

CORRESPONDENCE



Local Paclitaxel Delivery in Peripheral Vascular Disease

TO THE EDITOR: With regard to the Local Taxane with Short Exposure for Reduction of Restenosis in Distal Arteries (THUNDER) trial, reported by Tepe et al. (Feb. 14 issue),¹ paclitaxel, like endovascular brachytherapy, may postpone rather than inhibit restenosis. Morphologic follow-up for more than 6 months therefore seems desirable. The usefulness of relying on target-lesion revascularization as an end point in studies of peripheral vascular disease is debatable,² particularly in an unblinded trial, such as the THUNDER study, which might be prone to bias. Indeed, a 6-month reintervention rate of 37% in the control group (mean lesion length, 74 mm) seems high as compared with a 12-month reintervention rate of 31% in the control group of the Balloon Angioplasty versus Stenting in the Superficial Femoral Artery (ABSOLUTE) trial (mean treated length, 127 mm).^{3,4} Furthermore, over the course of 6 months, the ankle-brachial indexes and Rutherford stages in the THUNDER control group worsened only slightly. It therefore seems remarkable that 20 of

21 patients with binary restenosis in this group were symptomatic and required target-lesion revascularization. In our experience, many patients with restenosis remain asymptomatic. Finally, in Figure 1 of the article by Tepe et al., Panels B and E (postintervention angiograms) show what appear to be technical failures according to the authors' definitions, and projections of the follow-up angiograms (Panels C and F) were not the same as the baseline studies.

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1. Tepe G, Zeller T, Albrecht T, et al. Local delivery of paclitaxel to inhibit restenosis during angioplasty of the leg. *N Engl J Med* 2008;358:689-99.
2. Diehm N, Baumgartner I, Jaff M, et al. A call for uniform reporting standards in studies assessing endovascular treatment for chronic ischaemia of lower limb arteries. *Eur Heart J* 2007;28:798-805.
3. Schillinger M, Sabeti S, Loewe C, et al. Balloon angioplasty versus implantation of nitinol stents in the superficial femoral artery. *N Engl J Med* 2006;354:1879-88.
4. Schillinger M, Sabeti S, Dick P, et al. Sustained benefit at 2 years of primary femoropopliteal stenting compared with balloon angioplasty with optional stenting. *Circulation* 2007;115:2745-9.

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TO THE EDITOR: Tepe et al. have assessed a promising technology aimed at inhibition of restenosis after femoropopliteal angioplasty. The clinical severity of peripheral arterial disease was gauged with the use of the classification suggested by Rutherford et al.,¹ with ratings from 0 to 6 and higher numbers indicating worse disease.

The authors summarize Rutherford stages as means and standard deviations. This implies that the data are of a continuous nature. However, Rutherford stages are ordinal variables,^{1,2} with

definitions of stages based on a combination of signs and symptoms. Therefore, means are difficult to interpret. Rather, data should be summarized transparently as numbers and percentages of patients in each stage and then analyzed with the use of contingency tables.^{2,3}

In addition, the authors use vessel patency as an end point, the definition of which is the presence of uninterrupted flow.¹ According to this definition, high-grade restenosis would be considered to indicate successful treatment, which is inappropriate for head-to-head trials of devices used for endovascular revascularization.² These concerns highlight the need for uniform reporting standards for the evaluation of different approaches to endovascular revascularization.²

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1. Rutherford RB, Flanigan DP, Gupta SK, et al. Suggested standards for reports dealing with lower extremity ischemia. *J Vasc Surg* 1986;4:80-94. [Erratum, *J Vasc Surg* 1986;4:350.]
2. Diehm N, Baumgartner I, Jaff M, et al. A call for uniform reporting standards in studies assessing endovascular treatment for chronic ischaemia of lower limb arteries. *Eur Heart J* 2007; 28:798-805.
3. Schillinger M, Sabeti S, Loewe C, et al. Balloon angioplasty versus implantation of nitinol stents in the superficial femoral artery. *N Engl J Med* 2006;354:1879-88.

THE AUTHORS REPLY: Schillinger and Minar express concern about the long-term outcome of single-dose therapy with a drug that has immediate bioavailability; we share their concern. After 2 years, the proportion of patients in the group treated with coated balloons who underwent target-lesion revascularization was significantly lower than that in either of the other two groups (Table 2 of our article). Blinding of the clinical investigators to the different devices might have been desirable for this end point but was not possible. Two-year angiographic data, which are now available, indicate target-lesion restenosis of 70% or more in 2 of 28 patients (7%) without previous target-lesion revascularization in the group treated with coated balloons, as compared with 6 of 19 patients (32%) in the control group. This confirms a persistent benefit.

The slightly higher 12-month reintervention

rate in our trial than in the trial by Schillinger et al. may be explained by the fact that we did not exclude previously stented lesions and that it is difficult to achieve exactly the same results as those reported by other investigators. In their letter, Schillinger and Minar contrast lesion length from our study with treated length from theirs; but when the mean lesion lengths in the two studies are compared, the difference is smaller (92 ± 64 mm in the control group in the study by Schillinger et al. vs. 74 ± 67 mm in our control group). The 12-month rate of target-lesion revascularization in our trial was 48% in the control group and 35% in the group treated with paclitaxel in the contrast medium, which is probably ineffective, versus 31% in the control group in the study by Schillinger et al.

The core laboratory findings for the angiograms presented in Figure 1 of our article were as follows: for the segment defined as the target lesion, residual stenosis after percutaneous transluminal angioplasty was 6.7%, with a minimal lumen diameter of 4.9 mm, in the patient in the control group (Panel B) versus 24% and 4.0 mm in the patient treated with a coated balloon (Panel E).

We agree with Diehm et al. regarding the nature of Rutherford data and the definition of patency. However, analysis of Rutherford data by class would require a lengthy presentation, and comparison of these data with the use of the Cochran–Mantel–Haenszel test did not yield different results. We will add only that the Cochran–Mantel–Haenszel test indicated a greater improvement in Rutherford stage from baseline to 6 months for the group treated with coated balloons as compared with the control group ($P=0.03$). Although patency has limitations as an end point, it was only one of several angiographic findings to be assessed (see Table 2 of our article).

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