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ORIGINAL ARTICLE

Analysis of Temperature During Storage and the Period of Warm Ischemia of the Graft in Kidney Transplants

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ABSTRACT

Objective: This study aims to analyze the temperatures of kidney transplants performed at Hospital Municipal São José, Joinville/SC, throughout the period of cold ischemia and whether this temperature is in line with what is recommended in the literature. **Method**: Prospective analysis based on all kidney grafts that was used for kidney transplant in the unit of kidney transplant of Hospital Municipal São José. **Results**: The study analyzed that the current method of graft conservation partially meets the expected values, to maintain the recommended temperature. **Conclusion**: It is important to maintain studies and analyzes on the subject for continuous improvement in graft storage.

Descriptors: Kidney Transplantation; Graft Transplantation; Cold Ischemia; Reperfusion.

Análise da Temperatura Durante o Armazenamento e o Período de Isquemia Morna do Enxerto em Transplantes Renais

RESUMO

Objetivo: Este estudo tem por objetivo analisar as temperaturas dos transplantes renais realizados no Hospital Municipal São José, Joinville/SC, durante todo o período de isquemia fria e se essa temperatura se adéqua ao preconizado em literatura. **Método**: Foi realizado um trabalho prospectivo com a coleta de dados dos enxertos renais utilizados para transplante renal com órgãos de doador falecido no serviço de transplante renal do Hospital Municipal São José. **Resultados**: O estudo analisou que o método atual de conservação do enxerto atende parcialmente aos valores esperados para manter a temperatura preconizada. **Conclusão**: Importante que se mantenham estudos e análises sobre o tema para melhoria continua no armazenamento do enxerto.

Descritores: Transplante de Rim; Transplante de Órgãos; Isquemia Fria; Reperfusão.

INTRODUCTION

The temperature at which the graft is exposed during the preoperative period is essential for the clinical outcome of the recipient, being related to the function of the transplanted organ, as well as the long-term survival of the graft.[1]

Most of the time, the storage of organs for transplantation is done in hypothermia, and the storage temperature must remain between 0 and 4 °C. Hypothermia is induced during organ harvesting surgery. It is associated with the infusion of preservation solution, characterizing the cold ischemia stage. The purpose of reducing the graft's temperature is to reduce the organ's metabolism when there

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is no blood flow, avoiding graft dysfunction during hot ischemia, that is, the period that comprises the clamping of the donor's artery until the infusion with the preservation solution. Hot ischemia is the period in which cellular damage becomes more evident since there is an abrupt interruption of the supply of oxygen to the cells and, as a consequence, there is a reduction in aerobic metabolism, suspension of glucose and fatty acid oxidation and transfer of glycolysis to the anaerobic pathway, which significantly reduces the amount of intracellular adenosine triphosphate (ATP). With a reduced ATP supply, the decrease in the activity of the Na/K/ATPase enzyme creates a hydro electrolytic imbalance between the intra and extracellular environments, which favors the formation of cellular edema.[2w]

Most organs tolerate warm ischemia for 30 to 60 minutes until their complete loss of function. Pegg et al. showed that when the period lasts longer than 5 minutes, it is already related to unfavorable results with reperfusion injuries, but they also showed that cold ischemia associated with an appropriate solution could increase graft viability in up to 30 hours.[1]

OBJECTIVE

Analyze the temperature measurements from storage of the renal graft at the time of opening the organ transport box, during the back-table up to reperfusion, including warm ischemia, to assess whether the temperature is adequate to the value recommended by the literature.

MATERIALS AND METHODS

Data were collected prospectively on all kidney grafts accepted for transplantation at the Renal Transplantation Service of Hospital São José de Joinville, SC, from June to December 2019.

Temperature measurements were performed according to the instructions in the Scantemp ST-600 digital infrared thermometer manual. The standardized distance was 24 ± 5 cm for each item measured, and the measurement time was 1 s according to the device's manual. The first measurement (T1) was performed at the bottom of the transport box right after removing the vial with the graft. The second measurement (T2) was performed after removing the graft from the last package that wrapped it, and at that exact moment, the graft was exposed on the organ preparation table (back table). The third measurement (T3) occurred at the beginning of warm ischemia (in which the organ leaves the table and comes into contact with the patient in the implantation phase). The fourth measurement (T4) was taken before reperfusion (post-implantation). The T1, T2, T3 and T4 measurements were standardized, taking the renal parenchyma close to the hilum as the point. All grafts were maintained with the same preservation liquid (histidine-tryptophan-ketoglutarate; Custodiol, Contatti Medical, São Geraldo, Brazil) at all storage stages, the same solution used by the liver transplant team.

Data were stored and crossed using statistical calculations (minimum, maximum, standard deviation) and significance value, with $p < 0.05$ in Microsoft Excel 2016 and IBM SPSS programs.

The grafts were collected, stored and transported according to the state protocol for packaging organs for transport in the state of Santa Catarina (RDC-66/2009).[7]

RESULTS

Statistical analysis consists of the Shapiro–Wilk data normality test, as shown in Table 1. Table 2 shows temperature measurements, mean and standard deviation.

Table 1. Normality test of the study's quantitative variables.

Groups (variables)	n	W	P	Normality
Age	39	0,8992	0,0021	No
T1 (°C)	39	0,9523	0,0986	Yes
T2 (°C)	39	0,8138	0,0000	No
T3 (°C)	37	0,9847	0,8813	Yes
T4 (°C)	31	0,9745	0,6491	Yes
CIT (h)	39	0,9233	0,0111	No

W: Shapiro–Wilk normality test statistics; P: Shapiro–Wilk test p-value; If $P < 0.05$, the observed distribution does not approximate the normal distribution; CIT: cold ischemia time;°C: degrees Celsius; h: hour.

Tabela 2. Principais medidas descritivas dos grupos de dados de mensuração quantitativa do estudo.

Variables	n	Amplitude	(Mean ± SD)	CI (95%)	(Mean ± QD)	CV
Age	39	(14,0–72,0)	(48,05 ± 15,79)	(43,1–53,01)	(54,0 ± 8,0)	32,86%
T1 (°C)	39	(–5,4–2,8)	(–1,18 ± 2,18)	(0–0,49)	(–1,4 ± 1,1)	185,23%
T2 (°C)	39	(–1,6–15,4)	(3,46 ± 3,68)	(2,3–4,61)	(2,4 ± 1,7)	106,47%
T3 (°C)	37	(5,0–30,2)	(16,46 ± 5,76)	(14,61–18,32)	(16,7 ± 3,6)	34,98%
T4 (°C)	31	(16,3–30,1)	(24,13 ± 3,01)	(23,07–25,19)	(24,4 ± 2,6)	12,47%
CIT (h)	39	(0,0–33,0)	(18,37 ± 6,48)	(16,33–20,4)	(18,0 ± 4,2)	35,28%

SD: standard deviation; CI: confidence interval; QD: quartile deviation; CV: coefficient of variation ; CIT: cold ischemia time; °C: degrees Celsius; h: hour. II –In some cases, *n* has lower than expected values due to a lack of data.

Table 3 presents the absolute and relative frequencies of each temperature, and we observe that 64% of the temperature measurements in T2 are within the range of 0 to 4° C, and 33% are above 4° C. We also saw that 100% of the measurements at T3 and T4 are above 4° C. All these findings with a $P < 0.001$. Analyzing the results obtained in T1, only 25.6% of the measurements were within the range of 0 to 4° C, and the rest of the data are below 0° C. However, as seen in Table 3, there is no relationship between T1 and any other measured temperature.

Table 3. Frequency distribution of the classification of each temperature.

Temperature	n (%)	CI (95%)	P
T1 (°C)			
Below 0	29 (74,4%)	(60,65–88,06)	0,0023
Between 0 and 4	10 (25,6%)	(11,94–39,35)	
T2 (°C)			
Below 0	1 (2,6%)	(0–7,52)	0,0000
Between 0 and 4	25 (64,1%)	(49,05–79,16)	
Above 4	13 (33,3%)	(18,54–48,13)	
T3 (°C)			
Below 0	0 (0,0%)	(0,00–0,00)	0,0000
Between 0 and 4	0 (0,0%)	(0,00–0,00)	
Above 4	37 (94,9%)	(87,95–101,79)	
Não informado	2 (5,1%)	(0,00–12,05)	
T4 (°C)			
Below 0	0 (0,0%)	(0,00–0,00)	0,0000
Between 0 and 4	0 (0,0%)	(0,00–0,00)	
Above 4	31 (79,5%)	(66,81–92,16)	
Não informado	8 (20,5%)	(7,84–33,19)	

CI: confidence interval; P: P-value of the Chi-square Test of Adherence (This test compares frequencies with each other within the same distribution)

DISCUSSION

Organ preservation and perfusion techniques are one of the tremendous technical challenges for the viability and success of transplants. Given this, two phases stand out, hypothermic and normothermic (through perfusion machines). In the area of organ preservation, the search for new preservation solutions, such as an enriched substrate saturated with oxygen and with leukocyte depletion, to help organ quality.[3]

The acute interruption of blood flow in any organ generates a significant reduction in oxygen supply, generating hypoxia and, consequently, ischemic cell damage. The alternative to reverse this process would be tissue reperfusion, but rapid revascularization causes ischemia-reperfusion injury (IRI). Furthermore, reoxygenation leads to the direct activation of the sterile environment's innate and adaptive immune responses. As a reaction, the inflammatory cascade activates, which in turn causes distinct pathological lesions, including endothelial dysfunction with increased vascular permeability, apoptosis, and cell necrosis.[3]

Cell necrosis is clinically manifested as IRI; it leads to organ dysfunction and death. It is worth noting that IRI is present in several clinical situations in addition to transplantation, such as acute myocardial infarction and massive hemorrhage in traumatic accidents.[3]

Strategies are used to mitigate the effects of ischemia/reperfusion injury, especially concerning adequate care for the donor, avoiding hemodynamic instability, vasoactive drugs, electrolyte variations and increased cold ischemia time (CIT).[3]

Preservation solutions try to mimic the hydro electrolytic and intracellular environment, aiming to stabilize the plasma membrane, prevent edema and reduce the cell damage caused by ischemia and acidosis as much as possible.[5] Added to the cooling of the graft at a temperature of 0 to 4 °C, reducing metabolism rates by 90 to 95%, reducing the lack of ATP and the deviation of metabolism to anaerobic pathways.[4]

Although the warm ischemia time (the period between arterial clamping and the start of perfusion with preservation solution) is more harmful to the organ, with trained teams, nowadays, this time rarely exceeds 5 minutes, with CIT being one of the main variables related to delayed renal allograft function.[4]

In T2, 64% of the cases are within the range of 0 to 4 °C, with only one measurement with a negative temperature at –1.6 °C and 13 measurements above 4 °C, which, according to the literature, may impair the function of the graft.[4] Warm ischemia before implantation leads to a high rate of delay in graft function and acute tubular necrosis, depending on the duration of ischemia.[6]

Regarding the analysis of temperatures at the beginning and end of warm ischemia, T3 and T4, respectively, no case had a temperature within the range of 0 to 4 °C, as recommended in the literature,[3] which further favors the negative impact of the cellular effects of oxygen deprivation. It is worth mentioning the enormous difficulty with the current technology in maintaining a temperature between 0 and 4 °C in the preparation of the graft in back-table and surgical manipulation, where the teams, in this case, have in their favor the accomplishment of the same in the shortest time possible.[4]

CONCLUSION

This study demonstrates that the temperature of the organs during storage and bench surgery is adequate and follows what is recommended in the literature (0 to 4 °C) in 64%, with statistical significance; however, 33% are above 4 °C, specifically in bench surgery. We also observed that T3 values are above the values recommended in the literature. Therefore, it is concluded that the method of conservation of the graft in the transport box meets the expected values by 64%. Still, this temperature is outside the recommended range after preparing the graft until implantation. Expansion of the number of transplants analyzed is necessary to confirm and improve the data. Still, reviewing techniques for maintaining temperature in the back table is a great challenge for all teams.

CONFLICT OF INTEREST

Nothing to declare.

AUTHORS' CONTRIBUTION

Substa**ntive scientific and intellectual contributions to the study:** Lima AC, Alves JCR, Borga AL, Deboni LM, Guterres JCP, Garcia CE; **Conception and design**: Lima AC, Deboni LM, Guterres JCP, Garcia CE; **Analysis and data interpretation:** Lima AC, Deboni LM, Guterres JCP, Garcia CE; **Article writing**: Lima AC, Deboni LM, Guterres JCP, Garcia CE; **Critical revision**: Lima AC, Alves JCR, Borga AL, Deboni LM, Guterres JCP, Garcia CE; **Final approval**: Lima AC, Deboni LM, Guterres JCP, Garcia CE.

DATA AVAILABILITY STATEMENT

All dataset were generated or analyzed in the current study.

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Not applicable.

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