NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Machine perfusion systems and cold static storage of donated kidneys

Final scope

Remit/appraisal objective

To appraise the clinical and cost-effectiveness of cold machine (pulsatile) perfusion systems and cold (static) storage solutions for the preservation of donated kidneys.

Background

End-stage renal disease is defined as irreversible decline in a person's kidney function that is severe enough to be fatal in the absence of renal replacement therapy. Kidney transplantation is the best form of renal replacement therapy for people with end-stage renal disease where it is possible. Unfortunately, the demand for organs greatly outstrips the supply of donor organs.

Most kidneys for transplantation are obtained from cadaveric heart beating (HB) donors, that is, people in whom death has been diagnosed by brain stem tests who are maintained on a ventilator in an intensive care unit. The availability of organs from this type of donor has declined by about 20% over the last decade, possibly because of a reduction in fatal road traffic accidents and a decrease in the number of deaths from intracranial haemorrhage.

One means of meeting the shortfall in organs has been the encouragement of living donor programmes, where the kidney is obtained from a living relative of the recipient or sometimes from a non-related donor such as a long term partner. Living donor transplantation has increased in recent years and accounted for 26.6% of the kidney transplants conducted in the financial year 2004-2005. Living donor transplantation is associated with a superior success rate compared to cadaveric transplantation.

A second means of expanding the pool of HB donors is through the use of extended criteria donors. These are kidneys from donors who would not normally meet the criteria for donation. The extended criteria include kidneys from donors who are either over sixty, or are over fifty and with two or more of the following features (2) a history of hypertension, (3) death by cerebral vascular accident, (3) terminal creatinine levels greater than 1.5mg/dl. Kidneys from extended criteria donors have a lower chance of long term success and a higher incidence of delayed graft function.

A different means of expanding the donor pool is to use organs retrieved from non-heartbeating (NHB) donors. NHB donors are categorised according to their presentation using the Maastricht criteria, with an important distinction made between controlled (e.g. where cardiac arrest is expected) and

uncontrolled donors (e.g. where cardiac arrest is unexpected). The use of kidneys from NHB donors is not new. Before the concept of brainstem death was legally defined in the 1970s, all cadaveric kidneys came from NHB donors.

The critical difference between organs from NHB and HB donors is the duration of warm ischaemic time, that is, the time that the organ spends deprived of oxygen before it is retrieved and cooled (in some cases a cannula can be placed for perfusion and cooling of the organs prior to retrieval). After retrieval, cooling the organ suppresses the metabolic rate and so reduces the rate of damage.

In NHB donors (particularly uncontrolled NHB donors) warm ischaemic time may be prolonged and as a result, kidneys from NHB donors tend to suffer higher rates of delayed graft function than those from HB donors. Delayed graft function (DGF) is a delay in recovery of renal function post transplantation. It gives rise to the need for continuing dialysis, longer hospitalisation and is associated with poorer long term outcome.

Transplants from NHB donors accounted for 143 (8%) of the 1783 kidney transplants conducted in the financial year 2004-2005. At present kidneys from NHB donors are only used for patients on the local waiting list, and are not shared through the national allocation system.

The technologies

In machine perfusion, cold preservation solution is pumped through the organ with the intention of supplying nutrients to the organ and removing metabolic end products there by reducing the damage associated with cold ischaemic time. Machine perfusion can be used to preserve grafts from both HB and NHB donors. It is suggested that machine perfusion may also allow the viability of the kidney to be tested ex vivo and improve the viability of donated kidneys. Up to 10% of kidneys from NHB donors never function after transplantation (known as primary non-function).

Two commercially available machine perfusion systems have been identified: the LifePort Kidney Transporter (Organ Recovery Systems) and Waters' RM3 Renal Preservation System (Waters Medical Sytems). In cold static storage, the kidney is flushed through with a preservation solution, and kept on ice. Two preservation solutions are widely used on the NHS; Marshall’s, (Soltran, Baxter Healthcare) and University of Wisconsin (Viaspan, Bristol Myers Squibb). The preservation solutions used in cold static storage are different from those used in machine perfusion.

Intervention(s)	Cold machine perfusion systems for kidney preservation including: • LifePort Kidney Transporter • RM3 Renal Preservation System Cold static storage solutions including: • Marshall's solution • University of Wisconsin solution
Population(s)	Recipients of kidney transplants.
Standard comparators	Each of the interventions should be compared with the others
Outcomes	The outcome measures to be considered include: • incidence and duration of delayed graft function • incidence of primary non-function • rejection rates • graft survival • graft function (glomerular filtration rate) • patient mortality • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The time horizon for the economic evaluation should reflect the life expectancy of recipients of kidney transplants. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	The devices will be appraised according to approved uses. Guidance will only be issued in accordance with the CE mark or marketing authorisation. If the evidence allows, the appraisal should consider the implications of assessing graft-viability using machine perfusion. If the evidence allows, the appraisal should consider the following subgroups: • recipients of kidneys from controlled NHB donors • recipients of kidneys from uncontrolled NHB donors • recipients of kidneys from extended criteria HB donors Further subgroups should be identified where the evidence allows. If the evidence allows, the appraisal should consider factors such as ease of use where this may impact on the clinical and/or cost effectiveness.

Related NICE recommendations	*Related Technology Appraisals*: National Institute for Clinical Excellence (2006) Guidance on the use of immunosuppressive therapy for renal transplantation in children and adolescents. *NICE Technology Appraisals Guidance* No. 99. London: National Institute for Clinical Excellence. National Institute for Clinical Excellence (2004) Guidance on the use of immunosuppressive therapy for renal transplantation in adults. NICE Technology Appraisals Guidance No. 85. London: National Institute for Clinical Excellence. National Institute for Clinical Excellence (2002) Guidance on the use of home compared with hospital haemodialysis for patients with end-stage renal failure. *NICE Technology Appraisal Guidance* No. 48. London: National Institute for Clinical Excellence. *Related Guidelines:* National Institute for Health and Clinical Excellence (2006) Anaemia management in people with chronic kidney disease (CKD. *NICE Clinical Guideline CG39.* London: National Institute for Health and Clinical Excellence.