

# A contemporary meta-analysis of Dacron versus polytetrafluoroethylene grafts for femoropopliteal bypass grafting

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**Background:** The present study provides a contemporary and comprehensive summation of midterm patency rates of polyester (Dacron) or polytetrafluoroethylene (PTFE) grafts in femoropopliteal bypass grafting based on a meta-analysis consisting only of randomized controlled trials.

**Methods:** MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched to identify all randomized controlled trials of Dacron vs PTFE grafts in femoropopliteal bypass grafting. Seven trials were found. Survival data were combined to yield the pooled cumulative primary patency. We estimated the log hazard ratio (HR) for each 1-month interval and then combined the HRs in a stratified way across intervals to obtain an overall log HR for each trial. Study-specific estimates were combined using inverse variance-weighted averages of logarithmic HRs in fixed-effects and random-effects models.

**Results:** The pooled cumulative primary patency of Dacron and PTFE grafts was, respectively, 60.2% (95% confidence interval [CI], 56.4%-64.0%) and 53.8% (95% CI, 46.8%-60.9%) at 3 years, and 49.2% (95% CI, 45.6%-52.7%) and 38.4% (95% CI, 32.2%-44.6%) at 5 years. Pooled analysis of the seven trials demonstrated no difference in HR for graft occlusion with Dacron relative to PTFE grafts (random-effects HR, 0.87; 95% CI, 0.67-1.12;  $P = .27$  for effect;  $P = .03$  for heterogeneity).

**Conclusion:** Either Dacron or PTFE grafts can be used in femoropopliteal bypass grafting with no significant differences in midterm graft patency at 5 years (49.2% vs 38.4%) when the autologous saphenous vein is unavailable. (*J Vasc Surg* 2010;52:232-6.)

Different materials can be used for femoropopliteal bypass grafting, including autologous and homologous grafts from the saphenous vein or the human umbilical vein as well as prosthetic graft materials such as polytetrafluoroethylene (PTFE) or polyester (Dacron) grafts.<sup>1</sup> Meta-analyses<sup>2,3</sup> of randomized controlled trials (RCTs) have demonstrated that saphenous vein graft patency is superior to PTFE graft patency in above-knee femoropopliteal bypass grafting.

A recent meta-analysis of RCTs of Dacron vs PTFE grafts as bypass materials for peripheral vascular surgery showed no evidence of a patency advantage of one synthetic material compared with the other.<sup>1</sup> The study, however, included not only femoropopliteal but also femorofemoral,<sup>4,5</sup> axillofemoral,<sup>5</sup> and aortoiliac<sup>6</sup> bypass grafting. It also did not meta-analyze RCTs of femoropopliteal bypass grafting exclusively. Furthermore, a most recent RCT,<sup>7</sup> not included in the previous meta-analysis,<sup>1</sup> showed that Dacron femoropopliteal bypass graft patency was superior to PTFE graft patency.

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The objective of the present study was to provide a contemporary meta-analysis of patency rates of Dacron and PTFE using only RCTs of extremity bypass below the inguinal ligament. An additional objective was to establish a comprehensive but concise midterm patency benchmark for vascular providers.

## METHODS

**Search strategy.** All RCTs of Dacron vs PTFE grafts in femoropopliteal bypass grafting were identified using a two-level search strategy. First, public domain databases, including MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials, were searched using the PubMed and OVID Web-based search engines. Second, relevant studies were identified through a manual search of secondary sources, including references of initially identified articles and a search of reviews and commentaries. All references were downloaded for consolidation, elimination of duplicates, and further analysis.

The MEDLINE (from January 1966), EMBASE databases (from January 1991), and the Cochrane Library and Central Register of Controlled Trials were searched through October 2009. MeSH keywords included *polyethylene terephthalate*, *polytetrafluoroethylene*, and *randomized controlled trial*. Exploding keywords included *femoropopliteal*, *polyethylene terephthalate*, *Dacron*, *polytetrafluoroethylene*, *PTFE*, and *randomized controlled trial*.

**Study selection and data abstraction.** Studies considered for inclusion met the following criteria: the design was an RCT, the study population comprised patients

undergoing femoropopliteal bypass grafting, and patients were randomly assigned to femoropopliteal bypass grafting with Dacron vs PTFE grafts. Data regarding detailed inclusion criteria, graft type, duration of follow-up, primary patency, and hazard ratio (HR) for graft occlusion were abstracted (as available) from each individual study. The survival (patency) data were extracted from the text, life tables, and survival curves that showed the number of grafts at risk for at least some intervals.

**Statistical analysis.** The pooled cumulative primary patency was yielded by means of a strategy to combine survival data constructed by Pereira et al.<sup>8</sup> In the first step, we redistributed in equal quantities at 1-month intervals grafts censored at intervals >1 month. Next, we obtained the numbers of failed grafts for intervals of 1 month by using the grafts at risk at the start of an interval, the redistributed censored units, and the interval hazard rates. We then calculated the Kaplan-Meier success rates for each series and each month of follow-up and used these rates as treatment effects.

In the second step, we calculated a within-series variance for each monthly success rate in each series; next, we calculated a between-series variance for each month. To obtain pooled measures of treatment effect for each month of follow-up, we used in the third step random-effects modeling. Finally, the product of successive monthly pooled measures of treatment effect allowed us to obtain pooled measures of cumulative success and to calculate approximate standard errors.

Using the method of Parmar et al,<sup>9</sup> we estimated the log HR for each 1-month interval and then combined them in a stratified way across intervals to obtain an overall log HR for each trial. We exploited the fact that when time to an event and censoring are not formally included in the calculation, the HR is estimated by the relative risk. Difficulties with calculating the log HR and its variance arose whenever the effective number of graft occlusions in the Dacron or PTFE arm was zero; that is, there was no graft occlusion in that interval in the Dacron or PTFE arms. To calculate the log HR and its variance in such circumstances, the zero was replaced by a small number of graft occlusions, say  $10^{-6}$ , in that interval.

The overall log HR for each trial was given by a weighted sum of the individual estimates of the log HR during each time interval, where the weights are inversely proportional to the variance of each estimate. Estimated ratios and their variances were used to construct 95% confidence intervals (CIs) for parameters of interest for individual studies and for the summary measure.

Study-specific estimates were combined using inverse variance-weighted averages of logarithmic HRs in both fixed-effects and random-effects models. Where no significant statistical heterogeneity was identified, the fixed-effect estimate was used preferentially as the summary measure. Between-study heterogeneity was analyzed by means of standard  $\chi^2$  tests. Sensitivity analyses were performed to assess the contribution of each study to the pooled estimate by excluding individual trials one at a time and recalculating

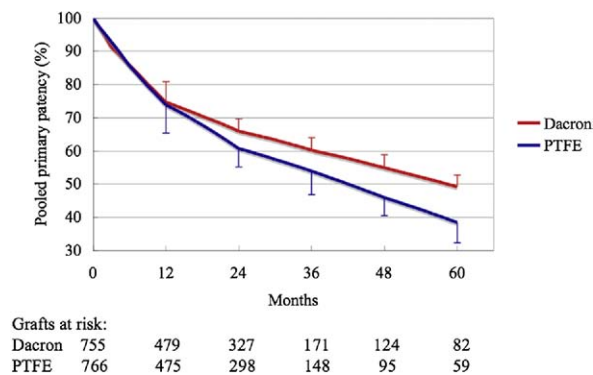


Fig 1. Pooled primary patency. PTFE, polytetrafluoroethylene.

the pooled HR estimates for the remaining studies. Publication bias was assessed graphically using a funnel plot and mathematically using a linear regression test, according to the method of Egger et al.<sup>10</sup> All analyses were conducted using Excel 11.5.0 software (Microsoft Corp, Redmond, Wash), Review Manager (RevMan) 5.0 software,<sup>11</sup> and MIX 1.61 software.<sup>12</sup>

## RESULTS

Our search identified seven RCTs<sup>7,13-18</sup> of Dacron vs PTFE grafts in femoropopliteal bypass grafting. Our meta-analysis included data on 1521 patients, of whom 755 were randomized to femoropopliteal bypass grafting with Dacron and 766 with PTFE. Dacron graft types included collagen-impregnated,<sup>7,17</sup> gelatin-sealed (gelatin-coated),<sup>13,18</sup> collagen-coated heparin-bonded,<sup>14</sup> fluoropolymer-coated,<sup>15</sup> and unsealed.<sup>16</sup> Expanded PTFE grafts were used in two trials.<sup>7,17</sup> Three<sup>7,13,17</sup> of the seven RCTs consisted of patients undergoing above knee femoropopliteal bypass grafting only, whereas four trials included below knee grafting in 14%,<sup>14</sup> 27%,<sup>16</sup> 31%,<sup>18</sup> and 41%<sup>15</sup> of patients, respectively. Duration of follow-up was 2 years,<sup>13</sup> 3 years,<sup>15</sup> 4 years,<sup>16,18</sup> 5 years,<sup>14,17</sup> and 10 years.<sup>7</sup> Although only van Det et al<sup>7</sup> reported 10-year results, we abstracted the 5-year outcomes because the other six RCTs provided <5-year results.

The pooled cumulative primary patency of Dacron and PTFE grafts was respectively 74.7% (95% CI, 68.5%-80.8%) and 73.9% (95% CI, 65.4%-82.4%) at 1 year; 65.9% (95% CI, 62.2%-69.7%) and 60.7% (95% CI, 55.1%-66.3%) at 2 years; 60.2% (95% CI, 56.4%-64.0%) and 53.8% (95% CI, 46.8%-60.9%) at 3 years; 54.9% (95% CI, 51.0%-58.8%) and 45.9% (95% CI, 40.4%-51.4%) at 4 years; and 49.2% (95% CI, 45.6%-52.7%) and 38.4% (95% CI, 32.2%-44.6%) at 5 years (Fig 1).

Two<sup>7,13</sup> of the seven RCTs demonstrated a statistically significant benefit of Dacron over PTFE grafts for patency in patients undergoing femoropopliteal bypass grafting. Only the trial by Robinson et al (2003),<sup>15</sup> which used fluoropolymer-coated Dacron grafts, demonstrated a statistically significant reduction in patency with Dacron compared with PTFE grafts. Pooled analysis of the seven trials

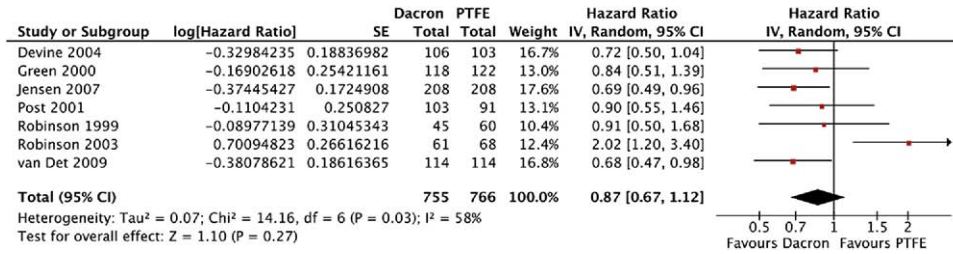


Fig 2. Forest plot shows the hazard ratio for graft occlusion of Dacron vs polytetrafluoroethylene (PTFE) grafts in all seven trials. CI, Confidence interval; IV, inverse variance; SE, standard error.

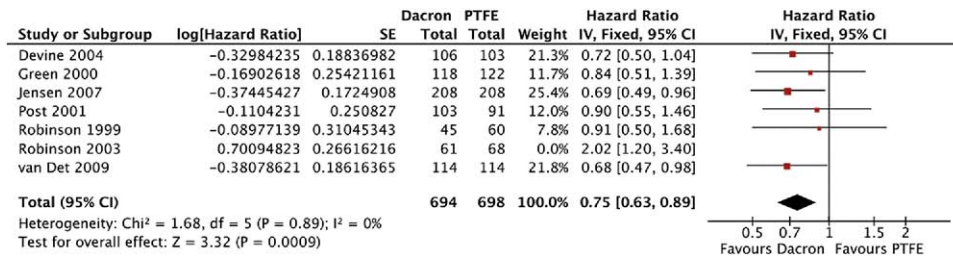


Fig 3. Forest plot shows the hazard ratio for graft occlusion of Dacron vs polytetrafluoroethylene (PTFE) grafts in six trials, except for the trial by Robinson et al (2003).<sup>15</sup> CI, Confidence interval; IV, inverse variance; SE, standard error.

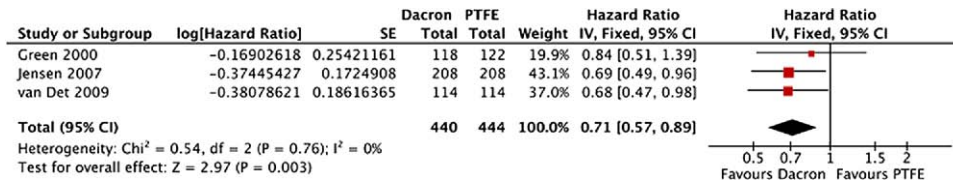


Fig 4. Forest plot shows the hazard ratio for graft occlusion of Dacron vs polytetrafluoroethylene (PTFE) grafts in three trials consisting exclusively of above-knee femoropopliteal bypass grafting. CI, Confidence interval; IV, inverse variance; SE, standard error.

demonstrated no difference in hazard for graft occlusion with Dacron relative to PTFE grafts (random-effects HR, 0.87; 95% CI, 0.67-1.12; P = .27 for effect; P = .03 for heterogeneity; Fig 2).

We performed several sensitivity analyses to assess the effect of qualitative heterogeneity in trial design and patient selection on the pooled effect estimate. Exclusion of any single trial from analysis, except for the trial by Robinson et al,<sup>15</sup> did not substantively alter the overall result of our analysis. Eliminating the Robinson et al trial substantially changed the pooled point estimate (fixed effects HR, 0.75; 95% CI, 0.63-0.89; P = .0009 for effect; P = .89 for heterogeneity; Fig 3).

When data from the three trials<sup>7,13,17</sup> consisting exclusively of above-knee femoropopliteal bypass grafting were pooled (representing 884 patients), Dacron grafts were associated with a statistically significant reduction in hazard for graft occlusion relative to PTFE grafts (fixed effects HR, 0.71; 95% CI, 0.57-0.89; P = .003 for effect; P = .76 for heterogeneity; Fig 4). To assess publication bias, we generated a funnel plot of the effect size vs the standard error

for each trial (Fig 5) and found no evidence of significant publication bias (P = .102 by Egger regression test).

## DISCUSSION

The results of our analysis suggest that there may be no difference in patency between Dacron and PTFE grafts in femoropopliteal bypass grafting at 5 years (49.2% vs 38.4%). Our analysis must be viewed in the context of its limitations:

First, the Dacron arms included collagen-impregnated, gelatin-sealed (gelatin-coated); collagen-coated, heparin-bonded; fluoropolymer-coated; and unsealed grafts. Excluding the trial that used fluoropolymer-coated Dacron grafts demonstrated a statistically significant reduction in the hazard for graft occlusion with Dacron relative to PTFE grafts.

Second, three of the seven trials included in our analysis consisted of patients undergoing above-knee femoropopliteal bypass grafting only, whereas four trials included below-knee grafting. Combining the three trials consisting of above-knee femoropopliteal bypass grafting exclusively showed a

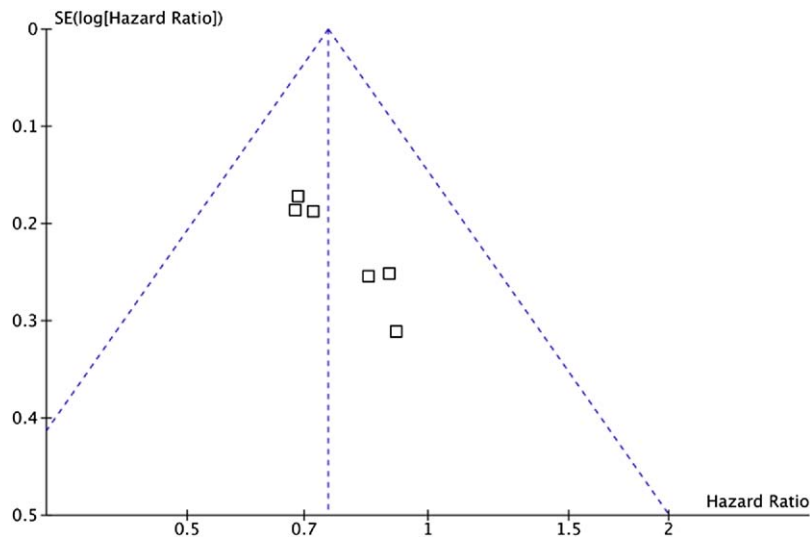


Fig 5. Funnel plot shows the effect size vs the standard error (SE).

statistically significant benefit of Dacron over PTFE grafts for occlusion.

Despite these limitations, however, our study has merit as a contemporary, comprehensive summation of 2- to 5-year patency rates using the best studies available (ie, RCTs and infrainguinal only).

Although the saphenous vein is considered to be the gold standard for below-knee femoropopliteal bypass grafting, there had been controversy about whether prosthetic materials (PTFE, Dacron, and the human umbilical vein) are equivalent to the autologous saphenous vein for above-knee femoropopliteal bypass grafting.<sup>3</sup> Prosthetic bypass material, however, may be needed if the saphenous vein is absent or not suitable for bypass grafting.

Klinkert et al<sup>3</sup> performed systematic review of studies comparing the patency of saphenous vein and PTFE as bypass material for above-knee femoropopliteal bypass. When only RCTs were considered, venous bypasses were superior to PTFE bypasses at all intervals studied. The primary patency rate of venous and PTFE bypasses was 80% and 69%, respectively, after 2 years and was 74% and 39%, respectively, after 5 years.

Those authors, however, could not perform a statistical comparison of the patency rates for vein and PTFE; therefore, we<sup>2</sup> performed an updated meta-analysis of RCTs. The pooled primary graft patency of saphenous vein and PTFE were 82.6% and 74.6% at 2 years (risk ratio for occlusion in PTFE vs saphenous vein, 1.34; 95% CI, 1.05-1.70;  $P = .0198$ ) and 76.4% and 56.1% at 5 years (risk ratio, 1.68; 95% CI, 1.34-2.11;  $P < .0001$ ), respectively. These results of the meta-analyses suggest that saphenous vein graft patency is superior to PTFE graft patency in above-knee femoropopliteal bypass grafting.

Meanwhile, PTFE with a vein cuff interposed at the distal anastomosis is a reasonable substitute when vein is not available.<sup>19,20</sup> Heparin-bonded expanded PTFE grafts

also provide good long-term results in infragenicular bypasses<sup>21</sup> and had primary patency results that were not significantly different from those for saphenous vein grafts.<sup>22</sup> Furthermore, the patency rates of PTFE grafts to infrageniculate vessels may be improved by effective anticoagulation with warfarin, and this improved patency rate may also result in improved limb salvage and further supports the use of PTFE grafts for critical limb ischemia when autogenous vein is not available.<sup>23</sup>

The next issue is which Dacron or PTFE grafts should be used when the autologous saphenous vein is unavailable. Roll et al<sup>1</sup> performed a systematic review and meta-analysis of RCTs to compare the effectiveness of Dacron and PTFE grafts in peripheral vascular bypass surgery. Meta-analysis on the comparison of PTFE vs Dacron grafts yielded no differences with regard to primary patency rates (HR for occlusion in PTFE vs Dacron, 1.04; 95% CI, 0.85-1.28;  $P = .72$ ). The meta-analysis, however, included not only femoropopliteal but also femorofemoral,<sup>4,5</sup> axillofemoral,<sup>5</sup> and aortoiliac<sup>6</sup> bypass grafting.

The results of RCTs of Dacron vs PTFE grafts for femoropopliteal bypass grafting are controversial. The results of our meta-analysis of RCTs of Dacron vs PTFE grafts exclusively in femoropopliteal bypass grafting suggest that Dacron and PTFE grafts have similar midterm (2- to 5-year) primary patency. However, the RCT by van Det et al<sup>7</sup> showed that Dacron femoropopliteal bypass grafts had superior patency compared with PTFE grafts during prolonged 10-year follow-up. Long-term (>5-year) follow-up results may be needed to assess which graft should be used in femoropopliteal bypass grafting.

Only the trial by Robinson et al<sup>15</sup> demonstrated a statistically significant occlusion increase with Dacron over PTFE grafts, and our sensitivity analysis eliminating that particular trial resulted in a statistically significant reduction in hazard for graft occlusion with Dacron relative to PTFE

grafts. Lower primary patency of the fluoropolymer-coated Dacron graft in the Robinson et al<sup>15</sup> trial was due to graft thrombosis mostly in the first month. The reason for the early thrombosis in the fluoropolymer-coated Dacron graft is unknown; however, it occurred more frequently in patients with previously documented poor prognostic indicators of graft survival, namely, critical limb ischemia, below-knee distal anastomosis, and grafts with a smaller diameter (6 mm). A possible explanation is that differences between graft types are more likely to be detected in patients with poor prognostic indicators and a higher rate of occlusion because the statistical power of a study for a given number of patients is greater if the occlusion rate is higher.<sup>15</sup>

## CONCLUSIONS

Either Dacron or PTFE grafts can be used in femoropopliteal bypass grafting with no significant differences in midterm graft patency (49.2% vs 38.4% at 5 years) when the autologous saphenous vein is unavailable. Dacron grafts, however, when not fluoropolymer-coated or used in above-knee bypass grafting, may be superior to PTFE grafts for patency.

## AUTHOR CONTRIBUTIONS

Conception and design: HT, TU

Analysis and interpretation: HT, HM, MM

Data collection: HM, MM, SG

Writing the article: HT

Critical revision of the article: HT, TU

Final approval of the article: HT, HM, MM, SG, TU

Statistical analysis: HT, HM, MM

Obtained funding: Not applicable

Overall responsibility: HT

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