

Europe's Newspaper for Vascular Specialists

vascularNEWS

ISSUE 34

June 2007

Randomised study assesses heparin-bonded vs. non-heparin-bonded PTFE-grafts

At the recent European Vascular Course, in Marseilles, France, Professor Frank Vermassen, Gent, Belgium, reported on initial findings from a prospective, randomised, open-label, comparative study of femoropopliteal bypass with ePTFE and heparin coated ePTFE.

He began by stating that the long term-results in femoro-popliteal reconstructions with synthetic grafts are less good than with autologous veins, due to the higher thrombogenicity of the inner surface of these grafts compared to the endothelium at the inner surface of autologous veins and the more pronounced formation of intimal hyper-

plasia. Vermassen then theorised that heparin-bonding could reduce thrombogenicity and diminish intimal hyperplasia. Heparin is bonded to PTFE by means of a covalent binding and ionic interactions.

Limited data

He said that there is currently a lack of clinical data with no randomised studies in PTFE grafts and one randomised study in dacron grafts (Devine, et al; *Journal of Vascular Surgery*, 33(3):533-539). In this study, patients demonstrated a significant improvement after receiving a heparin-bonded Dacron prosthesis compared to those



Frank Vermassen

who received an uncoated PTFE.

In animals, studies have shown that heparin-bonded PTFE-grafts cause less distal micro-embolisation than PTFE-grafts irrigated with heparin (Ritter et al; *Surgery*, 122(5):888-892) and patency rates are higher and thrombus deposition less in an interposition experiment in dogs (Begovac, et al; *European Journal of Vascular and Endovascular Surgery*, 25(5):432-437). Moreover, heparin-coated PTFE-grafts had a better patency than uncoated grafts in a rat experiment (Walpoth, et al; *Circulation*, 98(19):II319-II323, suppl S, Nov 10, 1998). *In vitro* tests have shown less platelet adhesion to the surface, also resulting in a thinner neo-intimal layer. However, studies on results *in vivo* or on the influence on patency are not available.

Study design

As a result, a study was set up as a prospective, open label, randomised, multi-centre study comparing heparin-bonded PTFE-grafts with the same PTFE-grafts without heparin-bonding. The study began enrolment in May 2004 with the aim randomising 520 patients in 20 centres over a three year inclusion period, with two years of follow-up. The primary endpoint is primary patency; secondary endpoints are secondary patency, limb salvage and mortality.

The study design calls for randomisation at each centre on a 1/1 basis between both grafts and no difference is made between above the knee (ATK) and below the knee (BTK) interventions, nor for other risk factors. According to Vermassen, stratification, separate analysis and multivariate analysis will compensate for differences between both groups if these risk factors prove to be significant or unevenly distributed between both groups.

Patency-results will be analysed according to an actuarial life-table analysis and differences analysed with the logrank test. A $p < 0.05$ value will be considered as significant and a multi-variate analysis will be performed for potential risk-factors. The study has a power of 0.8 to detect a relative difference of 1.3, assuming a patency of 50% after three years with a two-sided alpha error of 0.05. Patency by clinical examination and ankle brachial index will be assessed at one, three, six, 12 and 24 months,

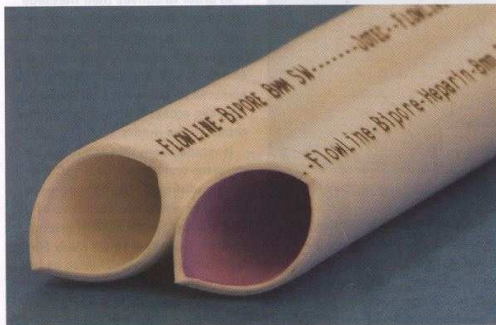
and by Duplex at one, 12 and 24 months and when graft occlusion is suspected. Interim analyses are foreseen every six months and sub-analyses will be performed for ATK and BTK reconstructions separately.

Vermassen reported that so far 467 patients have been enrolled in 29 centres (mean follow-up of 636 days), with 450 patients treated (325 ATK, 125 BTK). Of the 325 ATK patients, 154 received a heparin-bonded PTFE-graft and 171 a non-heparin-bonded PTFE-graft. In addition, of the 125 BTK patients, 74 received a heparin-bonded PTFE-graft and 51 a non-heparin-bonded PTFE-graft.

Interim analysis

An interim analysis revealed that there have been a total of 110 occlusions; 90 primary (19%), 16 secondary and four tertiary. Of the 72 occlusions ATK, 25 occurred in the heparin group and 47 in the non-heparin group. Of the 38 occlusions BTK, 23 were in the heparin group and 15 in the non-heparin group. In managing the occlusions, 21 were treated conservatively, 40 received thrombolysis, 27 received thrombectomy, 23 received a new bypass and four had an amputation.

In conclusion, Vermassen said that heparin-bonding on PTFE-grafts can theoretically improve patency, however he added that randomised trials are needed to prove this with level 1 evidence. He added that the results with the Jotec-prostheses in the femoropopliteal area are 'promising' and the final results are expected in 2008.



Heparin-bonded graft

Siemens Medical Solutions that help