Non-heart-beating organ donors as a source of kidneys for transplantation: a chart review

Graham M.D. Campbell, MD; Francis R. Sutherland, MD

Abstract

Background: Organ transplantation is the treatment of choice for patients with end-stage organ failure, but the supply of organs has not increased to meet demand. This study was undertaken to determine the potential for kidney donation from patients with irremediable brain injuries who do not meet the criteria for brain death and who experience cardiopulmonary arrest after withdrawal of ventilatory support (controlled non-heart-beating organ donors).

Methods: The charts of 209 patients who died during 1995 in the Emergency Department and the intensive care unit at the Foothills Hospital in Calgary were reviewed. The records of patients who met the criteria for controlled non-heart-beating organ donation were studied in detail. The main outcome measure was the time from discontinuation of ventilation until cardiopulmonary arrest.

Results: Seventeen potential controlled non-heart-beating organ donors were identified. Their mean age was 62 (standard deviation 19) years. Twelve of the patients (71%) had had a cerebrovascular accident, and more than half (10 [59%]) did not meet the criteria for brain death because one or more brain stem reflexes were present. At the time of withdrawal of ventilatory support, the mean serum creatinine level was 71 (29) μmol/L, mean urine output was 214 (178) mL/h, and 9 (53%) patients were receiving inotropic agents. The mean time from withdrawal of ventilatory support to cardiac arrest was 2.3 (5.0) hours; 13 of the 17 patients died within 1 hour, and all but one died within 6 hours. For the year for which charts were reviewed, 33 potential conventional donors (people whose hearts were beating) were identified, of whom 21 (64%) became donors. On the assumption that 40% of the potential controlled non-heart-beating donors would not in fact have been donors (25% because of family refusal and 15% because of nonviability of the organs), there might have been 10 additional donors, which would have increased the supply of cadaveric kidneys for transplantation by 48%.

Interpretation: A significant number of viable kidneys could be retrieved and transplanted if eligibility for kidney donation was extended to include controlled non-heart-beating organ donors.

The advent of better organ preservation, surgical techniques and immunosuppression has dramatically improved the success of solid organ transplantation.[1] This therapy has become the treatment of choice for patients with end-stage organ failure. However, the supply of organs has not increased to meet the demand. In Canada the number of organ donors has remained static at about 14 or 15 donors per million population.[2] The list of patients waiting for kidney transplantation in Canada has increased by 57% over the past decade, from 1606 patients in 1991 to 2528 in 1997.[2]

There are 2 ways to increase the availability of organs for transplantation: increase the number of organ donors from within the present pool or increase the size of the pool by expanding the eligibility criteria for donors. Achieving the first of these options is difficult. Even where organ procurement organizations are extremely efficient, as is the case in Spain,[3] donor rates have not exceeded 25 donors per million population. There are 3 major difficulties in increasing the number of organ donors from the present pool: failure to identify all possible donors, failure to ask the family (or failure to ask in a timely and compassionate manner), and refusal of consent by the family.[4] Although continuing efforts to increase the efficiency of existing programs

Evidence

Études

Dr. Campbell recently completed his medical studies at the University of Calgary, and Dr. Sutherland is an Associate Professor with the Department of Surgery, University of Calgary, and is affiliated with the Transplant Program, Foothills Hospital, Calgary, Alta.

This article has been peer reviewed.

CMAJ 1999;160:1573-6

See related article page 1590

may enhance Canada's rate of organ retrieval, improvements to levels above 25 donors per million population will probably depend on expanding the donor pool. One of the options to increase the size of the donor pool is to use organs from people whose hearts have stopped beating.

Non-heart-beating organ donors are defined as patients with brain injuries incompatible with recovery whose condition does not meet formal criteria for brain death and whose cardiopulmonary function ceases before organs have been retrieved. These donors can be classified as "uncontrolled" or "controlled" depending on whether cardiorespiratory function ceases spontaneously or after support is withdrawn, respectively. When organ transplantation began in the 1950s and 1960s, all kidneys used for transplantation were from either non-heart-beating organ donors or living relatives of the recipient. However, after the establishment of brain death guidelines[5] in 1968, it became standard practice to use organs from brain-dead donors whose hearts were still beating.[6]

This study was designed to determine whether the establishment of a protocol for non-heart-beating organ donation would significantly affect the availability of kidneys for transplantation. Both livers and kidneys have been taken from non-heart-beating donors,[7] but organs from this type of donor have a higher rate of initial non-functioning after transplantation than organs from conventional donors.[8] Our study focused on potential kidney donation, because kidney recipients can undergo dialysis if there is an initial period during which the transplanted organ does not function.

Methods

The charts of 209 patients who died between Jan. 1 and Dec. 31, 1995, in either the Emergency Department or the intensive care unit (ICU) at the Foothills Hospital in Calgary were reviewed. The criteria for eligibility for non-heart-beating organ donation were defined before the chart review.

Candidates for non-heart-beating organ donation were classified in 2 categories: controlled and uncontrolled. Candidates for controlled non-heart-beating donation were patients who had suffered irremediable brain damage as a result of head trauma or stroke and who were hemodynamically stable on ventilator support. These patients did not meet the criteria for brain death and were therefore ineligible for conventional heart-beating organ donation. In all such cases active care had been withdrawn, ventilation had been discontinued, and the patients had experienced cardiopulmonary arrest within 24 hours. It was felt that patients who lived for longer than 24 hours after withdrawal of ventilatory support were inappropriate as potential donors because of expected damage to the organs, family stress during the waiting period and impracticalities related to resource utilization.

Candidates for uncontrolled non-heart-beating donation were patients who had experienced cardiopulmonary arrest without withdrawal of support, either on the way to the hospital, in the Emergency Department or in the ICU, and who had subsequently died. Because of ethical considerations and because of the resource implications of having a team ready to procure organs quickly from such patients, we felt that they did not represent an appropriate source of organs, and data for these patients were not analysed in detail.

The patients' charts were reviewed for evidence of the following exclusion criteria: cancer; systemic sepsis, indicated by positive blood culture results, fever or leukocytosis; high-risk lifestyle; previously documented HIV, hepatitis C virus, hepatitis B surface antigen, or human T-lymphotropic virus types I and II; pre-existing kidney disease; or diabetes with renal damage. Patients with any of these conditions were excluded, as they would have been unsuitable for organ donation. The following information was then extracted from the charts of potential organ donors: diagnosis on admission; age; sex; health before admission; length of stay in hospital; whether brain death had been declared and if it was not, the reason; serum creatinine level; hourly urine output; serum electrolyte levels; use of inotropes; prothrombin time and partial thromboplastin time; duration of ventilatory support; time to cardiopulmonary death after ventilatory support was withdrawn; and cause of death. For each variable, we used the last value recorded before withdrawal of support. Because hourly urine output was highly variable, we calculated a mean for the 8 hours before withdrawal of support.

Data were also retrieved on the number of patients who met the criteria for brain death, the number who actually became donors, the number whose families refused consent and the number who met the criteria for organ donation (as determined during the chart review) but who were apparently missed at the time.

This project was approved by the Conjoint Scientific Review Committee and the Ethics Review Board of the Calgary Regional Health Authority.

Results

Of the 209 patients whose charts were reviewed, 25 (12%) met the criteria for non-heart-beating organ donation. Two of these were deemed ineligible for organ donation, one because death did not occur until 24 hours after ventilation was discontinued and the other because of massive burns to the body and organ damage. Twenty-three patients (11%) remained eligible for our analysis.

Seventeen patients (8% of the total) were classified as potential controlled non-heart-beating organ donors (Table 1), and the other 6 (3%) were classified as potential uncontrolled non-heart-beating donors. Of the 17 potential controlled non-heart-beating donors, 3 (18%) had been seen only in the Emergency Department, and 14 (82%) had been admitted to the ICU before death. Of the 6 potential uncontrolled non-heart-beating donors, 4 were from the Emergency Department and 2 were from the ICU.

The mean age (and standard deviation) of the potential controlled non-heart-beating donors was 62 (19) years (Table 1). Nine (53%) of the patients were older than 70 years, whereas only 6 (35%) were younger than 60 years. Of the 17 patients, 12 (71%) had experienced cerebrovascular accidents, 3 (18%) had hypoxic brain injuries, and 2 (12%) had suffered massive head trauma. The unmet criteria for brain death differed from one patient to another, and for some patients there was more than one such criterion. One patient had no clinical life signs but was not declared dead because a brain scan showed slight diffuse activity. Brain death was not declared for 10 patients (59%) because one or more brain stem reflexes were present. Six patients (35%) maintained the ability to withdraw from pain, and 4 (24%) had some spontaneous respirations. For one patient the criteria for clinical brain death could have been met, but the chart indicated that the examination was not completed.

The mean serum creatinine level was 71 (29) μmol/L; creatinine level was not recorded for 2 of the patients. One patient, who had type 2 diabetes, had a slightly elevated creatinine level (143 μmol/L) at the time of death but had no history of renal damage. Urine output varied greatly among these patients; the mean over the 8 hours before ventilatory support was withdrawn was 214 (178) mL/h. Data were unavailable for 4 patients from the Emergency Department. Nine (53%) of the patients had been receiving inotropes for at least part of their stay in hospital.

The mean duration of ventilation was 59.4 (70.5) hours. After discontinuation of ventilation, the mean period until death was 2.3 (5.0) hours. Thirteen patients (76%) died within 1 hour after ventilation was stopped, and 16 (94%) died within 6 hours.

For the period studied (calendar year 1995) we identified 33 potential conventional organ donors (people for whom brain death had been declared and whose hearts were still beating); of these, 21 (64%) became donors. The families of 8 patients (25%) refused consent. For 4 patients (12%), our review indicated that the criteria for donation had been met, but these patients did not become donors; there was no documentation of family refusal.

We estimate that, if a protocol for non-heart-beating organ donation had been in place during 1995, kidneys would have been retrieved and transplanted from 10 (60%) of the 17 potential controlled non-heart-beating donors that we identified. For this calculation, we assumed that 25% of families would have refused consent and that 15% of kidneys would have been discarded because of extensive glomerulosclerosis. The latter assumption was based on our current experience in the Transplant Program at the Foothills Hospital: we perform biopsy on all kidneys retrieved from elderly patients and discard approximately 15% because of glomerulosclerosis (unpublished data). The kidneys from these 10 patients would have increased our rate of cadaveric kidney transplantation by 48%.

Interpretation

There are many issues involved in the use of organs from non-heart-beating organ donors. Controversy exists about how such donors are defined and about which group (controlled or uncontrolled) should be considered suitable. Questions have been raised about whether there would be enough non-heart-beating organ donors to justify the expense of setting up a retrieval program and whether the quality of the organs retrieved would be adequate. It is also unclear which of the many procurement techniques and protocols proposed are best. Finally, ethical concerns about defining death need to be addressed.

Non-heart-beating donors have been divided into 4 categories:[9] dead on arrival, unsuccessful resuscitation, awaiting cardiac arrest and cardiac arrest while brain dead. We preferred to classify non-heart-beating donors as uncontrolled or controlled, depending on whether cardiopulmonary arrest was spontaneous or occurred after support was withdrawn, respectively. We feel that this classification is more appropriate in terms of both ethical and practical considerations. Ethical considerations inhibit the use of organs from uncontrolled non-heart-beating donors. These patients die suddenly and family is usually not available to

Table 1: Characteristics of 17 patients who died in the Emergency Department or the intensive care unit of the Foothills Hospital, Calgary, in 1995 and who met criteria for controlled non-heart-beating organ donation

Patient no.	Age, yr	Reason brain death not declared*	Serum creatinine, μmol/L	Urine output, mL/h	Inotropes	Ventilation time, h	Time to asystole,† h
Cerebrovascular accident							
1	73	Withdrawal	ND	27	N	23.2	5.7
2	72	Withdrawal	119	171	Y	83.8	0.5
3	67	BSR, respirations	98	222	Y	21.8	0.4
4	71	Withdrawal, BSR	32	109	Y	221	0.9
5	54	Respirations	48	143	Y	249	0.2
6	45	BSR	63	278	Y	40.7	2.9
7	75	Respirations	ND	ND	Y	1.5	0.4
8	87	Examination incomplete	83	82	N	22.9	0.1
9	75	Withdrawal, BSR	143	ND	N	2.5	1.0
10	67	BSR	65	ND	N	3.5	0.4
11	88	BSR	76	726	N	5.5	0.4
12	33	Brain scan activity	64	350	N	61.0	0.6
Hypoxic brain injury							
13	71	Withdrawal, BSR, respirations	83	ND	N	3.2	0.1
14	81	BSR	62	54	Y	97.0	0.4
15	50	BSR	44	101	Y	64.6	4.1
Head trauma							
16	39	Withdrawal	46	350	Y	61.7	21.1
17	15	BSR	47	167	N	47.2	0.1
Summary‡	62 (19)		71 (29)	214 (178)		59.4 (70.5)	2.3 (5.0)

Note: ND = no data available.
*"Withdrawal" = withdrawal from painful stimuli, BSR = brain stem reflexes present, "respirations" = some spontaneous respirations.
†After ventilatory support was withdrawn.
‡Mean (and standard deviation).

give consent for organ donation. The invasion of a patient's body with flushing apparatus to cool and preserve the organs without prior consent, for whatever good intention, has potential negative consequences if the family objects, when consent is finally sought. Organs from controlled non-heart-beating donors have better graft viability than those from uncontrolled non-heart-beating donors.[7]

We estimated that 10 of the 17 potential controlled non-heart-beating donors would have been able to donate kidneys for transplantation. A large number of the potential non-heart-beating donors were older than 70 years, an age at which graft viability diminishes. Biopsy of these kidneys would have eliminated any that were unlikely to function because of extensive glomerulosclerosis. Ten additional donors would have increased by 20 the number of kidneys available and hence our rate of cadaveric kidney transplantation by 48%. Kootstra[10] reported a similar increase in cadaveric kidney supply (by 40%) in a study of non-heart-beating organ donation.

The medical records indicated that kidney function in the 17 potential controlled non-heart-beating donors was adequate at the time of withdrawal of ventilatory support. However, the mean age of the patients was 62 years, significantly older than the mean of 38 years for donors in Canada in 1996.[2] Only 6 (35%) of the potential controlled non-heart-beating donors were younger than 55 years, the age group in which renal function is likely well preserved. Of these, 3 might not have become donors because they died more than 1 hour after withdrawal of support. After 1 hour, renal damage may be significant, and the logistics of retrieving the organs become more difficult. In a previous study of 229 non-heart-beating kidney donors, mean age was 46 years and kidney allograft survival was the same as for donors with a heart beat.[8] It seems unlikely that kidneys from our pool of older non-heart-beating donors would have fared as well. The development of reliable tests for kidney viability may address this problem.[11]

For potential controlled non-heart-beating donors, ventilatory support may be withdrawn either on the ward or in the operating room. If the patient is declared dead on the ward, there may be a significant delay in getting the body to the operating room for organ retrieval. Withdrawing support in the operating room would obviate this problem, provided that the patient dies within a reasonable length of time (1–6 hours). Our data support withdrawal of care in the operating room, given that 13 of the 17 potential controlled non-heart-beating donors experienced cardiopulmonary arrest within 1 hour of ventilation being discontinued, and 16 died within 6 hours. Patients who do not die within this period would be returned to the ward and ultimately might not become organ donors; this possibility would have to be fully explained to the family.

Brain death evolves over a variable period, and if ventilatory support had been continued, many of the 17 potential controlled non-heart-beating donors in this study would have progressed to brain death. Although it may be appropriate to provide ventilatory support to a patient with rapidly evolving brain death, providing such support for an extended period would undoubtedly cause much distress to the family and the ICU staff. In this circumstance providing ventilatory support may not be in the patient's best interests. However, denying the patient and his or her family the opportunity to donate organs for transplantation may also have consequences for the grieving process of family members. Furthermore, a person who, during his or her lifetime, indicated a high motivation to donate organs might have consented to prolongation of ventilatory support to allow for organ donation. Non-heart-beating organ donation circumvents this problem.

In this study we did not attempt to address the problem of defining when a patient has died and thus when organs can be taken. The thought of retrieving organs from a patient who is not dead is abhorrent. Efforts to reduce warm ischemic time (the time between a cessation of blood perfusion and preservation with a cooling flush solution) by defining death as occurring as close as possible to the time of cardiopulmonary failure leads to the risk of removing organs from patients who have not died. Protocols for non-heart-beating organ donation must ensure that uncoerced, informed consent be obtained from relatives and must allow a third party to judge when the patient has died and organ retrieval can begin. The criteria for death should not be altered from presently accepted criteria to facilitate organ donation.

Our results indicate that a significant number of viable kidneys could be retrieved for transplantation from controlled non-heart-beating organ donors. With a carefully devised protocol, this type of organ donation offers better health for patients with renal failure, improved compliance with the wishes of families and patients motivated to donate organs, and greater comfort for the ICU staff who deal with these problems.

Competing interests: None declared.

References

1. D'Alessandro AM, Southard JH, Love RB, Belzer FO. Organ preservation. *Surg Clin North Am* 1994;74:1083-5.
2. *Annual report 1998*. vol 2. Ottawa: Organ Donation and Renal Transplantation, Canadian Organ Replacement Register, Canadian Institute for Health Information; 1998.
3. Miranda B, Segovia C, Sanchez M, Felipe C, Naya MT, Matesan, R. Evolution of organ procurement and donor characteristics in Spain. *Transplant Proc* 1995;27:2384-8.
4. D'Alessandro AM, Hoffmann RM, Knechtle SJ, Eckhoff DE, Love RB, Kalayagio M, et al. Successful extrarenal transplantation from non-heart-beating donors. *Transplantation* 1995;59:977-82.
5. CMA. Guidelines for the diagnosis of brain death. *CMAJ* 1987;136:200A-B.
6. Spoor MT, Sutherland F. The evolution of the concept of brain death. *Ann R Coll Physicians Surg Can* 1995;28:30-2.
7. Casavilla A, Ramirez C, Shapiro R, Nghiem D, Minacle K, Fung JJ, et al. Experience with liver and kidney allografts from non-heart-beating donors. *Transplantation* 1995;59:197-203.
8. Cho YW, Terasaki PI, Cecka JM, Gjertson DW. Transplantation of kidneys from donors whose hearts have stopped beating. *N Engl J Med* 1998;338:221-5.
9. Kootstra G, Daemen JHC, Oomen APA. Categories of non-heart-beating donors. *Transplant Proc* 1995;27:2893-4.
10. Kootstra G. The asystolic, or non-heartbeating donor. *Transplantation* 1997;63:917-21.
11. Kievit JK, Oomen APA, Janssen MA, van Kreel BK, Heineman E, Kootstra G. Viability assessment of non-heart-beating donor kidneys by alpha glutathione S-transferase in the machine perfusate. *Transplant Proc* 1997;29:1381-3.

Reprint requests to: *Dr. Francis Sutherland, Department of Surgery, Peter Lougheed Centre, 3500 – 26th Ave. NE, Calgary AB T1J 6J4; fax 403 219-3574; Francis.Sutherland@CRHA-health.ab.ca*