Used donor renal pathology scores</p> <p>Biopsy protocol</p> <p>Discard if > 20% interstitial fibrosis</p> <p>Also discard if vascular disease</p>
<p>Allografts with DGF had significantly > GS and tubular atrophy/interstitial fibrosis/vascular disease on biopsy</p> <p>Histology score donor kidney alone did not influence allograft function at 1 yr</p>	Di Paolo et al	Deceased (n=60)	Not stated	<p>Discard if > 30% GS</p> <p>Donor hypertension independently associated with DGF</p> <p>Allocated > 55 yr old donor allografts to recipient > 45 yr only</p> <p>Mean CI = 12 hr</p>

81/210 allografts GS, range 1-60%	Escofet et al	210 allografts (implantation biopsy)	?	%GS correlated with allograft function at 1 and 4 yr %GS correlated with allograft function at 4 yr (multivariate) 5 yr allograft survival 35% if GS > 20%
17 allografts GS > 20% (actuarial 5 yr graft survival 35%) 69% donors aged > 55 yr had GS 0-10%				
Creatinine significantly higher in recipients with moderate vasculopathy vs none up to 2 yr post transplant	Lu et al	89 allografts	1995–98	CI = 14 hr if > 20% GS vs 19 hr if < 20% GS and 22 hr if no GS

* GS = glomerulosclerosis, † DGF = delayed graft function

Table 3. Discardment of potential renal allografts

% RA discarded	Years	Source	Donors
1–5.5% (Aust)	1995-2002	ANZOD Report 2003	All deceased
5–11% (USA)	1990-1999	Chang et al 2003 (US SRTR Registry data)	All deceased
10–21% (Spain)	1989-1999	Chang et al 2003 (Spain ONT data)	All deceased
8% (Aust)	1990-1997	Verran et al 2001 (NSW data)	Deceased > 55 yr