NICE National Institute for Health and Care Excellence

NICE guidance

Normothermic extracorporeal preservation of hearts for transplantation following donation after brainstem death

HealthTech guidance
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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guidance replaces IPG549.

1 Recommendations

1.1 Current evidence on the efficacy of normothermic extracorporeal preservation of hearts for transplantation following donation after brainstem death shows that the procedure extends preservation times compared with conventional cold storage. The evidence on safety is adequate in the short term. Therefore, this procedure may be used with standard arrangements for clinical governance and audit. The usual consent procedures (see Human Tissue Authority's guidance for professionals) for organ donation and implantation must also be followed.

1.2 NICE encourages further research into normothermic extracorporeal preservation of hearts for transplantation following donation after brainstem death. Outcomes should include primary graft function, graft function in the long term and device-related complications.

2 Indications and current treatments

2.1 Heart failure is a complex clinical syndrome that occurs when the efficiency of the heart as a pump is impaired. It leads to reduced blood flow to body tissues and increased filling pressure in the heart. This causes congestion and oedema in the lungs (causing breathlessness) or the body (causing swelling of the legs). Other symptoms include reduced exercise tolerance, fatigue and malaise.

2.2 Medical treatment of heart failure involves drugs, including diuretics and inotropic agents. Invasive therapies include electrophysiological interventions, such as pacemakers and implantable cardioverter defibrillators, revascularisation by percutaneous coronary angioplasty and stenting or coronary artery bypass grafting, valve replacement or repair, and temporary use of intra-aortic balloon pumps.

2.3 In chronic heart failure, conventional treatment strategies may not work, resulting in the need for heart transplantation or implantation of a ventricular assist device to provide permanent circulatory support (destination therapy). A ventricular assist device may also be used to provide temporary circulatory support while a patient waits for heart transplantation (bridge-to-transplantation).

2.4 Conventional heart transplantation involves removing the heart of a donor who no longer has any activity in their brainstem, and has permanently lost the potential for consciousness and the capacity to breathe autonomously. The donor heart is usually preserved using cold ischaemic storage until it is implanted into the recipient. Prolonged cold storage times may result in ischaemic and reperfusion injuries that can impair heart function after transplantation.

3 The procedure

3.1 Normothermic extracorporeal preservation aims to keep the donor's heart beating outside the body, using a perfusion machine that delivers warm oxygenated blood supplemented with catecholamine, nutrients and electrolytes. This technique aims to decrease the amount of damage that occurs to the heart after removal, by reducing the rate of tissue deterioration compared with conventional cold ischaemic storage. The aim is to improve clinical outcomes for the recipient. The technique was initially used to preserve hearts donated after brainstem death, but has recently been adapted to preserve hearts donated after circulatory death (death that has been diagnosed and confirmed using cardio-respiratory criteria). This overview considers only normothermic extracorporeal preservation of hearts donated after brainstem death.

3.2 In this procedure, the donor heart is inspected and arrested with cold cardioplegia solution before being removed. After removal, the heart is placed in a perfusion machine and re-animated. The perfusion machine comprises a blood reservoir (which stores the donor's blood), pulsatile-flow pump, blood oxygenator, blood warming unit and monitoring equipment. Oxygenated blood from the reservoir is warmed and pumped into the aorta, perfusing the coronary arteries of the donor heart. Coronary venous blood drains into the right atrium, through the coronary sinus, and passes into the right ventricle. The blood flows through the pulmonary artery, into the oxygenator, and passes back into the reservoir. Aortic pressure, coronary flow, blood temperature and heart rate are all monitored. Immediately before the transplantation procedure, the heart is arrested with cold cardioplegia solution and disconnected from the perfusion machine. It is then implanted into the recipient. This procedure has been used to store donor hearts for up to 8 hours before transplantation.

4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

4.1 In a randomised non-inferiority trial of 128 patients who received donor hearts stored by normothermic extracorporeal preservation (n=62) or standard cold ischaemic storage (n=66), the mean out-of-body times (the duration from the time the donor heart was stopped to the time of reperfusion after transplantation) were 324±79 minutes and 195±165 minutes respectively ($p<0.001$). The 30-day survival rate was 94% (58 of 62) in the normothermic extracorporeal preservation group and 97% (64 of 66) in the cold ischaemic storage group (not significant).

4.2 In a non-randomised comparative study of 159 patients who received donor hearts stored by normothermic extracorporeal preservation (n=29) or standard cold ischaemic storage (n=130), the mean hospital length of stay was 26 days in the normothermic extracorporeal preservation group and 28 days in the standard cold ischaemic storage group (not significant). Cumulative survival rates were 96% and 95% respectively at 30-day follow-up (not significant).

4.3 In a case series of 30 patients, biventricular allograft function was well preserved in 92% (24 of 25) of patients at mean follow-up of 257 days; the mean left ventricular ejection fraction was 66%, the mean fractional shortening was 37%, and the mean longitudinal right ventricular systolic function was 13.6 mm.

4.4 In the non-randomised controlled study of 159 patients who received donor hearts stored by normothermic extracorporeal preservation (n=29) or standard cold ischaemic storage (n=130), the cumulative survival rates were 89% and 81% respectively at 1-year follow-up (not significant). At 2-year follow-up, the cumulative survival rates were 89% and 79% respectively (not significant).

4.5 Specialist advisers listed the following as key efficacy outcomes: an increase in preservation times; a decrease in ischaemia times, the need for organ reconditioning, length of stay in an intensive care unit, primary graft function, and

30-day survival or mortality rates; and an increase in the number of hearts available for transplantation.

5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

5.1 Death was reported in 14% (4 of 29) of patients in the normothermic extracorporeal preservation group in a non-randomised comparative study of 159 patients who received donor hearts stored by normothermic extracorporeal preservation (n=29) or standard cold ischaemic storage (n=130). Deaths were caused by severe multi-organ failure (n=2), graft failure (n=1) and graft vasculopathy (n=1). Authors did not report the death rate in the standard cold ischaemic storage group. Death because of bowel ischaemia was reported in 1 patient, 44 days after transplantation, in a case series of 30 patients.

5.2 A haemorrhagic stroke was reported in 1 patient in a case series of 20 patients. No further details were provided.

5.3 Severe rejection was reported in 18% (11 of 62) of patients in the normothermic extracorporeal preservation group and 14% (9 of 66) of patients in the standard cold ischaemic storage group in a randomised non-inferiority trial of 128 patients (not significant).

5.4 Graft failure was reported in 1 patient in the normothermic extracorporeal preservation group (n=62) and in no patients in the standard cold ischaemic storage group (n=66) in the randomised non-inferiority trial of 128 patients (not significant). Primary graft failure was reported in 7% (2 of 29) of patients in the normothermic extracorporeal preservation group and 15% (20 of 130) of patients in the standard cold ischaemic storage group in the non-randomised comparative study of 159 patients (not significant).

5.5 Left ventricular dysfunction was reported in 8% (5 of 62) of patients in the normothermic extracorporeal preservation group and 6% (4 of 66) of patients in the standard cold ischaemic storage group in the randomised non-inferiority trial of 128 patients (not significant). In the same study, right ventricular dysfunction was reported in 3% (2 of 62) of patients in the normothermic extracorporeal

preservation group and 9% (6 of 66) of patients in the standard cold ischaemic storage group (not significant).

5.6 Moderate right ventricular failure was reported in 19% (5 of 26) of patients in the case series of 30 patients.

5.7 A need for haemodialysis was reported in 10% (3 of 29) of patients in the normothermic extracorporeal preservation group and 25% (33 of 130) of patients in the standard cold ischaemic storage group in the non-randomised comparative study of 159 patients (p=0.05).

5.8 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed the following anecdotal adverse events: inadequate perfusion leading to ischaemic damage and the need for inotropes, extracorporeal membrane oxygenation or ventricular assist device support; clotting of the circuit during perfusion; and loss of the donor heart because of detachment from the perfusion system. They considered that the following were theoretical adverse events: 'over-perfusion' of the donor heart leading to myocardial oedema and loss of the donor heart because of mechanical failure of the perfusion system during transportation.

6 Committee comments

6.1 The committee was advised that normothermic extracorporeal preservation might allow better assessment and more frequent use of marginal hearts, so increasing the number of hearts available for transplantation. However, the available evidence did not provide data to draw any conclusions about this potential benefit.

Update information

Minor changes after publication

January 2026: Interventional procedures guidance 549 has been migrated to HealthTech guidance 404. The recommendations and accompanying content remain unchanged.

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Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.