Evaluation of outcomes in renal transplantation using machine perfusion for the preservation of kidneys from expanded criteria donors



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Context

The shortage of kidney grafts led to retrieve organs from old donors with one or more co-morbidities, considered as "expanded criteria donors" (ECD). In France, since 2012, the "Agence de la biomedecine" (ABM) has recommended machines perfusion (MP) preservation for kidneys from ECD to improve kidney preservation and transplantation outcomes, with the creation of a specific lump sum financing the additional costs of this strategy. The program recommends MP preservation starts at the organ removal and ends at the organ transplant, enabling the rehabilitation of the organ during its transport. This study evaluates the impact of MP vs cold storage (CS), for the period 2011-2014 with kidneys from ECD.

Method

From the ABM database (Cristal), the effect of MP on the delayed graft function (DGF) was analyzed using a multivariate logistic model excluding pre-emptive transplants and primary non functions (PNF).

In addition, transplants from the same donor, whose one kidney was preserved by MP and the other by CS (population of twins), were analyzed using a mixed model.

We observed 4 316 grafts from ECD between 2011-2014

- 801 grafts with MP (18,5%)
- 3 515 grafts in CS

Stratification by CIT level or eGFR donor level was done.

Results on DGF of MP vs CS with kidneys from ECD

Candidate population MP vs. CS

We significantly found in MP population

- More recipients with comorbidities (54% vs 48%)
- Older recipients (63.9y vs 62.7y) •
- More donors with HTA (61% vs 58%) ٠
- Older donors (68.6y vs 67.8y)
- Shorter cold ischemia time (CIT) (16.9h vs 17.4h)

Transplant outcomes MP vs. CS

- Graft survival at 1 year with and without death censored similar between MP and CS recipients
- PNF: 4% for MP vs 6% for CS, p=0.03

Table 1. Multivariate analysis of DGF (logistic regression)

	Variable	Level	OR	95% Cl	p-value
Storage method (ref CS)		MP	0,45	[0,36 - 0,56]	<0.001
Recipient Factors	BMI (ref. <25 kg/m²)	25-29	1,30	[1,09 - 1,54]	<0.001
		≥ 30	1,63	[1,33 - 1,99]	
	Cause of ESRD (ref. Other)	PKD	0,73	[0,58 - 0,91]	0,006
	Time spent on dialysis (ref.<3y)	≥ 3 y	1,61	[1,36 - 1,90]	<0.001
	Retransplants (ref. No)	Yes	1,74	[1,38 - 2,19]	<0.001
	Number of comorbidities (ref.0)	1	1,04	[0,86 - 1,26]	<0.001
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- DGF: 16% for MP vs. 29% for CS, p<0.001 •
- MP has a protective effect on the DGF ٠ adjusted OR = 0.45 [0,36 - 0,56]
- The durations of hospitalization and dialysis after ٠ transplantation are shorter with fewer sessions of dialysis.

Transplant outcomes MP vs. CS in twin population

- 84 pairs analysis •
- Survival at 1 year with and without death censored ٠ MP vs. CS recipients not significantly different
- 2% of PNF for MP vs. 6% for CS, NS
- 7% of DGF for MP vs. 33% for CS, p<0.001 •
- MP has a protective effect on the DGF ٠ adjusted OR = 0.18 [0.06 - 0.58]

Figure 1. Forest plot of the treatment effect in stratified analyses

Subgroup		MP (n=672)	CS (n=2,995)	Adjusted Odds Ratio of MP (CS ref)			
		no. of L	DGF (%)		OR	CI at 95%	р*
Overall		109 (16%)	862 (29%)		0.45	(0.36 - 0.56)	
CIT (h)							0.59
	<14	40 (14%)	266 (23%)	<u> </u>	0.50	(0.34-0.72)	
	15-22	49 (17%)	411 (30%)	<u> </u>	0.43	(0.31-0.6)	
	>22	20 (19%)	185 (37%)	<u> </u>	0.37	(0.22-0.64)	
eGFR donor (ml/mn)						0.019
	<60	53 (23%)	327 (32%)	¢	0.62	(0.44-0.87)	
	≥ 60	56 (13%)	535 (27%)		0.36	(0.26-0.48)	
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				0,1 0,2 0,3 0,4 0,5 0,6 0,7 0,8 0,9 1	1,1		

≥2 1,59 [1,31 - 1,94] eGFR donor (ml/mn) Donor 0,99 [0,99 - 1,00] <0.001 **Factors** Gender (ref. Male) [0,65 - 0,89] <0.001 Female 0,76 HTA (ref. No) 1,24 [1,06 - 1,45] 0,007 Yes Antidiuretic hormone (ref. Yes) No 1,22 [1,03 - 1,45] 0,08 1,06 [0,83 - 1,35] Missing Transplant CIT (h) 1,03 [1,02 - 1,04] <0.001 Factors ATG, Polyclonal anti-lymphocyte Yes [0,57 - 0,79] <0.001 0,67 antibodies (ref. No) Missing 0,75 [0,50 - 1,14]

Conclusions

Comorbidities of recipients are more frequent and the age of donors and recipients is significantly higher for kidneys preserved by MP vs. CS.

Our results confirm a significant reduction of DGF incidence for ECD kidneys preserved by machines, with 2.2 times lower risk despite a population more at risk in this group, and a 5.2 times lower risk in the population of the kidneys "twins".

There is no significant difference in graft survival at 1 year between MP and CS recipients but without adjustment.

It remains to assess the impact of less recipients with DGF on the long term graft survival and to evaluate the cost effectiveness of this strategy.

*p-value of interaction test with MP/CS factor in multivariate analysis

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