Fluoropolymer-coated Dacron Versus PTFE Grafts for Femorofemoral Crossover Bypass: Randomised Trial


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Objectives. To investigate whether patency of a thin walled 8 mm fluoropassivated Dacron graft was similar to that of a standard 8 mm PTFE graft for femorofemoral crossover bypass surgery.

Design. A randomised multicentre clinical trial comparing two vascular grafts with participation of 10 departments of vascular surgery in Denmark, Sweden and Norway.

Patients and methods. 198 patients were randomised to PTFE (n = 107) or fluoropolymer-coated Dacron grafts (n = 91), 63% underwent surgery for claudication, 27% for ischaemic rest pain and 10% for tissue loss. The median follow-up time was 24 months (IQR 19–26 months).

Results. The primary patency rate of the two grafts was similar (log rank test: p = 0.35). The primary patency rates (95% CI) for coated Dacron and PTFE grafts were 92% (86–98) and 94% (89–99) at 12 months and 87% (74–95) and 93% (87–99) at 24 months, respectively.

Conclusion. In patients with unilateral iliac artery disease not amenable to angioplasty, the femoral-femoral bypass is durable and effective. No difference in patency was found between the two graft materials (fluoropolymer coated Dacron and PTFE).

Keywords: Femorofemoral bypass; Patency; Fluoropassivated Dacron; PTFE.

Introduction

Femorofemoral crossover bypass surgery has been used for nearly 4 decades for extra anatomic reconstructions in patients with unilateral iliac artery disease. When introduced, the crossover bypass was reserved for patients with a high surgical risk as an alternative to aortobifemoral bypass.1,2 Today it is considered a less invasive alternative when endovascular management is impossible or considered unfavourable.3,4

There is no solid evidence concerning the best graft material. Experimental data indicate that PTFE may be less thrombogenic and have less affinity towards bacteria, as compared to Dacron.5–10 Though other studies have indicate equal performance of PTFE and Dacron, PTFE has become the preferred graft for infrainguinal procedures in many centres.11–15 Specific studies in the femorofemoral position are sparse and so are randomised trials.

A recently developed fluoropolymer coated Dacron graft (fluoropassivated Dacron) aims at combining some of the desirable clinical features of Dacron (ease of handling, freedom of suture hole bleeding and lower price) with those of PTFE (lower thrombogenicity, less intimal hyperplasia and less bacterial affinity).16

The objective of this trial was to investigate whether patency of thin walled 8 mm fluoropassivated Dacron graft was comparable to that of
a standard 8 mm PTFE graft for femorofemoral cross-over bypass surgery.

Material and Methods

Study design

The study was a prospective multicentre clinical trial comparing two vascular grafts with participation of vascular surgical units in Denmark, Sweden and Norway. The study was conducted in accordance with the Declaration of Helsinki, with the European Good Clinical Practice Guidelines, and with the European EN540 standards for Clinical Trials. The protocol was approved by the regional ethical committees in Denmark, Norway and Sweden (KF 01-149/99) according to local requirements.

Inclusion criteria

Patients scheduled for elective femorofemoral cross-over bypass surgery for uni-iliac occlusive disease. Patients with significant aorto- or donor-iliac artery disease were eligible, provided vascular or endovascular treatment before or in connection with the femorofemoral bypass procedure could secure uninhibited inflow.

Exclusion criteria

Exclusion criteria included: age <18 or >85 years, pregnancy, patients who could not give fully informed consent in writing, patients with serious concomitant medical disease with a life expectancy less than the span of the study, persons mentally not able to understand and give fully informed consent, when adequate follow-up could not be arranged, emergency surgery for trauma, acute thrombosis or embolism and a proximal anastomosis above the inguinal ligament.

Study centres, length of study

Initially 21 centres, expressed interest, but before the first patients were included, 6 centres withdrew, due to logistic or financial reasons. Five other centres withdrew within the first year after they had enrolled either none or a few patients. Any patients from these centres were not included in the study. Therefore we recruited patients from 10 centres (8 Danish centres, 1 Swedish and 1 Norwegian). Recruitment of patients started in January 2000 and was terminated after 34 months in November 2002 having recruited 198 patients. Though the initial recruitment period of 18 months was extended by 16 months we were approximately 100 patients short of the number estimated from the power calculation, due to the participation of only half the initially planned centres.

The surgical procedure and the graft

For the purpose of this study a femorofemoral bypass was defined as the insertion of a bypass graft described by inverse “U” shape with both anastomoses to the common, the profunda or the superficial femoral artery of the right and left groin, respectively.

The prostheses used were thin walled fluoropassivated Dacron grafts (a knitted Dacron prosthesis in which the surface was treated with a fluoropolymer before sealing with gelatin (Sulzer Vascutek Ltd, Inchinnan Renfrewshire, Scotland, UK)) and thin walled expanded polytetrafluoroethylene (PTFE) grafts (W.L. Gore & Associates Inc., Flagstaff, Arizona, USA or Impra Inc., Tempe, Arizona, USA). In all cases 8 mm externally supported grafts were used. The costs of the grafts were comparable (~ €740 in 2005) (Personal communication, Vingmed Denmark, Dec 2005). Patients were enrolled consecutively and randomisation took place in the operating theatre after surgical exposure and only when the possibility of the intended bypass procedure was confirmed. Assignment to either a PTFE or a fluoropassivated Dacron graft was determined using sealed envelopes using computerised block randomisation.

Endpoints and patency evaluation

Primary uncorrected graft patency was the primary outcome. Procedures performed for disease beyond the graft and its two anastomoses were not considered as corrections to improve primary graft patency. Secondary patency, limb survival, perioperative complications and effect on symptoms were secondary endpoints.

Patency assessment was based on the following objective findings: Accepted imaging techniques (duplex, angiography or MR-angiography) or Doppler signal with handheld Doppler at two points directly over a superficially located graft in addition to maintenance of ankle-arm index improvement or maintenance of achieved improvement in ankle-arm index no more than 0.10 below the highest post operative index or direct observation at operation or post-mortem examination.
If patency was restored after occlusion by thrombectomy, thrombolysis or transluminal angioplasty, and/or problems with the graft itself or one of its anastomoses requiring revision, but not a redo-procedure the graft was considered as having secondary patency.

Patients were classified preoperatively and during follow-up as being asymptomatic, suffering claudication or suffering critical limb ischaemia. Each limb was considered separately.

Sample size and study period

This study was designed as a non-inferiority study, i.e. that patency of the fluoro passivated Dacron graft was not inferior to that of the PTFE graft. Assuming a 2-year patency rate of PTFE of 75% (based on the available literature when initiating the study in 19993,18) and an attrition rate over a 2-year period of 25% (20% mortality and 5% lost to follow-up), the numbers required for 80% power (type two error: 0.2) and 95% confidence (type one error: 0.05) were 150 patients in each group. Based on the number of interested centres and the number of femorofemoral procedures performed in those centres in the year 1998, we estimated that it would take 18 months to recruit 300 patients.

Follow-up

All patients were evaluated at least on the day after surgery and on the day of discharge. Thereafter all patients were assessed at 1, 12, and 24 months for the current status of symptoms, pulses and ankle pressures and the graft was examined by hand held Doppler or duplex-ultrasound, as appropriate. If graft occlusion was suspected a duplex examination or arteriography was performed. One primary investigator at each centre was asked to fill in the follow-up forms at the time of each patient review. Extraordinary visits were performed in case of any clinical or subjective deterioration.

Statistical analyses

Analysis was by intention to treat. When appropriate, the $\chi^2$-test or Fischer exact test was used for comparison of categorical data, and the Mann-Whitney U-test for continuous data. Kaplan-Meier statistics were used for analysis of graft failure and survival, and differences between groups were assessed by the log-rank tests. Multivariate analysis was performed with Cox proportional-hazards models with stepwise variable selection. Analyses were performed by the SPSS statistical software package (SPSS Inc, Chicago, Illinois, USA).

Results

Patients were randomised to PTFE ($n = 107$) or fluoro-passivated Dacron ($n = 91$) (see flowchart, Fig. 1). In total 124 (63%) patients underwent surgery for claudication, and 72 (37%) for critical limb ischaemia (CLI). The baseline characteristics are presented in Table 1. The patients in the two groups did not differ significantly with respect to the listed co-morbidity.

Donor limb inflow was improved in 76 (38%) patients of whom 35 (18%) patients had a preoperative iliac angioplasty (PTA) while 41 patients (21%) had a simultaneous intra-operative procedure performed: iliac PTA in 7, iliofemoral bypass or endarterectomy in 15, femoral endarterectomy in 15 and other procedures in 4. The patients in the two groups did not differ significantly with respect to the number of inflow procedures performed.

The preoperative angiogram allowed runoff assessment in 193 (97%) patients, 86 (45%) of whom revealed occlusion ({$n = 76$}) or >50% stenoses ({$n = 10$}) of the superficial femoral artery (SFA). In this subgroup of patients, intraoperative outflow procedures were performed in 39 (45%): a popliteal or crural bypass in 17 patients and thrombendarterectomy of the common and/or profound femoral artery in 22.

30-day results

The 30-day operative mortality was 0.5% (1/198). One 79-year-old female suffered a fatal myocardial infarction during the first post-operative day. However, 21 patients (11%) suffered a peri-operative (within 30 days) complication. Within the first month, 14 (7%) patients experienced infectious complications, equally distributed between the patients groups (Dacron 7 (8%)/PTFE: 7 (7%)): superficial wound infections occurred in 6 (7%) and 6 (6%) while graft-infections developed in 1 (1%) and 1 (1%), respectively. Three patients had thrombosis of graft, 2 had postoperative bleeding necessitating reoperation and 2 patients suffered thrombosis of a femoro-popliteal bypass of the recipient limb.

Additionally 3 graft infections occurred within 2, 3 and 12 months postoperatively, giving a incidence of graft-infections of 2.5% (5/198) and in total 9% (17/198) having infectious complications. All five patients with graft infection had their graft removed but none required amputation.
During follow-up, median 24 months (IQR 19–26 months), there were 20 graft failures (10%) (Dacron: 11, PTFE: 9) and 24 (12%) deaths. Another 6 patients (3%) were lost to follow-up. A further 6 patients had their graft removed due to graft-infection (n = 5) or graft-occlusion resulting in a redo procedure (n = 1) (Fig. 1). The primary patency rate of the two grafts was not significantly different (log rank: p = 0.35).

The primary patency rates for fluropassivated Dacron and PTFE grafts were 92% (95%-confidence interval: 86–98) and 94% (89–99) at 12 months and 87% (74–95) and 93% (87–99) at 24 months, respectively (Fig. 2, Table 2). Pooling the two groups yielded patency rates (95%CI) at 12 and 24 months of 92% (89–96) and 90% (86–95), respectively. Only 4 of 20 occluded grafts were successfully revascularised after thrombectomy or thrombolysis. Analysis of the occluded grafts (n = 20) revealed that 12 (10%) had...
been operated on for claudication and 8 (11%) for CLI. Of those 12 with claudication and graft occlusion, three eventually had a major amputation while nine (75%) remained stable or improved. Among those operated on for CLI, 2 underwent major amputation following graft occlusion, while 6 remained clinically stable or improved. Finally, 2 further patients had a major amputation due to progression of disease. Thus, in total seven (3.5%) patients underwent major amputation (Dacron \( n = 3 \)/PTFE \( n = 4 \)). There were no cases of donor limb amputation.

Survival (95%CI) in patients operated on for claudication was 98% (95–100%) and 93% (86–99%) at 12 and 24 months, respectively, as compared to the survival in patients operated on for critical limb ischaemia: 88% (79–97%) and 79% (64–94%) (log rank: \( p = 0.0068 \); Hazard ratio 3.6 (95%-CI: 1.5–8.8) after adjustment for gender and age.

**Table 1. Baseline characteristics of 198 femorofemoral bypass**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Fluoro-Dacron</th>
<th>PTFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>( n )</td>
<td>91</td>
<td>107</td>
</tr>
<tr>
<td>Age (median [IQ-range])</td>
<td>71 (65–76)</td>
<td>68 (61–77)</td>
</tr>
<tr>
<td>ABI (median [IQ-range])</td>
<td>0.60 (0.50–0.77)</td>
<td>0.60 (0.42–0.88)</td>
</tr>
<tr>
<td>Indication surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Claudication</td>
<td>60 (66%)</td>
<td>66 (62%)</td>
</tr>
<tr>
<td>Rest pain</td>
<td>23 (25%)</td>
<td>30 (28%)</td>
</tr>
<tr>
<td>Ulcer</td>
<td>8 (9%)</td>
<td>11 (10%)</td>
</tr>
<tr>
<td>Male sex</td>
<td>51 (56%)</td>
<td>50 (47%)</td>
</tr>
<tr>
<td>Never smoked</td>
<td>8 (9%)</td>
<td>15 (14%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not using insulin</td>
<td>9 (10%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>On insulin</td>
<td>1 (1%)</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>History of stroke</td>
<td>2 (2%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>21 (23%)</td>
<td>30 (28%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>31 (34%)</td>
<td>41 (38%)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>5 (6%)</td>
<td>7 (7%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>12 (13%)</td>
<td>21 (20%)</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>23 (26%)</td>
<td>19 (18%)</td>
</tr>
<tr>
<td>Previous amputation</td>
<td>3 (3%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Duration of operation (min)</td>
<td>median [IQ-range]</td>
<td>105 (85–140)</td>
</tr>
</tbody>
</table>

**Fig. 2. Primary patency of the two graft materials (PTFE and Fluoropassivated Dacron).**

**Risk factors for graft occlusion**

As patency of the two grafts did not differ significantly, data were pooled for further analysis. Neither indication for surgery (claudication or critical limb ischaemia) did not affect patency (log rank: \( p = 0.518 \)) nor did runoff (0–49% SFA stenosis vs >50% or occlusion of SFA) (log rank: \( p = 0.143 \)) (Fig. 3). Preoperative donor iliac PTA was not associated to patency rate (Log rank: \( p = 0.440 \)). However, endarterectomy of the donor common femoral artery was associated to an increased risk of graft failure (log rank: \( p = 0.011 \), Hazard ratio 4.1 (95%-CI: 1.4–12.4)).

**Table 2. Patency data**

<table>
<thead>
<tr>
<th>Interval start (months)</th>
<th>Number entering interval</th>
<th>Number exposed to risk</th>
<th>Kaplan Meyer cumulative patency at 1, 6, 12 and 24 months. (95%-CI and SE).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoropassivated Dacron</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>91</td>
<td>88</td>
<td>98% (95–100%) [0.02]</td>
</tr>
<tr>
<td>6</td>
<td>80</td>
<td>80</td>
<td>95% (90–100%) [0.02]</td>
</tr>
<tr>
<td>12</td>
<td>76</td>
<td>74</td>
<td>92% (86–98%) [0.03]</td>
</tr>
<tr>
<td>18+</td>
<td>69</td>
<td>63</td>
<td>87% (74–95%) [0.04]</td>
</tr>
<tr>
<td>PTFE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>107</td>
<td>104</td>
<td>100% (100–100%) [0]</td>
</tr>
<tr>
<td>6</td>
<td>97</td>
<td>95</td>
<td>97% (94–100%) [0.02]</td>
</tr>
<tr>
<td>12</td>
<td>90</td>
<td>87</td>
<td>94% (89–99%) [0.03]</td>
</tr>
<tr>
<td>18+</td>
<td>82</td>
<td>73</td>
<td>93% (87–99%) [0.03]</td>
</tr>
</tbody>
</table>

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Recipient limb ankle-brachial index increased from a median of 0.41 (interquartile range: 0.30–0.54) preoperatively to 0.80 (0.64–0.96) and 0.80 (0.62–0.95) at 12 and 24 months, respectively (Fig. 4). A total of 75% and 77% patients were reported to be free of symptoms at 12 and 24 months respectively (Fig. 5).

Donor limb ankle-brachial index remained unchanged, from a preoperative median value of 0.82 (0.64–0.99) to 0.82 (0.64–1.00) and 0.82 (0.60–1.00) at 12 and 24 months, respectively (Fig. 4). Preoperatively, 78% reported no symptoms related to the donor limb, compared with 79% and 80% at 12 and 24 months postoperatively. One month postoperatively 17 patients (9%) reported onset or worsening of ischaemic symptoms of the donor limb.

**Discussion**

*Patency and survival*

This trial found that a fluoropassivated Dacron graft performed as well as a standard PTFE graft used in the femorofemoral position. Moreover, the crossover bypass seemed durable and effective for treating patients with uni-iliac occlusive disease. In fact, results obtained in patients with critical limb ischaemia equalled those obtained in patients with claudication, although survival was inferior in the former group, as expected\(^\text{19}\) (Table 3). However, the study was underpowered, as we did not reach the planned number of patients, in spite of a prolonged period of patient recruitment.

Only a few studies have compared different graft material for femorofemoral grafts. In 1999, Johnson et al. found no difference in patency of PTFE and preclotted knitted Dacron grafts in a randomised trial.\(^\text{20}\) For many simple Dacron is the gold standard for femoro-femoral bypass and a 3rd arm of simple Dacron would have been tempting but unrealistic due to insufficient available patients. In the only recent randomised controlled trial, Johnson et al. reported the 2 year patency of simple Dacron as 68% (n = 340, CLI: 72%).\(^\text{21}\) A retrospective study found a 2 year patency of Dacron of 79% (n = 86, 48% CLI).\(^\text{18}\) When pooling patients who received Dacron and patients who
received PTFE, the patency rate of the crossover-by-
bypass in our study (90% at 2y) is comparable with
both the unilateral iliac bypass (92% at 2y) and the
aorto-bifemoral bypass (91% at 2y) as reported by
van der Vliet et al. in an retrospective review of 184 uni-
lateral and 350 aorto-bifemoral reconstructions for ob-
structive disease.21

**Risk factors**

Over the years several risk factors for femorofemoral
bypass graft failure have been analysed. Indication
for surgery, quality of inflow, superficial femoral ar-
tery outflow and more recently hypertension have
been identified, though results are not consist-
te.18,22–26 In our prospective study no correlation
between patency and any of the co-variables listed
in Table 1 was observed.

**Complications**

Ever since the introduction of the femorofemoral by-
pass deterioration of donor limb haemodynamics
causing a “steal syndrome” has been a concern.4,27
In our study 9% reported new or worsening of ischae-
mic symptoms in the donor limb, though no signi-
ficant reduction of ABI was recorded. These new
donor limb symptoms represent both “silent” arterial
insufficiency of the donor limb becoming apparent
when the recipient leg was improved, real haemo-
dynamic steal as well as progression of the athero-
sclerotic process. These results are comparable with
others reporting progression of donor limb symptoms
in approximately 10%.28 More than one third (38%)
had an additional inflow improving procedure ex-
plaining why 14% experienced clinical improvement
of both limbs.

Though infectious complications occurred in 9%
the frequency of graft-infections was only 2.5%, com-
parable with results reported in the literature.20,23

There was no evidence to indicate a higher rate of in-
fected complications with Dacron grafts as com-
pared with PTFE, corroborating other randomised
prospective clinical trials.10,14,15,20 However, the abso-
lute number graft-related complications were low and
this randomised study was probably not large enough
to detect a difference between Dacron and PTFE.

The major limitation of this trial is the risk of over-
looking a smaller difference (type II error) due to
under-recruitment, a fact that weakens our conclu-
sions. Nevertheless, the present study is one of the
largest controlled femorofemoral bypass trials ob-
tained within a relative short recruitment-period. In
previous trials, comparing two graft materials for
femoro-femoral bypass20 and femoropopliteal by-
pass11,29 approximately 200 patients were found to
be sufficient, according to power calculations.

Because the randomisation was stratified per
centre, the imbalance between the sizes of the two
arms (91/107) may be a consequence of the unexpect-
edly low number of patients being recruited in some
centres.

Although vascular imaging is the gold standard
for determining patency, only two of the participating
centres had duplex-ultrasound for routine follow-up
of crossover bypass. Instead continued improvements
in the ankle-arm index and/or Doppler insonation
directly over the graft was considered to indicate
patency, both methods that are generally
acceptable.17,20

Although our trial was under-recruited and hence
underpowered, we found that fluoropassivated
Dacron grafts performed as well as PTFE grafts for
femorofemoral cross-over bypass surgery, both
having excellent patency at up to 2 years.

**Founding**

The study was partly financially supported by Sulzer Vascu-
tek Ltd, Inchinnan Renfrewshire, Scotland, UK.

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**Table 3. Primary patency of femorofemoral bypass reported in recent literature**

<table>
<thead>
<tr>
<th></th>
<th>Primary patency</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Critical Limb Ischaemia/</td>
<td>Critical Limb Ischaemia/</td>
</tr>
<tr>
<td></td>
<td>Claudication</td>
<td>Claudication</td>
</tr>
<tr>
<td></td>
<td>1 year</td>
<td>2 years</td>
</tr>
<tr>
<td>Criado 199318</td>
<td>110</td>
<td>88%/82%</td>
</tr>
<tr>
<td>Johnson 199920</td>
<td>340</td>
<td>78%/a</td>
</tr>
<tr>
<td>Purcell 200524</td>
<td>144</td>
<td>88%/93%</td>
</tr>
<tr>
<td>Kim 200526</td>
<td>192</td>
<td>86%/95%</td>
</tr>
<tr>
<td>Elberg 2006</td>
<td>198</td>
<td>90%/95%</td>
</tr>
</tbody>
</table>

* Both CLI and claudicants.
References


Accepted 4th June 2006
Available online 27 June 2006

Eur J Vasc Endovasc Surg Vol 32, October 2006