Preservation solutions for static cold storage of kidney allografts: a systematic review and meta-analysis

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CRD summary
This review concluded that kidneys stored in University of Wisconsin, histidine-tryptophan-ketoglutarate and Celsior preservation solutions appeared to be at lower comparable risk of delayed graft function. Although the review was mainly well conducted, the small number of mostly low quality studies for each comparison, and the differences between them, mean that the authors' conclusions may not be reliable.

Authors' objectives
To examine the effectiveness of preservation solutions for static cold storage of kidney allografts.

Searching
MEDLINE, EMBASE, The Cochrane Library, Transplant Library from the Centre for Evidence in Transplantation, and International Clinical Trials Registry Platform (ICTRP) were searched up to July 2011. References from included studies and reviews were checked. No language limitations were applied.

Study selection
Eligible comparative studies were of preservation solutions for static cold storage of deceased donor (adult or child) renal allografts. First and subsequent transplants were included. Retrospective, animal, non-comparative or live donor studies were excluded. The primary outcome was delayed graft function.

Included studies were conducted in a number of different countries including a range of Western European countries (two specifically in the UK), USA, Japan, Russia, Latvia, and Brazil. The University of Wisconsin method was the most common preservation solution used. Types of donor differed between studies; approximately half of the studies did not limit the type of donor; some studies focused on donors after brain death or after cardiac death. Definitions for delayed graft function differed between studies; the most common definition was the need for dialysis in the first week.

Two reviewers independently selected studies for inclusion. Any differences were resolved through discussion.

Assessment of study quality
Randomised controlled trials (RCTs) were assessed using the Jadad score, which assessed randomisation method, blinding and reporting of withdrawals (highest score possible was 5 points). A score of 3 or more points was considered good quality.

In addition, both RCTs and non-RCTs were assessed for allocation concealment, intention-to-treat analyses, sample size calculation, description of withdrawals, and appropriateness of statistical tests.

Two reviewers independently assessed study quality.

Data extraction
Outcomes (delayed graft function, primary non function, graft survival, renal function, biopsy proven acute rejection, and patient survival) were extracted from each study to calculate risk ratios (RRs) with 95% confidence intervals (CIs).

Two reviewers extracted the data. Any differences were resolved through discussion or consultation with two other authors.

Methods of synthesis
Data from the studies were pooled using a fixed-effect model where studies were judged to be conceptually statistically similar enough. Heterogeneity was assessed using the Q statistic and I².

Results of the review
Fifteen studies were included in the review (3,584 patients) comprising 10 RCTs (3,004 patients) and five non-RCTs (580 patients). Of the 10 RCTs, only two were rated as high quality according to the Jadad score. Only four RCTs reported allocation concealment. Seven RCTs reported on withdrawals. No studies reported using blinding.

These result focus on primary outcome of delayed graft function.

**Eurocollins versus University of Wisconsin solution** (three RCTs): The trials were too heterogeneous to pool their results. There were mixed results. The largest RCT (695 kidneys) found that Eurocollins solution had a higher rate of delayed graft function in stored kidneys than the University of Wisconsin solution (RR 1.46; 95% CI 1.15 to 1.87). The two smaller RCTs (40 kidneys and 90 kidneys) did not find a difference.

**Eurocollins versus histidine-tryptophan-ketoglutarate (HTK) solution** (two RCTs and two non-RCTs): The studies were too heterogeneous to pool their results. Both RCTs found higher delayed graft function for Eurocollins solution compared with HTK solution stored kidneys; the larger RCT found a smaller but precise effect (RR 1.48; 95% CI 1.18 to 1.85) compared with the smaller RCT (RR 23.55; 95% CI 1.47 to 378.34). One of the non-RCTs also found delayed graft function to be higher for Eurocollins solution stored kidneys (RR 2.64; 95% CI 1.46 to 4.77), but the other study did not find a statistically significant difference.

**Celsior versus University of Wisconsin solution** (three RCTs): The trials used the same definition of delayed graft function (requiring dialysis within a week). The meta-analysis found no statistically significant difference between preservation solutions (RR 0.97; 95% CI 0.76 to 1.23; $I^2=0\%$).

**Histidine-tryptophan-ketoglutarate (HTK) versus University of Wisconsin solution** (two RCTs): As there were only two RCTs, meta-analyses were not conducted. Neither trial found a statistically significant difference between preservation solutions.

**Other comparisons**: One small non-RCT (45 kidneys) found that delayed graft function of stored kidneys was statistically significantly higher with Perfudex compared with hyperosmolar citrate solution (p<.01). One non-RCT (104 kidneys) did not find a statistically significant difference between hyperosmolar citrate and phosphate buffered sucrose solutions. One RCT and one non-RCT did not find a statistically significant difference between University of Wisconsin and University of Wisconsin-modified preservation solutions.

**Authors' conclusions**
Kidneys stored in Eurocollins solution were at greater risk of delayed graft function compared with those stored in University of Wisconsin or histidine-tryptophan-ketoglutarate solution in the largest and highest quality RCTs. No differences were found between University of Wisconsin, histidine-tryptophan-ketoglutarate and Celsior preservation solutions.

**CRD commentary**
The review question and inclusion criteria were clear. The search included a good coverage of relevant databases. No language restrictions were applied, which reduced the risk of language bias. A large clinical trial register was searched which reduced the risk of publication bias. Appropriate methods were used to minimise error and bias for review processes.

Most included studies were rated as low quality. There were a limited number of studies for each comparison of preservation solutions. The primary outcome measure (delayed graft function) was measured variably across studies. The authors only conducted meta-analyses when studies were sufficiently similar.

Although the review was mainly well conducted, the lack of trials, the low quality of trials, and the differences in definitions of delayed graft function between studies mean that the authors' conclusions may not be reliable.

**Implications of the review for practice and research**

**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that further research was required to examine the efficacy of preservation solutions for non-renal organs.
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