What is the evidence for oxygenated hypothermic machine preservation in kidney transplantation? A systematic review

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Background

Methods of hypothermic ex-vivo oxygenated preservation (HOP) were historically used to support the metabolism of kidneys and to preserve the cellular integrity of donor organs under hypothermic conditions before transplantation [1]. However the superiority of HOP has not been confirmed and therefore we performed a systematic review comparing HOP with non oxygenated hypothermic preservation (NHOP) techniques in kidney transplantation.

Methods

A systematic literature search was performed using Medline, Embase, Cochrane's CENTRAL and the Transplant Library including all study designs.

- Registered with PROSPERO 2013, ID: CRD42013005170
- Reviewers screened abstracts, identified studies for inclusion and extracted data independently
- Methodological quality of human RCTs and case series were assessed using the Jadad scale and quality assessment tool (developed by Health Technology Assessment experts) respectively [2].
  A modified risk of bias tool developed by Krauth et al. [3] was used to assess animal studies
- Studies were categorised into comparative and non-comparative for both humans and animals
- Data were analysed as a narrative synthesis

Results

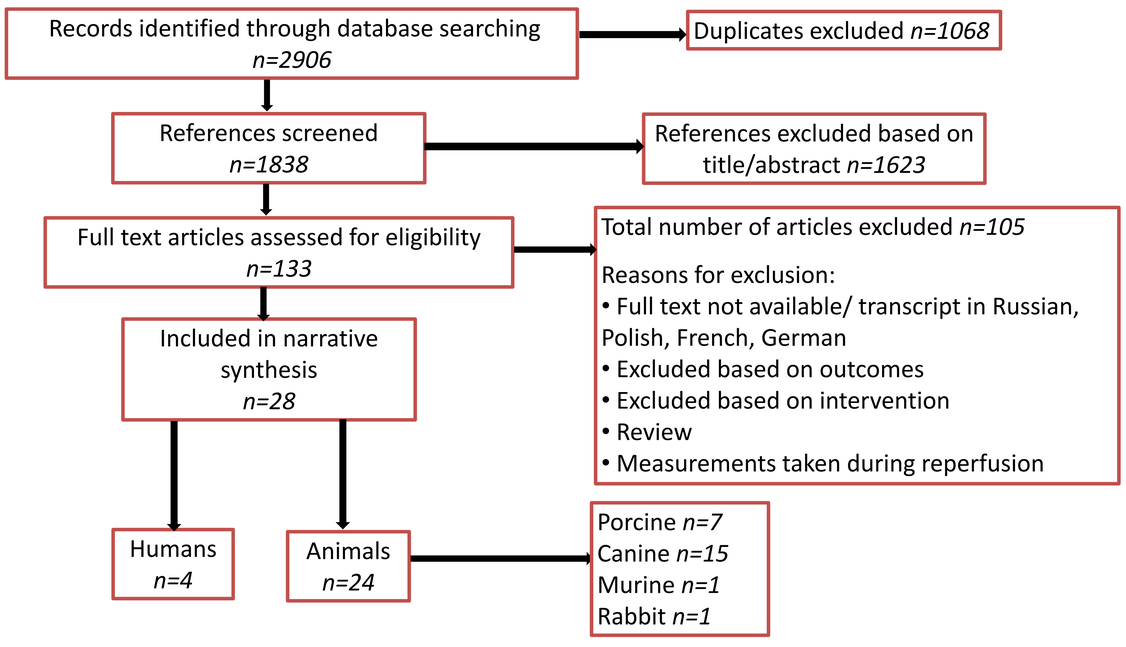

Fig 1. Flow chart of search results

Hypothermic oxygenated preservation (HOP) in human kidneys			
Author (year), study design (no. of donors)*	**Total groups compared (no. of organs transplanted)**	**Follow up time**	**Patient survival**
Rolles (1989), RCT (10)	a) Oxygen persufflation (10) b) Stored in RME solution (10)	15 days	a) 100% (10/10) b) 100% (10/10)
Flatmark (1975), case series (4)	a) Continuous machine perfusion, oxygenated persufflation and reperfusion (4)	4 weeks	a) 75% (3/4) at 4 weeks
Fuchinoue (1986), case series (30)	a) Cold machine perfusion with Oxypherol (44)	1 year	-
Manax (1965), case report (2)	a)Cold perfused, hyperbaric chamber, 3atm b)Cold perfused, hyperbaric chamber, 5OHP	7 months	a) 100% b) 0%

Fig 2. Results from human studies. *All deceased donors

Human data is limited to four studies. One RCT compared HOP and cold storage (CS) following a mean warm ischemia time (WIT) of 55 minutes [4]. Patient survival did not differ between groups and the difference in renal function was not significant. It is possible that the difference in survival rates across the human studies may be attributed to the range in follow up time (15 days to 4 weeks) or WIT (0-55 minutes). The methodological quality across all four studies were poor.

Two porcine studies (one RCT, one cohort) compared HOP (oxygenated perfusate) with NHOP (non oxygenated perfusate). Following immediate preservation and no WIT there was no difference in renal function between the HOP and HNOP RCT groups. In contrast the cohort study showed good renal function in kidneys following 60 minutes WIT and preservation with oxygen, however the difference between the HOP and NHOP groups were not statistically significant. A total of five porcine studies compared HOP with cold storage. Renal function was significantly better in porcine kidneys that were preserved with oxygen than cold stored, however the survival rates between HOP and CS were inconclusive.

Seven canine studies presented survival rates for kidneys that underwent HOP within a hyperbaric chamber. The highest rates of survival (67-100%, n=3 studies) were presented in kidneys preserved within the chamber for 4-7 hours compared with kidneys preserved for a period >7 hours (0-40%, 4 studies). The animal studies accounted for attrition bias, primary outcomes and described the animal characteristics but reported poorly on sample size calculation and co-morbidities.

Conclusions

The addition of oxygen during hypothermic preservation presents varying results but may improve renal function in kidneys that have undergone a period of warm ischemia. The evidence from clinical studies is limited and RCTs in humans using new technology are needed to validate whether oxygenated preservation improves renal function and patient or graft survival.

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