LETTER TO THE EDITORS

Machine perfusion use for combined staged kidney transplantation after heart re-transplantation: keep calm and stabilize the recipient!

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Dear Editor,

In kidney transplantation (KT), a prolonged cold ischemia time (CIT) in static cold storage and a perioperative hemodynamic instability of the recipient have been identified as independent negative prognostic factors for postoperative morbidity and poor graft survival [1]. Even the development of hyperdynamic states and the massive use of inotropic drugs have been shown to have a detrimental effect on kidney graft [2]. Under this perspective, the management of combined heart–kidney transplant (HKT) recipients must face significant complexities [2,3] which are reflected by an increased risk of kidney graft loss compared to KT alone (hazard ratio 1.43 [4]). Moreover, kidney graft loss has been identified as a negative prognostic factor for HKT recipient survival [3]. The overall risks further increase in the case of heart re-transplantation for late graft dysfunction, making the need of dialysis a relative contraindication for a second heart transplantation (HT) [5]. In 2015, the HT group of our Transplant Unit reported on our experience with three cases of combined simultaneous kidney transplant and heart re-transplant, showing the feasibility and safety of this procedure [5]. Nonetheless, in that series as well as in other previous reports on HKT [2,3], several ischemia-related complications of the kidney grafts were noted, comprising delayed graft function (DGF), long-term dysfunction, graft rejection, and ureteral ischemia. Following that preliminary experience and thanks to technology advances, we have consequently implemented our surgical management of HKT with the use of an hypothermic machine perfusion (HMP) for the kidney graft, switching from a simultaneous HKT to a staged procedure. The aim of this approach is to protect the kidney graft from any potential ischemic injury related to the early post-HT phase. Three patients were treated, and their clinical characteristics and their surgical details are reported in Table 1. The mean time interval between the end of HT and the start of KT was nearly 17 h, and KT was performed only when an adequate hemodynamic stability was ensured, as defined by the following criteria:

1. no mechanical circulatory support,
2. no inotropic therapy with adrenaline, dobutamine, or enoximone,
3. serum hemoglobin over 9 g/dl with no blood transfusion in the last 12 h.

A maximum CIT of 36 h was fixed as time limit for staged KT. If the HT recipient was not hemodynamically stable by that time, the kidney graft was transplanted to a backup recipient. The HT postoperative course was uneventful for patient 2 and 3. Patient 1 developed two episodes of mild–moderate cell-mediated heart rejection, proven at protocol biopsy, and treated with steroid pulse and switching to tacrolimus therapy (standard immunosuppression protocol was based on cyclosporine, mycophenolate mofetil, and prednisone). At hospital discharge, the left ventricular ejection fraction of patient 1, 2, and 3 was 59%, 75%, and 68%, respectively. The KT postoperative course was characterized by a prompt trend toward normalization of the estimated glomerular filtrate rate, progressive increase of urine output, and disappearance of proteinuria (Fig. 1). None of the recipients developed DGF or other ischemia-related complications. The use of HMP for staged KT has been also recently reported after liver transplantation, with analogue good results [6]. Moreover, a staged rather than simultanoeus HKT has been previously described, although without HMP and with

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Table 1. Demographic and clinical data of donors and recipients.

	Patient 1	Patient 2	Patient 3
Recipient			
Gender	M	M	M
Age (years)	46	47	53
BMI	23	20	32
Diabetes mellitus	No	No	No
Arterial vasculopathy	No	No	No
Cause of renal failure	Calcineurin inhibitors toxicity	Chronic glomerulonephritis	Chronic glomerulonephritis
Dialysis	Preemptive†	Preemptive†	2 years
Pretransplant creatinine serum level (mg/dl)	2.21	3.59	5.13
PRA‡	0	0	0
HLA compatibility	A1 B0 DR1	A1 B0 DR0	A1 B1 DR 0
Time interval between first HT and re-HT (years)	20	30	15
Donors			
Gender	M	M	F
Age (years)	47	55	48
BMI	48	21	23
Diabetes mellitus	No	No	No
Hypertension	Yes	Yes	No
Arterial vasculopathy	No	No	No
Creatinine serum level (mg/dl)	0.94	0.55	0.62
Causes of brain death	Anoxia	Trauma	Trauma
HKT surgical details			
Re-HT operative time	8 h 10 min	7 h 10 min	7 h 50 min
Time interval between re-HT and KT	14 h 25 min	22 h 15 min	14 h
Mean arterial pressure, at kidney graft reperfusion (mmHg)	92	70	75
Inotropic drugs use, at kidney graft reperfusion	No	No	No
Kidney graft cold ischemia time (min)			
Static cold storage*	515	347	420
HMP	860	1441	640
Renal graft artery resistive index			
HMP-start	0.56	0.64	0.72
HMP-end	0.20	0.24	0.25
Kidney graft warm ischemia time (min)	46	30	50
Recipient's status	Death due to melanoma (13 months post-transplant)	Alive (7 months follow-up)	Alive (21 months follow-up)

BMI, body mass index; HLA, human leukocyte antigen; HMP, hypothermic machine perfusion; HT, heart transplantation; KT, kidney transplantation; PRA, panel reactive antibodies.

‡Measured with Luminex testing. None of the patients was positive for donor specific antibodies at HKT.

†The indication to KT was based on a daily proteinuria >2 g, signs of chronic ischemic damage of the native kidneys (small size and reduced cortical thickness at ultrasound scan), and long history of calcineurin inhibitors use.

*Static cold storage was used during the shipping time of organs from the hospital where the organ procurement was performed.

results comparable to the simultaneous procedure [7]. In conclusion, we believe that an HMP-driven staged HKT may currently represent the surgical strategy with the best safety profile and improved KT outcome, particularly when the hemodynamic stabilization of the recipients after the HT procedure cannot be promptly ensured. We tend to support the use of HMP systematically in all HKT cases, to protect a kidney graft which

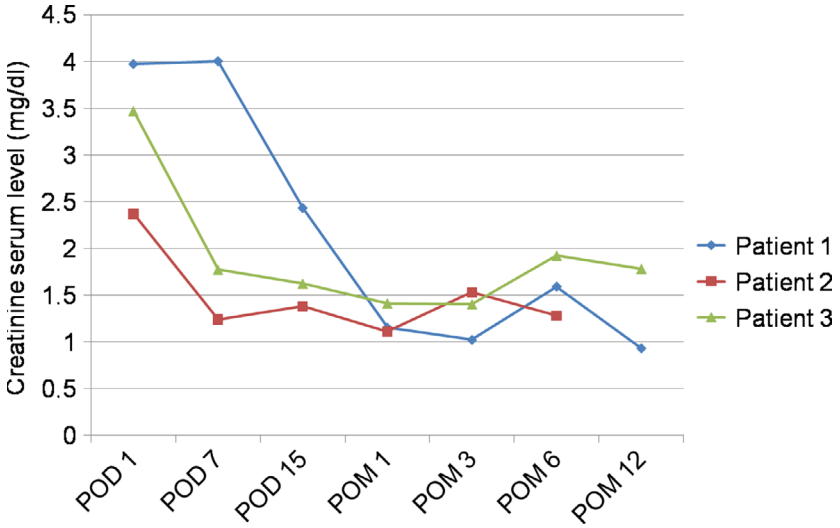

Figure 1 Postoperative trend of creatinine serum levels in patient 1, 2 and 3. POD, postoperative day, POM, postoperative month.

not only must accumulate the ischemic time associated with HT procedure, but also may potentially need to be re-allocated. This approach may guarantee the chance of not only planning the surgical strategy in advance, but also of modifying it electively as the clinical conditions of the recipient evolve.

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Conflicts of interest

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