Transplant International

LETTER TO THE EDITOR

'When good kidneys pump badly': outcomes of deceased donor renal allografts with poor pulsatile perfusion characteristics

doi:10.1111/j.1432-2277.2009.00970.x

Hypothermic machine perfusion (HMP) is a dynamic preservation technique utilizing a continuous pulsatile flow of solution, rich in metabolic substrates, to enhance viability after reperfusion. HMP has been associated with microvascular stabilization, decrease in oxidative stress as well as improved adenosine triphosphate availability upon reperfusion [1]. HMP has recently evolved into the preferred method of extended criteria donor (ECD) kidney preservation, with extensive utilization in deceased donor (DD) renal transplantation [2–6]. Strong evidence now exists that renal HMP improved early graft function [5–7] and increased the utilization of ECD kidneys [7], with recent reports suggesting a long-term graft survival benefit of HMP [3,6].

Pulsatile perfusion parameters (PPP) of flow (FL) and resistance (RES) are frequently used in the evaluation of donor kidneys and have been thought to be predictive of outcomes. Poor PPP triggered discard in many cases [2,8,9]. We sought to evaluate outcomes of DD kidneys with poor PPP that were transplanted. We identified DD grafts preserved with HMP on the Waters RM3 between 9/1/04 and 2/1/06. Kidneys were perfused with Belzer MPS at 4–6 °C with settings of 50 mmHg and 60 pulses/min. Cases with poor PPP (defined as FL <80 ml/min/100 g and RES > 0.4 mmHg/(ml/min/100 g) at the time of organ offer and arrival at our center were included. Donor, preservation and recipient outcomes were recorded. Eighty-nine DD kidneys underwent HMP and were transplanted during the study period. Eleven (12.4%) had PPP. Donor and Recipient age was 45.8 ± 13 and 48.6 ± 11 years respectively. Median donor terminal creatinine was 0.8 mg/dl (*r*, 0.7–3.7). The median cold ischemia time was 22 h (range: 14–48 h) with a median of 13 h of HMP (range: 6–30 h). Mean flow and renal resistance were 74 ± 6 cc/g/min and 0.46 ± 0.1 respectively. Case-specific donor and recipient variables are summarized in the Tables 1 and 2. All patients received thymoglobulin induction with tacrolimus, mycophenolate mofetil and steroid was discontinued within 7 days. Four patients (36.3%) required hemodialysis (HD) post-transplant, although two required only one HD session for hyperkalemia. The biopsy-proven rejection

Table 1. Donor and preservation characteristics.

Donor	Donor age	Donor terminal SCr.	CIT (h)	MP time (h)	WIT (min)	Flow*	Res†	DGF	Donor biopsy
1	42	0.8	20	15	39	69	0.45	No	Not done
2	42	0.8	26	19	42	68	0.44	Yes	Not done
3	44	0.8	40	30	32	65	0.61	No	Not done
4	65	0.6	48	15	42	79	0.35	No	Normal: <5% glomerulosclerosis
5	25	3.7	39	13	45	72	0.54	Yes	ATN/+Glomerular Fibrin thrombi
6	53	0.7	22	18	27	59	0.42	No	Not done
7	53	0.7	15	11	33	72	0.45	Yes	Not done
8	43	1.4	21	9.5	35	77	0.41	No	Not done
9	43	1.4	18	12	35	74	0.43	No	Not done
10	56	1.7	30	5.5	40	80	0.45	Yes	Not done
11	38	2.9	14	10	30	79	0.6	No	Not done

SCr., serum creatinine (mg/dl); CIT, cold-ischemic time; WIT, warm-ischemic time; DGF, delayed graft function.
*PP flow (ml/min/100 g).
†PP resistance mm Hg/(ml/min/100 g).

Table 2. Recipient characteristics and outcomes.

Recipient	Gender	Age (years)	F/U Time (months)	No. HD	LOS	1 Month SCr.	3 Months SCr.	6 Months SCr.	Most recent SCr.	Biopsy-proven rejection	Functional graft	Comments/ complications
1	F	61.2	47.1	0	6	1.8	1.4	1.3	1.3	No	Yes	–
2	M	50	47.1	1	6	2.1	N/A	2.3	2.0	Yes	Yes	Aspergillus pneumonia
3	M	31.7	46.4	0	7	2.9	2.8	2.1	2.0	No	Yes	–
4	M	63	45.2	0	5	1.9	2.2	1.7	1.8	No	Yes	incisional hernia
5	F	44	42.4	>3	5	4.5	1.2	1.3	1.1	Yes	Yes	AMR
6	F	59	41.9	0	4	1.4	1.6	1.7	–	Yes	No	2 Episodes of ACR → graft lost at 3 years
7	M	50	41.9	1	4	1.7	1.6	2.2	4.5	No	Yes	BK virus infection
8	M	35	35.3	0	4	1.9	1.5	1.7	1.3	No	Yes	UTI
9	M	55	35.3	0	4	1.9	1.8	2.6	3.1	No	Yes	ARF from ACEI
10	M	49	34.5	>3	4	HD	HD	5	–	No	No (graft removed because of life-threatening infection)	Multiple admissions for cryptosporidium → dehydration/ATN → 1 month SCr 5.1
11	M	37	44.9	0	5	1.4	1.5	1.3	1.3	No	Yes	Sepsis, pyelo DKA

HD, hemodialysis; LOS, length of stay; SCr., serum creatinine (mg/dl); AMR, antibody-mediated rejection; DKA, diabetic ketoacidosis.

rate was 27%. Median follow-up was 42.4 months. (range: 36–47) At the end of the follow-up period, all patients were alive and 9/11 (81.8%) had functioning grafts.

Pulsatile perfusion parameters are frequently used in the evaluation of DD kidneys and are thought to be a measure of graft quality that is predictive of outcomes. Some groups routinely discard DD kidneys if PPP are poor [3–7,9]. While it is impossible to determine whether discard was prudent in such reports, our small series does suggest that poor PPP should be taken in context with other donor variables. There are few reports on this topic, Sonneday *et al.*[8] reported a series of imported kidneys with poor PPP and actually found when HMP was reinitiated at their center most kidneys actually had acceptable parameters. Furthermore, Mozes *et al.* [10] cautioned on discard of kidneys solely based on poor PPP. While the messages of these reports are similar to ours, we are the first to specifically report transplant outcomes when kidneys that have persistent PPP are transplanted.

Acceptable short- and long-term outcomes were seen in obtained in kidneys with PPP that were otherwise acceptable for transplantation. While PPP may correlate with delayed graft function, there is little data showing a relationship between perfusion parameters and long-term function. If parameters are used in conjunction with other variables that indicate a poor quality organ, then discard is appropriate. In our small series, poor perfusion parameters in the absence of other high-risk donor variables were not correlated with a negative outcome. We recommend further study. In the absence of contradictory reports, we recommend utilization of low-risk DD kidneys with poor PPP.

James V. Guarrera, Michael J. Goldstein, Benjamin Samstein, Scot Henry, Christopher Reverte, Ben Arrington, Tod Brown, Theresa K. Coleman, Gabriel Mattei, Natasha Mendez, Joan Kelly and Lloyd E. Ratner
Division of Abdominal Organ Transplantation, Department of Surgery, Columbia University Medical Center, New York, NY, USA

References

1. Maathuis MH, Manekeller S, van der Plaats A, *et al.* Improved kidney graft function after preservation using a novel hypothermic machine perfusion device. *Ann Surg* 2007; **246**: 982. Discussion 989.
2. Wight JP, Chilcott JB, Holmes MW, *et al.* Pulsatile machine perfusion vs. cold storage of kidneys for transplantation: a rapid and systematic review. *Clin Transplant* 2003; **17**: 293.
3. Kwiatkowski A, Wszola M, Kosieradzki M, *et al.* Machine perfusion preservation improves renal allograft survival. *Am J Transplant* 2007; **7**: 1942.
4. Sellers MT, Gallichio MH, Hudson SL, *et al.* Improved outcomes in cadaveric renal allografts with pulsatile preservation. *Clin Transplant* 2000; **14**: 543.
5. Matsuoka L, Shah T, Aswad S, *et al.* Pulsatile perfusion reduces the incidence of delayed graft function in expanded criteria donor kidney transplantation. *Am J Transplant* 2006; **6**: 1473.
6. Moers C, Smits JM, Maathuis MH, *et al.* Machine perfusion or cold storage in deceased-donor kidney transplantation. *N Engl J Med* 2009; **360**: 7.

7. Schold JD, Kaplan B, Howard RJ, *et al.* Are we frozen in time? Analysis of the utilization and efficacy of pulsatile perfusion in renal transplantation. *Am J Transplant* 2005; **5**: 1681.
8. Sonnenday CJ, Cooper M, Kraus E, *et al.* The hazards of basing acceptance of cadaveric renal allografts on pulsatile perfusion parameters alone. *Transplantation* 2003; **75**: 2029.
9. Nyberg SL, Baskin-Bey ES, Kremers W, *et al.* Improving the prediction of donor kidney quality: deceased donor score and resistive indices. *Transplantation* 2005; **80**: 925.
10. Mozes MF, Skolek RB, Korf BC. Use of perfusion parameters in predicting outcomes of machine-preserved kidneys. *Transplant Proc* 2005; **37**: 350.

