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EFFECT OF SECOND WARM ISCHEMIA ELIMINATION ON KIDNEY GRAFT FUNCTION: AN EXPERIMENT AND CLINICAL STUDY

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Objective: to evaluate the effectiveness of a new device for second warm ischemia (SWI) elimination in kidney transplantation (KT). **Materials and methods.** The study included clinical and experimental stages. The clinical stage included 63 patients out of 219 who underwent KT at Botkin Moscow City Clinical Hospital between July 2018 and August 2022. The inclusion criteria were kidneys from donation after brain death (DBD) donors with expanded criteria or kidneys from donation after circulatory death (DCD) donors, and an SWI time greater than 45 minutes. The first group consisted of 24 recipients operated on using the new SWI elimination device. The second retrospective control group consisted of 39 patients where sterile ice bags were used at the implantation stage. The groups had no statistically significant differences in the main recipient and donor characteristics, as well as in perioperative parameters. Also, from November 2021 to April 2022, 23 kidney autotransplantation experiments in female Landrace pigs were performed. The animals were cared for in accordance with the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasbourg, 18 March 1986). Efficiency of different SWI elimination techniques was compared on two experimental models: standard donor (group 1, n = 12) and asystolic donor (group 2, n = 11). **Results.** In the clinical trial group, mean graft temperature (t_m) before reperfusion was statistically significantly lower in group 1 using the special SWI elimination device: 6.4 ± 1.7 °C (95% CI 3.2–8.5) versus 22.1 ± 2.3 °C (18.1–24.6), $p < 0.001$. The risk of delayed graft function (DGF) was 3.86 times higher (95% CI 1.11–13.43) with the standard SWI elimination technique. In the experimental group, in the subgroups using the new device (n = 12), graft t_m before reperfusion was 5.1 ± 0.4 °C (95% CI 4.5–5.8), whereas in the ice bag subgroups (n = 11), t_m was 29.3 ± 1.3 °C (95% CI 27.7–30.8), which was significantly higher ($p < 0.001$). The overall 1-week survival of the experimental animals was significantly higher in the SWI elimination device subgroup (logrank p = 0.036). **Conclusion.** The developed device is effective in eliminating SWI of renal graft.

Keywords: kidney transplantation, second warm ischemia, delayed graft function, DGF, SWI.

INTRODUCTION

Kidney transplantation (KT) is the gold standard therapy for end-stage kidney disease in patients without absolute contraindications for KT [1]. Delayed graft function (DGF) is one of the most frequent postoperative complications. According to various reports, DGF occurs in more than 20% of cases on average [2, 3]. It should be noted that DGF is associated with many long-term adverse effects of LT, including increased incidence of postoperative complications and decreased graft survival [3–8].

Prolonged secondary warm ischemia time (>45 minutes) is one of the significant risk factors for DGF [9]. It has been found that with every minute of formation of vascular anastomoses, graft temperature increases on average by 10 °C [10], which can aggravate its ischemic preservative injury. To prevent graft heating during vascular anastomosis formation, various methods of graft surface cooling have been suggested. The classic technique for elimination of second warm ischemia (SWI) is to wrap the kidney in a sterile ice bag [11]. It is universally used but comes with a number of disadvantages. For example, during implantation, ice may melt or spill into the wound, resulting in not achieving optimal graft cooling. This probably gave rise to the development of other methods of SWI elimination by means of "packages" made of silicone, polyurethane, polyethylene and other materials [9, 12–14]. Many of these devices are complex and expensive.

In our previous work, prolonged SWI was strongly associated with DGF [15]. This was the reason for developing a new SWI elimination device, whose efficiency we evaluated in experimental and clinical conditions.

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MATERIAL AND METHODS

From July 2018 to November 2021, 219 isolated LTs from deceased donors were performed at the transplant ward of Botkin Hospital. In order to eliminate SWI of the graft, standard packaging in an ice bag was used in all cases. During retrospective analysis of treatment outcomes, it was found that there was prolonged SWI time (>45 minutes) in 61 cases (27.9%). These patients were 1.98 (95% CI: 1.04 to 3.77) times more likely to develop DGF, which was statistically significant ($p = 0.035$). In order to prevent ischemic injury to the graft during implantation, our center developed a special SWI elimination device.

Description of the special SWI elimination device

The device is a gauze/fabric pack for a renal graft and an ice slush. It has three spaces isolated from each other. The middle space has two openings through which it communicates with the external environment. The renal vascular pedicle and the ureter is placed into these openings. Ice chips are placed in the two outer spaces that do not communicate with the environment (Fig. 1).

All three spaces are closed from above by tightening a purse-string suture. During formation of vascular anastomoses, the purse-string suture can be loosened, and ice chips can be added to the outer spaces as needed (Fig. 2). Upon completion of formation of vascular anastomoses, the device is dissected along the anterior wall and disposed of.

The safety and efficacy of the developed device in comparison with the standard SWI elimination technique based on the standard ice bag were studied in an experiment and then, in clinical conditions.

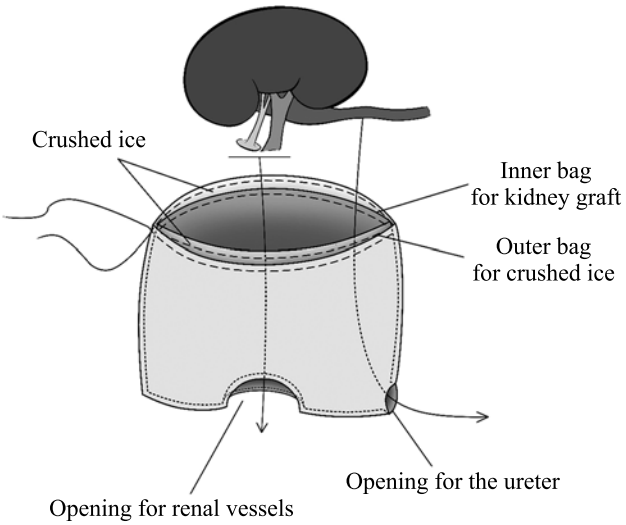

Fig. 1. SWI elimination device. Placing the kidney

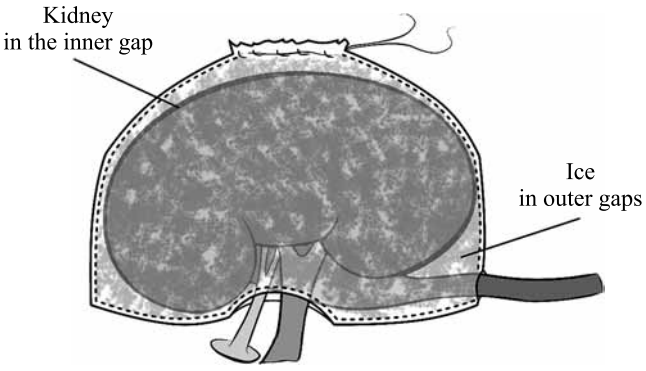

Fig. 2. SWI elimination device. Tightening the purse-string suture

Experimental stage

From November 2021 till April 2022, we carried out 23 experiments on kidney autotransplantation in female Landrace pigs with the average weight of 31 ± 1.4 (from 29 to 34) kg. Preoperative preparation, anesthetic support, care of the animal in the postoperative period, and withdrawal from the experiment were all performed in accordance with the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasbourg, 18 March 1986). A comparative study of the efficacy of different SWI elimination methods was performed in the experimental models of the standard donor (n = 12) and asystolic donor (n = 11). The study design is shown in Fig. 3.

Kidney autotransplantation was performed according to the following protocol:

1. Midline total laparotomy, kidney mobilization from the retroperitoneal space. At this stage, the anatomical features of each of the renal pedicles were evaluated and a decision was made as to which kidney would be subsequently transplanted (Fig. 4, a, b).
   a) when performing KT in the standard donor model, immediate cold preservation was performed after the future graft has been removed;
   b) when performing KT in the asystolic donor model, before removal and preservation of the future graft, its vessels were clamped with atraumatic clamps for 30 minutes (Fig. 4, c).
2. Removal of the contralateral kidney for the most accurate assessment of graft function after surgery.
3. Custodiol HTK solution was used in all cases for static cold preservation. After perfusion, the graft vessels were treated on a back-table. The median cold ischemia time of the renal graft was 180 minutes (IQR: 175–190).
4. Before implantation, the aorta and inferior vena cava were mobilized in the lower half of the abdominal cavity.
5. The kidney was implanted by means of arterial and venous anastomoses with the main vessels in an end-to-side manner. Experimental conditions made it pos-

sible to create identical prolonged implantation times in each operation. Thus, the median second warm ischemia time was 70 minutes (IQR: 70–75). We used the SWI elimination device (Fig. 5, b) and the standard ice bag technique (Fig. 5, a) in 12 experiments and 11 experiments, respectively).

6. Upon completion of vascular anastomosis formation, we performed graft reperfusion, formed ureteroneocystostomy anastomosis, performed revision and layer-by-layer suturing of the wound.

At the stages of graft immersion into the wound and immediately before reperfusion, its surface temperature was recorded using a remote thermometer at a distance of 2–3 cm (Fig. 6).

Laboratory monitoring of graft function was performed for 7 days after surgery: creatinine, urea, blood gases and electrolytes were determined once every 2 days. Daily diuresis was also monitored during the first 3–4 days, then the urethral catheter was removed for humanitarian reasons. Euthanasia under anesthesia was used to withdraw the animals from the experiment. After the animal's death, an autopsy was performed followed by morphological study of the renal autograft.

The presence of oliguria (<500 ml/day) at postoperative day 3–4 and/or hyperkalemia (>6.0 mmol/l) within a week after surgery were considered as criteria for DGF. If DGF developed, the animal was withdrawn from the experiment ahead of time. We assessed and compared the dynamics of creatinine and potassium levels, daily diuresis rates and frequency of DGF between the subgroups.

Clinical stage

The study included 63 patients operated at Botkin Hospital from July 2018 to August 2022. The inclusion

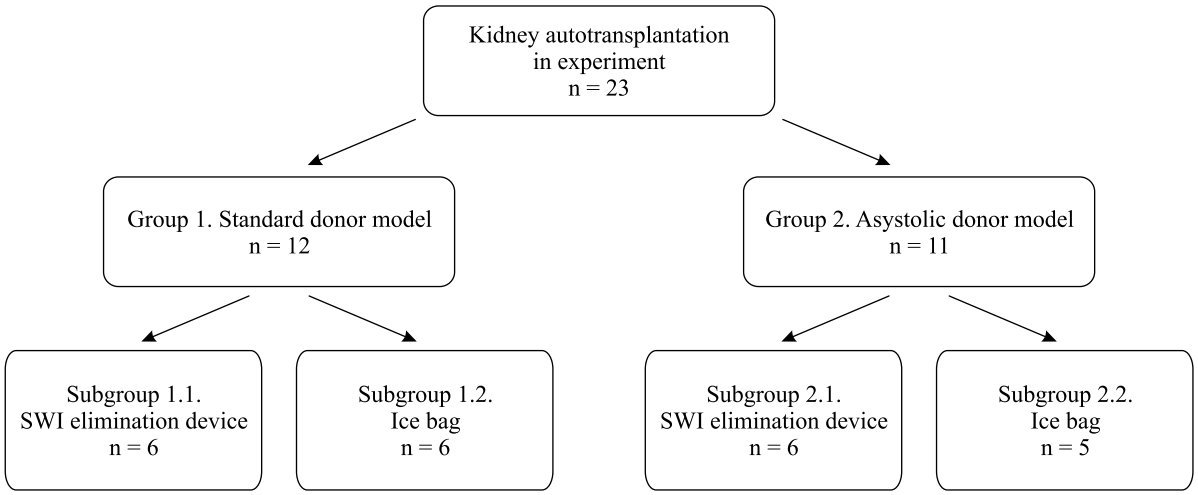

Fig. 3. Experimental stage of the comparative study of SWI elimination techniques

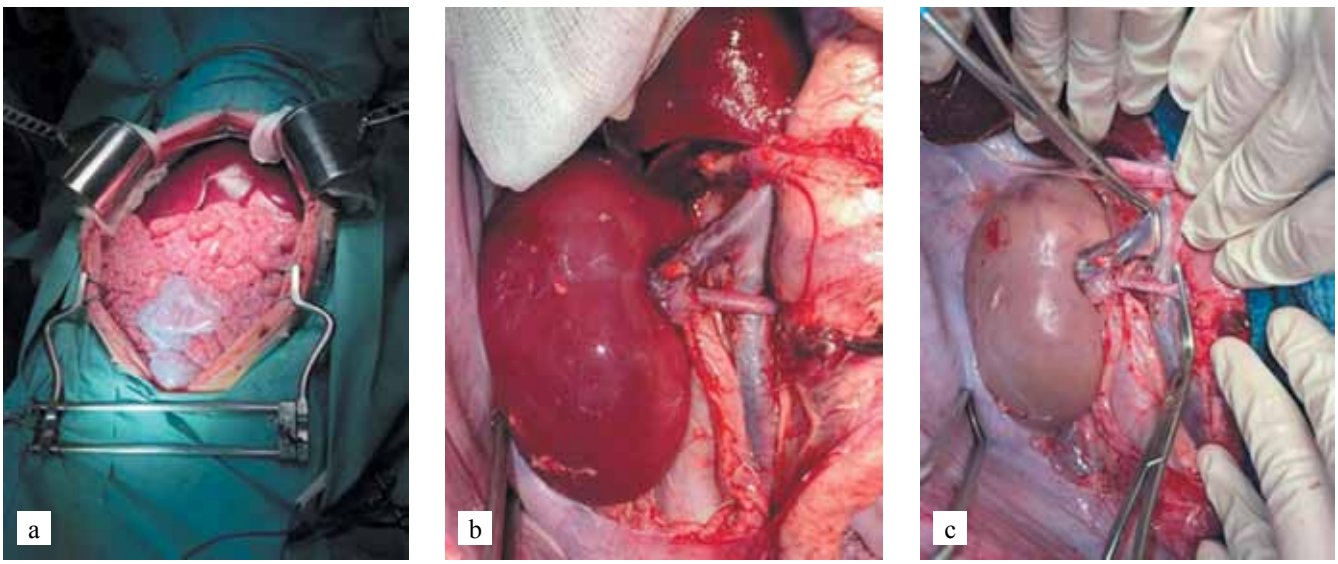

Fig. 4. Experimental kidney autotransplantation in a pig model: nephrectomy stage (intraoperative photo): a, midline total laparotomy, installing the retractors; b, isolation of the right kidney from retroperitoneal space, vascular stem dissection; c, placing clamps on renal vessels

criteria were: use of a renal graft obtained from a DBD donor with expanded criteria or DCD donor, and prolonged SWI time (>45 minutes). A patient was excluded from the study if they developed primary nonfunction, died or underwent emergency graftectomy within 7 days after surgery, and if hypothermic oxygenated machine perfusion was used during organ preservation. Preoperative examination, KT and postoperative management of the recipients were performed in accordance with national clinical guidelines. A prolonged-release tacrolimus-based triple-drug immunosuppression regimen was used as a supportive immunosuppressive therapy. The starting dose of the drug was administered at 0.2 mg per kg of the recipient's weight and was taken before surgery. The target tacrolimus level was considered to be 10–12 ng/ml. Delayed graft function was defined as the need for hemodialysis within week 1 after surgery.

The first group consisted of 24 kidney transplant recipients who used the developed special SWI elimination device during the operation. Among them were 14 men (58.3%) and 10 women (41.7%). Median recipient age was 48 (IQR: 39–55) years, median BMI was 27.5 (IQR: 23.0–31.0) kg/m^2. The main causes of end-stage renal disease were chronic glomerulonephritis (16/24, 66.7%),

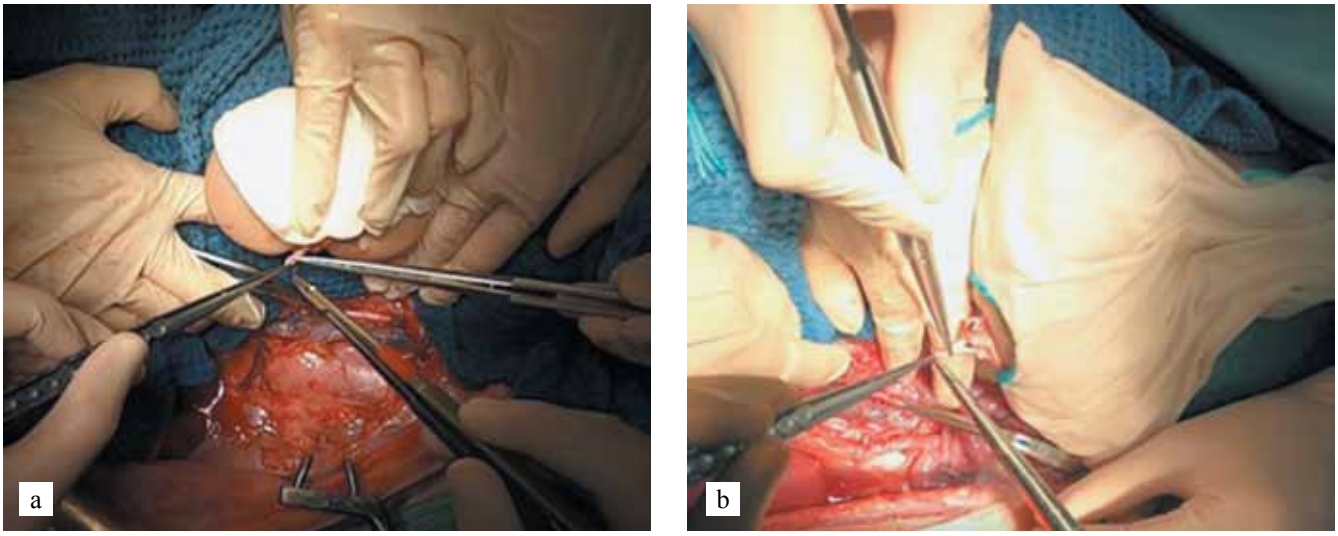

Fig. 5. Experimental kidney autotransplantation in a pig model: implantation stage (intraoperative photo): a, implantation using an ice bag; b, implantation using the special SWI elimination device

Fig. 6. Measuring the graft surface temperature with a remote thermometer

diabetes (3/24, 12.5%), and others (5/24, 20.8%). Median residual daily urine output before transplantation was 300 (IQR: 100–600) ml. In all cases, the kidney graft was obtained from an expanded criteria brain-dead donor. Median donor age was 65 (IQR: 54–68) years, the median BMI was 34.0 (IQR: 27.2 to 36.0).

Retrospective control group 2 consisted of 39 patients who had used an ice bag for SWI elimination during surgery. Among them were 28 men (71.8%) and 11 women (28.2%). Median recipient age was 51 (IQR: 39–54) years, median BMI was 26.0 (IQR: 24.0–28.3) kg/m^2. The main causes of end-stage renal disease were chronic glomerulonephritis (21/39, 53.8%), diabetes (4/39, 10.2%), chronic tubulointerstitial nephritis (3/39, 7.7%), and others (11/39, 28.2%). Median residual daily urine output before transplantation was 300 (IQR: 0–700) ml. In 37 cases (94.9%), the kidney graft was obtained from an expanded criteria brain-dead donor; in 2 cases, the graft was procured from a donor with irreversible effective circulatory arrest (5.1%). Median donor age was 62 (IQR: 53–67) years, median BMI was 32.5 (IQR: 25.3–34.5).

The groups had no statistically significant differences in the main recipient and donor characteristics, as well as a number of perioperative parameters. Detailed comparative characteristics are presented in Table 1.

Statistical analysis

Statistical processing and data analysis were performed using IBM SPSS Statistics 26 version for Microsoft Windows (USA). Mann–Whitney U test was used to compare two groups of quantitative indicators, given the small sample size, regardless of the distribution type. Qualitative data were compared using Pearson's chi-squared test or Fisher's exact test to determine the OR and 95% CI, as well as the closeness of association of the studied characteristics according to Cramer's V. Survival analysis was performed using Kaplan–Meier estimate with determination of statistically significant differences using Mantel–Cox long-rank test. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Experimental stage

In all 23 experimental operations, mean graft temperature before immersion into the wound was 4.8 ± 1.1 (95% CI: 4.2–5.9) °C and did not differ between subgroups ($p > 0.05$). In subgroups 1.1 and 2.1, where SWI elimination was performed with the developed device (n = 12), mean graft temperature at the completion of vascular anastomoses was 5.1 ± 0.4 (95% CI: 4.5–5.8) °C, whereas in subgroups 1.2 and 2.2 featuring ice bags (n = 11) it was 29.3 ± 1.3 (95% CI: 27.7–30.8) °C, which was statistically significantly higher ($p < 0.001$).

Life-threatening surgical complications developed in the first 3/23 (13.04%) experiments: renal autograft artery thrombosis (n = 2) and massive lymphorrhea in the abdominal cavity (n = 1). These animals were withdrawn from the experiment early.

In group 1 (experimental model of KT from a standard donor), we found statistically significant differences in creatinine levels on day 1, 3 and 5, and diuresis rates on postoperative day 1 between the subgroups. In subgroup 1.1, the differences were statistically significantly higher ($p < 0.05$). In contrast, the studied subgroups had no significant differences in potassium levels ($p > 0.05$), and in no case was there DGF. The results of the comparative study in group 1 are presented in Table 2.

Morphological study showed that in group 1 (experimental kidney autotransplantation in the standard donor model), renal grafts implanted using the standard SWI elimination technique, had slightly more pronounced microscopic signs of renal tubular injury (Fig. 7).

In the experimental kidney autotransplantation group in the asystolic donor model, there were no surgical complications and associated mortality. In subgroup 2.1 featuring the special SWI elimination device, a condition meeting the DGF criteria accepted for experimental animals developed in one case (1/6, 16.7%). As a result, the animal was withdrawn from the experiment on postoperative day 4. In subgroup 2.2, in turn, DGF developed in 4 out of 5 cases (80%), and therefore the animals were withdrawn from the experiment on postoperative day 2, 4, and 5. Thus, the survival rate of experimental animals in postoperative week 1 was statistically significantly higher in the "special SWI elimination device" subgroup (log-rank $p = 0.036$). Plots of survival of experimental animals with immediate renal graft function depending on the SWI elimination method used are shown in Fig. 8.

Morphological study revealed that in group 2 (experimental kidney autotransplantation in the asystolic donor model), grafts implanted using the ice bag SWI elimination technique, had significantly more pronounced signs of renal tubular necrosis and injury (Fig. 9).

Clinical stage

Of the 63 cases selected in the clinical phase of the study, there were no hospital mortality or severe surgical complications of KT (Clavien–Dindo >II) in the early postoperative period. mean graft temperature before reperfusion was statistically significantly lower in group 1 that used the developed special SWI elimination de-

Table 1

Comparative characteristics of the groups based on the SWI elimination method

Parameter	Group 1 SWI elimination device n = 24		Group 2 Ice bag n = 39		p-value
	M	IQR	M	IQR	
Recipient age (years)	48	39–55	51	39–54	0.657
Recipient's BMI (kg/m^2)	27.5	23.0–31.0	26.0	24.0–27.3	0.725
Residual diuresis (ml)	300	100–600	300	0–700	0.756
Donor age (years)	65	54–68	62	53–67	0.645
Donor's BMI (kg/m^2)	34.0	27.2–36.0	32.5	25.3–35.0	0.238
Cold preservation time (min)	725	550–820	775	640–790	0.343
Second warm ischemia time (min)	58	50–65	62	55–75	0.411
Highest tacrolimus C_0 in the first week (ng/ml)	19.2	17.0–25.1	22.4	18.6–28.3	0.19

vice: 6.4 ± 1.7 (95% CI: 3.2–8.5) °C versus 22.1 ± 2.3 (18.1–24.6) °C ($p < 0.001$).

In the retrospective group, DGF developed in 17 of 39 recipients (43.6%), which was statistically significantly lower than in group 1: 4/24 (16.7%) ($p = 0.032$). The odds of developing DGF for the standard SWI elimination technique were 3.86 times higher (95% CI: 1.11–13.43) and there was a moderate association between the traits ($V = 0.277$). The average length of stay in the hospital in group 1 was 14.5 ± 4.4 (12 to 18) bed days, which was also statistically significantly lower ($p = 0.024$) than in the retrospective control group – 18.3 ± 3.2 (16 to 25) bed days. The results of the clinical phase of the study of the safety and efficacy of the developed SWI elimination device in comparison with the standard method are presented in Table 3.

DISCUSSION

DGF, according to Russian and foreign authors, is a common early post-transplant complication in recipients. Undoubtedly, its increased frequency is mainly associated with the inevitable – expansion of the deceased donor selection criteria, in view of the enormous demand for KT. At the same time, understanding the extreme urgency

Table 2

Dynamics of laboratory and clinical indicators of graft function after kidney autotransplantation in the standard donor model

Parameter	Subgroup 1.1 SWI elimination device n = 5		Subgroup 1.2 Ice bag n = 4		p-value
	M	IQR	M	IQR	
Creatinine (before surgery)	53.4	52.0–54.2	53.0	52.2–54.0	0.758
Creatinine (day 0), μmol/l	159.2	156.4–163.0	173.2	158.1–175.1	0.152
Creatinine (day 1), μmol/l	252.0	235.3–282.1	324.8	301.4–356.5	**0.031**
Creatinine (day 3), μmol/l	221.4	213.3–253.6	345.0	322.4–398.3	**0.008**
Creatinine (day 5), μmol/l	168.9	142.2–211.5	234.4	201.6–269.5	**0.043**
Potassium (before surgery), mmol/l	4.3	4.3–4.5	4.2	4.1–4.5	0.823
Potassium (day 0), mmol/l	4.7	4.4–5.0	4.9	4.5–5.0	0.743
Potassium (day 1), mmol/l	4.0	3.8–4.3	4.5	3.9–4.7	0.521
Potassium (day 3), mmol/l	4.4	4.3–5.4	5.3	4.2–5.3	0.213
Potassium (day 5), mmol/l	4.7	4.3–4.8	4.6	4.3–4.9	0.642
Diuresis (day 1), ml	1200	1000–1200	600	600–700	**0.025**
Diuresis (day 2), ml	1500	1300–1600	1300	1200–1500	0.342
Diuresis (day 3), ml	1300	1000–1500	1400	1100–1400	0.412

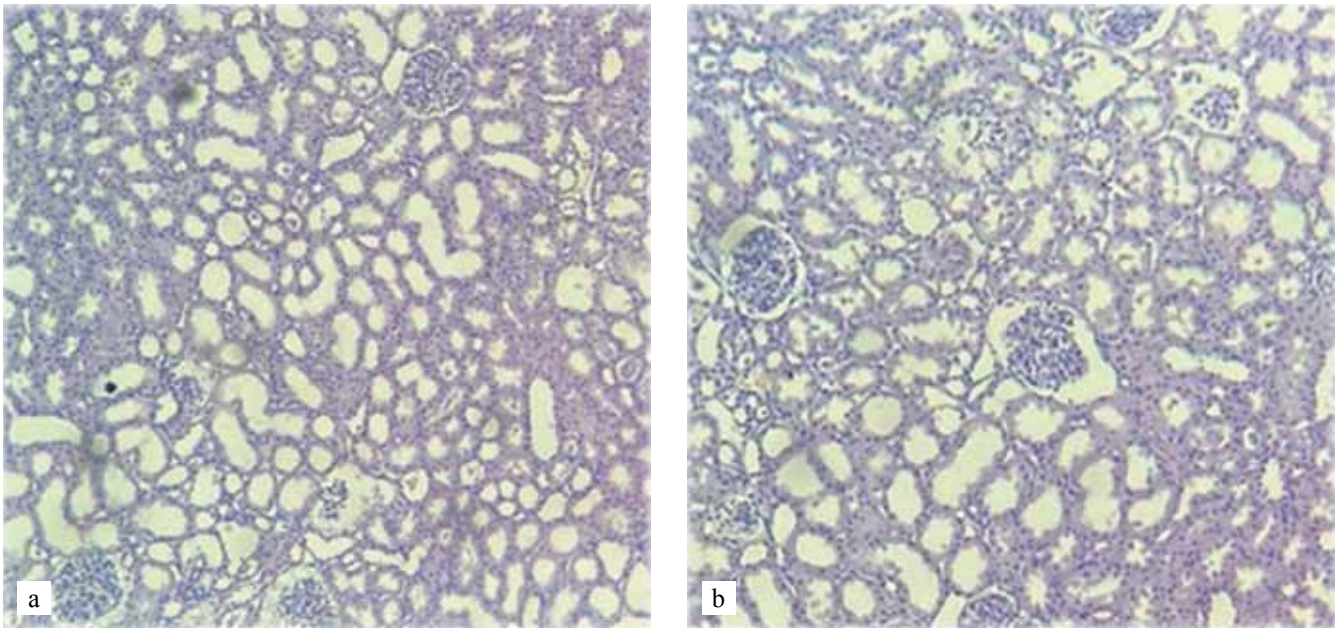

Fig. 7. Microscopic examination of kidney grafts after kidney autotransplantation in the standard donor model: a, after using the special SWI elimination device; b, after using the standard SWI elimination technique

of this problem, taking into account the increased risk of complications and decreased long-term graft survival, it is necessary to strive to influence every modifiable factor that increases the risk of DGF.

Table 3

Outcomes of treatment of renal transplant recipients in the early postoperative period depending on the SWI elimination technique used during surgery

Parameter	Group 1 SWI elimination device (n = 24)	Group 2 Ice bag (n = 39)	p-value
Mean graft temperature before reperfusion	6.4 ± 1.7 (3.2–9.5) °C	17.1 ± 2.3 (13.1–24.6) °C	**0.013**
DGF frequency	4/24 (16.7%)	17/39 (43.6%)	**0.032**
Length of hospital stay	14.5 ± 4.4 (12–18)	18.3 ± 3.2 (16–25)	**0.024**
Hospital mortality	0	0	1
Complications (Clavien–Dindo >II)	0	0	1

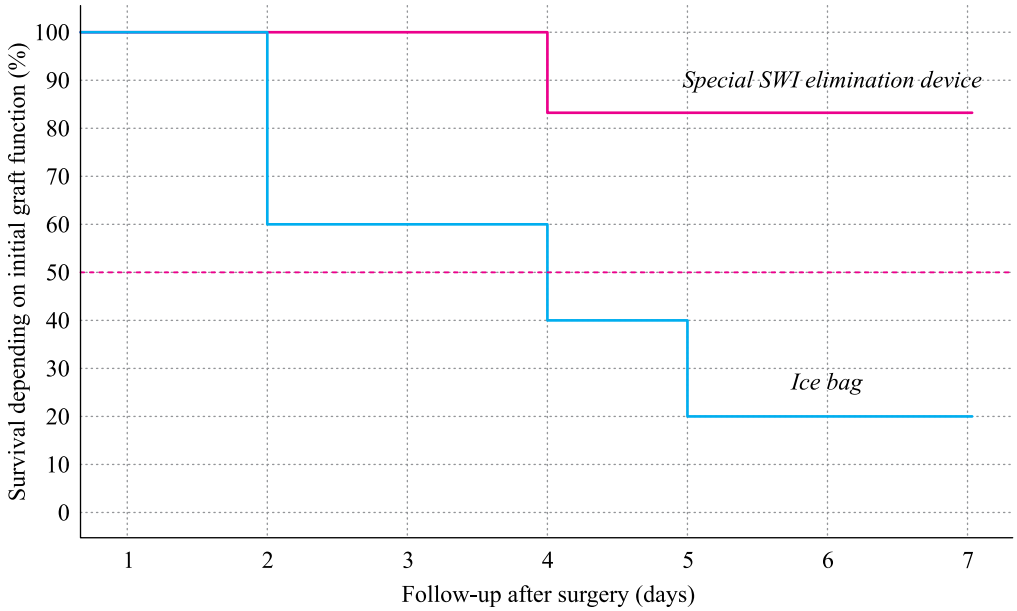

Fig. 8. Survival with immediate renal graft function in the early postoperative period depending on the SWI elimination technique used during kidney autotransplantation in the asystolic donor model

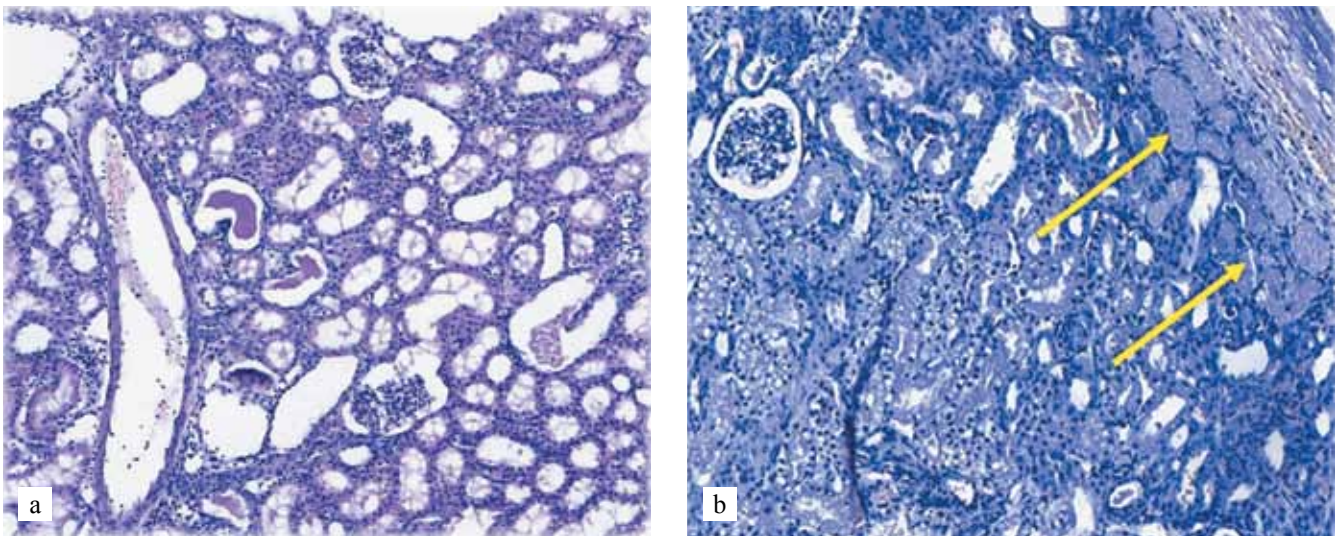

Fig. 9. Microscopic examination of kidney grafts after kidney autotransplantation in the asystolic donor model: a, after using a special SWI elimination device; b, after using the standard SWI elimination technique (yellow arrows indicate foci of acute tubular necrosis)

Both in many works and in our study, prolonged SWI time was a statistically significant and modifiable risk factor for DGF ($p = 0.035$). Nevertheless, the need for SWI elimination to date, is not clear. According to a retrospective study by Karipineni et al. (2014), SWI elimination did not improve graft function after surgery and did not influence long-term outcomes [12]. This was probably due to the fact that DGF has many risk factors on both the donor and recipient side, which was not taken into account by the authors when forming comparison groups. In contrast, Kamińska et al. (2016) investigated the effect of SWI elimination on paired kidneys and, by virtually eliminating the effect of donor-side DGF risk factors, the authors obtained the expected result: SWI was an independent predictor of DGF and acute renal graft rejection in both single- and multivariate analyses, confirming the need to eliminate it [14]. The authors also noted that grafts obtained from donors with expanded criteria are probably more sensitive to SWI.

We took this assumption as the basis, and it was reflected in two stages of the study. The first experimental stage was performed on large pigs, a generally recognized optimal model for preclinical studies in nephrotransplantology. The use of experimental model of kidney autotransplantation made it possible at the planning stage of the study to exclude potential risk factors of DGF besides the one under study at the planning stage of the study: all experimental operations were performed in pigs of the same breed, age and body weight, and use of kidney autograft made it possible to exclude immunological conflict. Also, experimental conditions made it possible to create identical cold preservation time and SWI time in the groups. In KT from a standard donor, DGF did not develop in any of the cases in our study. Probably, the contribution of SWI time factor alone is not enough for the development of severe ischemic injury and poor initial graft function. However, when combined with other risk factors, prolonged vascular anastomosis formation can lead to DGF. Thus, in the model of kidney transplantation from an asystolic donor, DGF incidence in the subgroup using the standard SWI elimination method was 4.8-fold higher than that using the developed SWI elimination device, which was statistically significant ($p = 0.036$).

Thus, we have proved that the developed device allows for more effective cooling of the renal graft during formation of vascular anastomoses, even under prolonged implantation periods ($p < 0.001$). The use of this device in KT from a standard donor can slightly improve graft function, but without affecting the DGF incidence. Its use in KT from an asystolic donor significantly reduces the severity of graft ischemic injury and DGF incidence ($p = 0.036$).

Indeed, prolonged SWI is often an unpredictable risk factor for DGF. Patients with end-stage renal disease, being on hemodialysis for a long time, almost always have atherosclerotic lesion and/or calcinosis of iliac arteries. When transplanting a kidney from suboptimal age donors, the aortic area and the renal artery wall may also be affected by atherosclerotic process. So, even with an experienced surgeon, vascular reconstruction may require more time, during which graft heating is inevitable. Our SWI elimination device allows to maintain an optimally low graft temperature for long during implantation, in contrast to the classical ice bag technique ($p < 0.001$), which we demonstrated both in an experiment and in a clinical study. "Effective" SWI elimination with the developed new device was associated with statistically significantly lower incidence of DGF ($p = 0.032$) and length of hospital stay ($p = 0.024$) in patient groups comparable in terms of the main risk factors of DGF.

Thus, the use of our developed special SWI elimination device significantly reduced the burden of DGF and, thus, improved treatment outcomes in recipients of a kidney obtained from a suboptimal donor.

CONCLUSIONS

1. Prolonged SWI time (>45 minutes) is a statistically significant risk factor for DGF ($p = 0.035$).
2. The most sensitive to SWI are grafts obtained from expanded criteria donors. We provided evidence to this in an experimental model of kidney autotransplantation from an asystolic donor. The incidence of DGF in "ineffective" SWI elimination can reach 80%.
3. Our developed special SWI elimination device allows to optimally cool a graft during the entire implantation procedure, even if the surgery is prolonged. This is in contrast to the classical ice bag technique ($p < 0.001$).
4. The use of the developed special SWI elimination device in clinical practice reduces DGF incidence safely and effectively ($p = 0.032$) for grafts obtained from expanded criteria donors and with prolonged implantation time.

The authors declare no conflict of interest.

REFERENCES

1. *Chadban SJ, Ahn C, Axelrod DA, Foster BJ, Kasiske BL, Kher V et al.* KDIGO clinical practice guideline on the evaluation and management of candidates for kidney transplantation. *Transplantation*. 2020; 104 (4S1): S11–S103. PMID: 32301874. https://doi.org/10.1097/TP.0000000000003136.
2. *Chen R, Wang H, Song L, Hou J, Peng J, Dai H et al.* Predictors and one-year outcomes of patients with delayed graft function after deceased donor kidney transplantation. *BMC Nephrology.* 2020; 21 (1): 1–10. PMID: 33276737. https://doi.org/10.1186/s12882-020-02181-1.
3. *Siedlecki A, Irish W, Brennan DC.* Delayed graft function in the kidney transplant. *American Journal of Transplantation*. 2011; 11 (11): 2279–2296. PMID: 21929642. https://doi.org/10.1111/j.1600-6143.2011.03754.x.

4. *Narayanan R, Cardella CJ, Cattran DC, Cole HC, Tinckam KJ, Schiff J et al.* Delayed graft function and the risk of death with graft function in living donor kidney transplant recipients. *Am J Kidney Dis*. 2010; 56 (5): 961–970. PMID: 20870331. https://doi.org/10.1053/j.ajkd.2010.06.024.
5. *Tapiawala SN, Tinckam KJ, Cardella CJ, Schiff J, Cattranet DC, Cole EH et al.* Delayed graft function and the risk for death with a functioning graft. *J Am Soc Nephrol.* 2010; 21 (1): 153–161. PMID: 19875806. https://doi.org/10.1681/ASN.2009040412.
6. *Nagaraja P, Roberts GW, Stephens M, Horvath S, Fialovaet J, Chavez R et al.* Influence of delayed graft function and acute rejection on outcomes after kidney transplantation from donors after cardiac death. *Transplantation.* 2012; 94 (12): 1218–1223. PMID: 23154212. https://doi.org/10.1097/TP.0b013e3182708e30.
7. *Kayler LK, Magliocca J, Zendejas I, Srinivas TR, SholdImpact JD.* Impact of cold ischemia time on graft survival among ECD transplant recipients: a paired kidney analysis. *American Journal of Transplantation.* 2011; 11 (12): 2647–2656. PMID: 21906257. https://doi.org/10.1111/j.1600-6143.2011.03741.x.
8. *Wu WK, Famure O, Li Y, Kim SJ*. Delayed graft function and the risk of acute rejection in the modern era of kidney transplantation. *Kidney International*. 2015; 88 (4): 851–858. PMID: 26108067. https://doi.org/10.1038/ki.2015.190.
9. *Hameed AM, Yuen L, Pang T, Rogers N, Hawthorne WJ, Pleass HC.* Techniques to Ameliorate the Impact of Second Warm Ischemic Time on Kidney Transplantation Outcomes. *Transplantation Proceedings.* 2018; 50 (10): 3144–3151. PMID: 30577180. https://doi.org/10.1016/j.transproceed.2018.09.003.
10. *Dienst SG, Ansari MR.* Use of a Cooling Jacket During Kidney Transplantation. *Henry Ford Hospital Medical Journal*. 1971; 19 (3): 127–134.
11. *Danovitch GM* (Ed.). Handbook of kidney transplantation. Lippincott Williams & Wilkins. 2009.
12. *Karipineni F, Campos S, Parsikia A, Durinka JB, Chang PN, Khanmoradi K et al.* Elimination of warm ischemia using the Ice Bag Technique does not decrease delayed graft function. *International Journal of Surgery.* 2014; 12 (6): 551–556. PMID: 24735894. https://doi.org/10.1016/j.ijsu.2014.04.002.
13. *Khan T, Kwarcinski J, Pang T, Hameed A, Boughton P, O'Grady G et al.* Protection From the Second Warm Ischemic Injury in Kidney Transplantation Using an *Ex Vivo* Porcine Model and Thermally Insulating Jackets. *Transplantation Proceedings*. 2021; 53 (2): 750–754. PMID: 33581848. https://doi.org/10.1016/j.transproceed.2021.01.037.
14. *Kamińska D, Kościelska-Kasprzak K, Chudoba P, Hałoń A, Mazanowska O, Gomółkiewicz A et al.* The influence of warm ischemia elimination on kidney injury during transplantation – clinical and molecular study. *Scientific Reports*. 2016; 6 (1): 1–10. PMID: 27808277. https://doi.org/10.1038/srep36118.
15. *Shabunin AV, Drozdov PA, Nesterenko IV, Makeev DA, Zhuravel OS, Astapovich SA*. Risk factors for delayed kidney graft function from a deseased donor. *Transplantologiya. The Russian Journal of Transplantation*. 2022; 14 (3): 265–277. https://doi.org/10.23873/2074-0506-2022-14-3-265-277.

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