LETTER TO THE EDITOR

# Hypothermic machine perfusion versus cold-storage for expanded criteria donor: A Single-center's first experience

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## To the Editor

It is a priority for the world of transplants to employ multiple and new strategies to reduce the discrepancy between organ availability and constantly growing waiting lists. Kidney transplantation (KT) is the gold standard treatment for patients with end-stage renal disease (ESRD). KT reduces mortality, extends life expectancy, and improves quality of life compared with dialysis (1). In this scenario of organ shortage, one strategy to reduce the gap between supply and demand is the use of donors in the expanded criteria donors (ECD) category. The Organ Procurement and Transplantation Network instituted a formalized definition of marginal kidneys with the advent of the Expanded Criteria Donor (ECD). Kidneys from ECDs are those from either a brain-dead donor ≥ 60 years of age or a donor 50 to 59 years of age with at least 2 of the following features: history of hypertension, terminal serum creatinine > 1.5 mg/dL (133 mmol/L), or cerebrovascular cause of death (2). The criteria for the definition of ECD was based on the presence of variables that increased the risk of graft failure by 70% (relative hazard ratio 1.70) versus that of standard criteria donor (SCD) kidney (3). ECD allografts are more susceptible to ischemia-reperfusion injury and are associated with higher discard rates due to an anticipated increased risk of primary non-function (PNF) or delayed graft function (DGF) (4). This clinical risk has necessitated a reconsideration of past preservation technologies; active organ preservation can have a wide spectrum of aims: from keeping the starting conditions stable to achieving an allograft's reconditioning. Static cold storage keeps cellular activity silent, inducing complete anaerobiosis of the tissues, whereas hypothermic dynamic perfusion with oxygenation, pragmatically far from regenerative medicine, could potentially stimulate cellular metabolic activity (5). At L'Aquila Transplant Center from November 2018 to January 2020, a total of 10 patients in ESRD (four women and six men; mean age 50 ± 9 years) with a median dialytic time of 2.5 years, underwent kidney transplantation from organs belonging to the ECD category. Five patients received an allograft subjected to static cold storage (SCSg) and five patients received a perfused allograft (HMPg). Perfusion parameters

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(renal resistance and flow rate) were recorded constantly during perfusion. The mean Karpinski score of the allografts was 2.9. The SCS group's mean preservation time was 660 minutes, HMP group's preservation time was 780 minutes. The allografts were perfused for an average of 210 min at a perfusion pressure of 15 mmHg. No allografts had supernumerary or polar renal arteries. During perfusion, a decrease in RR was accompanied by a parallel increase in renal flow, until reaching a stable washing plateau. Mean renal artery flow was 63 ± 18 ml/min at the start of perfusion and increased to 87 ± 46 ml/min after 60 min. The maximal flow was measured immediately before disconnecting the kidney from the machine with a mean of 90 ± 47 ml/min. Intraoperatively, the five perfused allografts showed excellent and homogeneous revascularization upon declamping at the end of the vascular anastomosis. No adverse events of a hemorrhagic or thrombotic nature occurred. As dictated in our internal protocol, all patients (SCSg and HMPg) underwent postoperative ultrasound and Doppler monitoring at one hour post-surgery. The grafts displayed good and homogeneous arterial vascularization at the parenchymal level with R.I between 0.6 and 0.7 on average. Good venous outflow was also visualized on the Doppler performed in the immediate postoperative time. The postoperative course was characterized by the absence of primary non-Function and by six episodes of DGF: 3 in SCSg and 3 in HMPg, with subsequent and gradual functional recovery at discharge. Delayed graft function did not differ significantly between the groups. In 2019, an episode of early graft function (EGF) was reported without the need for dialysis postoperatively, with an allograft subjected to machine perfusion. In 2020, however, we reported that a perfused organ, after a good and initial functional recovery underwent urgent transplantectomy following a spontaneous parenchymal rupture diagnosed by ultrasound and CT on the 14th postoperative day (Figure 1). In our opinion, there are no elements to link this event to pre-implantation perfusion treatment (6). The creatinine values in the 21th postoperative day were similar in all 10 cases studied .The functional performance was therefore excellent in the grafts subjected to treatment with HMP; Especially in the setting of longer cold ischemic times, on average 240 minutes longer. At the same time, they achieved appropriate clinical performance with regard to creatinine. There were similar

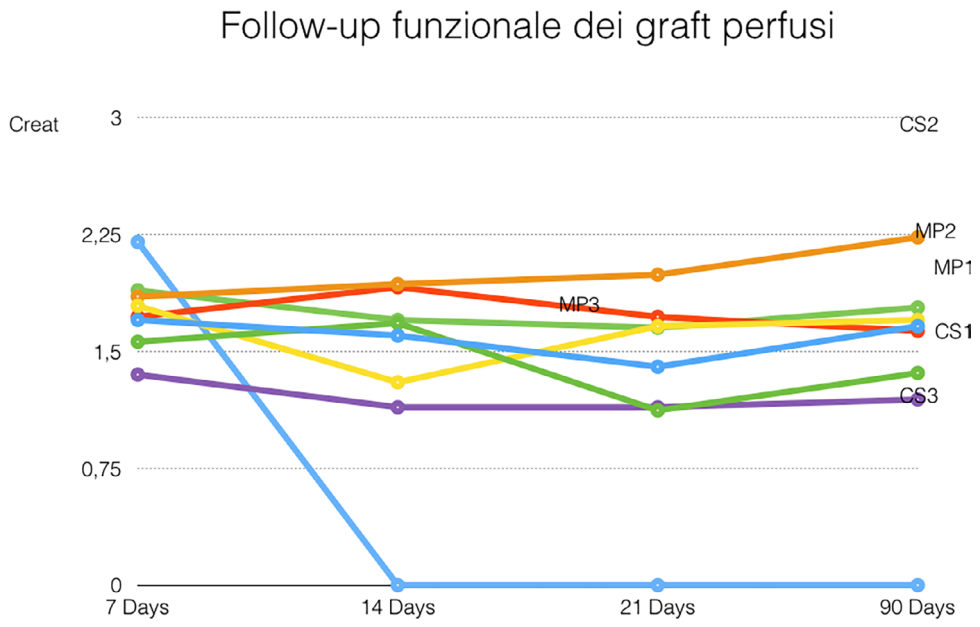


**Figure 1.** The serum creatinine levels of transplanted patients with static cold storage (CS) and machine perfusion (MP) at 7, 14, 21, 90 days after the surgery.

incidences of DGFs, in a better case (HMP3) and a worst case (HMP4) compared to kidneys transplanted without preconditioning with machine perfusion. Despite the small number of patients, the present study confirms that HMP can represent a beneficial step for ECD. The clinical outcomes, including DGF and serum creatinine, in the two groups are comparable, despite the HMP group having a statistically significant longer cold ischemia time. Machine perfusion could be a useful tool for evaluating graft viability, which is of particular importance in advanced age.

**Ethic Approval:** Approved by local commitee n°1603184 18/02/2019

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## Abbreviations:

ESRD End stage Renal Disease
DGF Delayed Graft Function
PNF Primary non Function
DBD Dead Brain Donor
ECD Expanded Criteria Donor
SCS Static Cold Storage
HMP Hypothermic Machine Perfusion
RR Renal vascoular Resistence

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