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Hypothermic machine perfusion in deceased donor kidney transplantation: a systematic review

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ABSTRACT

Background: Hypothermic machine perfusion (HMP) of kidneys is intended to mitigate the deleterious effects of cold storage on organ quality, particularly when the cold ischemic time is prolonged or the donor is otherwise marginal. The use of HMP has remained controversial; however, a number of randomized controlled trials (RCTs) have recently been conducted to clarify its benefits.

Methods: We undertook a systematic search of the Medline and Embase databases and of the Cochrane Central Register of Controlled Trials. We included only RCTs in the meta-analysis. Outcomes analyzed were the incidence of delayed graft function (DGF), primary nonfunction (PNF), graft loss, and patient death at 1 y.

Results: We identified seven RCT trials and subjected them to meta-analysis, including 1353 kidney transplant recipients. Hypothermic machine perfusion significantly reduced the incidence of DGF (risk ratio [RR] 0.83, 95% confidence interval [CI] 0.72–0.96). There was no difference in the incidence of PNF (RR 0.78, 95% CI 0.36–1.68), graft loss at 1 y (RR 0.87, 95% CI 0.64–1.19), and patient death at 1 y (RR 0.91, 95% CI 0.60–1.37) between HMP and donor kidneys preserved using cold storage.

Conclusions: There are few RCT comparing HMP and cold storage of kidneys in deceased donor kidney transplantation. Although these studies are small and heterogeneous in design, HMP appeared to be associated with a reduced incidence of DGF. No difference in the incidence of PNF, graft loss, or patient death at 1 y could be demonstrated.

1. Introduction

Delayed graft function (DGF) and primary nonfunction (PNF) are well-known complications after kidney transplantation. The frequency of DGF and PNF in deceased donor kidney transplantation ranges from 2% to 50% and 2% to 15%, respectively [1]. Delayed graft function is usually the result of ischemic injury to the graft before and during organ procurement, and is further aggravated by the reperfusion syndrome [2]. Optimization of graft quality under conditions of prolonged ischemia thus represents the primary goal of deceased donor kidney preservation. To date, the predominant organ preservation method of deceased donor kidneys used by most centers is static cold storage (CS). Cold storage

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preservation is based on the suppression of metabolism by hypothermia. Blood is removed by flushing the kidney and replaced with an appropriate cooled preservation solution [3]. The concept of hypothermic machine perfusion (HMP) of deceased donor kidneys, which had been developed before the routine use of CS preservation, provides an attractive alternative [4]. Hypothermic machine perfusion is based on a controlled continuous circulation of a perfusate, which, although not oxygenated or refreshed during storage, has been hypothesized to protect the deceased donor kidneys from injuries related to ischemia and reperfusion [5]. This protection may be particularly important when the cold ischemic time is prolonged or the donor is otherwise marginal.

Several clinical studies have compared HMP with CS preservation of deceased donor kidneys. Early reports showed no significant difference in DGF or graft survival rates when comparing HMP and CS preservation [6,7]. In 2003, Wight *et al* [8] published a systematic review and meta-analysis, and demonstrated a 20% reduction in DGF when HMP was used. More recently, two randomized controlled trials (RCTs) using modern immunosuppression were conducted and showed contradictory results [9,10].

The primary aim of this study was to assess evidence for the effect of HMP compared with CS of donor kidneys on delayed graft function using a systematic review and meta-analysis of the available RCTs. We assessed the impact of HMP on rates of primary nonfunction, graft loss, and patient death at 1 y.

2. Methods

2.1. Search methods

We undertook a comprehensive search through October 2011, including the Cochrane Central Register of Controlled Trials, MEDLINE, and EMABSE, with additional reports identified from hand-searching conference proceedings and reference lists of included studies. Two reviewers (V.L. and J.L.) independently performed search strategies. When there was more than one report from an individual trial, all reports were examined for any available data. The publication reporting the most outcome data was designated the index publication, and is referenced in this report. Figure 1 shows the search strategy.

2.2. Selection criteria and study outcomes

We included all RCTs of parallel design comparing HMP *versus* CS of kidneys for deceased donor kidney transplantation, irrespective of blinding, sample size, publication status (i.e., whether published as the full text or presented only as an abstract at a conference), and language. We excluded quasi-randomized trials and other study designs. Primary outcomes analyzed were the incidence of DGF and graft loss at 1 y. Secondary outcomes sought were the incidence of PNF and patient death at 1 y.

2.3. Data collection and analysis

Two reviewers (V.L. and J.L.) independently screened search results using titles, abstracts, and, where necessary, the full paper version to identify eligible trials. Two reviewers extracted data independently, using a standardized form. We assessed methodological quality of trials according to the method recommended by the Cochrane Collaboration [11]. We analyzed data using Review Manager (RevMan, Version 5.1.4; The Cochrane Collaboration, Copenhagen, Denmark).

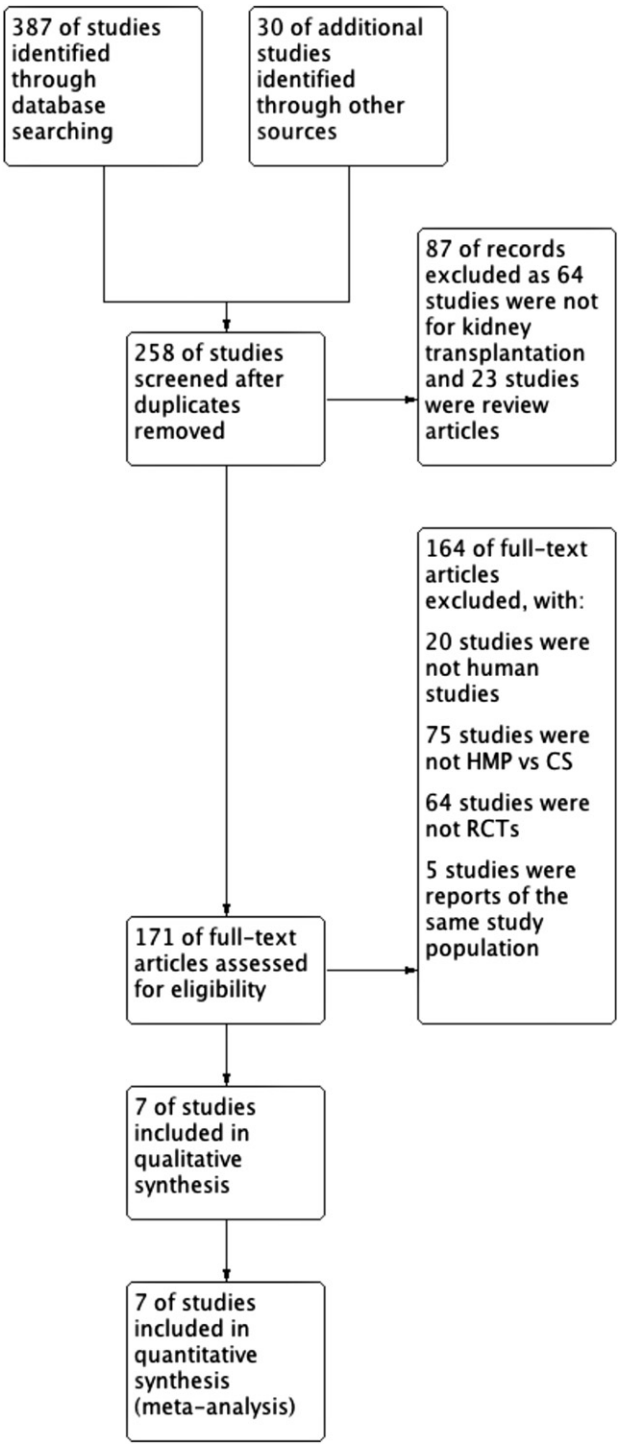

Fig. 1 – Flowchart showing the process of identifying randomized controlled trials for inclusion in systematic review. RCT = randomized controlled trial.