http://dx.doi.org/10.1590/0100-6991e-20192079

Review Article

Machine perfusion *versus* cold storage in renal preservation of deceased donors with brain death: systematic review and meta-analysis.

Máquina de perfusão *versus* armazenamento estático na preservação renal de doadores com morte encefálica: revisão sistemática e metanálise.

Ricardo Ribas de Almeida Leite, TCBC-RJ[1]; Alberto Schanaider, TCBC-RJ[2]; Eliana Rosa da-Fonseca[3]; Vinicius Layter Xavier[4]; Luiz Carlos Duarte de-Miranda, ACBC-RJ[2].

1. Federal University of Rio de Janeiro, Postgraduate Program in Surgical Sciences, Department of Surgery, Rio de Janeiro, RJ, Brazil.
2. Federal University of Rio de Janeiro, Department of Surgery, Rio de Janeiro, RJ, Brazil.
3. Federal University of Rio de Janeiro, Library, Rio de Janeiro, RJ, Brazil.
4. University of Rio de Janeiro State, Institute of Mathematics and Statistics, Department of Statistics, Rio de Janeiro, RJ, Brazil.

ABSTRACT

With the increasing use of machine perfusion in kidney transplantation, it has been observed that dynamic ischemia correlates with the improvement of organ preservation. In this context, we performed a systematic review that aimed to evaluate the efficacy of the portable machine perfusion (LifePort Kidney Transporter Machine®), used in Brazil, compared to cold storage, regarding the delayed graft function of deceased donors with brain death. Literature search was carried out in LILACS, MEDLINE via PubMed, Scopus, Clarivate Analytics, Cochrane Library, Embase, and SciELO, as well as in Google Scholar manually. The systematic review consisted only of randomized clinical trials. For meta-

analysis, relative risk and odds ratio were evaluated. Eighty-six documents were identified and two papers from European and Brazilian groups were selected at the end, with eligibility criteria for meta-analysis. In these, 374 kidneys were assigned to machine perfusion and 374 kidneys were assigned to cold storage. Delayed graft function was observed in 84 and 110 patients, respectively. In meta-analysis, a risk ratio of 0.7568 (p=0.0151) and an *odds ratio* of 0.6665 (p=0.0225) were obtained, both with a 95% confidence interval. Machine perfusion reduced the incidence of delayed graft function of deceased donors with brain death.
Keywords: Kidney Transplantation. Pulsatile Flow. Cold Ischemia. Delayed Graft Function. Brain Death.

INTRODUCTION

Since 1902, when European surgeon Emerich Ulmann decided to remove one kidney from a healthy dog and implant in the cervical region of another, resulting in the elimination of urine, renal transplantation has been constantly evolving in its various aspects: surgical (donors, access pathways, techniques), clinical (immunosuppressants, infectious markers, histopathological), and regarding organ preservation (cold storage and machine perfusion). Solid organ transplantation, once an experimental procedure with remote chances of success, has become the gold standard for the treatment of chronic kidney disease[1].

The importance of organ preservation following withdrawal has become evident as soon as surgeons have faced the challenge of storing the organs and transporting them from donors to recipients[2]. In one of the first articles on cold ischemia for renal preservation, Calne et al. have stated that damages from renal ischemia are of extreme importance to those interested in kidney transplantation with deceased donor and are probably responsible for more failures than immunological reactions[3]. All transplanted organs are susceptible to ischemic damage. In addition, after implantation, the kidney undergoes reperfusion, what, in turn, causes additional cellular damage associated with those of ischemia. In this context, the so-called ischemia-reperfusion process, linked to oxidative stress, seems to play a fundamental role in the clinical outcome of the renal graft[4].

The waiting list for renal transplantation in Brazil exceeds 20,000 patients. It is, therefore, the organ with the highest demand in the country, according to Brazilian Association of Organ Transplantation[5]. To meet this growing demand,

there has been a substantial increase in donors in borderline conditions, that is, deceased donors whose kidneys carry a higher risk of worse clinical outcomes. In these donors, called expanded-criteria donors, organ preservation during ischemia has assumed great importance[6]. The most widely accepted definition of expanded criteria in renal donors includes patients over 60 years of age or between 50 and 59 years old, comprising two of the following parameters: systemic arterial hypertension, history of stroke, or creatinine with a final value >1.5mg/dl. Another fundamental concept within the specialty is the delayed graft function (DGF), which is the need for the patient to undergo dialysis in the first week after transplantation, due to a slow recovery of function and resulting in a shorter survival of the transplanted kidney[7].

In the 1960s, Belzer *et al*.[8] refined the organ's cold storage (CS) process and developed a machine for dynamic ischemia, initially idealized by Charles Lindber and with the purpose of minimizing ischemic damages and improving clinical outcome in transplanted patients. Thus, its first successful use in a kidney transplant happened in 1968, after 17 hours of organ ischemia. In the machine perfusion (MP), after an initial infusion to remove blood from the organ, the kidney is coupled to an apparatus that maintains a continuous pulsatile perfusion through the arterial weft, as well as the temperature between 1^{o}C and 10^{o}C degrees[9]. This technology was implanted in our country about five years ago, and the lack of a national consensus guideline for its use in renal transplantation motivated us to conduct a thorough review of literature, searching for more current and consistent scientific evidences.

METHODS

The present study consisted of a systematic review with meta-analysis on the use of MP compared to CS, with the focus directed to the primary clinical outcome of DGF, in renal transplanted patients. Literature search aimed at identifying randomized clinical trials and subjecting them to quality and validity criteria established in scientific literature, ultimately, analyzing them statistically in relation to the clinical outcome of DGF.

The following inclusion criteria were used: randomized clinical trial (RCT) studies and articles on kidney transplantation from donor with brain death.

Regarding exclusion criteria, the following parameters were established: studies that were not only RCT; animal models; studies that included only donors with circulatory death; studies that did not use LifePort Kidney Transporter Machine®; isolated cost-effectiveness studies; multiple organ transplants.

Systematic Review

The systematic review was preceded by the strategy named PICO (The acronym stands for Patient/Problem, Intervention, Comparison, and Outcome)[10], aiming to construct the research question with the following configuration: Patient/Problem (P) to be studied: Transplantation and uptake of kidneys; Intervention (I): machine perfusion; Comparison (C): Static ischemia with dynamic ischemia; and Outcome (O): Identify clinical benefit of DGF in renal transplanted patients. It was considered as the question of the research: “for the delayed graft function of the renal transplanted patient, what is the efficacy of machine perfusion compared to cold storage?”

The search was completed in April 2017, using relevant databases in the health area, such as: MEDLINE, consulted via PubMed; Scopus (Elsevier) and Web of Science (current Clarivate Analytics), via Portal de Periódicos/CAPES. We also searched in Cochrane Library (Wiley), Embase (Elsevier), Scientific Electronic Library Online (SciELO), and LILACS/Portal Regional da Biblioteca Virtual em Saúde (BVS), as well as in Banco de Teses CAPES and Google Scholar manually.

The search terms were identified and mapped in the controlled vocabularies: Health Sciences Descriptors and Medical Subject Heading (MeSH), considering the standard terms and their synonyms (entry terms), as described in table 1.

Table 1. Health Sciences Descriptors and MeSH terms used in the bibliographic research.

	Descriptors/Synonyms	MeSH terms/Entry terms
Patient	"Kidney Transplant" OR "Kidney Graft" OR "Renal Transplant" OR "Kidney Transplantation" OR "Renal Transplantation"	"Kidney Transplantation" OR "Renal Transplantation" OR "Renal Transplantations" OR "Transplantations Renal" OR "Transplantation Renal" OR "Grafting, Kidney" OR "Kidney Grafting" OR "Transplantation Kidney" OR "Kidney Transplantations" OR "Transplantations Kidney"
Intervention	"Machine Perfusion"	"Kidney Perfusion" OR "Machine Perfusion in Kidney" OR "Machine Perfusion" OR "Renal Perfusion" OR "Perfusion Machines"
	"Pulsatile Flow" OR "Pulsatile Perfusion"	"Pulsatile Flow" OR "Pulsatile Flow" OR "Flow Pulsatile" OR "Flows Pulsatile" OR "Pulsatile Flows" OR "Flow Pulsating" OR "Flows Pulsating" OR "Pulsating Flow" OR "Pulsating Flows" OR "Perfusion Pulsatile" OR "Perfusions Pulsatile" OR "Pulsatile Perfusion" OR "Pulsatile Perfusions" OR "Static Storage"
Comparison	"Cold Ischemia" OR "Cold-Induced Ischemia"	"Cold Ischemia" OR "Ischemia Cold" OR "Cold Ischemia Time" OR "Cold Ischemia Times" OR "Time Cold Ischemia" OR "Cold Ischemic Time"
Outcome	"Delayed Graft Function"	"Delayed Graft Function" OR "Graft Function, Delayed"

Randomized clinical trial was the type of study selected for research. For its recovery, the following terms were used: "clinical trial" OR "random" OR "random allocation". For relationships among terms, we utilized quotation marks (""). For compound terms and mathematical operators, OR. For grouping/sum of synonyms, AND. For intersection of terms, PICO elements; NOT, in turn, was used to exclude the terms "cardiac death", because it is an unauthorized technique in Brazil, OR "circulatory death". Search strategies performed in scientific portals and databases are shown in Table 2.

Table 2. Search strategies in scientific databases.

Databases	Search strategies
PubMed	((((("kidney transplantation"[MeSH Terms] OR ("Kidney Transplantation"[Title/Abstract] OR "Renal Transplantation"[Title/Abstract] OR "Renal Transplantations"[Title/Abstract] OR "Transplantation Renal"[Title/Abstract] OR "Kidney Grafting"[Title/Abstract] OR "Transplantation Kidney"[Title/Abstract] OR "Kidney Transplantations"[Title/Abstract] OR "Transplantations Kidney"[Title/Abstract])) AND (("pulsatile flow"[MeSH Terms] OR ("Pulsatile Flow"[Title/Abstract] OR "Pulsatile Flow"[Title/Abstract] OR "Flow Pulsatile"[Title/Abstract] OR "Pulsatile Flows"[Title/Abstract] OR "Pulsating Flow"[Title/Abstract] OR "Pulsating Flows"[Title/Abstract] OR "Perfusion Pulsatile"[Title/Abstract] OR "Pulsatile Perfusion"[Title/Abstract] OR "Pulsatile Perfusions"[Title/Abstract])) OR ("kidney perfusion"[Title/Abstract] OR "Machine Perfusion"[Title/Abstract] OR "Renal perfusion"[Title/Abstract] OR "perfusion machines"[Title/Abstract]))) AND ("delayed graft function"[MeSH Terms] OR ("Delayed Graft Function"[Title/Abstract] OR DGF[Title/Abstract]))) AND (English[lang] OR Portuguese[lang] OR Spanish[lang])) AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR "clinical trials as topic"[MeSH Terms] OR clinical trial[Publication Type] OR random[Title/Abstract] OR "random allocation"[MeSH Terms] OR "randomized controlled trial"[All Fields] OR "clinical trial"[Title/Abstract] OR "prospective trial"[Title/Abstract] OR "randomized trial"[Title/Abstract]) AND (English[lang] OR Portuguese[lang] OR Spanish[lang])
Scopus	((((TITLE-ABS-KEY("Kidney Transplantation" OR "Renal Transplantation" OR "Renal Transplantations" OR "Transplantations Renal" OR "Transplantation Renal") OR TITLE-ABS-KEY("Grafting, Kidney" OR "Kidney Grafting" OR "Transplantation Kidney" OR "Kidney Transplantations" OR "Transplantations Kidney"))) AND ((TITLE-ABS-KEY("kidney perfusion" OR "machine perfusion in kidney" OR "Machine Perfusion" OR "Renal perfusion" OR "perfusion AND machines) OR TITLE-ABS-KEY("Pulsatile Flow" OR "Pulsatile Flow" OR "Flow Pulsatile" OR "Flows Pulsatile" OR "Pulsatile Flows" OR "Flow Pulsating") OR TITLE-ABS-KEY("Flows Pulsating" OR "Pulsating Flow" OR "Pulsating Flows" OR "Perfusion Pulsatile" OR "Perfusions Pulsatile" OR "Pulsatile Perfusion" OR "Pulsatile Perfusions"))) AND (TITLE-ABS-KEY("Delayed Graft Function" OR "Graft Function Delayed" OR dgf))) AND (TITLE-ABS-KEY("clinical trial" OR "clinical trials"))) AND (TITLE-ABS-KEY("circulatory death" OR "cardiac death"))
Clarivate Analytics (Web of Science)	("Kidney Transplantation" OR "Renal Transplantation" OR "Renal Transplantations" OR "Transplantations Renal" OR "Transplantation Renal" OR "Grafting, Kidney" OR "Kidney Grafting" OR "Transplantation Kidney" OR "Kidney Transplantations" OR "Transplantations Kidney") AND Topic: ("Pulsatile Flow" OR "Pulsatile Flow" OR "Flow Pulsatile" OR "Flows Pulsatile" OR "Pulsatile Flows" OR "Flow Pulsating" OR "Flows Pulsating" OR "Pulsating Flow" OR

	"Pulsating Flows" OR "Perfusion Pulsatile" OR "Perfusions Pulsatile" OR "Pulsatile Perfusion" OR "Pulsatile Perfusions") AND Topic: ("Delayed Graft Function" OR "Graft Function Delayed" OR DGF) AND Topic: ("clinical trial" OR "clinical trials" OR "random allocation") Stipulated time: every year. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, and ESCI.
Cochrane	ID Search Hits #1 "Kidney Transplantation":ti,ab,kw or "renal transplantation":ti,ab,kw or "Transplantations Renal":ti,ab,kw or "Kidney Transplantations":ti,ab,kw or "Kidney Grafting":ti,ab,kw (Word variations have been searched) 6873 #2 "Machine Perfusion":ti,ab,kw or "perfusion machines":ti,ab,kw or "pulsatile flow":ti,ab,kw or "Pulsatile Flows":ti,ab,kw or "Flow Pulsatile":ti,ab,kw (Word variations have been searched) 630 #3 "delayed graft function":ti,ab,kw or "Graft Function Delayed":ti,ab,kw or "DGF":ti,ab,kw (Word variations have been searched) 385 #4 #1 and #2 and #3 28 There are 25 results from 1039010 records for your search on #4 - #1 and #2 and #3 in Trials in the strategy currently being edited
Embase	'Kidney transplantation' AND ('pulsatile flow' OR 'machine perfusion') AND 'delayed graft function' AND ('clinical trial' OR randomization) 'kidney transplantation'/de AND 'machine perfusion'/exp AND 'delayed graft function'/exp AND 'machine perfusion' AND ('clinical trial'/exp OR 'clinical drug trial' OR 'clinical trial' OR 'major clinical trial' OR 'trial, clinical')

In the systematic review after the definition of the research protocol, followed by data analysis and synthesis, a search strategy was initiated and, then, in reference to the database, the references/articles were identified. After exclusion of duplications and also by title and abstract, references to read the full text were selected. We performed a new exclusion by specific criteria and the consolidation for quantitative and qualitative analyses. PRISMA 2009 Flow Diagram[11], which consists of the main items to report systematic reviews and meta-analyses, was followed.

Meta-analysis

Meta-analysis was performed using R 3.3.2 software, with metafor library[12]. Neperian logarithm of the risk ratio ln (RR) and the odds ratio ln (OR) were evaluated. The heterogeneity of the studies was assessed using Cochran's Q-test.

RESULTS

Systematic review

We selected 86 documents using our search strategy, out of which 25 were duplicated. Thus, analysis and selection were carried out in 61 studies. After applying the inclusion and exclusion criteria, other 35 studies were excluded by title and other 17 by abstract reading, and five were discarded after full reading. Among the four selected for qualitative evaluation[7,9,13,14], two[7,13] were excluded and two[9,14] were included in meta-analysis (Figure 1).

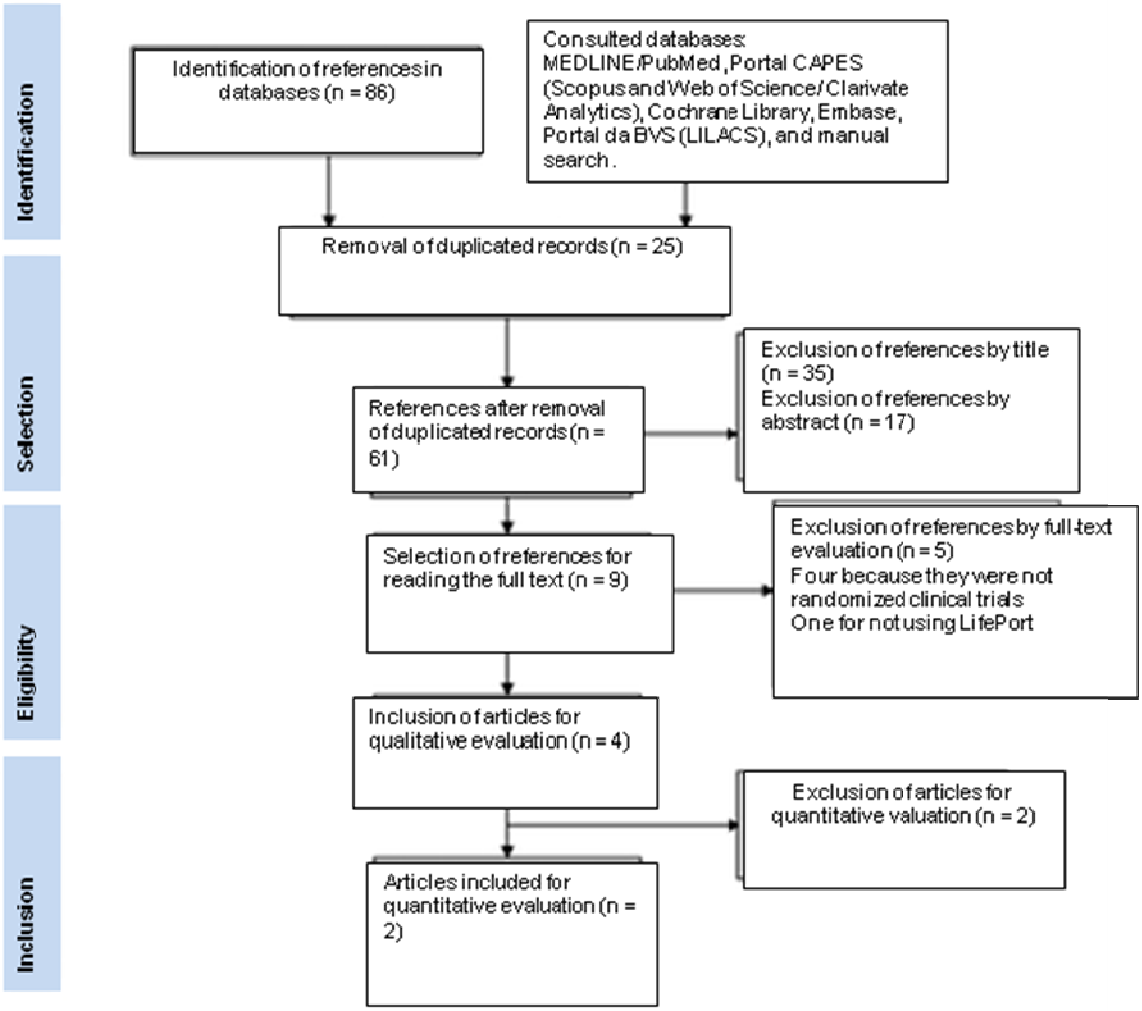

Figure 1. Result of the systematic review in the search flowchart.

The two randomized clinical trials selected for meta-analysis were published in 2009 and 2017[9,14]. There were 374 donors, 748 kidneys, half allocated in CS

and half in MP. The clinical outcome observed with DGF was verified in 84 patients who received kidneys from MP and in 110 patients where the organs were in CS.

Meta-analysis

Risk Ratio (RR)

The heterogeneity test presented q-value of 0.0879, with p-value of 0.7669. Therefore, the heterogeneity was not considered significant. Using the fixed-effect model, we obtained ln(RR) estimate =-0.2786, with standard deviation of 0.11147. Considering the bilateral test whose null hypothesis is ln(RR)=0, with Zval test statistics =-2.4289, the null hypothesis is rejected at significance level of 0.05, p=0.0151. Confidence interval was 95% for ln(RR) estimate: (-0.5034; -0.0538).

Figure 2 summarizes the result of the meta-analysis considering RR. This is a forest type chart (forest plot). For each study, the RR and the 95% confidence interval are presented. The vertical dotted line indicates the point where RR is equal to 1. In the two selected studies, the confidence interval comprised values very close to 1. The model results are presented at the bottom of the graph. The meta-analytic measure is represented by the rhomb. The estimated value of the RR for this meta-analysis was 0.7568, represented by the center of the rhomb, with 95% confidence interval (0.6044; 0.9476), represented by the rhomb edges. It is important to highlight that the meta-analytic measure was less than 1 and its 95% confidence interval (CI) did not contain one.

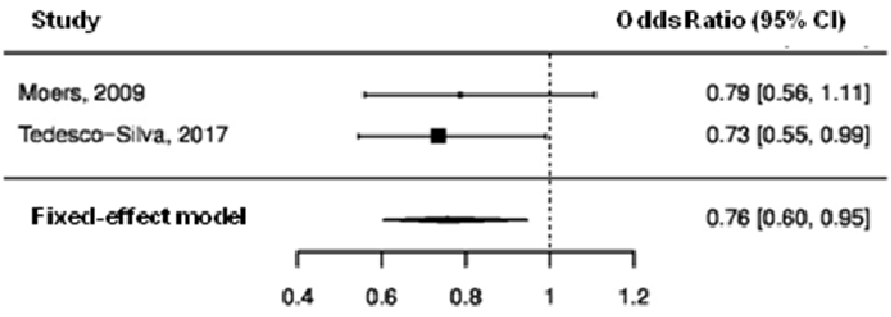

Figure 2. Forest plot for RR. In the meta-analysis, we observed the confidence intervals for both selected studies with RR estimate at 0.7568 (0.6044, 0.9476).

Odds Ratio (OR)

The heterogeneity test presented q-value of 0.8933, with p-value of 0.346. Therefore, the heterogeneity was not considered significant. Using the fixed-effect

model, we obtained ln(OR) estimate =-0.4057, with standard deviation of 0.1778. Considering the bilateral test whose null hypothesis is ln(OR)=0, with Zval test statistics =-2.2815, the null hypothesis is rejected at significance level of 0.01, p=0.0225. Confidence interval was 95% for ln(OR) estimate: (-0.7542; -0.0572).

Figure 3 summarizes the result of the meta-analysis considering OR. For each study, the OR and the 95% confidence interval are presented in a forest type chart (forest plot). The vertical line indicates the point where OR is equal to 1. In the two selected studies, the confidence interval comprised values very close to 1. The estimated value of the OR for this meta-analysis was 0.6665, represented by the center of the rhomb, with 95% confidence interval (0.4704; 0.9444), represented by the rhomb edges. It is important to highlight that the meta-analytic measure was less than 1 and its 95% confidence interval did not contain one.

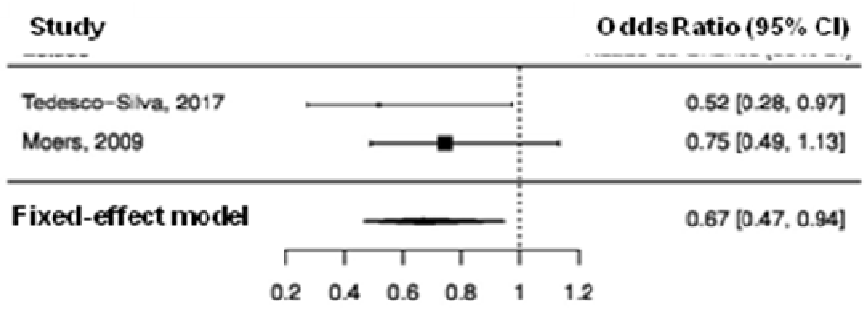

Figure 3. Forest plot for OR. In the meta-analysis, we observed the confidence intervals for both selected studies with OR estimate at 0.6665 (0.4704; 0.9444).

DISCUSSION

The lack of conclusive evidences on the portable MP and a better understanding of the clinical benefits resulting from its use by the professionals involved in the transplantation programs motivated the elaboration of the present study. In this sense, we tried to answer the following question: when compared to CS, does MP reduce DGF?

Among the 86 identified documents for the qualitative evaluation, there remained four articles[7,9,13,14]. The randomized clinical trial performed by Treckmann *et al*.[7] was excluded from the meta-analysis due to the fact that its sample had been rescued from the work of Moers *et al*.[9]. Thus, we avoided double-counting the patients of the sample. At this same eligibility stage, RCT by Gallinat *et al*.[10] was

also excluded from the meta-analysis due to the fact that 39 analyzed donors had also been rescued from Moers' essay[9]. Moreover, in the outcome, it was not possible to identify the 46 new cases, what made it impossible to add them in the statistical analysis.

The outcomes found in the RCTs of Moers *et al*.[9] and Tedesco-Silva *et al*.[14] were effectively used in the meta-analysis, in view of the presence of the inclusion criteria. With the eligibility of these two articles for meta-analysis, there were 748 kidneys in both studies, equally distributed: 374 to MP and the other half to CS. Regarding the clinical outcome studied, characterized by DGF, 84 kidneys placed in MP had DGF, while 110 patients in CS evolved with dialysis in the first week after transplantation.

In Moers' study[9], 336 deceased donors have had their kidneys randomly allocated between MP and CS. The 672 recipients have been followed for one year. The primary outcome characterized by DGF has also been analyzed. A total of 42 donors (84 kidneys) with circulatory death have been excluded from the meta-analysis. Out of the 294 with encephalic death, 242 have met the criterion of standard donors. The mean cold ischemia time has been 15 hours in both the MP and CS groups. In the sample comprising all types of donors, 70 patients of the MP group (20.8%) and 89 of the CS group (26.5%) have evolved with DGF. It has been found, therefore, that MP has reduced DGF in a statistically significant way (OR=0.57, p=0.01)[9]. These results corroborate those obtained in the present systematic review, in which 84 patients in the MP group (22.4%) and 110 (29.4%) in the CS group had DGF, with OR=0.6665 and p=0.0225.

In turn, in the essay of Tedesco-Silva *et al*.[14], 80 deceased donors with encephalic death have been included in the study. Out of these, 43 have been expanded-criteria donors. The analyzed primary outcome has been DGF. The mean cold ischemia time has been 25 hours in both the MP and CS groups. The DGF in the MP group (45%) has been lower than in the CS group (61%), with a p-value of 0.039[14]. Such study has extreme importance at national and international levels, being the first Brazilian clinical trial to prospectively and randomly evaluate the use of this technology in the national population, evidencing not only its clinical benefit but also its logistic and cultural differences in developing countries.

When comparing the European study[9] with the samples of Brazilian patients[14], the high incidence of DGF in these patients stands out. The explanation

lies in the hemodynamic instability of the donors, the highest creatinine levels at the time of collection, and the longer time of cold ischemia, with an increase of about ten hours in the mean time of cold ischemia[14]. In addition, in the European study, there was a lower percentage of expanded-criteria and brain-death donors (28% *versus* 54%). Such facts, whether due to the continental dimensions or to the scarcity of financial resources, showed a higher percentage of organs in situations more inclined to worse clinical outcomes than in developed countries. It was verified, therefore, that MP is linked to a protective effect against DGF and, so, it can be remembered as a strategy to be studied in order to optimize the quality of the offered organs, also in the Brazilian scenario.

The estimated values for risk ratio and odds ratio were 0.7568 (p=0.0151), with 95% CI (0.6044-0.9476), and 0.6665 (p=0.0225), with 95% CI (0.4704-0.9444), respectively. Therefore, the use of MP was statistically significant to reduce DGF in donors with encephalic death. These results demonstrate that the chance of a patient who received a kidney stored in MP to evolve into DGF is lower than if it was in CS.

It can be affirmed that the systematic review with meta-analysis, now undertaken, is in agreement with results of international literature when analyzing the reduction percentage of DGF with the use of MP[15-19]. It is of paramount importance to also point out that none of the selected studies have identified any adverse effect or clinical negative outcome with the use of MP[20].

The systematic review with the meta-analysis now undertaken, despite its careful selection of quality studies, presented some limitations that follow. In the four RCT selected for qualitative evaluation, different preservation liquids were used in CS (UW® and Euro Collins®, among others) and MP (KPS-1®), what may be a bias, since the different compositions of the liquids also influence DGF[21]. Only DGF was analyzed as clinical outcome and long-term outcomes, such as patient's and graft's survival, were not included. The need for further clinical trials, demonstrating the benefit of this device in late clinical outcomes, becomes evident. The rigorous selection criteria to ensure greater validity of the outcome at the end of the meta-analysis, according to the investigated objective, restricted selection to a small number of RCTs with the use of LifePort Kidney Transporter Machine®. Cost-effectiveness analysis of this technology was not included in the current systematic review with meta-analysis. Thus, additional studies that consider

investments for public health in Brazil will be able to add value to the subject's research. Further studies are still needed, including different populations and logistics of transplantation with different characteristics.

When choosing a systematic and impartial review of literature followed by meta-analysis, with careful statistical evaluation, it was possible to extract measures of association between independent studies, but similar and with evidence quality that will be able to substantiate the power of the recommendations coming from this study's conclusion. In Brazilian literature, we did not find other systematic reviews with meta-analysis comparing static cold ischemia with dynamics ischemia, and, in our opinion, despite some limitations already mentioned in relation to this review, our National Transplant System may benefit from the use of MP.

In this context, portable MP seems to configure a promising therapeutic option, both to choose and select the organ and to improve the clinical outcome of the transplanted patient, in comparison to the use of CS related to DGF reduction. Despite this conclusion, present in the systematic review with meta-analysis now undertaken, additional studies on hypothermic pulsatile MP will be needed. It is necessary to expand the sampling and to obtain new evidences about the contribution of this technology to patients submitted to solid organ transplantations, aiming to reach a consensual conduct with the medical-scientific community.

CONCLUSION

MP reduces the incidence of DGF of deceased donors with brain death, and it can be understood as one of the possible strategies to improve the prognosis of transplanted patients.

RESUMO

Com a utilização crescente da máquina de perfusão no transplante renal, tem sido constatado que a isquemia dinâmica correlaciona-se à melhora da preservação orgânica. Nesse contexto, realizamos uma revisão sistemática que procurou avaliar a eficácia do uso de máquina de perfusão portátil (Lifeport Kidney Transporter Machine®), utilizada no Brasil, comparada ao armazenamento estático, no que tange à função retardada do transplante renal de doadores com morte encefálica. Foi efetuada pesquisa bibliográfica, nas bases LILACS,

MEDLINE via PubMed, Scopus, Clarivate Analytics, Cochrane Library, Embase, SciELO, além de busca manual no Google acadêmico. A revisão sistemática, finalizada em abril 2017, foi constituída somente por ensaios clínicos randomizados. Para metanálise, foram avaliadas Razão de Risco e Razão de Chance. Foram identificados 86 documentos e selecionados, ao final, dois artigos com critérios de elegibilidade para metanálise, de grupos europeus e brasileiros. Nestes, 374 rins foram alocados para a máquina de perfusão, e igual número para o armazenamento estático. A função retardada do enxerto foi constatada em 84 e 110 pacientes, respectivamente. Na metanálise, foram obtidas uma Razão de Risco de 0,7568 (p=0,0151) e uma Razão de Chance de 0,6665 (p=0,0225), ambas com intervalo de confiança de 95%. A máquina de perfusão reduziu a incidência de função retardada do enxerto de doadores com morte encefálica.
Descritores: Transplante de Rim. Fluxo Pulsátil. Isquemia Fria. Função Retardada do Enxerto. Morte Encefálica.

REFERENCES

1. Henry SD, Guarrera JV. Protective effects of hypothermic ex vivo perfusion on ischemia/reperfusion injury and transplant outcomes. Transplant Rev (Orlando). 2012;26(2):163-75.
2. Fuller BJ, Lee CY. Hypothermic perfusion preservation: the future of organ preservation revisited? Cryobiology. 2007;54(2):129-45.
3. Calne RY, Pegg DE, Pryse-Davies J, Brown FL. Renal preservation by ice-cooling: an experimental study relating to kidney transplantation from cadavers. Br Med J. 1963;2(5358):651-5.
4. Bon D, Chatauret N, Giraud S, Thuillier R, Favreau F, Hauet T. New strategies to optimize kidney recovery and preservation in transplantation. Nat Rev Nephrol. 2012;8(6):339-47.
5. Associação Brasileira de Transplante de Órgãos. Registro Brasileiro de Transplantes (RBT) [Internet]. 2017 jan./set. [cited 2018 mar 08]; XXII(3).]. Available from: http://www.abto.org.br/abtov03/Upload/file/RBT/2017/rbttrim3-leitura.pdf.
6. Yuan X, Theruvath AJ, Ge X, Floerchinger B, Jurisch A, García-Cardeña G, et al. Machine perfusion or cold storage in organ transplantation: indication, mechanisms, and future perspectives. Transpl Int. 2010;23(6):561-70.

7. Treckmann J, Moers C, Smits JM, Gallinat A, Maathuis MH, van Kasterop-Kutz M, et al. Machine perfusion versus cold storage for preservation of kidneys from expanded criteria donors after brain death. Transpl Int. 2011;24(6):548-54.
8. Belzer FO, Ashby BS, Gulyassy PF, Powell M. Successful seventeen-hour preservation and transplantation of human-cadaver kidney. N Engl J Med. 1968;278(11):608-10.
9. Moers C, Smits JM, Maathuis MH, Treckmann J, van Gelder F, Napieralski BP, et al. Machine perfusion or cold storage in deceased-donor kidney transplantation. N Engl J Med. 2009;360(1):7-19.
10. Santos CMC, Pimenta CAM, Nobre MRC. The PICO strategy for the research question construction and evidence search. Rev Lat Am Enfermagem. 2007;15(3):508-11.
11. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med [Internet]. 2009 Jul [cited 2017 dez 17]; 6(7):e1000097. Available from: https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000097
12. Viechtbauer W. Conducting meta-analyses in R with the metaphor package. J Stat Softw [Internet]. 2010 Aug [cited 2015 dec 17]; 36(3):1-48. Available from: http://www.jstatsoft.org/v36/i03/.
13. Gallinat A, Moers C, Treckmann J, Smits JM, Leuvenink HG, Lefering R, van Heurn E, et al. Machine perfusion versus cold storage for the preservation of kidneys from donors ≥ 65 years allocated in the Eurotransplant Senior Programme. Nephrol Dial Transplant. 2012;27(12):4458-63.
14. Tedesco-Silva H Junior, Mello Offerni JC, Ayres Carneiro V, Ivani de Paula M, Neto ED, Brambate Carvalhinho Lemos F, et al. Randomized trial of machine perfusion versus cold storage in recipients of deceased donor kidney transplants with high incidence of delayed graft function. Transplant Direct. 2017;3(5):e155.
15. Wight JP, Chilcott JB, Holmes MW, Brewer N. Pulsatile machine perfusion vs. cold storage of kidneys for transplantation: a rapid and systematic review. Clin Transplant. 2003;17(4):293-307.

16. Lam VW, Laurence JM, Richardson AJ, Pleass HC, Allen RD. Hypothermic machine perfusion in deceased donor kidney transplantation: a systematic review. J Surg Res. 2013;180(1):176-82.
17. O'Callaghan JM, Morgan RD, Knight SR, Morris PJ. Systematic review and meta-analysis of hypothermic machine perfusion versus static cold storage of kidney allografts on transplant outcomes. Br J Surg. 2013;100(8):991-1001.
18. Jiao B, Liu S, Liu H, Cheng D, Cheng Y, Liu Y. Hypothermic machine perfusion reduces delayed graft function and improves one-year graft survival of kidneys from expanded criteria donors: a meta-analysis. PLoS One. 2013;8(12):e81826.
19. Hameed AM, Pleass HC, Wong G, Hawthorne WJ. Maximizing kidneys for transplantation using machine perfusion: from the past to the future: a comprehensive systematic review and meta-analysis. Medicine (Baltimore). 2016;95(40):e5083.
20. Matsuoka L, Almeda JL, Mateo R. Pulsatile perfusion of kidney allografts. Curr Opin Organ Transplant. 2009;14(4):365-9.
21. Chatauret N, Thuillier R, Barrou B, Hauet T, Eugene M. Machine perfusion in clinical trials: the preservation solution bias. Transpl Int. 2011;24(9):e81-2.

Received in: 12/03/2018
Accepted for publication: 02/05/2019
Conflict of interest: none.
Source of funding: none.

Mailing address:
Ricardo Ribas de Almeida Leite
E-mail: ribasricardo@yahoo.com.br