Dacron vs Polytetrafluoroethylene Grafts for Femoropopliteal Bypass: a Prospective Randomised Multicentre Trial


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Objectives: to compare the patency of PTFE (Polytetrafluoroethylene) and unsealed knitted Dacron femoro-popliteal bypasses.

Design: multi-centre prospective randomised trial.

Materials and methods: of 203 patients randomised, 194 were included in the final analysis (103 Dacron grafts and 91 PTFE grafts). The median follow-up was 36 months (range: 6–72 months); the distal anastomosis was above-knee in 141 and below-knee in 53 cases. Univariate comparisons of patency were made by the Kaplan–Meier method, multivariate calculations on the effects of covariables by a Cox regression analysis.

Results: there was no difference regarding primary and secondary patency or limb salvage between Dacron and PTFE. The primary 3-year patency for Dacron grafts was 64% (95% confidence interval [C.I.] 55–74%) and for PTFE grafts 61% (C.I. 49–72%). The corresponding 3-year secondary patency was 81% (C.I. 73–89%) and 75% (C.I. 65–86%) respectively, the limb salvage rate 90% (C.I. 84–96%) and 91% (C.I. 84–97%). Upon multivariate analysis below-knee anastomosis was the principal independent predictor of primary graft failure (risk ratio 1.7 [C.I. 1.05–2.8]), impaired secondary patency was associated with infragenicular bypass (risk ratio 3.3 [C.I. 1.8–6.3]) and distal gangrene (risk ratio [C.I. 1.01–3.8] p = 0.048), major amputation was independently predicted by below-knee bypass, tissue necrosis, and poor run-off index.

Conclusions: PTFE and Dacron are equally suitable for femoro-popliteal bypass.

Key Words: Vascular prosthesis; Femoro-popliteal bypass; Surgery.

Introduction

There is broad consensus that autologous vein results in superior long-term patency of infragenicular bypass. However, if autologous vein is not available, PTFE (Polytetrafluoroethylene) has been the most popular choice. However, the preference for PTFE over Dacron is not evidence based. This trial was planned at a time when no conclusive evidence was available to justify the preferential use of PTFE grafts.

Materials and Methods

Study design

The study included patients requiring a femoro-popliteal bypass either above-knee or below-knee where the surgeon considered a prosthetic graft to be the most appropriate choice. The protocol was in accordance with the declaration of Helsinki and was approved by the ethical committee of the University of Heidelberg. The following centres contributed to this study: Chirurgische Universitätsklinik Heidelberg, Universitätsklinikum Mannheim, Josefskrankenhaus Heidelberg, Diakonissenkrankenhaus Karlsruhe, Allgemeines Krankenhaus Hamburg-Altona, Alfried-Kurpp-Krankenhaus Essen.

Inclusion criteria

Indication for artificial graft of at least 20 cm length with proximal anastomosis at the femoral artery. Both atherosclerotic occlusions and popliteal aneurysms could be included. For above-knee bypass the choice between autologous vein and prosthetic graft was left to the decision of the surgeon who could opt for sparing the saphenous vein.
Exclusion criteria
- Infections at operation sites;
- Emergency surgery for acute ischaemia;
- Distal anastomosis below the origin of the anterior tibial artery;
- Composite grafts or jump grafts;
- No preoperative angiography available sufficient to judge distal run-off;
- Previous inclusion in this study either for a contralateral bypass or an earlier ipsilateral one (simultaneous bilateral grafts could be included just with one side);
- Concomitant diseases expected to limit life expectancy to below 3 years at the time of randomisation;
- No informed consent to randomisation or unlikelihood of regular follow-up (e.g. due to serious doubts regarding compliance);
- Contraindications to all types of anticoagulants perioperatively (upon discharge the patients were required to receive either anti-platelet drugs, heparin or coumadin); later withdrawal of anticoagulants for any reasons was recorded but was not considered violation of the protocol;
- Availability of suitable autologous vein (for infragenicular bypass only). Criteria for suitability of the saphenous vein were not pre-determined.

Randomisation
Patients were randomised to either treatment arm intraoperatively by sealed envelopes. The order of assignment had been generated by random digits from a statistical software package (SAS). The envelopes were drawn only following surgical exposure of the sites of proximal and distal anastomosis and judging the vessels appropriate for the intended reconstruction. Randomisation was stratified both for participating hospital and for the site of distal anastomosis (supra- vs infragenicular).

Materials
Patients assigned to the “DACRON” group received unsealed knitted polyester velour grafts (“Microvel” Meadox Company, Ratingen/Germany, taken over by Boston Scientific Vascular during the course of the study); for infragenicular anastomosis spiral-enforced prostheses were applied. Dacron prostheses were sealed by autologous blood intraoperatively. Patients assigned to the “PTFE” group received “Thin wall TW” grafts above knee and “Ring removable RTW” grafts infragenicular (W.L. Gore Associates, Putzbrunn/Germany). Both type and size of suture materials as well as the diameter of the prosthesis (6 or 8 mm) or the type of anastomosis (end-to-end vs end-to-side) was left to the choice of the surgeon. Only three of the patients with below-knee bypass received a distal vein cuff.

Concomitant therapy
Any type of pre- or intraoperative inflow reconstruction or perioperative minor amputations for gangrene were allowed but nevertheless recorded. All patients were treated with heparin perioperatively (dosage and type of administration not standardised). Upon discharge the patients were required to receive either anti-platelet drugs, heparin or coumadin.

Primary end-point
Any occlusion of the graft occurring after the patient left the operating theatre, i.e. primary patency was chosen as the primary outcome measure. This was used in the sense of unassisted primary patency, i.e. in those cases where impeding graft occlusion necessitated reinterventions, the primary end-point was reached at this moment. In case of graft occlusion outside medical supervision the time point of marked increase in pain or reduction in pain-free walking distance was considered as time of graft occlusion. In case of asymptomatic occlusion the half-time between two follow-up visits was considered. Duplex scan and/or angiography were performed in any case of clinical deterioration and/or clinical suspicion of graft occlusion.

Secondary end-points
Secondary patency and limb salvage (avoiding major amputation) were chosen as secondary outcome measures.

Sample size
The study was designed to detect a difference between 50% and 70% primary patency after 3 years with \( \alpha = 0.05 \) and \( \beta = 0.2 \). The expectation of a 20% difference came out of a retrospective analysis within the departmental records of the senior author demonstrating an advantage of this magnitude in favour of Dacron grafts. For actuarial analysis by two-sided log-rank test this would require 193 patients for analysis. Assuming a drop-out rate of 5% we planned to randomise a total of 203 patients. A planned interim analysis was performed after randomisation of 100 patients showing no conclusive evidence for early termination of the study according to preset criteria.

Follow-up
Patency of graft upon primary discharge had to be proven by either angiography or duplex sonography.
Table 1. Group comparison for patient and disease characteristics.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DACRON</th>
<th>PTFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>103</td>
<td>91</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>median [range] yrs</td>
<td>65 [40–84]</td>
<td>68 [47–84]</td>
</tr>
<tr>
<td>patients aged &gt;65</td>
<td>52 (50%)</td>
<td>51 (56%)</td>
</tr>
<tr>
<td>Female ()</td>
<td>27 (27%)</td>
<td>21 (24%)</td>
</tr>
<tr>
<td>Infragenicular bypass</td>
<td>27 (26%)</td>
<td>26 (29%)</td>
</tr>
<tr>
<td>Duration of operation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>median [range] min</td>
<td>130 [65–300]</td>
<td>135 [70–290]</td>
</tr>
<tr>
<td>cases with &gt; = 180 min</td>
<td>31 (30%)</td>
<td>23 (25%)</td>
</tr>
<tr>
<td>Simultaneous operations</td>
<td>33 (32%)</td>
<td>22 (24%)</td>
</tr>
<tr>
<td>Diameter of graft 8 mm*</td>
<td>11 (11%)</td>
<td>6 (7%)</td>
</tr>
<tr>
<td>Run-off Index*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>median [range] yrs</td>
<td>3.7 [1.0–7.5]</td>
<td>4.0 [1.0–10.0]</td>
</tr>
<tr>
<td>patients with index &gt; = 4</td>
<td>49 (46%)</td>
<td>51 (56%)</td>
</tr>
<tr>
<td>Diabetes mellitus non-insulin/insulin dep.</td>
<td>17/12</td>
<td>12/8</td>
</tr>
<tr>
<td>Smoker (never/previous/active)</td>
<td>34/30/39</td>
<td>28/24/39</td>
</tr>
<tr>
<td>Renal failure</td>
<td>13 (13%)</td>
<td>12 (13%)</td>
</tr>
<tr>
<td>Distal gangrene (Stage IV)</td>
<td>26 (25%)</td>
<td>17 (19%)</td>
</tr>
<tr>
<td>Critical limb ischaemia§</td>
<td>36 (35%)</td>
<td>26 (29%)</td>
</tr>
<tr>
<td>Contributing centre#</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>B</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>C</td>
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<td>D</td>
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<td>14</td>
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<tr>
<td>E</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

* All other grafts were 6 mm in diameter.
§ The remaining patients had intermittent claudication except two cases in each group operated for popliteal aneurysms.
# A sixth centre contributed the remaining seven cases.

Planned follow-up visits were scheduled to take place after 3 and 6 months as well as 1, 2, 3, 4, and 5 years postoperatively. Extraordinary visits were performed in case of any clinical or subjective deterioration.

Statistical analysis

Differences were considered significant at p<0.05 (two-sided). Patency and limb salvage data were estimated by the Kaplan–Meier method comparing both treatment arms by log-rank test. Multivariate analysis was performed by the Cox proportional-hazards model with stepwise variable selection (p<0.05 for entry and removal of variables from the model). The covariables listed in Table 1 were included in the multivariate analysis provided a p-value below 0.25 was reached on univariate analysis. The type of graft was always included in multivariate calculations. Calculations were performed by the SAS statistical software package (SAS Institute, Cary, NC, U.S.A.).

Results

Recruitment of patients started in September 1993 and was terminated after randomisation of the planned 203 patients in October 1998. Due to primary dropout of nine patients (violation of inclusion or exclusion criteria in three cases and refusal of patients to show up for any follow-up visit in six cases) a total of 194 patients were included in the final analysis. At the time of this analysis a median follow-up of 36 months (range: 6–72 months) was reached. A total of 141 patients received a supragenicular bypass, 53 an infragenicular bypass. Table 1 lists the distribution of important covariables among the treatment arms.

Primary patency

Figure 1 shows the data on overall unassisted primary patency of the grafts. As it is easily visible there was actually no difference between the two treatment arms (log-rank test p = 0.89): the actuarial 3-year patency for Dacron grafts was 64% (95% confidence interval [CI] 55–74%) and for PTFE grafts 61% (CI. 49–72%). Univariate analysis of the potentially important covariables revealed a significant impact on primary patency for infragenicular bypass (p = 0.03, log-rank test), poor run-off (p = 0.046), and the presence of critical limb ischaemia (p = 0.02). In multivariate analysis the only significant variable contributing to primary patency was the site of distal anastomosis where infragenicular bypass resulted in an increased risk ratio of 1.7 (CI. 1.05–2.8, p = 0.03). Upon subgroup analysis for this parameter it was obvious that there was a markedly worse outcome for infragenicular
success (26 Dacron grafts, 16 PTFE grafts). The increased number of early occlusions in Dacron grafts (Fig. 1) was no longer visible upon looking at secondary patency leading to almost identical secondary patency rates for both types of graft. The actuarial 3-year secondary patency for Dacron grafts was 81% (C.I. 73–89%) and for PTFE grafts 75% (C.I. 65–86%). Univariate analysis of the covariables showed a significantly decreased secondary patency for infragenicular bypass ($p=0.0001$), distal gangrene ($p=0.005$), as well as critical limb ischaemia ($p=0.002$). In addition, bypasses performed in centre A had decreased secondary patency ($p=0.009$) which was easily explainable by the increased incidence of below-knee bypass in this centre. Accordingly, on multivariate analysis infragenicular anastomosis (risk ratio 3.3 [C.I. 1.8–6.3] $p=0.0002$) and distal gangrene/Fontaine stage IV disease (risk ratio 2.0 [C.I. 1.01–3.8] $p=0.048$) were independently predictive of impaired secondary patency.

**Amputation**

Limb salvage was successfully achieved in most of the cases. At 3 years postoperatively the rate was 90% (C.I. 84–96%) in the DACRON arm and 91% (C.I. 84–97%) in the PTFE treatment arm ($p=0.56$). Univariate analysis showed six variables to be associated with impaired rates of limb salvage: infragenicular anastomosis ($p=0.0001$), distal gangrene ($p=0.0001$), critical limb ischaemia ($p=0.0004$), duration of primary operation exceeding 3 h ($p=0.003$), poor run-off index ($p=0.007$), and operation in centre A ($p=0.04$). Upon multivariate analysis three of these remained independently associated with major amputations: below-knee bypass (risk ratio 4.2 [C.I. 1.8–10.1] $p=0.001$), tissue necrosis/Fontaine stage IV disease (risk ratio 3.9 [C.I. 1.6–9.1] $p=0.002$), as well as a poor run-off index (risk ratio 3.4 [C.I. 1.1–10.1] $p=0.03$) decreased the chance of limb salvage.

**Discussion**

Due to the shortcomings of retrospective data the present results will be compared only with previous randomised trial data. An early prospective study which was partly randomised compared 36 PTFE with 10 composite Dacron-vein below-knee bypasses; the authors reached the conclusion that further use of Dacron-vein composites was not justified. A German
trial randomised 250 patients with supragenicular bypass. Unfortunately, since a preliminary report on the first 103 patients no further data of this trial have been published. Up to 18 months of follow-up no significant difference between PTFE and Dacron grafts had been detectable.15

A North American multicentre trial15 has been reported recently with a prolonged follow-up.15 In 240 above-knee grafts no difference in patency could be detected between PTFE and Dacron grafts. Lastly, a randomised trial from Australia with a total of 108 patients (75 above-knee and 33 below-knee grafts) confirmed that there is no difference in primary and secondary patency between PTFE and Dacron grafts in femoro-popliteal position.16 Unlike the present study both the North American and the Australian trial used collagen-impregnated Dacron grafts. However, there is no reason to expect major differences between impregnated and unimpregnated grafts except easier intraoperative handling of impregnated and lower costs for unsealed Dacron grafts.

In the present study, with its limited number of patients, there is still a risk of a type II error, i.e. smaller differences might have been overlooked. Although a meta-analysis is beyond the scope of this report the evidence accumulated by now in various trials strongly suggest that PTFE and Dacron are equally effective in femoro-popliteal bypass surgery. This firm statement should be restricted to supragenicular anastomoses as the total number of infragenicular bypasses was too small in the present as well as in the other studies. Nevertheless, the relevance of this conclusion extends beyond the scope of open bypass surgery as the question of graft material may be equally important for endovascular devices.

In the present study, as well as in the Australian trial, the most significant predictors of early graft failure were poor vessel run-off and critical limb ischaemia. In the North American trial the only independent predictor of occlusion were younger age and graft diameter below 7 mm. In our study patient age and graft diameter did not affect primary or secondary patency or limb salvage.

A recent analysis of the 2119 femoro-popliteal grafts included in the Dutch trial on anticoagulants revealed female gender, critical ischaemia, poor run-off and non-venous graft material to be independent risk factors for occlusion.17 This underlines the fact that the patency rates achieved with prosthetic materials in the present as well as other trials are far from being satisfactory and still fall short of autologous vein grafts even in the above-knee location.18 Although we may achieve improved quality of life in most of our patients19 there may be a remarkable workload to achieve long-term patency.20

Since the widespread acceptance of PTFE as graft material for infragenial bypass surgery it took more than two decades to prove that it may be no better than the old-fashioned Dacron. We do hope that ongoing or future developments of innovative prosthetic materials21,22 or modifications in surgical technique23 will reach the same level of evidence within shorter time.

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References


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