Pulsatile machine perfusion versus cold storage of kidneys for transplantation

The clinical and cost-effectiveness of pulsatile machine perfusion versus cold storage of kidneys for transplantation retrieved from heart-beating and non-heart-beating donors

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Executive summary

Health Technology Assessment 2003; Vol. 7: No. 25

Health Technology Assessment
NHS R&D HTA Programme

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Objectives

The aim of this review is to evaluate the clinical and cost-effectiveness of machine perfusion (MP), as opposed to cold storage (CS), as a means of preserving kidneys which are to be transplanted. It examines the use of MP for kidneys from both heart-beating donors (HBDs) and non-heart-beating donors (NHBDs), and the impact on graft function immediately post-transplantation as well as in the longer term. In addition, it examines whether or not the use of MP can allow valid testing of kidney viability prior to transplantation.

Background

There is a continuing (and growing) mismatch between the number of kidneys available for transplantation and the number of patients on the waiting list. One possible way to increase the supply of kidneys for transplantation would be to extend the range of donors. This could include NHBDs as well as donors with other adverse characteristics. Kidneys taken from such donors tend to suffer higher rates of primary non-function, delayed graft function (DGF) and reduced longer term survival than those taken from ideal donors.

It has been suggested that MP may lead to a reduction in DGF and an increase in graft survival. MP may also allow the valid testing of the viability of kidneys taken from 'marginal' donors (thus avoiding the transplantation of non-viable kidneys). This could then contribute to the safe extension of criteria for donor recruitment, and hence increase the transplantation rate. A reduction in DGF would also, *per se*, be cost saving – which may make the use of these machines cost-effective.

Methods

A literature search was undertaken to identify relevant studies. A meta-analysis was undertaken of those that had appropriate comparator groups and reported sufficient data. A structured review was undertaken of studies examining tests of viability of kidneys on MP. Economic modelling was used to determine the cost-effectiveness and cost–utility of MP.

Evidence available

Twenty papers (reporting 16 studies) were identified that reported on the clinical outcome of the use of MP and that had appropriate comparator groups. These were published between 1971 and 2001. In the majority of these, pairs of kidneys were split, with one being machine perfused and the other preserved using cold storage. Overall the studies were small and of poor quality, with only four of the 16 studies scoring two on the Jadad scale (none scored more).

Twenty-six papers were identified which reported studies of tests of kidney viability. Most were of limited quality, with non-ideal outcome measures and poor design. Only one contained sufficient information to be able to calculate the sensitivity and specificity of a test of viability.

Summary of findings

The meta-analysis suggests that the use of MP, as compared with CS, is associated with a relative risk of DGF of 0.804 (95% confidence limits 0.672 to 0.961). There was no evidence to suggest that this effect is different in kidneys taken from HBDs as opposed to NHBDs. Meta-analysis of 1-year graft survival data showed no significant effect, but the studies, even when aggregated, were severely underpowered with respect to the likely impact on graft survival. The size of effects demonstrated were in line with those predicted by an indirect model of graft survival based on the association of DGF with graft loss.

There is some evidence that the flow characteristics of the perfusate of kidneys undergoing MP may be an indicator of kidney viability, but data are inadequate to calculate the sensitivity and specificity of any test based on this. The concentration of α-glutathione-S-transferase (a marker of cell damage) in the perfusate may be the basis of a valid test. A threshold of 2800 μg/100 g

gives a sensitivity of 93% and specificity of 33% (and hence a likelihood ratio of 1.41).

The published economic evidence is of poor quality and the generalisability of the US studies to a UK healthcare setting is low. The economic assessment indicates that it is unlikely that in the UK health setting complete cost recovery will be obtained from a reduction in the incidence of DGF.

The baseline analysis indicates that in the long-term MP would be expected to be cheaper and more effective than CS for both HBD and NHBD recipients. The probability that this is the case is estimated at around 80% for NHBD recipients and 50–60% for HBD recipients.

Future research

A definitive study of the clinical benefit of MP (in the context of the current state of development of transplantation) needs to be undertaken, in order to establish its effect on DGF and longer term graft survival. Ideally this would be accompanied by an economic evaluation of the benefits.

While direct evidence relating to improvements in graft survival would be preferable, the small predicted improvement indicates that a very large sample size would be required in order to detect statistically significant results. In addition to seeking better direct evidence of the impact of MP on DGF rates, further research on quantifying the predicted impact of DGF on graft survival in this technology would be warranted.

Further research is also needed to establish whether or not a valid test (or combination of tests) of kidney viability can be developed. This should be accompanied by work with all interested parties (including patients) to establish what an appropriate trade-off between false-positive and false-negative results of such test(s) would be.

Publication

Wight J, Chilcott J, Holmes M, Brewer N. The clinical and cost-effectiveness of pulsatile machine perfusion versus cold storage of kidneys for transplantation retrieved from heart-beating and non-heart-beating donors. *Health Technol Assess* 2003;**7**(25).

NHS R&D HTA Programme

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The research reported in this monograph was commissioned by the HTA Programme and funded as project number 01/35/01. Technology assessment reports are completed in a limited time to inform decisions in key areas by bringing together evidence on the use of the technology concerned.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for any recommendations made by the authors.

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ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.