Non-Heart-Beating Donors: One Response to the Organ Shortage

Anthony M. D'Alessandro, Robert M. Hoffmann, and Folkert O. Belzer

The current shortage of organs for transplantation has resulted in renewed interest in the use of organs from non-heart-beating donors (NHBDS). The organ shortage has been created, in part, by steady improvements in transplant results. As results have improved, the indications have been broadened, thereby increasing the number of patients eligible for transplantation. This is clearly shown by the number of patients currently listed and waiting for transplants. As of January 1995, over 37,000 patients were awaiting transplants; over 27,000 of these patients were on the kidney transplant waiting list. Despite what appear to be very good educational efforts and required request laws, the rate of organ donation from heart-beating donors (HBDs) has remained relatively constant—approximately 4,000 organ donors per year.2 The actual number of HBDs is surprisingly low; the potential pool of HBDs in the United States has been estimated to be between 10,000 and 12,000 per year.2,3 Evans4 estimates that 43 to 55 HBDs per million population could realistically be recovered. Unfortunately, only 19 organ donors per million population are recovered on average in the United States. Clearly, increasing the number of HBDs would go a long way toward alleviating the current organ shortage crisis.

The current supply of organs from HBDs is insufficient to meet the clinical need. Until we are able to increase HBDs through sustained educational efforts and improvements in organ procurement organization (OPO) performance standards, the use of organs from NHBDS deserves to be thoroughly explored. Although it could be argued that dialysis is a satisfactory alternative to transplantation, dialysis is generally perceived to result in a less-than-acceptable quality of life. However, the need for extrarenal organs is dramatically more urgent. Without transplantation, as many as one third of all potential liver and heart transplant recipients will die awaiting organs.5 For these reasons, non-heart-beating organ donation should not only seek to increase the number of kidneys for transplantation, but should also be directed at maximizing the use of all intra-abdominal organs, the lungs, and possibly even the heart for transplantation.

History of NHB Organ Donation

Although the amount of discussion generated by NHBDS might lead to the belief that this is a new concept, the fact is that NHBDS formed the very foundation of modern clinical transplantation. After a hiatus of nearly 20 years, the use of NHBDS is being re-examined as a potential source of organs to alleviate the current shortage. "Back to the future," as Youngner and Arnold stated recently,6 is an appropriate reference to the use of organs from NHBDS. Since brain-death laws did not exist until the late 1970s and early 1980s, all organs transplanted were recovered from NHBDS. Reports from several programs during the early years of transplantation describe in detail many of the problems associated with kidney retrieval from NHBDS.7,11 Usually, the time from declaration of death until the recovery of organs resulted in prolonged warm ischemia and poor function after transplantation. Although the majority of early activity with NHBDS was with kidneys, the late 1960s and early 1970s saw the beginnings of liver, heart, and pancreas transplantation. The first attempts at transplantation of these extrarenal organs were, of course, from NHBDS. These first retrievals are described in detail by Starzl et al. and Calne and Williams for livers12,13 and by Kelly and others for the pancreas.14,15 In fact, the first heart transplanted by Barnard in 1967 was recovered from an NHBDS.16 In that instance, the donor was placed on cardiopulmonary bypass and cooled after five minutes’ absence of cardiac or respiratory activity. This case may represent the first case of cardiac reanimation, a phenomenon that has only recently

From the Department of Surgery, University of Wisconsin Medical School, Madison, WI.

Address reprint requests to Anthony M. D'Alessandro, MD, Department of Surgery, H11/780 University of Wisconsin Hospital, 600 Highland Avenue, Madison, WI 53792-1355.

Copyright © 1995 by W.B. Saunders Company

0036-1723(95)01061-0001/0

168 Transplantation Review, Vol 9, No 4 (October), 1995, pp 168-175
began to be explored as a method of increasing the number of hearts for transplantation from NHBDs.\textsuperscript{17} Despite the numerous obstacles that these early pioneers of transplantation faced, many of the organs transplanted from NHBDs functioned very well. These successes were achieved even though methods of preserving organs were just being developed, immunosuppression consisted of only azathioprine and prednisone, and recipient surgical technique was far from being refined. With improvements in each of these areas came improved results, broadened indications, longer waiting lists, and the organ shortage. The organ shortage has led to the need to re-examine NHBDs as a potential source of organs in light of the tremendous strides transplantation has made over the last 25 years.

**Experimental Studies**

**Warm Ischemia**

The main question regarding the use of NHBDs revolves around the issue of tolerance to warm ischemia—that is, how much warm ischemia can a specific organ tolerate and still be expected to yield acceptable results after transplantation. Early work in the laboratories of Garcia-Rinaldi\textsuperscript{18} and Ruers\textsuperscript{19} showed the possibility of using NHBDs kidneys that had sustained a warm ischemic insult. Anaisse et al.\textsuperscript{20} clearly showed in a canine model that 1 hour of warm ischemia followed by 5 hours of in situ cold ischemia and 24 hours of preservation resulted in excellent renal blood flow and sustained life after transplantation.\textsuperscript{20} We and others have shown that short periods of warm ischemia are well tolerated, resulting in long-term graft survival similar to that found in transplantation from HBDs.\textsuperscript{21,22} In fact, in a controlled setting, we would consider up to 2 hours of warm ischemic time acceptable. This position is supported, in part, by a study by Rigotti et al.,\textsuperscript{23} in which 120 minutes of warm ischemia in the porcine model of renal transplantation resulted in recovery of function in six of eight animals. Whereas warm ischemia is a major determinant of function after transplantation, it may not be the only factor, as recently suggested by Rowinski et al.\textsuperscript{24} They speculate that metabolic, hemodynamic, and hormonal changes may be as important as warm ischemia.

Although the liver is sensitive to warm ischemia, it actually tolerates up to 1 hour of warm ischemia in the setting of total vascular occlusion and hepatic resection.\textsuperscript{25,26} However, warm ischemia followed by organ retrieval, preservation, and transplantation is clearly different than in situ warm ischemia. Hoshino et al.\textsuperscript{27} have shown in a porcine model that a core cooling technique with cardiopulmonary bypass resulted in functional livers after short periods of cardiac arrest (5 and 10 minutes) or hypotension (30 minutes) followed by 5 minutes of cardiac arrest. However, prolonged cardiac arrest of 20 minutes resulted in nonfunction. These experimental findings would seem to explain, in part, results obtained after transplantation of livers from uncontrolled NHBDs after cardiopulmonary resuscitation.\textsuperscript{28} However, controlled NHBDs, in which there was a period of hypotension followed by a brief cardiac arrest, yielded excellent liver function in four of five livers transplanted at our center\textsuperscript{29} and in six of six livers transplanted at the University of Pittsburgh.\textsuperscript{30} The longest period of warm ischemia in our experience was 35 minutes, which still yielded excellent post-transplant function. Depending on the donor and recipient status, we would consider up to 1 hour of warm ischemic time as acceptable.

Previous reports have indicated that pancreatic islets are also relatively resistant to ischemic insult.\textsuperscript{30,31} Wantanabe et al.,\textsuperscript{32} using a core cooling technique and cardiopulmonary bypass, have shown that pancreatic grafts can also tolerate 30 minutes of warm ischemia followed by 24 hours of cold ischemia. Our group has reported on six clinical pancreas transplants from controlled NHBDs that had a mean warm ischemic time of 15.4 minutes (range 4 to 35 minutes). All pancreatic allograft recipients were immediately insulin-independent without evidence of graft pancreatitis.

Experimentally, lungs have been shown to be more resistant to warm ischemia than previously thought.\textsuperscript{33} Our group has reported the first successful lung transplant from an NHBD with 55 minutes of warm ischemia to a patient who was on extracorporeal membrane oxygenation (ECMO) before transplant and was weaned and extubated 4 days after transplantation.

Recent work by Gundry et al.\textsuperscript{34,35} has shown that lamb and baboon hearts could be transplanted and resuscitated after as much as 30 minutes of asphyxia. This work could lead the way in using hearts from NHBDs. However, before proceeding to using hearts from NHBDs, cardiothoracic surgeons should re-examine the low use of hearts in the United States from multiple organ donors.
Organ Preparation

No optimal method of flushing organs has been determined. Although core cooling with cardiopulmonary bypass has been shown to be effective experimentally, this technique in the clinical setting would seem to be cumbersome. As we have shown, in the controlled setting of renal retrieval from NHBDs it is not necessary to place any cannulas. However, in our experience, in the setting of controlled extrarenal NHBDs, simple chest tubes placed into the femoral artery and vein are adequate to provide a flushout of all the intra-abdominal organs. We believe that simplicity is important in the clinical setting of any organ procurement endeavor.

However, in the uncontrolled setting, it may be necessary to use special catheters to achieve a higher flushout pressure. Ana et al. have shown that higher flushout pressure resulted in better posttransplant function. Also, the addition of vasodilators such as trifluoperazine, agents that might mitigate the effects of warm ischemia, and free radical scavengers such as superoxide dismutase or allopurinol might improve function of kidneys retrieved from NHBDs.

Finally, we do not know the optimal method of preserving kidneys from NHBDs. It is clear from our group as well as others that continuous machine perfusion yields significantly lower rates of delayed graft function (DGF) compared with cold storage. Reducing DGF can also have implications for long-term graft survival. Light et al., Matsuno et al., and Ana et al. have shown superior rates of function when continuous machine perfusion was used instead of cold storage for NHBD organs. The presence of dissolved oxygen, a colloid such as hydroxyethyl starch, and substrates such as adenosine and phosphate to regenerate adenosine triphosphate, as well as free radical scavengers such as allopurinol might be important in limiting injury from warm ischemia after reperfusion.

Ethical Issues

Although not widely appreciated, current clinical transplantation was founded on the use of NHBDs. Without NHBDs, the current practice of transplantation could not have progressed to the prominent position it now occupies in American surgery. What then is the controversy, and what are the ethical issues frequently discussed?

Whenever changes in organ procurement procedures are contemplated, ethical questions are raised. For those of us in transplantation today, it is difficult to believe that Dr. David Hume, noted kidney transplant pioneer, was sued in 1968 for removing kidneys from a HBD. Today, an entire generation of transplant professionals does not consider the use of NHBDs because they are generally unaware of the history of NHBDs that preceded the era of brain-death laws. For this reason, open discussions regarding NHBDs must be conducted, not only to educate but to dispel fears of impropriety and to prevent undermining the public trust as they consider organ donation.

Younger and Arnold recently discussed some of the ethical, psychosocial, and public policy implications of NHBDs. Their paper summarizes the June 1993 issue of the *Kennedy Journal of Ethics*, which was dedicated to ethical issues of non-heart-beating donation, and discusses the University of Pittsburgh policy on procuring organs from patients from whom life support was withdrawn. They reiterate two fundamental rules of organ procurement: (1) The dead-donor rule, which states that vital organs should only be taken after death and that patients must not be killed by organ retrieval, and (2) care of living patients must not be compromised in favor of potential recipients. With regard to the first rule, it must be determined when death occurs and if it is irreversible; furthermore it must be determined whether the rule of the irreversibility should be applied to patients after the decision to withdraw support has been made usually for an irrecoverable process. The Pittsburgh protocol arbitrarily requires apnea, no pulse pressure, and 2 minutes of asystole, ventricular fibrillation, or electromechanical dissociation. The protocol at our center arbitrarily chose 4 minutes of absent cardiac function. It is understood that in some of these circumstances a patient could be resuscitated and might not be irreversibly dead; however, such resuscitation is considered inappropriate when a determination has been made that continued life support is not in the patient's best interest. Also, organ retrieval must not kill a patient. Care must be taken not to hasten a patient's death. To this end, the Pittsburgh protocol permits use of narcotics only if the potential donor shows signs of discomfort. Our protocol is similar in that it permits the use of analgesic medications if there is doubt about the patient's sensitivity to pain. Also, in our protocol, we administer heparin and phenolamine before withdrawal of support. In our experience with HBDs, the administration of these agents has not hastened a
potential donor’s death, although it has caused transient hypotension.

With regard to the second rule, there must be strict separation of physicians caring for the dying patient and those involved in transplantation procedures. Death of the patient must also be declared by a physician not involved with the transplant process. Although the Pittsburgh protocol does not allow physicians to bring up the topic of non-heart-beating donation, our center feels it is appropriate for the attending physician to bring up the topic of organ donation once a decision has been made to withdraw support. If the family requests further information, the center notifies a representative of our OPO.

Issues of consent are extremely important when discussing NHBDs. Clearly, with controlled NHBDs, adequate time is available to fully discuss the procedure with the donor’s family. Although the majority of families will allow organ retrieval in the operating room (OR), we feel comfortable allowing the patient to expire in the intensive care unit (ICU). Because patients being considered for non-heart-beating donation have in many instances preserved brain stem reflexes, it is important to discuss with the family the possibility of continued spontaneous respiration and cardiac activity. The family must be informed that, if this occurs and continues beyond a specified period of time after which retrieval of the organs is no longer possible, the patient will be returned to the ward or the ICU and allowed to expire. For extrarenal NHBDs, because our experience is preliminary, we will only attempt liver and pancreas retrieval in the OR and with placement of femoral canulas. Another question regarding controlled NHBDs centers around whether families of patients who are withdrawing life-sustaining measures be given the option of organ donation. Now that NHBD protocols are in place in over one third of the nation’s OPOs, perhaps required request should be extended to these cases.

Consent and logistics are more problematic for uncontrolled NHBDs. There has been sentiment that placement of femoral or peritoneal canulas without consent is a minimally invasive procedure and could be performed with consent, which would provide 4 to 6 hours of in situ cold ischemia and sufficient time to get consent for donation. However, we must be extremely careful not to create any impression of disrespect for the dead or to alienate other health professionals. For these reasons, our center believes consent is necessary for any procedures that are being performed in preparation for organ donation. Programs of uncontrolled NHBDs in the Netherlands and recently at the Washington Hospital Center have shown that this approach is possible and can still lead to viable transplanted kidneys.

Before implementing its extrarenal NHBD program, our center had no formal protocol. Because we had been procuring kidneys from controlled NHBDs for over 20 years, it was considered the standard of care at our center. We actually started our extrarenal NHBD program without a protocol in place. However, it became clear that discussion with our Ethics Committee and institutional approval were desirable. Because the use of NHBDs is not considered experimental at our center, Institutional Review Board (IRB) approval was not necessary. However, after recommendation by our Ethics Committee, the Medical Board approved our NHBD protocol. At this time our protocol includes only patients with severe neurological injury with no hope of recovery who are being withdrawn from life support. Within the framework of our protocol, discussions are ongoing regarding the advisability of organ retrieval from patients who do not have severe neurological impairment; likewise, the possibility of organ retrieval from uncontrolled NHBDs is being considered.

Clinical Status of NHBD Donation
Although a few centers continued using NHBDs, this method fell out of favor after the introduction of brain-death laws. The use of heart-beating brain-dead donors completely eliminated the warm ischemic times unavoidable in NHBDs. Kidneys and extrarenal organs could be transplanted without the fear of organ damage caused by anoxia and warm ischemia. Also, in the late 1970s and early 1980s, before the expansion of renal and extrarenal programs to their current levels, there were enough HBDs to fulfill the need for organs.

Although efforts to increase the number of HBDs to their full potential should continue, NHBDs will likely supplement HBDs out of necessity. A recent OPO survey indicated that 23 of 66 active OPOs procured and transplanted organs from NHBDs and that 7 of those 23 OPOs procured and transplanted extrarenal organs.

One of the main goals of OPOs recovering organs from NHBDs is to limit warm ischemic times. The approach to minimizing warm ischemic time depends on whether organ retrieval is occurring in a controlled or uncontrolled setting. Patients who are asystolic, usually as a result of trauma or a myocardial infarction, are potential candidates for uncon-
trolled donation. Controlled donation occurs in the setting in which a decision has been made by the patient’s family to withdraw life support in the absence of the usual brain-death criteria.

**Controlled NHBDs**

Controlled NHBDs are more desirable than uncontrolled NHBDs for a variety of reasons. First, warm ischemia is limited; organs are usually removed immediately after pronouncement of death in the operating room. Alternatively, in our experience and that of others with kidney retrieval, death can be pronounced in the ICU setting followed by transport to the OR for renal recovery. This allows family members to be present at the time of death. However, for extrarenal recovery our group prefers transporting potential NHBDs to the OR before the pronouncement of death. Perhaps as more experience with extrarenal NHBDs is obtained, withdrawal of life-sustaining measures could occur in the ICU setting. Another advantage of controlled NHBDs is the family’s opportunity to make an un hurried decision to donate organs. There is adequate time to discuss organ donation and obtain consent, particularly if placement of femoral cannulas before withdrawal of support. Although it is difficult to estimate the number of severely brain-injured but not brain-dead patients who would be potential donors, Nathan estimates the potential donor pool could increase by 20% to 25%.

**Controlled renal NHBDs.** Although the number of centers retrieving and transplanting kidneys from controlled NHBDs is increasing, published reports are few. Orloff et al. recently reported on 19 renal transplants from 12 NHBDs. The mean warm ischemic time in this study was 25 minutes, with a postoperative dialysis rate of 22% and a 1-year graft survival of 76%. Life support in this protocol was withdrawn in the ICU setting and the patient pronounced dead; only then were heparin and phenolamine administered and the abdomen lavaged with cold lactated Ringer’s solution. No episodes of primary nonfunction were seen in this study.

In a paper presented by Casavilla et al. from the University of Pittsburgh, 17 of 20 kidneys were transplanted from 10 controlled NHBDs; 81% developed acute tubular necrosis (ATN). Graft survival was 88% after a mean follow-up period of 12.5 ± 12.1 months. The Pittsburgh protocol did not use femoral cannulas or vasodilators such as phenolamine, but performed rapid laparotomy before in situ perfusion. The mean time from extubation until cardiac arrest was 23 ± 11 minutes and less than 4 minutes until in situ perfusion.

The University of Miami (Olson L, personal communication, January 1995) also has had experience with controlled renal NHBDs and has transplanted 25 kidneys from 20 donors over the last 10 years. Kidneys were continuously perfused and perfusion characteristics formed the basis of whether a kidney would be transplanted. Thirteen kidneys were discarded because of poor perfusion characteristics and 25 were transplanted; the ATN rate was 40%, although all kidneys (10) transplanted at the University functioned immediately. Seven potential donors could not be used because they did not undergo cardiopulmonary arrest after life support was discontinued. This point underscores the importance of discussing this possibility with family members as well as with nursing and OR personnel.

Although our center has an extensive experience over the last 21 years with controlled renal NHBDs, we have not previously published our results. Even after the introduction of brain-death laws, our center preferred controlled NHBDs for reasons of simplicity. After our extrarenal programs became established, recovery from NHBDs was preferred but NHBDs continued to supplement HBDs by approximately 10% per year. From January 1985 until December 1993, 239 kidneys from 125 NHBDs were transplanted at our center. Life support was withdrawn in the ICU or in the OR in accordance with family preference. Before withdrawal of support, heparin and phenolamine were administered. Kidneys were individually removed after cardiac arrest and were flushed only after retrieval and then placed on continuous machine perfusion. In 1993, when our center initiated extrarenal recovery from NHBDs, femoral catheters were placed prior to withdrawal of support, and kidneys were flushed in situ. Because the kidneys were removed individually, the warm ischemic time of the right kidney was 15.8 ± 7.7 minutes and that of the left kidney 18.2 ± 7.3 minutes. The mean preservation time was 30.2 hours. The need for dialysis for all causes in the postoperative period was 22%; dialysis for ATN only was 14.9%. This compares favorably with the national average of 28% for kidneys retrieved from HBDs and is similar to the series reported by Orloff et al. The 1-month and 1-year patient and graft survival in this series of patients was 99.1% and 94.3% and 94.6% and 83.4%, respectively.

**Controlled extrarenal NHBDs.** Although seven OPOs report using extrarenal organs from NHBDs, few
have reported their experience. One report from Sweden in 1987 revealed only one case of PNF in 17 livers recovered from controlled NHBDs. More recently, the University of Pittsburgh reported on six livers transplanted from seven controlled NHBDs. All functioned immediately but two developed hepatic artery thrombosis requiring retransplantation and three patients eventually survived. Our center recently reported on five livers transplanted into four patients from controlled NHBDs. The technique used by our group begins in the OR with placement of femoral cannulas and administration of heparin and phenolamine before withdrawal of support. An en-bloc removal of all intra-abdominal organs (Fig 1) is used and organs are separated and suitability for transplantation determined after returning to our center. The mean warm ischemic time is 15.4 ± 10.7 minutes and the mean preservation time is 10.4 ± 2.2 hours, which is similar to the 10.7 hours reported by the Pittsburgh group. In our series, one case of PNF occurred for technical reasons and three of the four patients are still alive. There were no episodes of hepatic artery thrombosis or ischemic-type biliary strictures. Our conclusion was similar to Pittsburgh’s in that, in controlled situations, livers from NHBDs functioned similarly to livers retrieved from HBDs.

Pancreas transplantation from controlled NHBDs has also been reported by our group. Six simultaneous pancreas-renal transplants were performed from controlled NHBDs from whom livers were also procured. The warm ischemic time was the same as that for the livers (15.4 ± 10.7 minutes) and preservation time of the pancreas was 17.4 ± 2.4 hours. All patients were immediately insulin-independent and free of graft pancreatitis and only one patient required hemodialysis after transplantation.

The experience reported by our group also included one lung transplant from an NHBD. The warm ischemic time in this case was 35 minutes and the lung was preserved for 3 hours with University of Wisconsin (UW) solution. Transplantation was immediately effective, extracorporeal membrane oxygenation was discontinued, and the patient was extubated 4 days after transplantation.

Uncontrolled NHBDs

The use of organs from uncontrolled NHBDs is more problematic, particularly from the logistical perspective. However, if the goal is to reduce the huge disparity between donors and recipients that currently exists, especially for kidneys, then uncontrolled NHBDs have the most potential. In a study by Nathan et al., 5,603 potential donors were identified; however, only 453 remained stable enough to be evaluated for donation. The remaining 4,169 patients expired from cardiac arrest and potentially could have been considered as uncontrolled renal NHBDs. In a Center for Disease Control study, in which the potential donor pool was estimated at 26,000, 11,500 patients expired within 24 hours. These patients, as in Nathan’s study, could also have been considered for uncontrolled NHBD donation.

Preventing warm ischemia in uncontrolled situations such as trauma or cardiac arrest, obtaining consent, placing femoral or peritoneal catheters, and removing organs are logistically very challenging. There are profound ethical, psychosocial, and perhaps even legal ramifications if the entire process is not carried out properly.

Figure 1. Technique of combined hepatic, pancreatic, and renal retrieval. Arrows indicate major steps in en bloc removal of intra-abdominal organs. Insert depicts flushout of portal circulation through a branch of the superior mesenteric vein. (Reprinted with permission. D'Alessandro AM, Hoffmann RM, Knechtle SJ, et al: Successful extrarenal transplantation from non-heart-beating donors. Transplantation [in press].)
Because retrieval of organs from uncontrolled NHBDs is necessarily more complicated, it stands to reason that protocols for doing so will also be more complicated. However, as recently shown by Light et al., from the Washington Hospital Center, it may be possible to satisfy issues of consent and placement of canulas, and to minimize warm ischemia in the uncontrolled setting. Clearly, the potential for establishing an uncontrolled NHBD program existed; a death audit at their center from 1992 to 1993 revealed only 55 potential brain-dead donors, but 351 potential NHBDs. The rapid organ recovery program (RORP) developed by the Washington Hospital Center has thoughtfully addressed these issues. First, their protocol accepts the fact that 30 to 45 minutes of warm ischemia of the kidney can be tolerated. Within this window, the Office of Decedent Affairs/Family Advocates obtains consent from the medical examiner and the family. Second, a staff of in-house catheter-placement specialists is trained to mix perfusion solutions, place femoral and peritoneal catheters and perform in situ flushout after consent is obtained. Third, an organ preservation laboratory has been established for pulsatile preservation of kidneys, which has been shown to be beneficial to warm ischemically damaged kidneys. Finally, a community oversight committee has been established to determine community viewpoints on organ donation and the RORP. Unfortunately, since the RORP was established in September 1994, only two kidneys have been retrieved and transplanted. The warm ischemic time was 40 minutes and both kidneys functioned immediately. It appears that 45 minutes may not be enough time to obtain consent before placing femoral and peritoneal canulas. Currently the Washington Hospital Center, through its community oversight committee, is trying to determine the public response to placing canulas before obtaining consent (Light J, personal communication, January 1995).

Uncontrolled renal NHBDs. Although the use of kidneys from controlled NHBDs will help alleviate the organ shortage, the disparity is so great between donors and potential recipients that the use of kidneys from uncontrolled NHBDs needs to be seriously considered. Even if the full potential of HBs were realized, based on the current waiting list for kidneys, there still would be a shortage of kidneys for transplantation.

Kootstra and his colleagues in Maastricht have pioneered efforts in the use of kidneys from uncontrolled NHBDs. His group has shown that kidneys retrieved from uncontrolled NHBDs have a higher rate of DGF (75%) but similar long-term graft survival. Twenty percent more kidneys have been transplanted through implementation of an uncontrolled NHBD program in Maastricht.54,55 This protocol requires consent for placement of catheters but, unlike the Washington Hospital Center protocol, CPR is continued after the patient is pronounced dead to circulate heparin and phenolamine and to maintain perfusion of the kidneys. ATN rates for uncontrolled renal NHBDs range from 60% to 70%, significantly higher than rates reported from controlled NHBDs.56 Graft survival reported by Boosler et al at 1 year was 80% and at 3 years 60%, at the same time, two groups from Japan reported a 70% 2-year graft survival.57,58 The group from Spain reported no difference in graft survival up to 6 years but early function was worse when compared with HBs.59 Although graft survival after renal transplantation from uncontrolled NHBDs is acceptable, it appears to be less favorable compared with controlled NHBDs and HBs. However, this should not curtail efforts to establish such programs.

Uncontrolled extrarenal NHBDs. Experience with uncontrolled extrarenal NHBDs has only recently been reported by the Pittsburgh group for liver transplantation. An earlier report indicated good function in six of seven livers recovered from uncontrolled NHBDs.60 However, more recently, in a group of 12 livers procured from uncontrolled NHBDs with a mean CPR time of 37 minutes, six were transplanted. Six livers were discarded for macroscopic or microscopic changes. Three of six livers developed primary nonfunction; one was lost to hepatic artery thrombosis, and one to cytomegalovirus hepatitis. Their conclusion was that procurement of livers from uncontrolled NHBDs was suboptimal and that the use of livers from these donors must be carefully assessed.60

Summary

The use of organs from NHBDs is beginning to gain acceptance as a method to help alleviate the current organ shortage. This is shown by the number of OPOs that now have protocols for retrieving organs from NHBDs. In a controlled setting, NHBDs can be expected to yield kidneys and, in preliminary studies, extrarenal organs that function similarly to those retrieved from HBs. The best method of renal preservation after retrieval from NHBDs appears to be machine perfusion—as a result of which, rates of
delayed graft function can be reduced significantly. Experimental work may help further limit the damaging effects of warm ischemia.

Although controlled NHBDs could have a significant impact on extrarenal transplantation, the impact on renal transplantation will be much smaller. For this reason, in the absence of HBDS, kidneys from uncontrolled NHBDs could have the most significant impact on decreasing the disparity between donors and potential renal recipients. However, protocols involving uncontrolled NHBDs are logistically more complex and must limit warm ischemia while, at the same time, satisfying issues of consent for any procedure performed in preparation for organ donation.

Because a large number of healthcare professionals are involved with potential NHBDs, discussions with them and with on-site ethics committees are extremely important. Although the use of NHBDs has a historical precedent, many are unaware that this concept is not new. Therefore, education of these same healthcare professionals is essential. Likewise, the transplant institution by way of medical boards or IRBs should approve protocols that involve the use of NHBDs. Active discussions regarding NHBDs should help allay any fears of impropriety and should help to maintain public trust. If our approach to NHBDs is scientifically sound, ethically based, and expertly applied, the use of NHBDs can be expected to have a major impact on organ donation.

Despite this resurgence of interest in NHBDs, we must not lose sight of the fact that we can and must do more to realize the full potential of HBDS.

References

1. United Network for Organ Sharing: UNOS Update 1994, 10 (12)
17. Orr JD, Cundry SR, Bailey LL: Reanimation may play role in increasing donor supply. UNOS Update 1994, 10(1):11
42. Henry MG, Sommer BG, Ferguson RM: Improved immediate function of renal allografts with Beiler perfusate. Transplantation 1988, 45:73
49. DeVita MA, Snyder JV: Development of the University of Pittsburgh Medical Center protocol for the care of terminally ill patients who may become organ donors after death following the removal of life support. Kennedy Institute of Ethics Journal 1993, 3:131