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COMPLEX USE OF PERFUSION TECHNIQUES IN KIDNEY TRANSPLANTATION FROM A DONOR WITH OUT-OF-HOSPITAL CARDIAC ARREST (CLINICAL CASE)

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Objective: to present the successful experience with a donor with out-of-hospital cardiac arrest (OHCA) in whom a set of modern perfusion techniques was used to obtain kidneys suitable for transplantation. **Materials and methods.** Automatic chest compression was resumed in an OHCA donor (after biological death has been confirmed in the hospital) to maintain minimal perfusion under mechanical ventilation with 100% FiO_2. With femoral vein cannulation, an extracorporeal circuit with a centrifuge pump and oxygenator was connected and abdominal normothermic regional perfusion was initiated. After 215 minutes, kidney was explanted under normothermic machine perfusion. Next, the left kidney was placed in the LifePort Kidney Transporter for hypothermic machine perfusion of donor kidneys. Perfusion time was 285 minutes. The right kidney was transplanted without additional ex-vivo perfusion. **Results.** Due to the complex use of perfusion techniques both in the donor body and ex-vivo, donor kidneys, after OHCA, with a total warm ischemia time of 110 minutes, were transplanted to recipients with good results. In the postoperative period, there was delayed function of the left and right renal grafts. The patients were discharged in a satisfactory condition under outpatient follow-up. **Conclusion.** The possibility and efficiency of organ donation after OHCA, facilitated by modern perfusion techniques and devices, open up a new perspective in addressing the organ shortage crisis.

Keywords: donors with out-of-hospital cardiac arrest, perfusion devices, kidney transplantation.

INTRODUCTION

Organ shortage crisis is a major public health problem. This has prompted the search for new solutions to increase the number of organ transplants. Patients with out-of-hospital cardiac arrest (OHCA) can constitute a very effective donor pool [1]. According to the modified Maastricht classification (Paris, 2013) [2], donors with OHCA are categorized as uncontrolled, IA (sudden OHCA without attempts at cardiopulmonary resuscitation), and IIA (sudden irreversible OHCA with ineffective cardiopulmonary resuscitation). The IIA donor category is most commonly used in clinical practice.

In 2013–2014, donors with OHCA class IIA accounted for about 64.2–54.1% of the total asystolic donation in Spain. With regulatory introduction of controlled organ donation, however, their proportion decreased to 15.6% in 2017 [2].

For Russia, this type of donation is undoubtedly relevant. In the first 10 years of the current century, there began to appear Russian publications concerning the beginning of the clinical use of automated chest compression (ACC) devices during cardiopulmonary resuscitation (CPR) [3, 4]. Among the advantages of these devices over manual CPR was the possibility of using them in OHCA conditions, primarily to achieve high-quality CPR when transporting a patient to the hospital. The current state of organ donation in Moscow, combined with the technical capabilities and experience of the Moscow Organ Donation Coordinating Center at Botkin Hospital, allow us to develop our own protocol for working with donors with OHCA and ensure its proper organization.

A clinical case study of OHCA donor management is presented in this publication.

CLINICAL CASE

From medical history. *A 33-year-old man was brought to the hospital in a state of clinical death with an incoming diagnosis of suspected pulmonary embolism (PE). Prehospital cardiac arrest. Acute heart failure. Acute respiratory failure. Artificial ventilation (AVL) at the prehospital stage.*

CPR was initiated by an emergency medical team using ACC devices. At the time of delivery to the hospi-

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tal, CPR had lasted for 53 minutes. In-hospital resuscitation lasted for 30 minutes, without effect. Biological death was confirmed. After death was confirmed, ACC devices together with AV (FiO_2 100%) were resumed to maintain perfusion of organs until the beginning of their preservation.

Preservation of abdominal organs under normothermic extracorporeal membrane oxygenation (nECMO). *A standard surgical access to the femoral vessels on the right side was performed. Using the Seldinger technique, 23 Fr (38 cm) and 19 Fr (23 cm) cannulas were inserted into the femoral vein and femoral artery, respectively, using an open method. On the left, a 16 Fr (90 cm) diameter double-balloon triple-lumen catheter (DBTL catheter) was placed into the femoral artery using an open method, and the thoracic balloon was inflated above the diaphragm level. The cannulas were retrogradely filled with donor blood and connected to an ECMO circuit. Abdominal normothermic perfusion was performed using Ex Stream (TransBioTech, Russia), an ECMO perfusion device. See Fig. 1.*

The perfusion temperature was maintained at 35 °C by means of a thermostat (Heater Unit HU 35, Maquet, Germany). Homeostasis was monitored by analyzing the acid-base state of arterial blood from the circuit at 1-hour intervals. The flow rate was maintained at ≥2.4 L/min. See Table 1.

During perfusion, solutions of alprostadil, furosemide, methylprednisolone, insulin, vancomycin hydrochloride or meropenem trihydrate were injected into the circuit. The required perfusion rate was achieved by infusing balanced crystalloid solutions into the extracorporeal circuit. Perfusion lasted for 215 minutes. With nECMO ongoing, the donor was transported to the operating room. See Fig. 2.

Kidney explantation for transplantation. *Median laparotomy was performed under nECMO. Warm scarlet blood was actively flowing from the edges of the surgical wound. Abdominal revision revealed no pathological effusion. The appearance of the abdominal organs (color, blood filling) corresponds to that in the case of organ*

Table 1

Acid-base status of donor arterial blood at the time of death and during nECMO

Acid-base status parameters	Death pronouncement	Hour 1 of perfusion	Hour 2 of perfusion
pH	6.61	7.031	7.772
pO_2 (mmHg)	63.1	595.6	666.2
pCO_2 (mmHg)	93.2	10.0	12.2
K^+ (mmol/L)	5.4	6.56	6.51
Na^+ (mmol/L)	148.0	133.3	142.6
BE (mmol/L)	–30		–1.34
Hemoglobin (g/L)	136	98.3	58.9
Glucose (mmol/L)	26.3	19.4	17.9
Lactate (mmol/L)	20.0	20.0	17.9
Urea (mmol/L),	6.3	–	–
Creatinine (μmol/L)	139	–	–

Fig. 1. Ex Stream, a perfusion device for extracorporeal membrane oxygenation

Fig. 2. Donor transportation (maintained by nECMO) to the operating room

explantation from a brain-dead donor. The organs were warm on palpation. Small bowel peristalsis was noted. A container with organ preservation solution "Custodiol" cooled to +4 °C was connected to the port in the venous part of the circuit, the preserving solution started to flow into the circuit and further through the oxygenator to abdominal organs. To drain the preserving solution after passage through the abdominal organs, a part of the venous circuit up to the port where Custodiol enters was isolated with clamps, the line was crossed, the free end was placed in a container to collect the drain. The rate of Custodiol inflow was 500.0 mL/min, washing to "clean water". In parallel with washing the organs with a preservative solution, sterile ice chips were placed in the abdominal cavity for local cooling. According to the standard technique, the right and left kidneys with vascular elements – a fragment of the aorta and inferior vena cava – were isolated and removed as a single block. The kidneys were separated on the table and examined in detail. On examination, the left renal graft was found to be of medium size, homogeneously colored, without tumor-like formations, with a single renal artery extending from the aorta and with a single renal vein. The right kidney graft was medium-sized, homogeneously colored, with a small cystic mass, there were two renal arteries branching from the aorta and a single renal vein. See Fig. 3.

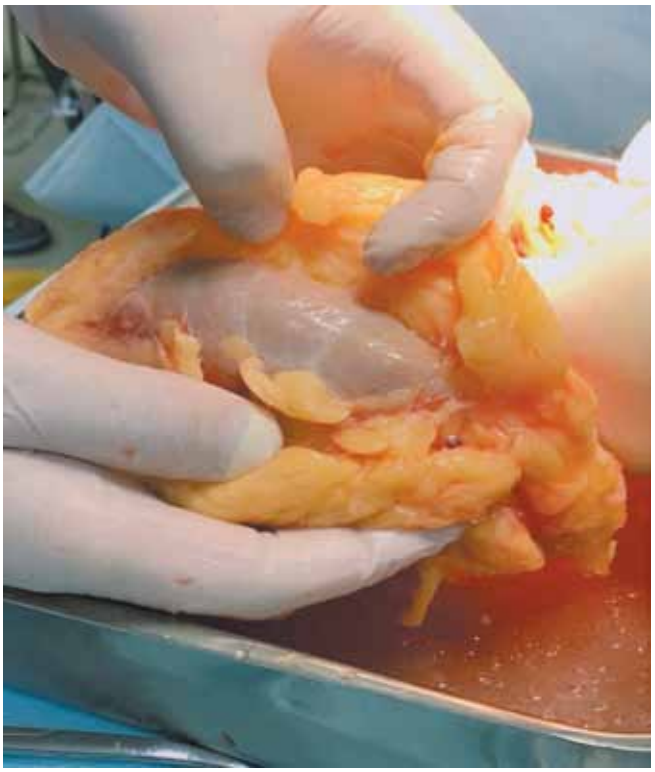

Fig. 3. Left donor kidney after explantation

Fig. 4. External view and baseline kidney perfusion parameters in the LifePort Kidney Transporter

Kidneys obtained from donors after OHCA have an increased risk of primary dysfunction or delayed function after transplantation because total warm ischemia time in this type of donation reaches critical values, up to 150 minutes. To reduce additional ischemic injury in kidneys recruited from expanded criteria donors and donors with irreversible circulatory arrest during static cold preservation, it is suggested to replace the latter partially/completely by perfusion preservation of donor kidneys provided by mechanical circulation of the perfusion solution through the donor kidney at different temperature regimes (hypothermic, normothermic) and possible oxygenation of the perfusion solution. Machine perfusion techniques have become an important tool in solving critical problems of organ transplantation, such as ischemia-reperfusion injury [5–7], unsatisfactory post-transplant graft function and lower graft survival [8, 9].

The experience of using commercially available machines for donor kidney perfusion in Russia is extremely limited, and there is no experience at all for kidney perfusion from a donor with OHCA [10]. At Botkin Hospital, it is possible to perform hypothermic machine perfusion of donor kidneys on the LifePort Kidney Transporter machine (Organ Recovery Systems, USA); accordingly, the left kidney graft sent to Botkin Hospital was placed in the mentioned machine for kidney perfusion. See Fig. 4.

Perfusion temperature did not exceed 8 °C. Perfusion pressure at the start of perfusion was 20/17 mmHg, taking into account pulsatile perfusion mode, with a flow rate of 94 ml/min and a resistivity index (RI) of 0.19 mmHg/mL/min. Machine perfusion lasted for 285 minutes. At the time of completion of donor kidney perfusion, perfusion pressure decreased to 10/3 mmHg, while the flow rate remained quite high, 79 ml/min, and the RI, which is calculated taking into account the above two parameters, decreased to 0.07 mmHg/mL/min. See Fig. 5.

The right kidney graft was sent to a transplant center where ex-vivo machine perfusion was not performed.

Recipients. *The donor-recipient pair was selected taking into account cross-match test and HLA compatibility results.*

Left kidney transplant recipient. *A 39-year-old woman, end-stage chronic kidney disease (CKD), diabetic nephropathy. Renal replacement therapy – hemodialysis, since February 11, 2017. Five HLA mismatches with the donor. On the waiting list since May 10, 2018. Kidney transplantation was performed on March 21, 2023. Surgery lasted from 05:50 to 09:25. After initiating blood flow at 07:47, the graft acquired physiological turgor, uniformly turned pink, and urine flow was noted. As the graft warmed up, pulsation of renal arteries was satisfactory, patency of vascular anastomoses was not impaired. After suturing the muscles of the anterior abdominal wall, an ultrasound examination was performed in the operating room, which found blood flow in the transplanted kidney to be satisfactory and resistivity index to be 0.50. See Fig. 6.*

Fig. 5. Final perfusion parameters

There was delayed graft function in the postoperative period. Therefore, five hemodialysis sessions were performed. At the moment of discharge from the clinic on day 36, urea and creatinine levels were 19 mmol/L and 117 μmol/L, respectively, diuresis was 1300 mL per day. See Table 2.

Right kidney transplant recipient. *A 51-year-old woman, end-stage CKD. Four HLA mismatches with the donor. Renal replacement therapy in the form of hemodialysis since September 22, 2008. On the waiting list since January 9, 2020. Kidney transplantation performed on March 21, 2023. After blood flow started, the graft acquired physiological turgor and color, urine flow was visualized along the ureter. On day 1 after the operation, 1700 mL diuresis was noted, which decreased on day 2. In the postoperative period, 3 hemodialysis sessions were performed. At the time of discharge on day 16, blood urea was 21 mmol/L, creatinine was 250 μmol/L, and diuresis was 3200 mL per day. See Table 2.*

DISCUSSION

OHCA is a major public health problem in both Europe and the United States. There are approximately 275,000 cardiac arrests annually and approximately 420,000 in the United States. Detailed epidemiologic information on this problem was, for the first time, presented in the international prospective multicenter study EuReCa ONE, which pooled data from 27 countries. The population of this study is represented by 10,682 cases of confirmed OHCA, of which 7,146 involved CPR. Of all patients hospitalized with OHCA, 25.2% had sponta-

Fig. 6. Doppler ultrasound of the left renal graft at the completion of surgery

neous circulatory recovery, 10.7% had continued CPR in the hospital, and 64.0% of patients were confirmed dead at the time of admission [11]. The high mortality rate of OHCA patients is noteworthy – according to EuReCa data, the survival rate among all patients who had CPR does not exceed 10.3%.

There is little Russian data on OHCA. Birkun A.A. (2017) points to the high prevalence of OHCA in a single administrative center of the Russian Federation, an order of magnitude higher than in many foreign countries [12]. The Center for the treatment of sudden cardiac death at Pavlov University provides data showing that there is extremely high mortality of patients with OHCA, which reached 92.6% [13].

The above foreign and Russian data suggest that there is a high proportion of potential donors among OHCA patients.

From the logistical and technological points of view, organ donation after OHCA is among the most challenging. Organizing this type of donation in a similar manner to leading foreign protocols, mainly from Spain and France, requires significant human and technical resources, which in turn raises the question of expediency and efficiency of the technologies under consideration. The most reliable data on outcomes of transplantations from such donors are presented by the corresponding programs in Spain, France, and Italy. The proportion of donors with OHCA from whom at least one organ was transplanted does not exceed 80.0% [14]. Poor preservation, associated with critical warm ischemia time, is the most common reason for not utilizing organs for transplantation [15]. However, outcomes of organ transplantation from donors with OHCA are considered acceptable, although with room for improvement. Kidney transplants have comparable short-term and long-term outcomes despite a higher incidence of primary dysfunction and delayed function compared with organs from brain-dead donors and controlled cardiac arrest donors [16–20].

The leading risk factor in organ donation with OHCA is the critical value of warm ischemia time. Normothermic regional perfusion significantly reduces the risk of graft dysfunction and is crucial for achieving optimal outcomes in kidney transplantation from such donors [19, 21]. However, even with careful donor selection and the use of normothermic regional perfusion, incidence of primary kidney graft dysfunction is 7–8% [22].

Because renal grafts from donors with OHCA are subject to prolonged and repeated ischemic injury, it is important to assess their viability before transplantation based on functional, anatomical and histological data, including *ex-vivo* machine perfusion [23].

Significant factors in evaluating a potential donor with OHCA are the time from the moment of cardiac arrest (the exact time can be known only if there are witnesses to this event) to the start of CPR (this time should not exceed 30 minutes for possible kidney donation and 15 minutes for possible liver donation) and the total warm ischemia time determined from cardiac arrest to initiation of organ preservation (this time should not exceed 150 minutes). As these time intervals increase, the risk of getting a non-functioning graft is significantly higher.

In the presented clinical case, the total warm ischemia time amounted to 110 minutes, which falls within the

Table 2

Characteristics of left and right kidney recipients

Characteristics	Left kidney recipient	Right kidney recipient
Gender (male/female)	Female	Female
Age (years)	39	51
Diagnosis	Stage 5 CKD, diabetic nephropathy	Chronic glomerulonephritis, stage 5 CKD
Date of hemodialysis initiation	February 11, 2017	September 22, 2008
Number of HLA-A, B, Dr mismatches	5	4
Length of stay on the waiting list (months)	57	38
Ex-vivo machine perfusion	Yes	No
Total cold ischemia time (hour)	17.7	21.3
Resistance index (RI) at end of surgery	0.50	–
RI on day 1	0.74	0.86
RI on day 7	0.7	0.80
RI at the time of discharge	0.80	1.0
Graft function	Delayed	Delayed
Number of post-transplant hemodialysis sessions	5	3
Urea/creatinine levels on day 1 (mmol/L) (μmol/L)	36/705	43/800
Urea/creatinine levels on day 7	37/381	24/360
Urea/creatinine levels at the time of discharge	19/117	21/250
Inpatient stay (bed days)	36	16

above-mentioned time limits. We consider the obtained outcomes, despite development of delayed renal graft function in recipients, to be satisfactory and comparable with foreign experience. Thus, incidence of delayed graft function for kidneys obtained from donors with OHCA is about 50–70%. Nevertheless, the authors note that such grafts have satisfactory 1-year, 5-year, and even 10-year survival rates [19, 24–27].

It should be noted that the paper presented is the first Russian experience of using *ex-vivo* machine perfusion of a kidney obtained from a donor with OHCA, in whom extracorporeal normothermic regional perfusion was used. *Ex-vivo* hypothermic machine perfusion of renal grafts allows us to obtain an objective assessment of organ transplantability through the renal resistive index (RRI).

Our experience of *ex-vivo* kidney perfusion is at the initial stage, and it is important to take into account many years of similar experience from leading foreign donor programs. Analysis of 302 *ex-vivo* hypothermic perfused donor kidney transplants, including kidneys from donors after circulatory death, showed that RRI is an independent risk factor for delayed graft function and graft dysfunction in the first year after transplantation. Hence, RRI can be considered as an additional tool for evaluation of kidney grafts, especially high-risk ones. However, the low prognostic value of RRI limits its isolated use in deciding whether to use or dispose of high-risk donor kidneys for transplantation [28]. In an analysis of 336 consecutive machine perfusion procedures of donor kidneys from expanded criteria donors, Mozes et al. showed that the transplant outcomes of kidneys with an unfavorable range of 0.40 mmHg/mL/min < RRI < 0.60 mmHg/mL/min were similar to those of kidneys with more acceptable perfusion rates [29]. I. Jochmans et al. also point out the need for cautious interpretation of RRI. In a cohort of 302 kidney transplants that received hypothermic machine perfusion, the RRI of donor kidneys with primary dysfunction was comparable to the RRI of kidneys with immediate and delayed function after transplantation. In a retrospective analysis of the above-mentioned cohort of transplanted kidneys, none of the kidney transplant cases with an RRI >0.40 mmHg/mL/min reported primary nonfunction [30].

In the clinical observation under consideration, *ex-vivo* hypothermic perfusion of one of the kidneys lasted 4.75 hours. Here, it is important to note that the RRI index, which was 0.19 at the beginning of perfusion, indicating that the donor kidney was in good condition and that it was suitable for transplantation, decreased to 0.07 by the end of perfusion. This allowed us to confidently recommend this kidney for transplantation. At the same time, similar to data from foreign publications given above, the RRI does not have a high prognostic ability, since there was delayed graft function in the postoperative period, when at such low RRI, we could expect immediate function. However, it is impossible not to note the practically reference blood urea and creatinine levels at the time of discharge of the patient who received the graft after *ex-vivo* hypothermic perfusion in the LifePort device.

It seems extremely important to further accumulate data on *ex-vivo* kidney perfusion parameters to form our own idea of the relationship between machine perfusion parameters and immediate and long-term kidney transplant outcomes.

CONCLUSION

Moscow city is developing its own practice of working with OHCA donors. Effective combination of the established organizational model of organ donation for transplantation in Moscow and modern perfusion technologies provided the very possibility of working with such a complex category of donors and laid serious prerequisites for further development in this direction. This, in turn, will significantly increase the number of transplants in Moscow and provide valuable scientific knowledge about organ donation where warm ischemia time reaches critical levels.

The authors declare no conflict of interest.

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