NICE Technologies Appraisal

Machine perfusion systems and solutions for cold (static) storage of donated kidneys

Personal Statement

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I have worked in renal transplantation both as a trainee and a consultant for over 20 years, appointed to my first consultant post (Birmingham) in 1995 and my current post in Glasgow in 2003. Initially my experience was with cold storage using Marshall's solution although I was aware that one transplant unit in the country (Liverpool) used machine perfusion of its locally retrieved kidneys. I remember the introduction of University of Wisconsin (UW) solution for cold storage and have used it in both liver and renal transplantation. In 2004 when starting a non-heart-beating donor programme I was convinced by the evidence from units such as Newcastle and South Thames of the benefits of machine perfusion in this type of kidney and compared the "Lifeport" system and the "Waters" machine. I preferred the "Lifeport" system and bought 2 of these machines which we have used with the perfusion machine version of UW solution in all but one of our non-heart-beating donor kidneys.

Machine perfusion

My experience is with the "Lifeport" system. I have no experience of using the "Waters" machine.

I find the machine easy to use. The attachments for putting on the kidney's artery are well designed and with a bit of practice easy to apply. The machine is well designed and has a number of very useful functions as well as being easy to transport and to clean after use. It allows real time monitoring of the kidney; pressure, flow, resistance and temperature and enables a decision to be made about the viability to the kidney and the likelihood of satisfactory function once transplanted (identifies kidneys unlikely to function). Not transplanting kidneys with high resistance reduces the incidence of primary non function which as well as making the unit's outcome figures look good reduces morbidity for the recipients. If a patient receives a kidney that doesn't work this has numerous implications – 2 operations that achieve nothing, an inpatient stay, numerous investigations including biopsies with their morbidities, immunological sensitization with the likelihood of reducing the chances for future transplants as well as considerable emotional strain and disappointment for the patient, their family and the team looking after them.

I believe that the pumping of perfusate through the kidney is beneficial for its function and that by using the machines we are able to keep our delayed graft function rate to less than 50% which is comparable with the rate in our kidneys from marginal / extended criteria donors. This is compared with a rate of about 70% reported in the literature for kidneys from NHBD preserved by cold storage. A reduced number of patients requiring dialysis for a period of time after transplant before the kidney works can only be a good thing.

There have been 2 recent trials of machine perfusion verses cold storage, the British one only considering kidneys from NHBDs and the European one considering kidneys from all types of cadaveric donors, which have given conflicting results. The European, multicentre trial from the Eurotransplant countries is a well designed randomised study where the machines were used properly. The results show a definite

benefit of machine perfusion compared to cold storage overall and in the subgroups particularly the NHBD subgroup. The British, multicentre study, which showed no benefit of machine perfusion I believe to be fundamentally flawed. It is a randomised study and was well planned although it involved a limited number of centres most of which did a small volume of NHBD transplants and who at the outset had limited or no experience of using machine perfusion. The statistical method was not one with which I am familiar and some questions have been raised by others because of this. What does not come out in the report but what is admitted by the presenter (Chris Watson) of the data in formal medical presentations is that the kidneys allocated to machine perfusion actually had an average of 6 hours of cold storage before being put on the perfusion machine. This is because the machines were not taken to the retrieval hospital and the kidneys were only connected up to them when the team returned to the transplant unit. This is not the way the machines are designed to be used and all the groups who use the machines properly take the machine to the retrieval hospital and pump perfuse from the time the kidney is removed. Since from experience of the machines and analysing the records of the resistance etc it is clear that the benefit of the machine is seen within the first hour of the preservation period then with a delay of 6 hour to machine perfusion any expected benefit of machine perfusion is lost and in fact this trial in real terms compared cold storage with cold storage so it is hardly surprising that there is no difference between the groups.

Since we now use an increasing number of extended criteria donors, the kidneys from which have an increased incidence of delayed graft function with its subsequent increased costs - financial and emotional, there is a case for using machine perfusion in kidneys from this group of donors as would be supported by the results of the recent European trial.

Cold Storage Solutions

Trials soon after the introduction of UW solution showed no significant benefit of this solution over the previously used Marshall’s solution. I therefore, in keeping with many of my renal transplant colleagues, continue to use Marshall’s solution for kidney preservation, believing that the extra cost of UW is not reflected in improved outcomes. However most cadaveric donors are multiorgan donors and UW has been shown to have benefit in liver transplantation so a liver retrieval team will perfuse all the organs in situ with UW solution and subsequently stores the organs including the kidneys in UW solution.

In a retrospective review in my unit (unpublished) we noticed that kidneys perfused with and stored in UW solution had less delayed graft function than the ones with Marshall’s solution. At that time our local liver unit was using Marshall’s solution for liver and kidney retrievals but UW if the pancreas was being retrieved as well. Imported kidneys preserved with UW also had less delayed graft function, despite a longer cold ischaemic time, than our local Marshall’s preserved kidneys. Since pancreata are only retrieved from younger / better donors this outcome could have been due to the better donors rather than the preservation solution. However after seeing our results our local liver retrieval team changed its protocol and started using

UW in all donors for in situ perfusion and cold storage and the delayed function rate of out transplanted kidneys fell.

Despite this I am still not convinced that in a kidney only donor the cost of UW solution is justified for the in situ perfusion when a large volume is used which ends up in a suction machine on the floor. I do think that UW has a place in cold storage particularly when it is anticipated that the cold ischaemic time will be prolonged.

Laura J Buist 17th June 2008