

A Successful Transplantation from Maastricht Category-4 Non-Heart Beating Donor

Kalp Atımsız Donörden (Maastricht Kategori 4) Yapılan Başarılı Bir Böbrek Nakli

ABSTRACT

The shortage of available organs is the limiting factor for kidney transplantation (Ktx). One of the strategies to increase access to Ktx is the use of non-heart beating (NHB) donors. We herein present a successful Ktx from an NHB (Maastricht Category-4) donor. The donor was a 21-year-old woman who had brain death due to cerebrovascular accident. She had severe hypotension for three hours despite 30 µg/kg/min dopamine infusion, followed by cardio-pulmonary arrest just before the operation began. Cardio-pulmonary resuscitation was consequently initiated and continued during the operation. Donor organ harvesting (hepatectomy and bilateral nephrectomy) was performed after direct aortic cannulation. The warm ischemia time was 35 minutes. The recipient was a 54-year-old man who had undergone hemodialysis for four years. There were 3/6 mismatches, and the lymphocyte cross-match was negative. The induction immunosuppressive was anti-thymocyte globulin, followed by tacrolimus/MMF/steroid after the 12th day. He had delayed graft function and hemodialysis was required at the third and sixth days. The urine output gradually increased and sCr slowly declined afterwards and he discharged with sCr 1.5 mg/dl on the 24th day. At the first year of transplantation, he is in good clinical condition with a stable baseline sCr of 1.5 mg/dl. NHB donors can be an alternative and important source to expand the kidney donation pool, and successful long-term outcomes favor this modality.

KEY WORDS: Non-heart beating donor, Kidney transplantation, Donor pool

ÖZ

Böbrek nakli bekleyen hasta sayısı, organ yetersizliğine bağlı olarak sürekli artmaktadır. Böbrek nakil sayısını artırma stratejilerden biriside kalp atımsız kadavra donörleri (NHB) kullanmaktır. Bu yazıda, Diyarbakır Eğitim ve Araştırma hastanesinde, Maastricht Kategori 4 NHB donörden yapılan başarılı bir böbrek nakli sunulmuştur. Yirmi bir yaşında kadın hastanın serebro-vasküler olay nedeniyle yoğun bakıma yatışının beşinci gününde beyin ölümü gerçekleşti. Serum kreatin 0,8 mg/dl iken uygunsuz donör bakımı nedeniyle 3,7 mg/dl'ye yükselmişti. Donör 30 µg/kg/dakika dopamin infüzyonu almasına rağmen ciddi hipotansiyonu vardı (60/40 mmHg). Donör operasyona alınmadan kardio-pulmoner arrest gelişti ve operasyon kardio-pulmoner resusitasyon eşliğinde gerçekleştirildi. Direk aortik kanulasyonu takiben hepatektomi ve bilateral nefrektomi yapıldı. Sıcak iskemi süresi 35 dakikaydı. Alıcı 54 yaşında erkekti ve hipertansif nefropatiye bağlı dört yıldır hemodiyalize giriyordu, 3/6 mismatch vardı, lenfosit cross-match negatifti. Soğuk iskemi süresi dokuz saattti. İndüksiyon olarak ATG (Anti-timosit globülin) kullanılıp 12. günden sonra immunsupresyona takrolimus/MMF/steroid ile devam edildi. Hastanın gecikmiş graft fonksiyonu olup üç ve altıncı günlerde hemodiyaliz gereksinimi oldu. Birinci haftanın sonunda idrar çıkımı artarken, kreatin 14. günden sonra 3 mg/dl'nin altına düştü. 24. günde kreatin 1,5 mg/dl olarak taburcu olan hastanın naklin birinci yılında klinik durumu iyi, kreatini bazal seviyededir. Organ nakli havuzunun genişletilmesinde NHB donörler önemli bir kaynak sağlayabilir. NHB donörlerde, gecikmiş graft fonksiyonu sık olmasına rağmen, başarılı uzun dönem sonuçları bu modaliteyi destekler niteliktedir

ANAHTAR SÖZCÜKLER: Kalp atımsız donör, Böbrek nakli, Donör havuzu

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INTRODUCTION

Kidney transplantation (Ktx) is the treatment of choice for end-stage renal disease (1). The shortage of organ donation is the limiting factor for this treatment modality. There is an increasing gap between the patients on the waiting list and number of available organs. In Turkey, there are about 22.000 patients on the kidney waiting list but only 3000 Ktx procedures were performed in 2012 (2). Another problem for Turkey is the dominance of living-related kidney donations (73%) (3). There are several strategies to increase access to kidney transplantation such as increasing the living-related Ktx, expansion of the brain death donation (DBD) pool by use of expanded criteria donors, increasing the quality of brain-death donor care and developing national programs for non-heart beating (NHB) donation.

We began a transplantation program at the Diyarbakır education and research hospital about one year ago. We herein present our first successful cadaveric Ktx in our hospital. The importance of the case is that the donor was an NHB (Maastricht category-4) donor who had received inappropriate donor care. The aim of this presentation is to draw attention to the importance of the prevention of organ loss due to inappropriate donor care and the potential use of NHB donors to expand the donor pool.

CASE REPORT

The donor was a 53 kg, 167 cm tall, 21-year-old woman who had suffered a cerebrovascular accident and followed-up at a state hospital's intensive care unit. At the fifth day of hospitalization, she was declared brain dead due to hypoxic brain injury. Her relatives refused organ donation until the 3rd day of brain death declaration. Serum creatinine on admission was 0.8 mg/dl, and then increased to 3.7 mg/dl progressively due to inappropriate donor care due to the initial refusal of organ donation. Our transplantation center was responsible for organ harvesting and one of the kidneys were offered to our center. At the arrival of our surgical team, she had hypotension (blood pressure 60/40 mmHg) for three hours despite the administration of 30 µg/kg/min dopamine infusion. The donor was taken to the operating room immediately but suffered cardio-pulmonary arrest just before the operation began. Cardio-pulmonary resuscitation (CPR) by external cardiac massage was consequently initiated and the operation was performed during continuous CPR. Donor organ harvesting (hepatectomy and bilateral nephrectomy) was performed after in-situ perfusion and cooling with the University of Wisconsin solution (UW) by insertion of a catheter directly into the aorta. Although the "real" warm ischemia time could not be determined, our estimation was at least 35 minutes (time between the cardiac arrest and completion of aortic perfusion). Pathological evaluation of kidney could not be performed due to technical issues but we accepted the kidney because of young donor age and no prior medical chronic disease history. The recipient was a 64 kg, 172 cm tall, 54 year-old male with end-stage renal failure due to hypertensive nephropathy. He had been on hemodialysis for four years. There were 3/6 mismatches and the lymphocyte cross-match was negative. The total cold

ischemia time was about nine hours. A written consent was obtained regarding the risk of an NHB donor and the left kidney was transplanted successfully to right iliac fossa.

The induction immunosuppressive was anti-thymocyte globulin (2.5 mg/kg/day) and continued through the 12th day with dose adjustments according to CD3 levels. At the 12th day, low-dose Tacrolimus was initiated with steroids and mycophenolate mofetil to stop ATG before the 14th day so as to prevent accumulated ATG toxicity. The patient had delayed graft function and hemodialysis was required at the third and sixth days. The urine output gradually increased afterwards, allowing discontinuation of hemodialysis. The serum Cr (sCr) exhibited a slow decline as expected, and at the 14th day fell to below 3 mg/dl. His sCr continued to decline and remained stable at 1.5 mg/dl. He was discharged from the hospital on the 24th day. He had no episode of acute rejection but suffered four episodes of urinary tract infection and was hospitalized due to urethral obstruction that was successfully treated by urology department. At the first year of transplantation, he was in good clinical condition with stable baseline sCr of 1.5 mg/dl.

DISCUSSION

We presented a successful Ktx from an NHB (Maastricht Category-4) donor. Although the donor had inappropriate donor care and prolonged hypotension followed by cardiac arrest, we decided to continue harvesting and transplant the kidney because of the young donor age and the medical history free of chronic diseases.

NHB Ktx popularity is increasing among western countries to expand the donor pool. This modality is expected to increase the kidneys available for transplantation up to 20-30% percent (4). In a previous study from Turkey, Ateş et al. have shown that nearly 18% of hospital deaths had the potential for NHB kidney donation (5). The increased number of published studies that reveal favorable graft-survival rates that are comparable with DBD donors at long-term follow-up also supports this Ktx modality (6,7).

NHB donors are classified with the Maastricht classification (8). Category 1 and 2 presents uncontrolled donors whereas category 3 and 4 presents controlled NHB donors (Table I). There are several medical, legal, and ethical issues regarding NHB kidney donation. Type 3 donors represent the cessation of advanced life support at intensive care units (ICU) and donation after cardiac arrest. This modality may be not suitable for every country, possibly including Turkey due to social, ethical, and religious reasons. Considering these reasons and the fact that some studies reported decreased declaration of DBD donors due to the use of Maastricht type 3 and 4 donors (9), it may be a better strategy to increase uncontrolled NHB donors to expand the donor pool. Although there were concerns about the success of uncontrolled NHB Ktx cause of unknown and increased warm ischemia time (WIT), a recent study has revealed similar rates of DGF, PNF and ten-year patient/graft survival with controlled NHB donation (10).

Table I: Maastricht categorization for non-heart beating donation.

NHBD Category	Alternative Categorization	Donor Status	Hospital Department
1	Uncontrolled	Death at arrival	Emergency Room
2	Uncontrolled	Unsuccessful resuscitation	Emergency Room
3	Controlled	Awaiting cardiac arrest	Intensive Care Unit
4	Controlled	Cardiac arrest while brain death	Intensive Care Unit

The most important determinant of success in NHB Ktx is the warm ischemia time. Warm ischemia time represents the time between the cardiac arrest or decrease of systolic blood pressure to less than 60 mmHg to the start of the cold perfusion. The optimal warm ischemia time for successful NHB Ktx is below 30 minutes. The main consequences and dilemma of prolonged WIT are delayed graft function or primary non-function (PNF). There is a high rate of PNF (about 5-9%) and DGF (60-95%) with NHB Ktx (6). DGF has been found to be significantly higher than with standard DBD in several series (4, 10). Conversely, DGF has been found not to negatively affect long-term graft survival (11). Despite the high DGF and PNF rates, it has been recently shown that NHB Ktx provides survival benefit to staying on dialysis treatment and waiting for a DBD Ktx (12).

In our case, WIT was about 35 minutes and, our patient suffered from DGF. However, he had a good functioning graft at one year of follow up. We used ATG as the induction immunosuppressive to avoid additional damage from calcineurine inhibitors. ATG prevents the attenuation of ischemia-reperfusion injury, however the nephrotoxic effects of calcineurine inhibitors increase with co-existing ischemic injury (13).

In conclusion, this report presents a successful Ktx from an NHB donor. Considered together with the current trend of using NHB donors to expand the donor pool in western countries, use of these donors may be an answer to the continuously growing Ktx waiting list for Turkey. However, it is clear that there is a need for a national health policy that is supported by legislation and highly organized transplantation centers to utilize this promising modality.

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