Non-Heart-Beating Donation: Current State of the Art


ABSTRACT

The use of non-heart-beating donors (NHBD) helps us to deal with the problem of the organ shortage. In addition to difficulties with legal and ethical acceptability, there are concerns regarding medical safety, which prevent the widespread use of these donors. To make optimum use of this potential organ supply, the ischemic injury that occurs after a period of warm ischemia needs to be reversed. To minimize the warm ischemia time, once the subject is declared dead, most centers commence in situ cold perfusion via a femoral access or a rapid aortic cannulation. This usually occurs within minutes of arriving at the emergency department, before the next of kin have been notified of the patient’s death. The European experience of kidney transplantation from NHBD shows promising results. The long-term outcomes are similar to HBD kidneys notwithstanding a higher rate of delayed graft function, which seems not to affect the long-term survival of these kidneys. In summary, NHBD may have an important impact on the large discrepancy that exists between the organ supply and the demand. Current data suggest that the results may be further improved by better patient selection and retrieval team organization.

A particularly important pool of donor organs, and the focus of considerable attention, is the non-heart-beating donor (NHBD). Kidneys from NHBD were the only source of cadaveric donors prior to the wide acceptance of brain-death criteria during the early 1970s. They have been used with excellent long-term results, especially in Japan, where brain death was only accepted legally in 1999. Now, NHBD present an untapped source of organs that could have an important impact on the large discrepancy that exists between supply and demand. Kidneys from NHBD may even double the donor pool.1,2 If such programs are reliable and successful, they could be widely promoted, significantly reducing waiting lists.

In the last few years, several reports have appeared in the medical literature showing good long-term function of kidneys from NHBD, with a graft survival probability similar to transplants from HB donors. However, several reasons have obstructed the widespread use of these organs. The main reason may be the concept of the transplantation community that NHBD are marginal or suboptimal donors who provide kidneys with poor function. Other problems include legal and ethical ones, as well as the logistics of the procedure.

Experience has shown that all legal and ethical problems can be solved by reaching agreements with the government, society, and medical community; however, logistical problems are more tricky. NHB donation remains a race against the clock. To obtain an acceptable warm ischemia period it is necessary to have good planning, management, and organization. Transplantation surgeons and coordinators must be within close reach of potential donor locations. Furthermore, enough trained staff members are required for uninterrupted on-call coverage. The risk that efforts in NHBD programs endanger regular HB programs, because of limited organizational resources, is not supported by published data. Indeed, it appears that NHBD consistently increase the number of available kidneys with no effect on HB donations.

The Maastricht group has defined 4 NHBD categories. Types I and II, also called “uncontrolled donors,” are subjects in whom cardiac death occurs in a sudden manner, usually in an out of hospital setting or in the Emergency Room. Transplant procurement teams are not alerted and a long time is required to fulfill the legal requirements for donation. Additionally, warm ischemia is always longer than in “controlled donors.” European countries perform the majority of this kind of donation.

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Types III and IV are also called "controlled donors." In type III, the patient is withdrawn from vital support because of a terminal illness; organs are retrieved after death is diagnosed, provided there is a previous agreement from the patient or the next of kin. The transplantation team is ready, and the donor is usually of a terminal illness; organs are retrieved after death is declared brain-dead. This type of donor is the main source of donors in Japan, even after approval of brain-death law. In this country, after diagnosing brain-death, the transplant procurement team has to wait until cardiac arrest occurs. The transplantation team is ready but the donor suffers a long period of instability before cardiac arrest. In western countries, it represents a sporadic source of organs, when the donor suffers a cardiac arrest while in the process of brain-death donation.

The unequal distribution of donors in the different categories in NHBD programs may explain some of the variation in outcome between the reports. The variable practice of withdrawing therapy from category III donors or inclusion of category IV donors in other countries, such as the United States or Japan, makes comparisons even more difficult.

For a proper interpretation of the results, it is necessary to account for the different time intervals in each type of NHBD. There are 3 crucial moments: first the cardiac arrest, second the time of death diagnosis, and finally the moment of organ retrieval. Between these points there are 2 important lapses of time. The time between cardiac arrest and death diagnosis is short or very short in controlled donors. Cardiac arrest is awaited and death diagnosis is done a few minutes after it. In uncontrolled donors, this lapse of time is usually long, because usually cardiopulmonary resuscitation maneuvers are performed. The diagnosis of death is done at least 30 minutes after cardiac arrest. In the case of type I NHBD, this interval is much longer. In our hospital, with an active type I NHBD program, it averages >100 minutes. The interval between death diagnosis and organ retrieval is also reduced to a minimum in the case of controlled donors. The retrieval team is ready and surgery starts immediately after death diagnosis. In the case of uncontrolled donors, this period is long: up to 2 to 3 hours are needed to fulfill all the legal requirements for organ donation, including the family interview. During this time the organs are perfused using a catheter placed in the aorta or using a cardiopulmonary bypass. Japanese NHBD have a prolonged period of hemodynamic instability due to previous cardiac arrest. Finally, cold ischemia time is characteristically long in the United States, short in Japan, and intermediate in European countries.

Short-term function of kidneys transplanted from NHBD is characterized by a rate of delayed graft function (DGF) that usually exceeds 70%. However, with proper donor selection, the rate of never-function kidneys can be similar to that obtained with HB donors. Usually a lower rate of DGF is seen in American type III donors, probably due to the use of stable donors with short warm ischemia times. In contrast, Japanese donors, with short warm ischemia but long periods of hemodynamic instability previous to cardiac arrest, show a DGF rate equal to the European groups with long warm ischemia but no period of hemodynamic instability prior to cardiac arrest.

Available data suggest that the delay in kidney retrieval is proportional to the rate of DGF, but the damage suffered by the kidney may be reversible as long as some limits are respected. Our NHBD program started in 1989. We have performed 217 renal transplantations from NHBD. Out of hospital deaths, after failed cardiovascular resuscitation, are taken to the hospital by the city emergency services. Cardiac arrest is considered as irreversible after a minimum resuscitation period of 30 minutes without an effective cardiac beat or when the nature of the injuries is not compatible with life. Cadavers with certain characteristics are considered potential donors: younger than 55 years; no thoracic or abdominal bleeding injuries; no external evidence of drug addiction; cause of death not physical violence; external cardiac massage and mechanical ventilation commenced within 15 minutes from the start of cardiac arrest; and continuous cardiac massage, mechanical ventilation, and intravenous saline perfusion during the transfer to the hospital. Cardiopulmonary bypass is performed while familial or judicial permission is obtained. In Spain, the current transplantation law includes the donation from NHBD. After the permission procedures are completed, organ extraction is performed. The majority of centers report on the use of NHBD type III and type IV. However, our main sources of NHBD are type I and type II. In fact, more than 80% of them were type I, transported to the hospital with the only purpose being donation. The incidence of DGF was higher among NHBD versus HBD donors (63.9% and 20.4%, respectively; relative risk 6.9, confidence interval 95%, 4.6–10.3). The number of dialyses and the days to function were similar between DGF kidneys from NHB and HB donors. A high rate of DGF in the NHBD setting can be accepted if this group is not associated with a poor long-term outcome, unlike DGF in the HBD setting, where it has been linked to compromised long-term results. In agreement with the results of other authors, we found that only kidneys from HBD and DGF showed diminished survival. NHBD with and without DGF showed the same survival curves.

We found no differences in long-term survival among NHBD when compared with the HBD kidneys. In fact, graft survival at 7 years shows a better tendency in NHBD group (93.3% vs 86.5%; P = .08). When patients older than 60 years of age were excluded from the group of patients receiving HBD kidneys, the results were the same, namely, 93.3% versus 89.8%.

The consequences of ischemic injury are less critical in kidney transplantation than in liver transplantation; pa-
tients receiving kidneys with DGF can be sustained with dialysis while the organ recovers. For this reason, the clinical use of NHBD has predominantly centered on kidney transplantation. The clinical experience of using livers from NHBD is currently limited. Under controlled circumstances, when the warm ischemia time is restricted to 20 or 30 minutes, the results are acceptable. In the uncontrolled setting, when cardiac arrest occurs outside the operating room, the results have been poor with a high rate of primary nonfunction. Most of the successful cases use continuous in vivo perfusion with cardiopulmonary bypass or chest compressions with oxygenation. It is likely that this provides some recovery of cellular energy stores before cold storage. Additionally, from experimental as well as clinical sources, there is good evidence that perfusing the liver at some point during the preservation period might be the best way to access the potential of the NHBD pool for liver transplantation.

We have retrieved 26 livers from NHBD. Because our institution does not have a liver transplantation program, some of these organs were sent by plane to another hospital 600 km away and 14 were finally transplanted. Among them, 5 showed primary nonfunction and the rest did well. The results are encouraging because we were able to retrospectively identify prognostic factors, such as warm ischemia period and time under bypass.

In summary, NHBD are a valuable source of cadaveric organs that have been the subject of renewed interest in recent years. The Institute of Medicine has studied the issues surrounding the use NHBD, reaching the conclusion that "the recovery of organs from NHBD is an important, medically effective, and ethically acceptable approach to reducing the gap that exists now and will continue to exist in the future between the demand for and available supply of organs for transplantation." Growing experience with these techniques demonstrates that when organs are transplanted from NHBD, the results are only slightly inferior to those from HB donors. Current data suggest that the results may be improved by better patient selection and retrieval team organization.

REFERENCES