NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA165; Machine perfusion systems and cold static storage of kidneys from deceased donors

This guidance was issued in January 2009.

The review date for this guidance is August 2010. In December 2010 the decision to review TA165 was deferred until the results of the Machine Preservation Trial became available.

1. Recommendation

The guidance should be transferred to the 'static guidance list'.

That we consult on this proposal.

2. Original remit(s)

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

3. Current guidance

1.1 Machine perfusion using the LifePort kidney transporter and cold static storage using Belzer UW storage solution or Marshall's hypertonic citrate solution are recommended as options for the storage of kidneys from deceased donors.

1.2 The choice of storage method should take into account clinical and logistical factors in both the retrieval teams and transplant centres. In situations where different storage methods are considered equally appropriate, then the least costly should be used.

4. Rationale[1]

This 3-year data from the machine perfusion trial confirms that the graft survival advantage for machine perfusion seen at 1 year (94% versus 90%, P=0.04) persists at 3 years (91% versus 87%; p=0.04). An economic analysis based on this trial (which was conducted in the Netherlands, Belgium, and the federal state of North Rhine–Westphalia in Germany) found that machine perfusion was associated with more quality-adjusted life-years (QALYs) at lower costs than cold static storage. This new evidence is consistent with that used for the original decision.

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

Although there may be an argument that a stronger recommendation in favour of machine perfusion could now be made (because the evidence is stronger on the basis longer-term data), the current guidance is positive in that it recommends machine perfusion as an option, with other considerations to be taken into account in choosing the form of preservation. The evidence used in the original decision also suggested a graft survival advantage for machine perfusion,

Some of the information in section 3.4 of TA165 (describing the regulatory status of Belzer UW storage solution made by Bristol-Meyers-Squibb) is no longer correct and this product does not have regulatory approval in the UK. However, an appropriately CE marked product is available from another manufacturer so the guidance is not affected by this change.

Therefore it is proposed that TA165 is moved to the static list.

5. Implications for other guidance producing programmes

There is a forthcoming guideline and quality standard on renal replacement therapy. If, following scoping, it is decided that organ preservation falls within the scope of that guideline and quality standard, a further review proposal for TA165 will be produced.

6. New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from November, 2010 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

TA165 was reviewed in August 2010, and in September 2010 it was decided that the guidance be transferred to the 'static guidance list' as there is no new evidence. Following consultation, it was decided that the decision to review the guidance should be deferred until the results of the Machine Preservation Trial are published.

The Machine Preservation Trial first reported results in 2009, in which hypothermic machine perfusion of deceased-donor kidneys significantly reduced the risk of delayed graft function compared with cold-storage perfusion (Moers et al. 2009). The follow-up period was extended to determine whether graft-survival advantage would persist 3 years after transplantation. Results for the follow-up period were reported in February 2012 (Moers et al. 2012). The 3-year graft survival remained better for machine-perfused kidneys (91% versus 87%; adjusted hazard ratio for graft failure, 0.60; p=0.04) than cold-storage perfusion. These updated results from the Machine Preservation Trial are generally in-line with the results reported in 2009 and do not change current NICE guidance as recommendation 1.1 list both machine perfusion and cold storage as options for the storage of kidneys from deceased donors.

The prices for the machine perfusion and cold storage products have remained largely unchanged.

When TA165 was developed and published, Belzer UW storage solution was not classified as either a medicine or a device. The manufacturer of Belzer UW storage solution (Bristol-Meyers-Squibb [Viaspan]) did not have an appropriate Marketing Authorisation or CE Mark at the time TA165 was published. However, the regulatory status of perfusion fluids has changed in the EU and perfusion fluids now require CE marking (they fall under the regulations for devices rather than medical products). One manufacturer of Belzer UW storage solution (Bristol-Meyers-Squibb [Viaspan]) has yet to indicate to the MHRA if they will apply for CE marking. However, a CE marked Belzer UW storage solution is now available from another manufacturer so the guidance on Belzer UW storage solution remains appropriate, although the information in the technology section about the regulatory status of this solution is no longer correct.

The conclusions from the Machine Preservation Trial demonstrate that machine-perfusion is superior to cold-storage (Moers et al. 2012). However, the current available evidence and the above information presented, it is proposed that TA165 be transferred to the ‘static list’.

8. Implementation

A submission from Implementation is included in Appendix 3.

9. Equality issues

No equality issues were raised during the course of the appraisal.

GE paper sign off: Janet Robertson, 1st February 2013

Contributors to this paper:

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Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed
- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

Early identification and management of chronic kidney disease in adults in primary and secondary care. linical guideline CG73. Published Sep 2008. Reviewed: December 2011 – decided to update guideline.

Anaemia management in people with chronic kidney disease (CKD). Clinical guideline CG114. Published Feb 2011. Reviewed: December 2011 - an update of this guideline is currently in the process of being scheduled into the work programme.

Renal transplantation - immuno-suppressive regimens (adults). Technology appraisal TA85. Published Sep 2004. Reviewed: August 2010 – decided to review guidance

Renal transplantation - immunosuppressive regimens for children and adolescents. Technology appraisal TA99 Apr 2006. Reviewed Sep 2009. Review scheduled.

Organ donation for transplantation: improving donor identification and consent rates for deceased organ donation CG135. Published: December 2011. Review date: TBC

In progress

Acute kidney injury: prevention, detection and management of acute kidney injury up to the point of renal replacement therapy. Clinical guideline. Anticipated publication date: Aug 2013

Referred - QSs and CGs

Acute kidney injury (non-traumatic) - quality standard. Anticipated publication: October 2014.

Renal replacement therapy services - quality standard. Anticipated publication: December 2014.

Details of new products

Drug (manufacturer)	**Details (phase of development, expected launch date,)**
WAVES Kidney Perfusion device (Waters Medical Systems)	This device appears to be replacing the RM3 kidney perfusion device, also manufactured by Waters Medical Systems
Celsior cold storage solution (Genzyme Corporation)	

Drug (manufacturer)	Details (phase of development, expected launch date,)
HTK cold storage solution (Custodial)	

Registered and unpublished trials

Trial name and registration number	Details
A multicentre randomised controlled study of cold Pulsatile Perfusion in Asystolic donor Renal Transplantion (PPART study). ISRCTN95022818	Anticipated date of completion: October 2013

References

Moers C, Smits JM, Maathuis MH, et al. (2009) Machine perfusion or cold storage in deceased-donor kidney transplantation. New England Journal of Medicine 360:7-19

Moers C, Pirenne J, Paul A, Ploeg RJ (2012) Machine perfusion or cold storage in deceased-donor kidney transplantation. New England Journal of Medicine 366:770-771

Appendix 3 – Implementation submission

Implementation feedback: review of NICE technology appraisal guidance 165

NICE Technology Appraisal 165 Machine perfusion systems and cold static storage of kidneys from deceased donors
Implementation input required by 15/10/2012
Please contact Rebecca Lea regarding any queries rebecca.lea@nice.org.uk

Contents

1 Routine healthcare activity data

The NICE implementation programme has not looked at any routinely collected data to determine the uptake of this technology appraisal guidance.

2 Implementation studies from published literature

Information is taken from the uptake database (ERNIE) website.

Nothing to add at this time.

3 Qualitative input from the field team

The implementation field team have recorded the following feedback in relation to this guidance:

Nothing to add at this time.