Perfusion of a Kidney Graft From a Donor After Cardiac Death Based on Immediately Started Pulsatile Machine Perfusion—An Experimental Study on a Small Animal

V. Opatrný[a,b], J. Moláček[a,b,*], V. Třeška[a,b], R. Matějka[d], and O. Hes[c]

[a]Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic; [b]Department of Surgery, University Hospital in Pilsen, Pilsen, Czech Republic; [c]Sikl's Institute of Pathological Anatomy, University Hospital in Pilsen, Pilsen, Czech Republic; and [d]Faculty of Biomedical Engineering, Czech Technical University in Prague, Prague, Czech Republic

ABSTRACT

Introduction. There is still a lack of organs for kidney transplantation. The aim of our experimental animal study was to improve the quality of the kidney grafts from donors after cardiac death (DCD) using immediate start of machine perfusion instead of perfusion based on hydrostatic pressure.

Methods. Ten rabbits were used as an experimental model. In group A, 5 kidneys after ischemic injury were perfused in situ using hydrostatic pressure. In group B, 5 kidneys were perfused in situ using machine pulsatile perfusion. After nephrectomy kidney parenchyma was histologically analyzed. We have evaluated the maximum perfusion flow rate, temperature drop rate, and degree of parenchymal injury.

Results. The flow rate in the group of machine-perfused animals (group B) was significantly higher than in the control group (group A), and temperature was significantly decreased in group B ($P < .001$). Qualitative histopathologic evaluation of the perfusion quality of the grafts was statistically significant, again in favor of machine perfusion in group B ($P = .005$).

Discussion. According to our results, the immediate start of machine perfusion is a superior method of kidney graft preservation in DCDs. All observed modalities were superior in the group with machine perfusion compared with usual clinical practice.

RENAL transplantation is the only chance for patients in the terminal stage of renal failure to maintain a good quality of life and mitigate the risk of complications arising from long-term peritoneal dialysis or hemodialysis. However, the number of patients on waiting lists for a kidney transplantation in the Czech Republic has increased from approximately 700 in 2006 up to nearly 1000 in 2013 [1], with the expectation that this number will gradually increase in the future. At the same time, the total annual number of transplantations carried out in the Czech Republic has remained the same for several years, approximately 500 to 600 a year [2]. This situation therefore requires so-called marginal donors (ie, donors with nonpremium quality grafts) to also be accepted. High-quality perioperative and postoperative care is able to cope with the associated problems. Typical examples of marginal donors are non–heart-beating donors, also called donors after cardiac death (DCD). The extension of the DCD program in the long run is of key importance for increasing the number of renal transplantations [3,4]. This program has been started at the Department of Surgery of the University Hospital and Faculty of Medicine in Pilsen since 2002 and was the first program of its kind in the Czech Republic [5].

Supported by Research Grant of Charles University Progres Q39.

*Address correspondence to Assoc Prof Jiri Moláček, MD, PhD, Vascular Surgery Department, University Hospital, Alej Svobody 80, Pilsen 304 60, Czech Republic. E-mail: molacek@fnplzen.cz

0041-1345/18
https://doi.org/10.1016/j.transproceed.2018.02.067

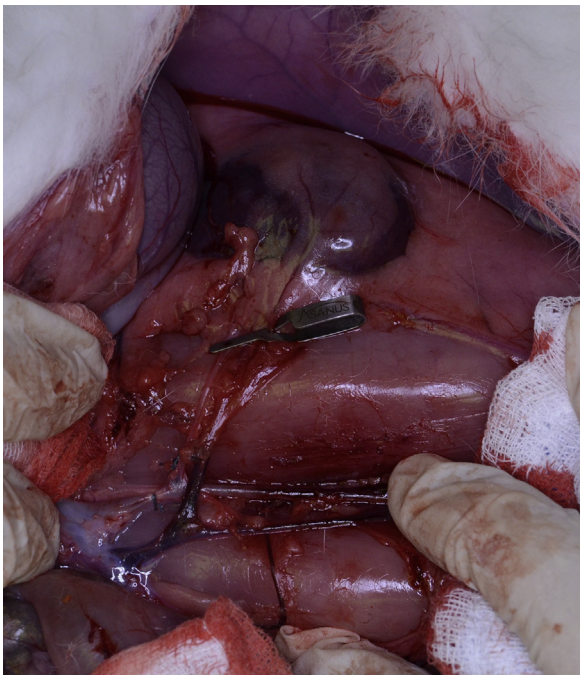

Fig 1. Clamp on the left renal artery and vein.

The DCDs at the center of this research are those patients in whom there was a primary failure of the cardiopulmonary functions and whose vital signs could not be recovered regardless of effective resuscitation lasting at least 30 minutes. Among the prevalent causes are multiple accidental traumas, myocardial infarctions, or devastating craniocerebral injuries. The approach in our institution is as follows. After resuscitation is stopped and a nontouch interval (10 minutes) has expired, measures are taken to ensure renal perfusion. Before the discontinuation of cardiopulmonary resuscitation, the donor is intravenously administered heparin (20,000 IU), which is then distributed into the blood circulation by indirect cardiac massage. In addition, the femoral artery is exposed in the donor's groin. A double-balloon triple-lumen catheter is inserted via the arteria femoralis communis into the abdominal

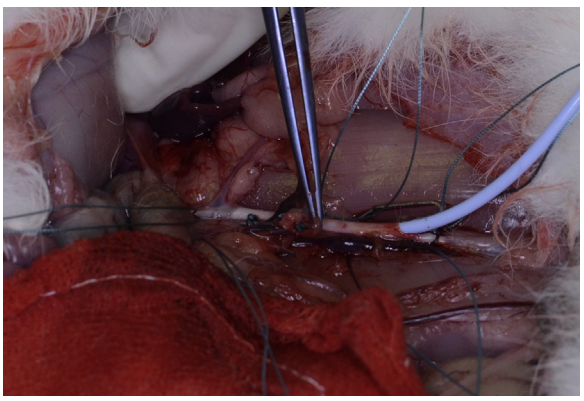

Fig 2. Perfusion catheter in the abdominal aorta.

Fig 3. The explanted kidney.

aorta, as a result of which the kidneys are flushed out with cold perfusion solution (CUSTODIOL HTK Solution, Dr Franz Köhler Chemie GmbH, Bensheim, Germany) thanks to the effect of hydrostatic pressure. The pressure is generated by suspending the bag containing the perfusate at least 1 m above the patient's bed.

After sufficient perfusion, the kidneys are explanted from the body and connected to a pulsatile machine perfusion system where they are further perfused with the same solution and cooled. In addition, the parameters of the renal grafts are monitored and samples of perfusate are taken to evaluate the markers of impaired renal parenchyma. After approximately 6 hours on the perfusion machine, a decision on the graft acceptance or refusal for transplantation is made. The graft indicated for transplantation is subsequently perfused until its transplantation to the recipient. The procedures may differ slightly at individual transplantation centers [6].

An alternative to machine perfusion is simple storage in a cold medium, so-called "cold storage," which was not applied to DCDs at our institution. Regardless of the long-term results of the grafts from DCDs, a higher prevalence of delayed graft function (DGF) as well as primary graft failure was reported for this group [7]. The aim of our animal experiment was to improve the quality of the kidney

Table 1. Evaluated Parameters for Individual Animals

Animal	Group	Flow rate Max (mL/min)	Temperature Drop Rate (°C)	Quality of Parenchyma (1–4)
1	A	8.7	3.7	3
2	A	6.9	2.4	3
3	A	1.26	3.46	3
4	A	5.7	3.3	3
5	A	8.5	4	3
6	B	14.15	19.53	1
7	B	12.08	17	2
8	B	9.74	14.3	1
9	B	15.25	20	2
10	B	13.82	16.9	2

Abbreviations: Group A, control; group B, machine perfusion.