

EX-VIVO PERFUSION MACHINES IN KIDNEY TRANSPLANTATION. THE SIGNIFICANCE OF THE RESISTIVITY INDEX.

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Abstract

Introduction. With a growing shortage of organs for transplantation, finding ways of increasing the donor organ pool remains of utmost importance. Perfusion machines (PM) have been proven to enhance the potential for kidney transplants to function sooner, last longer, giving patients the opportunity for a better life quality.

Objective. The aim of this study is to evaluate the relation between the resistance index provided by the PM, the postoperative resistance index measured by Doppler ultrasound and the initial graft outcome.

Material and method. Between January 2012-December 2012, clinical data obtained from 82 consecutive renal transplants from brain death donors (BDD) which underwent PM maintenance were analyzed in a transversal study. Prior transplantation we recorded the solution temperature, filtration rate and the resistance index provided by PM. After the surgical intervention, each patient had standard follow-up. Doppler ultrasound resistivity index (RI) was recorded on the first postoperative day.

Results. Out of 115 renal transplants, 98 (85.21%) were performed with grafts from BDD. The PM was used for 82 renal grafts. The Doppler resistance index in relation to the resistance index shows a highly statistical correlation by linear regression ($R=0.813$, $p<0.0001$). Primary graft function was recorded in 74 patients (90.24%) and it was highly statistically significant correlated with the resistance index measured by PM. Out of 8 patients with primary non-function, 6 patients recovered with normal graft function at one year.

Conclusion. The resistivity index recorded by the life-port machine is correlated with the vascular resistivity index measured by Doppler ultrasound and thus it may predicts the primary graft outcome.

Keywords: Graft quality, perfusion machine, post-transplant Doppler ultrasound, renal transplantation.

Introduction

Renal transplantation has been the treatment of choice for patients with end stage kidney disease since 1960's. This method has a good cost-efficiency ratio and offers a greater improvement in life quality over other methods like hemodialysis or peritoneal dialysis. Perfusion machines (PM) have been proven to enhance the potential for kidney transplants to function sooner and last longer, giving patients the opportunity for a better life quality with their new organ. By reducing the risk of delayed graft function (DGF) and the associated risk of transplant failure, kidney preservation with PM offers the potential for more kidneys to be suitable for transplantation, reducing the current waiting list and the

ongoing cost of care for people waiting for a kidney transplant. With a growing shortage of organs for transplantation, finding ways of increasing the donor organ pool remains an important issue.

Objective

The aim of this study was to evaluate the relation between the resistance index provided by the PM, the postoperative resistance index measured by Doppler ultrasound and the initial graft outcome.

Material and method

Out of 115 renal transplants performed at Clinical Institute of Urology and Renal Transplantation from Cluj-Napoca, between January 2012-December 2012, clinical data obtained from 82 consecutive renal transplants from BDD which underwent PM maintenance were - analyzed in a transversal study.

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Recipients were included in the study with ethics committee approval only after written and informed consent. Prior transplantation we recorded the solution temperature, filtration rate and resistance index provided by the PM.

After the surgical intervention, each patient had standard follow-up including, urine output and Doppler ultrasound. Initial urine output and Doppler ultrasound resistivity index (RI) of the segmentary renal arteries were recorded on the first postoperative day.

The collected data were analyzed using the EpiInfo program by linear regression in order to test the hypothesis that life-port machine indices are correlated with Doppler ultrasound indices and graft outcome.

Results

Of the 115 renal transplants, 98 (85.21%) were done with grafts from BDD. The PM was used for 82 renal grafts (Table I.) which required transportation from other centers.

The temperature of the perfusion solution was maintained between 2-6°C using ice. Wisconsin solution was used with mean filtration rate of 121.63 ml/min average resistance index 0.15. Data regarding the measured parameters are presented in Table I.

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Table I. Parameters recorded pre and post-transplantation.

Total number of renal transplants	115
BDD grafts	98
Perfused BDD grafts	82
Solution temperature	3.73±1.44 (2-6)°C
Filtration rate	121.63±32.88 (38-169) ml/min
Resistance index	0.15±0.087 (0.05-0.40)
Doppler resistance index	0.67±0.071 (0.55-0.86)
Primary graft function	90.24% (74/82)

BDD - brain death donor

Regression summary for the dependent variable: Doppler resistance index in relation to the resistance index shows a highly statistical correlation by linear regression ($R=0.813$, $R^2=0.661$, adjusted $R^2=0.657$, $F(1.80)=156.34$, $p<0.0001$, Std. Error of estimate: 0.04166).

Primary graft function was recorded in 74 patients (90.24%). The average resistance index measured by PM was statistically significantly higher in the cases of delayed / non-functional grafts as compared with the primary graft function cases (Table II).

Out of 8 patients with primary non-function, 6 patients recovered with normal graft function at one year.

Table II. Relation between graft function and resistance index.

Graft function	No.	Resistance index	p
Primary	74	0.13±0.073	<0.000
Delayed/Non function	8	0.30±0.058	

Discussion

Machine perfusion of deceased donor kidneys has been shown to improve graft performance. The randomized European multicenter trial published in the New England Journal of Medicine clearly proved beyond doubt the beneficial effect of machine perfusion on delayed graft function [1]. Life-port perfusion machines ensure pulsatile perfusion of the kidney with preservation solution at temperatures between 0 and 4 degrees Celsius. This continuous perfusion circuit maintains the electrolytic equilibrium of the interstitial fluid, the oxygen transport, as well as the removal of toxic metabolites. These advances have made possible the expanding of selection criteria for deceased donors: organ harvesting from Non Heart Beating Donors, extension of the donor's age beyond 65 years, prolonged exposure of organs to anoxia/hypoxia and ischemia (more than 22 hours at cold temperatures), and harvesting of the kidneys from marginal donors (hypertension, diabetes) and slightly elevated serum creatinine level [2,3]. In this context in which more and more harvesting centers are being opened and considerable efforts are being put into an efficient organization of the transplant program, the purchase and use of life-port systems is justified [4]. This could not only facilitate the transport and preservation of kidneys between harvesting and transplant centers, but also improve the graft evaluation prior to transplant as well as improve the graft quality, thus reducing the post-transplant primary non-function of the kidneys, with important economic impact [5,6]. Life-port systems display three perfusion indicators: pressure (low pressure can lead to a diminishing of the perfusion, while high pressure associated with mechanical stress can damage the endothelium), filtration rate (high values are associated with a lower rate of immediate post-transplant complications) and resistance indices (a high filtration resistance could foreshadow weak success of the post-transplant graft). Doppler ultrasound coupled with diuresis monitoring and biochemical examinations are performed for the evaluation of the graft functionality and used to detect post-transplant complications: perinephric collections (hematoma, urinoma, lymphocel), a reduction in the renal function (acute or chronic rejection, acute tubular necrosis, drug-related nephrotoxicity), vascular complications (renal artery stenosis, renal vein thrombosis, arterio-venous fistulas and pseudo-aneurysms).

Due to the shortage of donor organs to meet the growing demand, transplantation from an expanded criteria donor (ECD) may also be an option for some transplant candidates. ECD kidneys are not considered ideal or standard, but can significantly shorten the waiting time to transplantation. The final decision to accept a particular organ will remain the prerogative of the transplant surgeon. The Life-port contribution in this decisional process can be decisive regarding the suitability of the organ being offered for a specific candidate [7,8].

Our study shows that the PM indices are highly corre-

lated with the Doppler ultrasound resistance index and thus, with the graft outcome. The resistivity index measured by the PM may be used to discard kidneys prior to transplant, avoiding transplants with a high rate of failure that can compromise life quality of the recipient with negative economic impact [9].

Our study identify a relation between PM resistivity index and Doppler ultrasound resistivity index measured on the first postoperative day.

To our knowledge, our study is the first to assess the relation between the resistivity index provided by the PM and the Doppler ultrasound.

Conclusion

The resistivity index recorded by the life-port machine is correlated with the vascular resistivity index measured by Doppler ultrasound and thus it may predict the primary graft outcome.

References

1. Moers C, Smits JM, Maathius MH, et al. Machine Perfusion or Cold Storage in Deceased-Donor Kidney Transplantation. *N Engl J Med*, 2009; 360:7–19.
2. Cohen B, Smits JM, Haase B, et al. Expanding the donor pool to increase renal transplantation. *Nephrol Dial Transplant*, 2005; 20:34–41.
3. Treckmann J, Moers C, Smits JM, et al. Machine perfusion versus cold storage for preservation of kidneys from expanded criteria donors after brain death. *Transpl Int*, 2011; 24(6):548–54.
4. Wight J, Chilcott J, Holmes M, Brewer N. The clinical and cost-effectiveness of pulsatile machine perfusion versus cold storage of kidneys for transplantation retrieved from heart-beating and non-heartbeating donors. *Health Technol Assess*, 2003; 7:1–94.
5. Schold JD, Kaplan B, Howard RJ, Reed AI, Foley DP, Meier-Kriesche HU. Are we frozen in time? Analysis of the utilization and efficacy of pulsatile perfusion in renal transplantation. *Am J Transplant*, 2005; 5:1681–1688.
6. Wszola M, Kwiatkowski A, Latek M, et al. Long-term medical and economical benefit of machine perfusion (MP) kidney storage in comparison to cold storage (CS). *Ann Transplant*. 2009; 14(2):24–29.
7. Lodhi SA, Lamb KE, Uddin I, Meier-Kriesche HU. Pulsatile pump decreases risk of delayed graft function in kidneys donated after cardiac death. *Am J Transplant*, 2012; 12(10):2774–80.
8. Kwiatkowski A, Wszola M, Kosieradzki M, et al. Machine perfusion preservation improves renal allograft survival. *Am J Transplant*, 2007; 7(8):1942–1947.
9. Catena F, Coccolini F, Montori G, et al. Kidney preservation: review of present and future perspective. *Transplant Proc*, 2013; 45(9):3170–3177.