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Kidney warming during transplantation

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Abstract The objective of the present study was to describe kidney temperature variations during transplantation and to identify the factors responsible for kidney warming. Kidney temperature was recorded steadily during transplantation. Kidney weight, body mass index (BMI), second warm ischemia time (t), and kidney temperature at the time of being placed in the recipient were analyzed so that we could evaluate their influence on kidney temperature and on kidney warming during transplantation. Kidney temperature at the time of removal from the container was 1.6 °C and 6.3 °C when the kidney was placed in the recipient. Kidney temperature in the recipient depended on kidney temperature after serum washing ($P < 0.0001$), but was independent of kidney preparation time ($P = 0.94$). Then, kidney temperature (T) increased according to the logarithmic curve given in the following equation: $T = 7.2\ \ln(t) - 0.6$. Kidney temperature at the end of anastomosis was 26.7 °C. Kidney warming speed was 0.48 °/min and was dependent on the length of time of vascular anastomosis ($P < 0.0001$). Kidney weight decreased the kidney warming speed ($P = 0.02$). In conclusion, kidney warming increases slowly during ex vivo preparation. Kidney temperature stays below the damaging ischemic temperature of 18°C. Because of its major impact on kidney warming, it is desirable that vascular anastomosis time be reduced, and, consequently, ex vivo kidney preparation needs to be meticulous.

Keywords Renal transplantation · Warm ischemia · Temperature · Kidney preservation · Viability testing

Introduction

During renal transplantation, the bloodless kidney is in cold or warm ischemia, depending on its initial temperature. Its cellular metabolism depends on temperature [1, 11, 17]. Hypothermia decreases cellular metabolism, causing renal ischemia, and preserves kidney functions for many hours.

Second warm ischemia time begins at the end of transplantation. It constitutes the time necessary for vascular anastomosis to be performed. If it is prolonged, it can cause delayed graft function, and sometimes, is responsible for kidney non-function [8, 19]. Kidney temperature variations during transplantation are not well known. The studies performed on animals have shown kidney warming during vascular anastomosis time [3, 4]. However, the standardized time of vascular anastomosis and the models used are smaller than human models and can only partially reproduce the physiological conditions present in human renal transplantation. The aim of this study was to describe kidney temperature variations during transplantation and to determine the factors responsible for kidney warming.

Patients and methods

Between January 1999 and May 2000, kidney temperature was recorded during 65 transplantations performed on 40 men and 25 women by six surgeons. The mean (range) age of donors and recipients was 37 (10–67) years and 43 (2–68) years, respectively. The kidneys were obtained from 64 heart-beating donors, of whom one had had a temporary cardiac arrest, and from one non-heart-beating donor. There were 38 left kidneys (58.5%) and 27 right kidneys (41.5%). Two kidney–pancreas transplantations were performed, and two renal grafts were conducted on children. The same surgical technique was used for all transplantations.

After organ procurement, the kidney was preserved for several hours in University of Wisconsin (UW) solution in an ice-cooled container. Then, an ex vivo vascular preparation was made. During this time, the kidney was protected with ice-cooled paper tissues. At the end of this preparation, the kidney was put on a drip and washed with cold physiological serum, 0.9%. Then it was weighed and immersed in cold serum. Once the iliac vessels were ready for anastomosis, the kidney was placed in the recipient and protected with cold serum. Vascular anastomosis was performed on external iliac vessels.

A tissular thermosensor (ref.: 2423, Medtronic) connected to an electronic thermometer was implanted into the kidney parenchyma, 15 mm deep. The technical characteristics were as follows: thermal sensitivity between 0 and 50 °C, sensitivity of 0.2 °C at 25 °C, and gauge 22 in diameter.

The temperature was recorded every minute during ex vivo preparation and transplantation until blood flow was restored, which signaled the end of ischemia. The number of hours of principal operating time for renal transplantation was registered (removal from the container, washing, placing in the recipient, until the end of vascular anastomosis). The operating room temperature and psoas temperature were also registered, as were kidney weight and body mass index (BMI) of the recipient.

Statistical analysis

The mean curve of kidney warming, a tendency curve, was made, so that we could build a model for renal temperature evolution as a function of vascular anastomosis time. The relationships between quantitative factors (ex vivo preparation time, vascular anastomosis time, kidney weight, BMI, end kidney washing temperature, mean kidney temperature, end kidney temperature, and mean kidney warming speed) were tested with Pearson's correlation coefficient. To allow an adjustment on some significant quantitative factors, we did a partial correlation test with $P < 0.05$ as significance factor.

To study the influence of ischemia on graft function, we considered two groups: immediate and delayed graft function. Graft function was regarded as being delayed if there was any form of dialysis or if the rate of creatinine decreased by less than 10% per day after transplantation.

We analyzed recipient age, donor age, cold ischemia, second warm ischemia, kidney temperature, and kidney warming speed, to evaluate their influence on graft function. We used univariate then multivariate analysis to take into account the significant value of data after adjustment on other significant data. The Mann–Whitney U test and Spearman's correlation statistic test were used ($P < 0.05$). Kidneys with surgical complications were excluded from the statistical analyses.

Results

The mean (range) was as follows. Air temperature was 23.3 (19.6–26.4) °C. Ex vivo kidney preparation time (time of kidney preparation until the beginning of anastomosis) was 82 (36–170) min. Kidney temperature during ex vivo preparation was 5.1 (2.2–9.2) °C. At removal from the container, kidney temperature was 1.6 (0–4.6) °C. Then, kidney temperature varied between 0.7 and 12 °C during ex vivo preparation, depending on kidney manipulation, quality of kidney protection with cool paper tissues, and washing serum temperature. Before being washed, the kidneys were at 4.9 (0.7–9.8) °C, then they warmed up in a few minutes to reach 6.8 (2–12) °C at the end of washing. During preservation in cold serum, kidneys were cooled under ice added to the serum. The mean (range) kidney temperature was 6.3 (2–11.2) °C when the kidney was placed in the recipient. Mean kidney temperature during ex vivo preparation is shown in Fig. 1.

Kidney temperature was independent of ex vivo preparation time. On the other hand, when the kidney was placed in the recipient, its temperature depended on serum temperature (Table 1).

When placed in the recipient, the kidney warmed up under the influence of abdominal temperature, which was 34.8 (30.9–36.5) °C. The vascular anastomosis time was 45.5 (22–85) min. Kidney temperature at the end of vascular anastomosis was 26.7 (19–33.7) °C, that is to say a mean warming of 20.6 (12.9–30.2) °C corresponding to a mean warming speed of 0.48 (0.27–0.72) °/min. The kidney temperature was 19.5 (12.4–27.5) °C during second warm ischemia. Mean kidney warming during second warm ischemia is indicated in Fig. 2.

Kidney temperature evolution depending on time could be expressed by the following equation:

$$T = 7.2 \ln(t) - 0.6$$

where T = kidney temperature and t: = vascular anastomosis time.

When blood flow was restored, kidney temperature increased by several degrees in just a few seconds to reach the central body temperature of the recipient, from 34 to 36 °C, and then became stable. The factors responsible for kidney warming during second warm ischemia are summarized in Table 2.

The mean (range) BMI was 22.6 (14.7–30.1) kg/m^2. The weight of kidneys was 213 (90–360) g. Two kidneys were not weighed for material reasons. Adjusted on vascular anastomosis time, the correlation between kidney weight and mean kidney warming speed stayed significant ($r = 0.28$; $P = 0.02$). There was a significant relationship between mean kidney warming speed and kidney final temperature, but they varied in the opposite direction (Fig. 3).

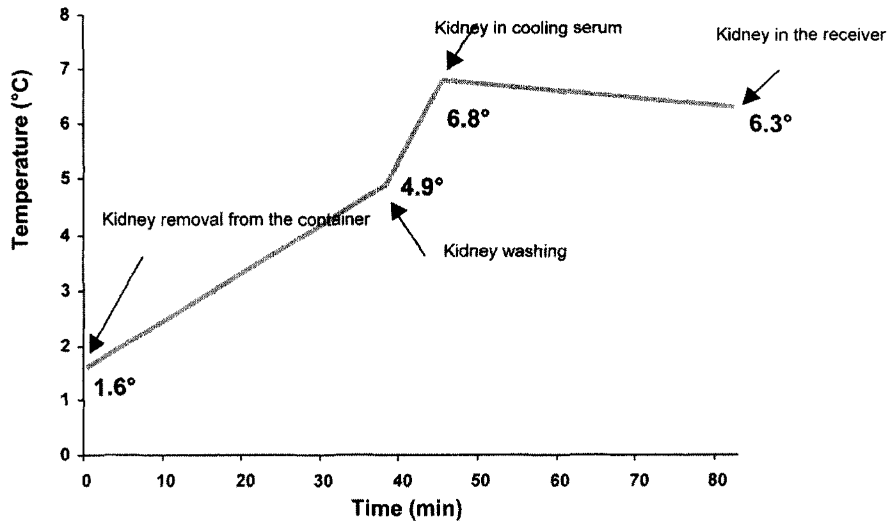

Fig. 1 Mean kidney temperature evolution during ex vivo preparation

Table 1 Relationship between preparation time, kidney temperature at the end of washing, and kidney warming during ex vivo preparation

Parameter	Mean kidney temperature		Kidney temperature in the recipient	
	r	P	r	P
Preparation time	0.10	0.4651	0.01	0.9420
Kidney temperature at the end of washing	0.8139	<0.0001	0.81	<0.0001

There were 39 (60%) kidneys with immediate graft function, 19 (29.2%) with delayed graft function, and seven kidneys (10.8%) had delayed graft function or did not function due to surgical complications:

- Two with delayed graft function, diagnosed by renal biopsy during harvesting, were due to cardiac arrest.
- Four with delayed graft function were due to urinary obstruction or renal bleeding.
- One had renal vein thrombosis.

Cold ischemia was significantly higher in the case of delayed graft function, and average warming speed was lower than with immediate graft function. After adjustment on average warming speed, the relationship between cold ischemia and graft function was still significant. There was no significant relationship between recipient age, donor age, warm ischemia and average kidney temperature during warm ischemia, initial kidney temperature, and graft function (Table 3).

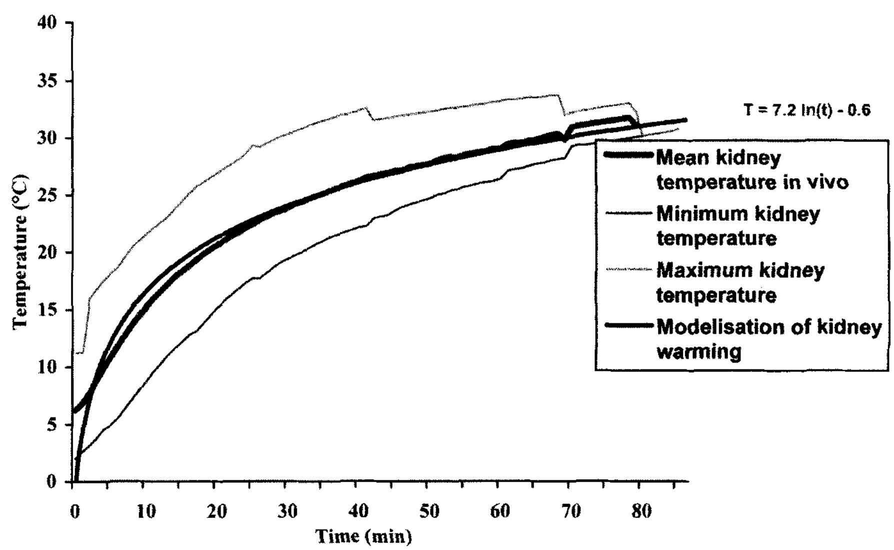

Fig. 2 Mean, minimum, and maximum kidney temperature evolution during vascular anastomosis time

Table 2 Factors responsible for kidney temperature during vascular anastomosis

Factor	Mean kidney temperature		End anastomosis kidney temperature		Mean kidney warming speed	
	r	*P*	*r*	*P*	*r*	*P*
Kidney temperature in the recipient	0.1856	0.1388	0.0795	0.5290	–0.38	0.0016
Anastomosis time	–	–	0.7969	< 0.0001	–	–
Mean kidney warming speed	–	–	–0.4382	0.0002	–	–
Kidney weight	0.00	0.9956	–0.1270	0.3214	–0.3590	0.0039
BMI	–0.0801	0.5292	–0.0408	0.7489	–0.2137	0.09

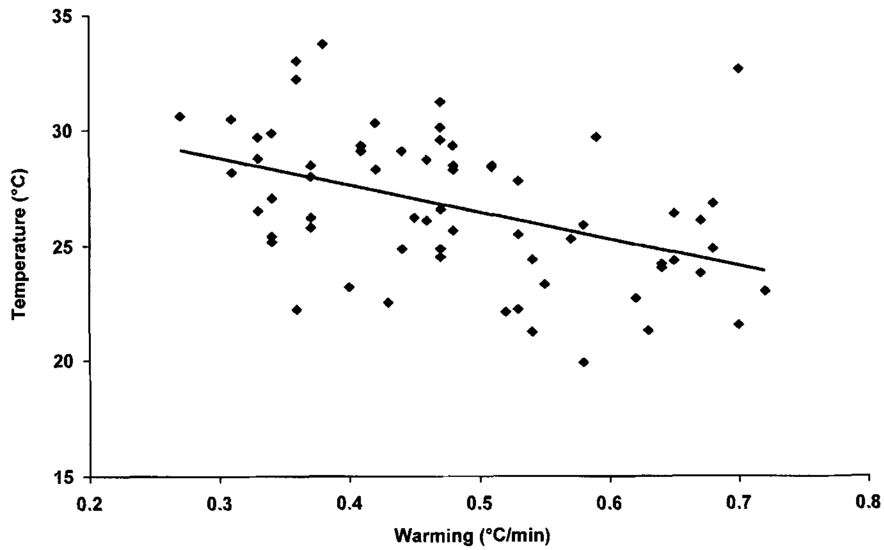

Fig. 3 Relationship between mean kidney warming speed and kidney temperature during vascular anastomosis

Table 3 Relationship between variables studied and graft function

Parameter	Immediate graft function ($n = 39$)	Delayed graft function ($n = 19$)	*P*
Mean donor age	35.5	41	0.15
Mean recipient age	43	45	0.52
Mean cold ischemia time (h)	17.7	23.5	0.05
Kidney temperature before beginning anastomosis (°C)	5.9	5.8	0.84
Mean kidney temperature at the end of anastomosis (°C)	26.5	26.8	0.91
Mean kidney temperature during anastomosis (°C)	19.2	19.6	0.72
Mean anastomosis time (min)	42.7	49.9	0.08
Mean warming speed (°C/min)	0.51	0.44	0.04

Discussion and conclusion

The lack of a reliable and reproducible technique to suppress warm ischemia may be a cause of renal nonfunction. To determine and prevent warm ischemia, this study measured precisely the intensity of renal warming during transplantation. The thermosensor placed at a depth of 15 mm allowed us to measure the temperature of the kidney parenchyma.

Ex vivo kidney preparation may be considered as cold ischemia time. The kidney warms up slightly. The mean kidney temperature was low at 5 °C, and the thermal threshold of glomerular and tubular activation functions, 18 °C [16, 22], was never reached, so kidney ischemic suffering was low. Moreover, there was no relationship between kidney temperature and ex vivo preparation time. The placing of cold, wet, paper tissues around the kidney is a simple and safe method that ensures good thermal protection without interfering with vascular preparation, provided that kidney manipulation is avoided by the surgeon, which would favor kidney warming.

The temperature when the kidney was placed in the recipient varied considerably, between 2 and 11.2 °C, and depended on serum temperature, which often warmed the kidney. Therefore, it is necessary that we control serum temperature to improve thermal kidney protection. Kidney temperature in the recipient was different from animal kidney temperature, which is less than 4 °C [2, 22]. In such studies, kidney temperature often corresponds to the kidney temperature at removal from the container [2] because it is an auto-transplantation or a kidney placed in an incubator [22, 23] without previous ex vivo preparation and washing. These situations do not exactly reproduce the specific physiological conditions in human renal transplantation.

These significant differences in kidney temperature were also observed by Szostek et al., who recorded kidney temperatures, at depths of 10 mm and 20 mm, of 8.87 °C [23] and 9.4 °C [24], respectively, but he did not specify the conditions of the ex vivo kidney preparation. These temperature differences show that the quality of kidney protection is not always adequate during ex vivo kidney preparation and differs according to transplantation team. Kidney temperature should be 4 °C for longer protection against the metabolic effects of warming when the kidney is placed in the recipient.

During vascular anastomosis time, kidney warming is not linear. It follows a logarithmic increase, which is characteristic of warming in a stable thermal environment. For the kidney, it is the abdominal temperature. The mean kidney warming speed is more elevated if the anastomosis time is short and the kidney temperature is low when placed in the recipient. Larger kidneys warm up more slowly than do smaller kidneys. The relationship between kidney weight and kidney warming speed was shown in vitro in pig kidneys [4, 26] and explains the limitations of animal studies because the animal kidneys used are smaller than human kidneys. Consequently, the kidneys warm faster and for a similar second warm ischemia time, the final and the mean renal temperatures are higher. Therefore, kidney ischemic suffering is more important. Conversely, large kidneys may be more resistant to second warm ischemia. Until now, there has been no study on the relationship between kidney temperature and graft function in physiological conditions. Our rate of delayed graft function was similar to that of other studies, where delayed graft function was between 20 and 30% for kidneys coming from heart-beating donors [3, 13, 20, 25]. Many studies have shown that observed delayed graft function increases with the time of cold ischemia, and we also found such results [12, 14, 15]. Considering warm ischemia, Szostek et al. observed an increased risk of delayed graft function when kidney temperature was over 15 °C [23]. But in this study, the transplantation procedure was quite experimental, with in situ cooling, and kidneys were harvested on hemodynamically unstable donors. Furthermore, this thermic threshold is not adapted to the physiological conditions of human renal transplantation, where such a temperature is reached after only 15 min.

Another aspect of warm ischemia after temperature is time. There is a risk of delayed graft function if second warm ischemia is over 30 and 45 min [7, 8, 10, 12]. The differences in second warm ischemia can be explained by different renal capital at the beginning of vascular anastomosis. It depends on harvesting conditions, cold ischemia, and probably, thermic renal conditions during vascular anastomosis. Actually, it is difficult for vascular anastomosis time to be reduced, which was similar for other transplantation teams [8, 9, 12]. To limit second warm ischemia, teams have proposed that the kidney be cooled in situ during the vascular anastomosis time [3, 4, 5, 6, 18, 21, 23]. This technique allows a stable kidney temperature to be maintained. It consists of the kidney being wrapped in a bag or a cooling isothermal shell at 5–15 °C, depending on the model used. However, it is still experimental and not commonly used in human renal transplantation because of its volume and the absence of sterile commercial products [5] or the necessity to renew the ice in the kidney bag [6].

In conclusion, we found that the kidney warms slowly during ex vivo preparation. Its temperature remains below the toxic thermal threshold of 18 °C. In vivo, its temperature increases as a logarithmic curve. It depends on vascular anastomosis time, kidney temperature in the recipient, and kidney weight. It is possible by simple means and during all transplantation steps to decrease kidney warming and to reduce kidney warm ischemia suffering. The ex vivo preparation must be meticulous if vascular anastomosis time is to be reduced. Renal manipulation must be avoided and simple kidney protection using ice is necessary and efficient. The washing serum temperature must be controlled and below 5 °C if we are to obtain better kidney cooling with metabolic necessity during vascular anastomosis time. Perhaps our description of kidney temperature during the whole kidney transplantation procedure will help further studies on renal graft function and renal metabolic needs.

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