Eur J Vasc Endovasc Surg (2018) ■, 1–7

Cost-Effectiveness Evaluation of Heparin Coated Versus Standard Graft for Bypass Surgery in Peripheral Artery Disease Alongside a Randomised Controlled Trial

Marie K. Villemoes [a], Jes S. Lindholt [b,c,*], Kim C. Houlind [c,d], Bo Gottschalksen [e], Christian N. Petersen [f], Martin Rasmussen [g], Charlotte Wedel [e], Morten B. Bramsen [h], Rikke Søgaard [i,j]

[a] Central Denmark Region, DEFACTUM, Aarhus, Denmark
[b] Department of Cardiovascular and Thoracic Surgery, Odense University Hospital, Odense, Denmark
[c] Cardiovascular Centre of Excellence in Southern Denmark, Odense University Hospital, Odense, Denmark
[d] Department of Vascular Surgery, Kolding Hospital, Kolding, Denmark
[e] Department of Vascular Surgery, Slagelse Hospital, Slagelse, Denmark
[f] Department of Vascular Surgery, Aalborg University, Aalborg, Denmark
[g] Department of Vascular Surgery, Rigshospitalet, Copenhagen, Denmark
[h] Cardiovascular Research Unit, Viborg Hospital, Viborg, Denmark
[i] Department of Public Health, Aarhus University, Aarhus, Denmark
[j] Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

WHAT THIS PAPER ADDS

This study assesses the cost-effectiveness of heparin coated versus standard polytetrafluoroethylene graft from a healthcare perspective, as this graft has recently been shown to reduce the risk of graft failure after revascularisation. Overall, heparin coating appears to be cost-effective, and, particularly for patients with critical ischaemia, it might improve outcomes while reducing costs.

Objective/Background: Heparin coating has recently been shown to reduce the risk of graft failure in arterial revascularisation, at least transiently. The aim of this study was to assess the cost-effectiveness of heparin coated versus standard polytetrafluoroethylene grafts for bypass surgery in peripheral artery disease from a long-term healthcare system perspective.

Methods: Cost-effectiveness evaluation was conducted alongside the Danish part of the Scandinavian Propaten trial in which 431 patients planned for femoro-femoral or femoro-popliteal bypass surgery were randomised to either type of graft and followed for 5 years. Based on the intention to treat principle, the differences in healthcare costs (general practice, prescription medication, hospital admission, rehabilitation, and long-term care in 2015 Euros), life years (LYs), and quality adjusted life years (QALYs) were analysed as arithmetic means with bootstrapped 95% confidence intervals. Cost-effectiveness acceptability curves were used to illustrate the probability of cost-effectiveness for a range of threshold values of willingness to pay (WTP).

Results: No statistically significant differences between the randomisation groups were observed for costs or gains of LYs or QALYs. The average cost per QALY was estimated at €10,792. For a WTP threshold of €40,000 per QALY, the overall probability of cost-effectiveness was estimated at 62%, but owing to cost savings in patients with critical ischaemia (cost per QALY $<$€0), it increased to 89% for this subgroup.

Conclusion: Until further evidence, heparin coated grafts appear overall, to be cost-effective over standard grafts, but important heterogeneity between claudication and critical ischaemia should be noted. While the optimal choice for claudication remains uncertain, heparin coated grafts should be used for critical ischaemia.

Article history: Received 31 October 2017, Accepted 1 March 2018, Available online XXX

Keywords: Blood vessel prosthesis, Cost benefit analysis, Peripheral arterial disease/surgery, Randomised controlled trials, Vascular patency

INTRODUCTION

The indication for bypass revascularisation is traditionally restricted to critical ischaemia, but claudicants are offered the procedure, although this indication is controversial.[1–3] In any case, the recommended procedure is arterial bypass surgery with autologous vein or vascular prostheses. However, neointimal hyperplasia formation at the

* Corresponding author. Department of Cardiothoracic and Vascular Surgery, Odense University Hospital, Elitary Research Centre of Individualised Medicine in Arterial Disease (CIMA), J.B. Winsløv Vej 4, DK-5000, Odense C, Denmark.

E-mail address: jes.sanddal.lindholt@rsyd.dk (Jes S. Lindholt).

https://doi.org/10.1016/j.ejvs.2018.03.012

Please cite this article in press as: Villemoes MK, et al., Cost-Effectiveness Evaluation of Heparin Coated Versus Standard Graft for Bypass Surgery in Peripheral Artery Disease Alongside a Randomised Controlled Trial, European Journal of Vascular and Endovascular Surgery (2018), https://doi.org/10.1016/j.ejvs.2018.03.012

anastomoses is a well known complication that threatens the patency of the reconstruction. In 1988, an animal study showed that prolonged heparin injection resulted in less neointimal hyperplasia,[4] and a subsequent randomised clinical trial showed that post-operative heparin treatment for 3 months was superior to low dose aspirin and dipyridamole.[5] This led later trials to test the efficacy of heparin coating versus no heparin coating of standard grafts, and positive results based on a short-term follow up have been reported.[6,7]

However, a standard graft is still preferred by many vascular centres, possibly because of the extra cost of the heparin coating and limited evidence on the long-term outcomes in terms of the patency. Non-randomised trials have indicated that long-term results could be positive,[8–10] but this has not been confirmed by a randomised trial until the recent reporting of the Scandinavian Propaten trial.[11] Overall, 569 patients were enrolled in the trial. Some 552 had follow up data available for analysis of the primary outcome. Use of heparin coating significantly improved patency by 37% after 2 years, whereas after 5 years there was no difference (adjusted hazard ratio [HR] 0.95, 95% confidence interval [CI] 0.71–1.28). In patients with critical limb ischaemia, the use of heparin coating reduced the 5 year risk of loss of primary patency by 37% (HR 0.63, 95% CI 0.40–0.99). What remains to be clarified from a societal point of view is whether the transient gain is likely to be cost-effective, and whether the subgroups of indications differ. The current study is a piggy back evaluation on the Danish part of the Scandinavian Propaten trial with the aim of assessing the cost-effectiveness of heparin coated versus standard graft based on a long-term healthcare perspective (trial registration: ISRCTN77471962).

METHODS

A cost-effectiveness evaluation was conducted in conjunction with the randomised Scandinavian Propaten Trial. The study design and clinical outcomes after 1 and 5 years have previously been reported in detail,[6,11] but a summary of design aspects for the present study is provided below.

Participants

Patients with peripheral arterial disease (PAD) scheduled for femoro-femoral or femoro-popliteal bypass surgery were recruited from seven of the eight specialised vascular surgery departments in Denmark during the years 2005–09. Non-Danish patients could not be included owing to register data being unavailable to the required level of detail. The resulting sample ($n = 431$) represents 80% of the sample included in the Scandinavian Propaten trial.

Setting and location

procedures were performed in highly specialised, hospital based centres of which there are eight to cover the population of almost six million. Denmark has a tax financed, universal national healthcare system. All patients are referred to specialised health care by their general practitioners. No centre used vein cuff above knee or for crossover bypass, and only a few prostheses were implanted below the knee. The stratified-by-centre randomisation ought to have secured an equal distribution of vein cuff or no cuff.

Study perspective

This study focused on a healthcare system perspective including the cost categories of primary care (general practice and physiotherapy), prescription medication related to cardiovascular disease, hospital based care relating to cardiovascular disease, and rehabilitation, home care, and assistive aids following eventual amputation.

Randomisation and comparators

Surgeons and patients were blinded to the randomisation, which was effected using computer generated random numbers at the time of referral for bypass surgery, and on obtaining informed consent from the patient. Following the methodology from the clinical study on which this economic evaluation was piggybacking, randomisation was undertaken at the surgical procedure level such that a patient, in principle could be randomised more than once. That applied to 15/431 patients (3.5%). All analysis follows the intention to treat (ITT) principle such that all patients ($n = 431$) were analysed as randomised in the first instance.

Comparators were femoro-femoral or femoro-popliteal bypass surgery of identical nature except for the graft, which was either standard polytetrafluoroethylene graft (standard group) or heparin coated graft (heparin group).

Time horizon

Evaluation was based on a fixed follow up of 5 years, regardless of which year the patient entered the study. The first patient had a surgery in May 2005 and follow up for the last patient ended in February 2014. Patients who died during follow up were included until the time of their death.

Costing

The healthcare cost perspective included the revascularisation procedure, including additional graft costs for the heparin group; post-operative care; readmission, including eventual re-intervention, amputation or other procedures related to cardiovascular disease; prescription medication; general practice and physiotherapy in primary care; and care costs after amputation. Details on data sources are provided below.

Hospital admissions were identified in Danish National Patient Registry and their costs were estimated from the national tariffs of the diagnosis related grouping system.[12] Revascularisation procedure codes KPD, KPE, and KPF, and amputation procedure codes KNFQ, KNGQ, and KNHQ were used to identify surgical interventions (see Table S1). In relation to revascularisation, a general graft cost is included in the standard tariff, but as this does not cover the additional cost of the heparin coating, the tariff by the extra

Please cite this article in press as: Villemoes MK, et al., Cost-Effectiveness Evaluation of Heparin Coated Versus Standard Graft for Bypass Surgery in Peripheral Artery Disease Alongside a Randomised Controlled Trial, European Journal of Vascular and Endovascular Surgery (2018), https://doi.org/10.1016/j.ejvs.2018.03.012