

Renal transplantation using non-heart-beating donors: a potential solution to the organ donor shortage in Canada

Julie D. Lacroix, BSc(OT);* John E. Mahoney, MD, MSc;† Greg A. Knoll, MD, MSc‡

Introduction: There is a chronic shortage of cadaveric organ donors for renal transplantation, which might be solved by the use of non-heart-beating donors (patients who suffer cardiac arrest and whose kidneys are harvested subsequently when irreversible heart and respiratory function occur). We carried out a chart review to determine whether the renal transplantation rate would improve if a non-heart-beating donor program was introduced at a Canadian centre. **Methods:** We reviewed the charts of all 1547 patients who died in the emergency department or intensive care unit of the Ottawa Hospital, a tertiary care centre serving 1.2 million people in eastern Ontario, between January 1999 and May 2001. The number of potential non-heart-beating donors was determined by the use of predefined criteria. The number of additional kidneys that could be obtained with a non-heart-beating donor program was estimated and compared to the actual number of kidneys procured from conventional brain-dead donors during the same period. The potential increase in the renal transplantation rate was calculated. **Results:** There were 83 potential non-heart-beating donors during the 29-month study period. The mean (and standard deviation) age of the donors was 40.6 (13.1) years, and 20% were female. The mean serum creatinine value was 75 (29) $\mu\text{mol/L}$; 44.6% of donors died secondary to trauma. We estimated that the use of non-heart-beating donors would have provided 14 to 41 additional donors during the study period (12–34 kidneys/yr). The cadaveric renal transplantation rate would have increased between 30% and 87%. **Conclusion:** The cadaveric renal transplantation rate could improve significantly if non-heart-beating donors were used in Canadian hospitals.

Introduction : On pourrait résoudre la pénurie chronique de donneurs d'organes de cadavre pour les transplantations rénales en recourant à des donneurs à cœur arrêté (patients en état d'arrêt cardiaque dont les reins sont prélevés par la suite lorsqu'il se produit une défaillance irréversible de la fonction cardiaque et respiratoire). Nous avons procédé à une étude de dossiers dans un centre canadien pour déterminer si la mise en œuvre d'un programme de donneurs à cœur arrêté améliorerait le taux de transplantations rénales. **Méthodes :** Nous avons étudié les dossiers des 1547 patients morts à l'urgence ou aux soins intensifs à l'Hôpital d'Ottawa, centre de soins tertiaires desservant 1,2 million de personnes dans l'est de l'Ontario, entre janvier 1999 et mai 2001. On a calculé le nombre de donneurs à cœur arrêté possibles en utilisant des critères prédéfinis. On a calculé le nombre de reins supplémentaires qu'il serait possible de prélever après avoir mis en œuvre un programme de donneurs à cœur arrêté et on l'a comparé au nombre réel de reins prélevés de donneurs conventionnels en état de mort cérébrale au cours de la même période. On a calculé l'augmentation possible du taux de transplantations rénales. **Résultats :** Il y a eu 83 donneurs à cœur arrêté possibles au cours de la période d'étude de 29 mois. L'âge moyen (et l'écart type) des donneurs s'établissait à 40,6 (13,1) ans et 20 % étaient des femmes. La valeur moyenne de la créatinine sérique était de 75 (29) $\mu\text{mol/L}$; 44,6 % des donneurs sont morts des suites d'un traumatisme. Nous avons calculé que le recours aux donneurs à cœur arrêté aurait produit de 14 à 41 donneurs supplémentaires pendant la période à l'étude (12–34 reins/année). Le taux de transplantation de reins de cadavre aurait augmenté dans une proportion de 30 % à 87 %. **Conclusion :** Le taux de transplantation de reins de cadavre pourrait s'améliorer considérablement si les hôpitaux de Canada utilisaient des donneurs à cœur arrêté.

From the *Faculty of Medicine, the †Division of Urology, Department of Surgery, and the ‡Division of Nephrology, Department of Medicine, University of Ottawa, Ottawa, Ont.

Accepted for publication Apr. 29, 2003.

Correspondence to: Dr. John E. Mahoney, Division of Urology, Ottawa Hospital — General Campus, 501 Smyth Rd., Ottawa ON K1H 8L6; fax 613 737-8982; jmahoney@ottawahospital.on.ca

The prevalence of end-stage renal disease (ESRD) has increased steadily since 1981.¹ It has been estimated that 32 952 Canadians will need treatment for ESRD by 2005.² The preferred treatment for ESRD is renal transplantation, which prolongs survival, enhances quality of life and is less costly than dialysis.^{3,4}

Despite the demonstrated benefit of renal transplantation, only 41% of Canadians with ESRD have a functioning kidney transplant, and this proportion has gradually declined since 1988.¹ This reflects the growing rate of ESRD and the relatively static number of cadaveric organ donors.¹ Since 1989, the number of Canadians on a waiting list for a kidney transplant has more than doubled,¹ but the number of cadaveric kidneys transplanted has remained essentially unchanged.¹

A potential solution to the cadaveric donor shortage is the use of non-heart-beating organ donors.⁵ A non-heart-beating donor is defined as one who first sustains cardiorespiratory arrest; organs are retrieved after irreversible cessation of cardiac and respiratory function.⁶ Death in this case is based on cardiac criteria.⁶ In contrast, a conventional heart-beating donor is one who sustains irreversible brain injury, and death is based on neurologic criteria.⁶ The concept of non-heart-beating organ donation is not new. In the early days of transplantation all cadaveric donors were non-heart-beating, as there were no laws governing brain death.⁷ Once the concept of brain death was established, the use of non-heart-beating donors decreased significantly.

Four categories of non-heart-beating donors have been identified as follows: category 1 — dead on arrival at the hospital; category 2 — unsuccessful resuscitation; category 3 — awaiting cardiac arrest; category 4 — cardiac arrest while brain dead (Table 1).⁶ Donors from categories 1, 2 and 4 have also been classified as uncontrolled donors because cardiac arrest occurs spontaneously without

warning.⁸ Category 3 donors have been classified as controlled donors because cardiac arrest only occurs after support is withdrawn.⁸

The results using non-heart-beating donors for kidney transplantation have been encouraging. Recent data from the United States have shown that recipients of a non-heart-beating donor kidney have a 5-year renal allograft survival that is the same as those who received a conventional heart-beating donor kidney.⁹ In a study from the United Kingdom, Nicholson and colleagues¹⁰ showed that recipients of non-heart-beating and heart-beating cadaveric donor kidneys had similar 5-year renal allograft survival rates. An even more impressive finding was that the non-heart-beating donor kidneys had a 5-year allograft survival rate that was not significantly different from recipients of a living donor kidney.¹⁰ Weber and colleagues¹¹ have recently reported long-term results using non-heart-beating donors in Switzerland. Using a matched-pair analysis, they showed that kidney-graft survival 10 years after transplantation was 78.7% for kidneys from a non-heart-beating donor and 76.7% for kidneys from a conventional heart-beating donor.

Two studies have examined the potential impact of non-heart-beating organ donation in Canada.^{8,12} Taylor and colleagues¹² demonstrated that the introduction of a non-heart-beating donor program would have

the greatest opportunity to increase the cadaveric organ pool. However, they included donors up to the age of 80 years, which is generally not recommended for non-heart-beating donation.¹⁰ Campbell and Sutherland⁸ showed that a non-heart-beating donor program would have increased their cadaveric renal transplantation rate by 48%. However, they only analyzed controlled non-heart-beating donors and once again included older donors (64% > 65 yr).⁸

Given that a non-heart-beating organ donor program may generate a substantial workload,¹³ we wanted to estimate the full impact that such a program would have if it was introduced at a Canadian hospital. The specific objective of this study was to determine how many additional kidneys could be transplanted at a Canadian centre if such a program were introduced. We chose to study both controlled and uncontrolled non-heart-beating donors since previous reports have shown the greatest potential from uncontrolled donors.^{6,10} In addition, we limited our analysis to donors 60 years of age or younger since there is a high failure rate with older non-heart-beating donors.¹⁰

Methods

We used the health records database of the Ottawa Hospital to identify all patient deaths that occurred in

Table 1

Categories of Non-Heart-Beating Donors

Category & description	Explanation
1 Dead on arrival	Victims of an accident, cardiac arrest or suicide outside the hospital. Resuscitation not initiated or stopped before arrival at the hospital. A protocol is needed for emergency personnel to initiate and continue resuscitation if these donors are to be made use of.
2 Unsuccessful resuscitation	Victims of an accident, cardiac arrest or suicide who receive cardiopulmonary resuscitation. If the treating team decides to discontinue resuscitation, the patient could be considered as a potential non-heart-beating donor at that time.
3 Awaiting cardiac arrest	Situation in which active care is withdrawn by the treating team in the intensive care unit.
4 Cardiac arrest while brain dead	Patients who suffer an unexpected cardiac arrest either during the process of being identified as brain dead or after the determination of brain death but before they are taken to the operating room.

the intensive care unit or the emergency department of the Ottawa Hospital between Jan. 1, 1999, and May 31, 2001 (29-month study period). The Ottawa Hospital is a 1047-bed tertiary care facility with 65 critical care beds serving approximately 1.2 million people in eastern Ontario. The study was approved by the Ottawa Hospital Research Ethics Board.

Patient records were reviewed to determine if there were any contraindications to non-heart-beating organ donation. Patients were excluded from the analysis if any of the following were present: age less than 16 years or more than 60 years; a known history of malignant disease, renal disease, diabetes or hypertension; documented history of hepatitis B, hepatitis C or HIV infection; history of intravenous drug use; sepsis during hospitalization; a conventional (brain dead) heart-beating donor; a brain dead potential heart-beating donor but consent declined by coroner or family; or a serum creatinine level greater than 125 $\mu\text{mol/L}$. All remaining patients were considered potential non-heart-beating donors and included in the analysis. The following data were abstracted from the charts of all

potential non-heart-beating donors: age, gender, cause of death, location of death and serum creatinine value.

Using the methods of Daemen and associates,¹⁴ we made a low, moderate and high projection of the number of additional kidneys that could be transplanted if a non-heart-beating donor program were in place. The low projection was a conservative estimate that included only controlled (category 3) donors. The moderate estimate, which is the protocol in Leicester (UK)¹⁰ and Zurich,¹¹ included categories 2, 3 and 4. The high estimate included all categories of donors and is the protocol in many Spanish centres.¹⁵ We assumed that consent for organ donation would be obtained in 75%. This value represents the average of actual consent rates obtained from existing non-heart-beating organ donor programs.^{13,14,16} We assumed that 40% of category 1, 2 and 4 donor organs¹³⁻¹⁵ and 15% of category 3 donor organs^{8,15} would not be suitable for transplantation because of poor renal function, prolonged ischemia, renal trauma, renal damage on biopsy or technical problems during organ perfusion and procurement.

During the same time period of this study, we obtained data on the number of heart-beating donors at our institution. These findings were used to compare the potential number of kidneys obtained from a non-heart-beating program to the actual number of kidneys obtained from conventional heart-beating donors.

Results

During the study period, 1547 patients died in the emergency department or the intensive care unit; 83 (5.4%) did not have any exclusion criteria and were considered potential non-heart-beating donors. The majority of the patients were male and the average age was 40.6 years (Table 2). Most of the patients died in the emergency department as a result of trauma (Table 2).

Patients dead on arrival at the emergency department (category 1) accounted for 28% of the cases (Table 3). Controlled donors (category 3) accounted for 26%, and the remaining 74% were uncontrolled donors (categories 1, 2 and 4). The most common source of potential

Table 2

Characteristics of the 83 Potential Non-Heart-Beating Donors

Characteristic	No. (and %)*
Location of death	
Emergency department	62 (75)
Intensive care unit	21 (25)
Female	17 (20)
Age, yr	
Mean (and SD)	40.6 (13)
Range	18-60
Mean (and SD) serum creatinine, $\mu\text{mol/L}\ddagger$	75 (29)
Cause of death	
Trauma	37 (44)
Cardiac	12 (14)
Suicide	7 (8)
Pulmonary	5 (6)
Neurologic	4 (5)
Other	3 (4)
Unknown	15 (18)

*Unless otherwise indicated.

†Chart recorded the serum creatinine value for only 26 patients.

Table 3

Categories of Potential Non-Heart-Beating Donors

Characteristic	Category; no. (and %) of subjects*			
	1 (n = 23)	2 (n = 37)	3 (n = 22)	4 (n = 1)
Location of death				
Emergency department	23	37	2	0
Intensive care unit	0	0	20	1
Female	1 (4)	6 (16)	10 (46)	0
Age, yr				
Mean (SD)	44.8 (10.6)	39.5 (14.5)	38.9 (11.7)	19
Range	19-60	18-60	22-57	—
Mean (and SD) serum creatinine, $\mu\text{mol/L}\ddagger$	—	103 (24)	70 (28)	61
Cause of death				
Trauma	6 (26)	20 (54)	10 (46)	1 (100)
Cardiac	4 (17)	7 (19)	1 (4)	0
Suicide	2 (9)	4 (11)	1 (4)	0
Pulmonary	0	1 (3)	4 (18)	0
Neurologic	0	0	4 (18)	0
Other	0	1 (3)	2 (9)	0
Unknown	11 (48)	4 (11)	0	0

*Unless otherwise indicated.

†No patient in category 1, 4 patients in category 2, 21 patients in category 3 and 1 patient in category 4 had a serum creatinine value recorded.

non-heart-beating donor kidneys was from patients who died after unsuccessful resuscitation (category 2), accounting for 44% of all cases. The cause of death was unknown for 48% of category 1 donors (Table 3). In the other 3 categories, trauma was the commonest cause of death (Table 3).

We estimate that a non-heart-beating organ donor program would have resulted in an additional 28 to 82 kidney transplants during the study period (Table 4). This translates into an additional 12 to 34 kidney transplants per year. During the study period there were 47 actual heart-beating organ donors leading to 94 kidney transplants. A non-heart-beating donor program would have increased our cadaveric renal transplantation rate by 30% to 87%.

Discussion

One of the greatest problems facing organ transplantation is the lack of donors with an ever-increasing number of potential recipients. Without a substantial increase in the number of donor organs, relatively fewer Canadians will enjoy the benefits of transplantation. This analysis demonstrated that a non-heart-beating organ donor program would significantly increase the number of cadaveric kidneys available for transplantation at a Canadian hospital. These findings are consistent with previous studies on non-heart-beating organ donation.

With the use of non-heart-beating donors, the cadaveric renal transplantation rate increased by 27% in a Spanish hospital,¹⁵ 34% in a British hospital¹⁰ and 66% at a transplant centre in the Netherlands.¹⁷ Our projected increase was 30% to 87%. Campbell and Sutherland⁸ showed that the renal transplantation rate would have increased by 48% in Calgary using only controlled non-heart-beating donors.

From 1989 to 1999 an average of 700 cadaveric kidneys were transplanted annually in Canada, while the number of patients waiting for a kidney transplant increased from 1386 to 2808.¹ If the results of our study were applied nationally an additional 210 to 610 kidneys annually would be available for transplantation. Such an increase in the cadaveric donor pool would help slow down the growth in the renal wait list¹ and likely decrease the waiting time to transplantation. A decrease in waiting time would not only improve the quality of life for patients with ESRD but may also improve survival after kidney transplantation.¹⁸

At the request of the United States Department of Health and Human Services, the Institute of Medicine conducted an exhaustive review of non-heart-beating organ transplantation. The report, published in 1997, concluded that “the recovery of organs from non-heart-beating donors is an important, medically effective,

and ethically acceptable approach to reducing the gap that exists now and will exist in the future between the demand for and the available supply of organs for transplantation.”¹⁹ The report suggested principles that should be followed in non-heart-beating organ donation, the most important of which included the commitment to informed consent, respect for donor and family wishes and the creation of locally approved protocols that are open to the general public.¹⁹ Since the release of this report, the number of kidneys transplanted from non-heart-beating donors has increased annually in the US.^{20,21} In 2001, surgeons in 68 hospitals in the US transplanted at least 1 kidney from a non-heart-beating donor.²¹

Non-heart-beating organ donation tends to occur in a time-pressured environment. Each step in the process from donor identification to procurement must occur within a certain period to minimize warm ischemia to the kidneys.²² After death is declared, a special catheter is inserted into the femoral artery to perfuse the kidneys with cold preservation fluid.²² Once in situ perfusion has been completed, the donor is transported to the operating room. The donor nephrectomy should be completed within 2 hours of in situ perfusion.²² Given the current economic restraints in most Canadian hospitals, non-heart-beating organ donation could not proceed without significant changes. Additional resources would be needed to staff a special operating room that would be available for urgent donor procedures. Given that it costs approximately \$74 000 per year to keep 1 patient alive on hemodialysis,²³ the costs to set-up and operate a non-heart-beating donor program should be quickly recovered. Bibo and associates²⁴ showed that the use of non-heart-beating donors for kidney transplantation was as cost-effective as conventional heart-beating donors and more cost-effective than dialysis.

What is the best way to proceed with non-heart-beating donation in

Table 4
Projected Number of Non-Heart-Beating Donors*

Factors considered	Estimate		
	Low	Moderate	High
Category	3	2,3,4	1,2,3,4
Potential donors	22	60	83
Consent obtained†	17	45	62
Organs discarded‡	3	14	21
Donors remaining	14	31	41
Kidneys available			
Per 29-month study	28	62	82
Per year	12	26	34

*Unless otherwise indicated.
†We assumed that consent would be obtained in 75% of cases (see Methods).
‡We assumed that 40% of categories 1, 2 and 4 and 15% of category 3 donor organs would be discarded for technical reasons (see Methods).

Canada? Although many western countries^{9,10,15} already use both controlled and uncontrolled non-heart-beating donors, we recommend gradual introduction in Canada. From a logistical point of view, it would be easiest to start with controlled (category 3) donors. Once a controlled non-heart-beating donor program has been established, expansion could include categories 2 and 4 donors. Category 1 donors, although successfully used in Spain,¹⁵ would likely be introduced in Canada only after several years' experience with the other types of non-heart-beating donors.

The strengths of this study include a large number of patient deaths evaluated, a predefined set of exclusion criteria applied consistently and the use of conservative exclusion criteria (e.g., age > 60 yr) that would not overestimate our results. However, the study also has limitations. We assumed that family consent for non-heart-beating donation would be 75%, the same as our current consent rate for heart-beating donors. Conceivably, the consent rate for organ donation after an unexpected cardiac arrest would not be optimal. However, Daemen and associates¹⁴ have reported equal consent rates for heart-beating and non-heart-beating organ donation. Alvarez and Rosario del Barrio¹⁶ reported a higher consent rate for non-heart-beating than for heart-beating donors. Nicholson and associates¹³ have reported a 72% consent rate in their non-heart-beating donor program. A substantial number of category 1 donors died of unknown causes and likely would not be used. However, even when these were excluded (Table 4), a significant number of kidneys were available for transplantation.

Conclusions

At a Canadian centre, we have shown that the cadaveric renal transplantation rate could improve significantly with the use of a non-heart-beating donor program. We believe

it is time for Canadian centres to move forward in this area and begin developing such programs. With the implementation of properly designed protocols, Canada could significantly increase its organ donor rate and improve the quality of life for Canadians with end-stage renal failure.

Acknowledgements: Ms. Lacroix completed this project during a summer research studentship with the University of Ottawa Faculty of Medicine. Salary support was provided by the Burroughs Wellcome Fund Student Research Awards of the Canadian Institutes of Health Research and the University of Ottawa Division of Urology Research Fund.

Competing interests: None declared.

References

1. 2001 Report, volume 1: Dialysis and renal transplantation, Canadian Organ Replacement Register. Ottawa: Canadian Institute for Health Information; 2001.
2. Schaubel DE, Morrison HI, Desmeules M, Parsons D, Fenton S. End-stage renal disease in Canada: prevalence projections to 2005. *CMAJ* 1999;160:1557-63.
3. Schnuelle P, Lorenz D, Trede M, Van der Woude FJ. Impact of renal cadaveric transplantation on survival in end-stage renal failure: evidence for reduced mortality risk compared with hemodialysis during long-term follow-up. *J Am Soc Nephrol* 1998;9:2135-41.
4. Laupacis A, Keown P, Pus N, Krueger H, Ferguson B, Wong C, et al. A study of the quality of life and cost-utility of renal transplantation. *Kidney Int* 1996;50:235-42.
5. Terasaki PI, Cho YW, Cecka JM. Strategy for eliminating the kidney shortage. In: Cecka JM, Terasaki PI, editors. *Clinical transplants*. Los Angeles: UCLA Tissue Typing Laboratory; 1998. p. 265-7.
6. Kootstra G. The asystolic, or non-heart-beating, donor. *Transplantation* 1997;63:917-21.
7. Starzl TE, Marchioro TL, Brittain RS, Holmes JH, Waddell WR. Problems in renal homotransplantation. *JAMA* 1964;187:158-64.
8. Campbell GM, Sutherland FR. Non-heart-beating organ donors as a source of kidneys for transplantation: a chart review. *CMAJ* 1999;160:1573-6.
9. Cecka JM. The UNOS Renal Transplant Registry. In: Cecka JM, Terasaki PI, editors. *Clinical transplants*. Los Angeles: UCLA Tissue Typing Laboratory; 2002. p. 1-18.
10. Nicholson ML, Metcalfe MS, White SA, Waller JR, Doughman TM, Horsburgh T, et al. A comparison of the results of renal transplantation from non-heart-beating, conventional cadaveric, and living donors [published erratum appears in *Kidney Int* 2001; 59:821]. *Kidney Int* 2000;58:2585-91.
11. Weber M, Dindo D, Demartines N, Ambuhl PM, Clavien PA. Kidney transplantation from donors without a heart-beat. *N Engl J Med* 2002;347:248-55.
12. Taylor PE, Field PA, Kneteman NM. Non-heart-beating donors: one answer to the organ shortage. *Transplant Proc* 1996;28:201.
13. Nicholson ML, Dunlop P, Doughman TM, Wheatley TJ, Butterworth PC, Varty K, et al. Work-load generated by the establishment of a non-heart beating kidney transplant programme. *Transpl Int* 1996;9:603-6.
14. Daemen JH, Oomen AP, Kelders WP, Kootstra G. The potential pool of non-heart-beating kidney donors. *Clin Transplant* 1997;11:149-54.
15. Sanchez-Fructuoso AI, Prats D, Torrente J, Perez-Contin MJ, Fernandez C, Alvarez J, et al. Renal transplantation from non-heart beating donors: a promising alternative to enlarge the donor pool. *J Am Soc Nephrol* 2000;11:350-8.
16. Alvarez J, Rosario del Barrio M. Transplant coordination as the "keystone" in non-heart-beating donations. *Prog Transplant* 2002;12:181-4.
17. Daemen JH, de Wit RJ, Bronkhorst MW, Yin M, Heineman E, Kootstra G. Non-heart-beating donor program contributes 40% of kidneys for transplantation. *Transplant Proc* 1996;28:105-6.
18. Meier-Kriesche HU, Port FK, Ojo AO, Rudich SM, Hanson JA, Cibrik DM, et al. Effect of waiting time on renal transplant outcome. *Kidney Int* 2000;58:1311-7.
19. Institute of Medicine. *Non-heart-beating organ transplantation: medical and ethical issues in procurement*. Washington: National Academy Press; 1997.
20. Rosendale JD, McBride MA, Davies DB. Organ donation in the United States: 1988-2000. In: Cecka JM, Terasaki PI, editors. *Clinical transplants*. Los Angeles: UCLA Tissue Typing Laboratory; 2002. p. 87-96.
21. OPTN: Organ Procurement and Transplantation Network. Data as of 2002 Aug 9. Available: www.optn.org (accessed 2003 Oct 22).
22. Brook NR, Waller JR, Nicholson ML. Nonheart-beating kidney donation: current practice and future developments. *Kidney Int* 2003;63:1516-29.
23. Lee H, Manns B, Taub K, Ghali WA, Dean S, Johnson D, et al. Cost analysis of ongoing care of patients with end-stage renal disease: the impact of dialysis modality and dialysis access. *Am J Kidney Dis* 2002;40:611-22.
24. Bibo JC, Engel GL, Kootstra G, Daemen JH. Cost analysis of transplantation with is-chemically damaged kidneys: preliminary results. *Transplant Proc* 1995;27:2959-61.