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Routine stent implantation vs. percutaneous transluminal angioplasty in femoropopliteal artery disease: a meta-analysis of randomized controlled trials

We read with great interest the article on routine stent implantation vs. plain balloon angioplasty in femoropopliteal artery obstructions by Kasapis *et al.*[1]

The endpoints of interest in the present meta-analysis were immediate technical success, rate of target vessel revascularization (TVR) as well as restenosis rates.

From our perspective, substantial heterogeneity of endpoint definitions in individual trials included in the present meta-analysis clearly hamper both the deduction of meaningful conclusions and the generalizability of results from the present meta-analysis.[2–4]

There were subtle but crucial differences among included individual studies regarding all three endpoints analysed. First, there was a substantial variability in the definitions of immediate technical success by residual stenosis thresholds between <20 and $<50\%$ rendering a direct comparison of results very challenging.[2]

Second, TVR was defined as 'repeat revascularization of the same superficial femoropopliteal artery (SFPA), proximal or distal to, or involving the index lesion, or surgical bypass of the SFPA'. In this context, the authors state that 'TVR, arguably, represents a more robust endpoint than restenosis by itself, as it is a decision driven by both the clinical status and by the angiographic or Doppler evidence of restenosis'. We feel that exactly the contrary is the case. It is obvious that TVR is influenced by many factors such as patient or physician preference or various other circumstances such as local reimbursement policy, especially in patients treated for claudication.[2] Thus, in the absence of a specific analysis of target lesion revascularization, providing only TVR rates does not allow to differentiate between restenosis in the index segment (which is attributable to the revascularization method to be scrutinized) and progression of atherosclerosis leading to the need for further revascularization not associated with the index procedure.[2–4] Therefore, solely reporting TVR rates does not allow for a precise outcome analysis related to the initially treated target lesion.

Third, binary restenosis in the present meta-analysis was defined as 'a reduction in the luminal diameter of more than 50% on follow-up conventional angiography or restenosis more than 50%, as determined by follow-up duplex ultrasound peak velocity ratio, except for one study that used the cut-off of 70% of angiographic restenosis'. Remarkably, four included studies used angiographic follow-up, four used duplex follow-up, and two studies used both. Unfortunately, the authors fail to describe that the definition of restenosis, however, varied substantially based on duplex criteria applied.[2] The peak systolic velocity ratio cut-off for restenosis ranged from 1.5[5] to $\geq$2.5[6] in included trials.

In conclusion, we feel that this article does more to confuse than to enlighten the ongoing debate about the clinical utility of modern stents in endovascular revascularization of femoropopliteal arteries. These concerns once again highlight the clear need for uniform reporting standards for the scientific evaluation of various innovative endovascular treatment approaches.[2–4]

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Routine stent implantation vs. percutaneous transluminal angioplasty in femoropopliteal artery disease: a meta-analysis of randomized controlled trials: reply

We are thankful to Diehm *et al.* for their interest in our meta-analysis on routine stent implantation vs. percutaneous transluminal angioplasty in femoropopliteal artery

disease published in the January issue of the *European Heart Journal*.[1] Several key issues are raised about the endpoint definitions used in individual studies included in the meta-analysis. We concur about the need for uniform reporting standards for the scientific evaluation of various innovative endovascular treatment approaches and congratulate Diehm *et al.*[2] on their work to that effect. However, this need neither hampers the deduction of meaningful conclusions nor nullifies the importance of the existing randomized controlled trials published in the current literature. In addition, we recognize that our meta-analysis is susceptible to the major limitations of all meta-analyses, including the difficulties in comparing the results because of different study populations, study designs, and reporting methods as well as the absence of individual patient data and it invokes the need for large adequately powered, high-quality randomized trial. Despite the inherent limitations, as the number of published clinical trials continues to increase, a meta-analysis can provide a systematic synthesis of research results through an explicit, quantitative, and more rigorous approach than the traditional method of narrative research review.[3]

Furthermore, the subtle differences in the definitions of endpoints in individual studies would not statistically impede the results since the same definitions were applied to both treatment arms in each study. Moreover, the assessment of immediate technical success or binary restenosis in real life are based on visual estimation with a reported intra- and inter-observer variability of an average of 22.76% with an average SD of 8.99.[4] Diehm and Baumgartner also criticize the use of studies with different Doppler criteria for restenosis. Notably, all four studies that used only duplex follow-up defined restenosis uniformly as a peak systolic velocity ratio (PSVR) ranging between >2 and ≥ 2.5.[5–8] The only study that used different PSVR of ≥ 1.5 included a small number of patients ($n = 53$) and there was additionally angiographic follow-up at 6 months.[9] In addition, influence analysis suggests that exclusion of this (or any other trial) would not significantly change the results.

We disagree with Diehm and Baumgartner's assertion that target lesion revascularization (TLR) is superior to target vessel revascularization (TVR) as an endpoint. Arguably, from the perspective of the patient, clinician, and resource utilization, the more important endpoint is the need for ipsilateral reintervention in the same vessel, rather than the exact distinction between TVR and TLR. The pre-eminence of TVR over TLR has been recognized by clinical trialists evaluating coronary and non-coronary revascularization and all the trials included in our meta-analysis uniformly reported TVR with only a few reporting TLR. In addition, there is no apparent reason that why in the setting of a randomized controlled trial the TVR would be influenced more by factors, such as physician or patient preference or local reimbursement policy compared with TLR. We are in complete agreement that a specific analysis of TLR and TVR would have allowed to differentiate between restenosis in the index segment vs. progression of atherosclerosis elsewhere in the vessel. Although mechanistically interesting, the differentiation between TVR and TLR means little for the patient who needs a second procedure.

In conclusion, despite the acknowledged limitations, we feel that the meta-analysis is conducted with rigour, the results are extant, and it provides a thorough and critical review of the existing randomized controlled trials underlining the current guidelines from both the American College of Cardiology and the Trans-Atlantic Intersociety Consensus that balloon angioplasty is the preferred initial endovascular treatment of symptomatic femoropopliteal disease with provisional stenting after a suboptimal angioplasty result.

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