

DuraGraft for preserving vascular grafts

Medtech innovation briefing

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Summary

- The **technology** described in this briefing is DuraGraft. It is a preservation solution used during operations for storing harvested blood vessels that will be used in coronary artery bypass graft (CABG) surgery.
- The **innovative aspects** are that it is the only CE-marked ionically and pH-balanced preservation solution for vascular grafts. It contains antioxidants that aim to prevent ischaemic damage to the vascular graft and associated endothelium.
- The intended **place in therapy** would be in people with coronary artery disease who are having CABG surgery.
- The **main points from the evidence** summarised in this briefing are from 2 published studies involving a total of 2,555 people having CABG. These suggest DuraGraft is likely to be associated with a lower risk of developing complications such as intimal hyperplasia after CABG compared with grafts stored in saline solution. However, the studies may be open to bias from allocation concealment and patient selection.

- **Key uncertainties** around the evidence are that the study results may not be generalisable to the NHS if the population having CABG differs between countries. The evidence is limited in quality and quantity and there is no evidence of the longer-term effects of DuraGraft use in the context of follow-up in a randomised controlled trial.
- The **cost** of DuraGraft is £630 per patient (including VAT). The **resource impact** is that DuraGraft increases costs compared with standard CABG using saline or blood solutions. This could be offset if it results in a reduction in the rates of CABG complications and repeat revascularisation, but there is very limited evidence to support this at present.

The technology

DuraGraft is a preservation solution used for storing harvested vessels that will be used for coronary artery bypass grafts (CABG) or peripheral vascular procedures. It can also flush isolated blood vessels harvested through anastomosis. It is a single-use, intraoperative vascular graft treatment to protect the structure and function of the vascular endothelium from ischaemic damage. The technology is also called endothelial damage inhibitor. It is an ionically and pH-balanced physiological salt solution containing L-glutathione, L-ascorbic acid, L-arginine and other additives that protect the graft from the damaging effects of ischaemia and handling during CABG. It is claimed that these have pro-endothelial and pro-vasomotor properties that reduce the incidence of ischaemia reperfusion injury and oxidative damage, while avoiding metabolic storage lesions (biochemical and physiological changes to red blood cells), a pro-coagulant response and inflammation in the harvested graft.

The company notes that DuraGraft includes L-arginine which has been known to cause an allergic reaction in some patients. DuraGraft should not be given to people with known allergy or hypersensitivity to L-arginine.

Innovations

DuraGraft is the only ionically and pH-balanced preservation solution containing antioxidants for vascular grafts to prevent oxidative damage during vascular surgery. The company claims that it is the only approved endothelial damage inhibitor that has been designed to address issues known to happen during grafting, handling, and exposure to ischaemic conditions.

Current care pathway

CABG procedures are often done to improve the blood supply to the heart in people with coronary artery disease to reduce their chances of having a heart attack. CABG might also be used during or after a heart attack to treat blocked arteries. NICE's guideline on [stable angina: management](#) provides guidance on treating people with stable angina and revascularisation for people whose symptoms are not satisfactorily controlled with optimal medical treatment. There are 2 main revascularisation procedures used to treat CABG or percutaneous coronary intervention. The choice of revascularisation strategy will depend on many factors including the results of angiography, a patient's preferences, age, and whether they have diabetes or other comorbidities. The use of preservation solution during CABG procedure is not covered by NICE guidance. But, NICE provides guidance on assessing graft patency, including NICE medical technologies guidance on [MiraQ for assessing graft flow during CABG](#) and NICE interventional procedures guidance on [intraoperative fluorescence angiography for evaluating CABG patency](#).

In clinical practice, saline or blood-based solutions are commonly used in CABG to store the harvested blood vessels during surgery.

Population, setting and intended user

DuraGraft will be used by cardiac surgeons or nurses in hospital operating theatres, which may be in secondary or specialist tertiary care centres, for people with coronary heart disease.

The company states that no changes are needed to current surgical techniques or procedure.

Costs

Technology costs

DuraGraft costs £630 (including VAT) per CABG. No other consumables are needed according to the company.

Costs of standard care

The [2018/19 national tariff](#) for a CABG ranges from £6,594 (HRG code ED28C, standard CABG with CC score 0 to 4) to £13,547 (HRG code ED26A, complex CABG with CC score of 10 and above). All tariffs include the use of standard storage solutions (saline and blood).

Resource consequences

Using DuraGraft would increase the costs of CABG by £630 per patient. These costs could be offset if the device reduced the incidence of vein graft failure, and if this meant that fewer post-CABG complications and fewer repeat revascularisation procedures were needed.

An economic study abstract ([Tatar et al. 2017](#)) estimated the cost of CABG and complications including revascularisation and myocardial infarction, and assessed the cost effectiveness of DuraGraft in CABGs done in Turkey. It took the perspective of the Turkish Social Security Institution. The results suggested that using DuraGraft cost less than not using DuraGraft in CABG, and it was more effective. The predicted number of complications avoided was 2.7, the incremental cost savings were not reported. It is not clear how grafts were stored in the comparator arm of the study.

Regulatory information

DuraGraft was CE marked as a class IIa medical device in October 2014.

A search of the Medicines and Healthcare products Regulatory Agency website revealed that no manufacturer field safety notices or medical device alerts have been issued for this technology.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Coronary artery disease is more common in men and in people over the age of 50, with the risk of developing coronary artery disease increasing with age. Cardiovascular disease is

more common in people of South Asian and African or Caribbean family origin. The technology is only validated for use in people with an indication for coronary artery bypass graft. Sex, age and race are all protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [interim process and methods statement](#). This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Two studies are summarised in this briefing, including a total of 2,555 patients having a coronary artery bypass graft (CABG).

The evidence for DuraGraft includes 1 randomised control trial (conference abstract) and 1 observational study (full text).

Table 1 summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

In general, the evidence suggests that the use of DuraGraft may be associated with a lower risk of developing complications and adverse events after CABG compared with saline solution. However, there is little evidence of the long-term effects of DuraGraft in the context of a randomised, controlled trial. None of the included studies compared the effectiveness of DuraGraft with blood-based solutions, which are commonly used in CABG in clinical practice.

The evidence is limited in quantity; both included studies are not from the UK, which may limit the generalisability of the findings to the NHS. However, patients with coronary artery disease selected to have CABG using the preservation solution are not thought to differ substantially from those seen in NHS practice.

Table 1 Summary of selected studies

<u>Perrault et al. (2017), conference abstract 135</u>	
Study size, design and location	A prospective randomised, double-blinded study of 119 patients who had CABG. Seven investigational sites in Canada.
Intervention and comparator(s)	DuraGraft. Saline solution.
Key outcomes	More patients in the DuraGraft group had mean reduction or no change in wall thickness at 4 to 6 weeks ($p < 0.0001$) and 3 months ($p < 0.0003$) after CABG compared with the heparinised saline group. Results suggested that DuraGraft prevented early increased wall thickness as an expression of intimal hyperplasia. Progressive intimal hyperplasia would contribute to vein graft disease and vein graft failure.
Strengths and limitations	A randomised study design. No long-term outcomes (at 12 months study follow-up) were reported. Details of allocation and randomisation were not reported in the abstract.
<u>Haime et al. (2018)</u>	
Study size, design and location	A cross sectional study of 2,436 patients who had CABG. USA.
Intervention and comparator(s)	DuraGraft. Saline solution.

Key outcomes	<p>The study included patients aged between 29 and 92 years. During CABG procedures, 1,400 patients had heparinised saline and 1,036 patients had DuraGraft. Patient characteristics and surgical data were similar between 2 groups except patients in the heparinised saline group had a higher prevalence of COPD and previous MI.</p> <p>Mean follow-up was 8.5 ± 4.2 years for the DuraGraft group, and 9.9 ± 5.6 years in the heparinised saline group. The study examined the differences in short-term and long-term outcomes between the 2 groups.</p> <p>Short-term outcomes were defined as events occurring in the peri- and early postoperative period within the first 30 days after CABG or before discharge. The study reported the following short-term outcomes: perioperative MI, prolonged ventilation time (>48h), prolonged time in coma (>24h), renal failure, and death. Results suggested that patients in the DuraGraft group had a substantial risk reduction in (77%) perioperative MI compared with those in the heparinised saline group (OR 0.23, 95% CI 0.09 to 0.59; $p=0.0024$).</p> <p>Long-term outcomes were defined as events happening >30 days after CABG. Results suggested that treatment with DuraGraft was associated with a significantly lower risk of repeat revascularisation starting at 1,000 days after CABG compared with the heparinised saline group (HR 0.65, 95% CI 0.44 to 0.97, $p=0.037$). DuraGraft was also associated with statistically lower occurrence of MACE (HR 0.81, 95% CI 0.70 to 0.94, $p=0.0051$) and statistically significant risk reduction in non-fatal MI (HR=0.55, 95% CI 0.41 to 0.74, $p<0.0001$) than the saline group.</p>
Strengths and limitations	<p>A retrospective study design. The heparinised saline and DuraGraft groups were observed in 2 sequential time periods, which may have affected outcomes. Most of the study participants were male (99%). Patient characteristics and surgical data were similar for most parameters, but patients in the heparinised saline group had a higher prevalence of COPD and previous MI. The data analysis for this study was supported by an unrestricted grant by Somahlution (the manufacturer).</p>

Abbreviations: CABG, coronary artery bypass; CI, confidence interval; COPD, chronic obstructive pulmonary disease; MACE, major adverse cardiac event; MI, myocardial infarction; OR, odd ratio; HR, hazard ratio.

Recent and ongoing studies

- [EU Multicentre registry to assess outcomes in CABG patients: treatment of vascular conduits with DuraGraft](#). ClinicalTrial.gov identifier: NCT 02922088. Status: recruiting. Indication: cardiovascular diseases, coronary artery disease. Intervention: DuraGraft.

Specialist commentator comments

Comments on this technology were invited from clinical specialists working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Four specialists were familiar with or had used this technology before.

Level of innovation

All experts agreed that the technology is a novel concept. Two experts thought DuraGraft is innovative in its formulation, including components that preserve the endothelium of the grafts, and is better than the current standard of care formulations (saline or blood-based solutions). One said that no solution designed specifically for endothelial protection is available in the NHS. One expert thought the technology is innovative and potentially may improve the durability of vein grafts.

Potential patient impact

The potential to improve the patency of vein grafts was the main benefit identified by experts. This was said to minimise vein graft damage during coronary artery bypass graft (CABG) and to reduce vein graft failure after CABG. One expert noted that a retrospective study in the USA has seen a reduction in vein graft dysfunction in people having CABG in the short term, but this would need to be confirmed in the context of randomised controlled trials. Most experts said the technology was unlikely to lead to substantial changes to current care for people having CABG but could improve flow pattern in the

short term (4 to 6 weeks) after CABG, and may potentially reduce the need for repeat revascularisations in the long term. Most of the experts agreed that the technology would be of most benefit for patients having CABG using saphenous vein conduits, and especially patients who are prone to early graft failure as 2 experts said.

Potential system impact

The potential to reduce the need for repeat revascularisations was identified as a key benefit to the healthcare system. The possibility of a reduction in vein graft failure and hospital admissions after CABG were also identified by the experts. Two experts said the cost implications of the technology were unclear because of the lack of economic analyses, and thought more evidence was needed to evaluate the cost effectiveness of the technology in the NHS. All experts agreed that there would be little resource impact apart from the cost of the technology, and no extra staff or other equipment would be needed to adopt this technology. Experts thought that minimal training for staff such as theatre scrub nurses would be needed in preparing the technology.

General comments

Two experts noted that DuraGraft has only been used in small number of patients in a trial in the UK. None of the experts were aware of any safety issues however, 1 expert noted a potential risk of allergic reaction to L-arginine included in DuraGraft. The main barriers to adoption identified by 2 commentators were the lack of randomised controlled data on the long-term benefit of the technology and the cost of the technology. Two experts said the technology would become standard care but both noted that the technology would only replace current standard care for graft preservation after harvesting because they did not think the technology was licensed for injection while the vein is being harvested. The company have since confirmed that DuraGraft is licensed for this and they have clarified this point in an updated Instructions For Use approved by their CE-mark Notified Body. One expert thought that the technology would be an addition to the current standard of care.

Specialist commentators

The following clinicians contributed to this briefing:

- George Gradinariu, specialist registrar in cardiothoracic surgery, Golden Jubilee National Hospital, non-financial professional involving in the DuraGraft registry study.
- Nawwar Al-Attar, consultant cardiac and transplant surgeon, Golden Jubilee National Hospital, non-financial professional involving in the DuraGraft registry study.
- Amal Bose, consultant cardiothoracic surgeon, Blackpool Teaching Hospitals NHS Foundation Trust, did not declare any interests.
- Norman Briffa, consultant cardiac surgeon, Sheffield Teaching Hospitals NHS Foundation Trust, non-financial professional involving in clinical research of DuraGraft.

Development of this briefing

This briefing was developed by NICE. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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