A meta-analytical approach for the treatment of in-stent restenosis

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See doi:10.1016/S1095-668X(02)00202-6, for the article to which this editorial refers.

As noted repeatedly, the treatment of in-stent restenosis remains one of the most vexing shortcomings in interventional cardiology. Coronary restenosis is often manifested by symptom recurrence, which is translated into an increased rate of repeat revascularization.

In this issue, Radke and colleagues report the results of a well-conducted meta-analysis with data gathered from published reports of 28 different studies. These studies included a total of 3012 patients with in-stent restenosis treated with six different modalities (stent-in-stent, rotational atherectomy, balloon angioplasty, laser angioplasty, directional atherectomy and vascular brachytherapy) and their clinical outcome at a follow-up of 9±64 months. Any major adverse cardiac event (MACE) as defined by death, myocardial infarction, and target lesion revascularization (TLR) occurred in 30% of the patients, irrespective of the type of device used. In 90% of these cases, this MACE rate was driven by the need for TLR as a result of restenosis. In the meta-regression analysis, post-procedural diameter stenosis (DS post) was significantly correlated with the MACE rate. The lower the DS post, the lower the MACE rate.

After the adjustment of confounding factors (lesion length, pre-procedural diameter stenosis and diabetes), vascular brachytherapy was associated with a non-significant reduction of 16.9% in the probability of MACE, as compared to balloon angioplasty. The authors concluded that balloon angioplasty should be the preferred modality for the treatment of in-stent restenosis, particularly in focal lesions and that vascular brachytherapy should be considered in patients with diffuse in-stent restenosis.

Several other issues deserve further credit and are worth mentioning in the light of recently published data. First, the authors are to be commended for addressing the difficult issue of how to treat in-stent restenosis, an area where little randomized controlled clinical data is available. However, if one looks specifically at intracoronary radiation for in-stent restenosis, the authors included only four studies in this analysis.

These studies were two registries (Beta WRIST and Lausanne registry) and two randomized clinical trials (WRIST and GAMMA-1). In the mean time, several additional studies have emerged. A pooled analysis from the trials (SCRIPPS-2, WRIST, GAMMA-1, GAMMA-2, long WRIST, long WRIST high-dose and SVG WRIST) demonstrated a 36% relative reduction (RR) in MACE favouring brachytherapy. Similarly, a pooled analysis from the trials (SCRIPPS-2, WRIST, GAMMA-1, GAMMA-2, long WRIST, long WRIST high-dose and SVG WRIST) demonstrated a 36% RR and finally, when pooling the trials, altogether, a 35% RR was exhibited. These data clearly support vascular brachytherapy as the preferred treatment of in-stent restenosis.

Second, comparing individual treatment modalities (stent-in-stent, rotational atherectomy, laser angioplasty, directional atherectomy and vascular brachytherapy) to balloon angioplasty without taking into account the angiographic pattern of in-stent restenosis may be inappropriate. In this respect, the authors fall short in correlating the angiographic presentation (lesion length and...
geographic location of neointimal proliferation relative to the initially implanted stent) of in-stent restenosis (focal, diffuse intrastent, diffuse proliferative or total occlusion) with the subsequent need for TLR, which in turn, is the clinical event that mainly drives the MACE rate, as previously mentioned. The pre-intervention angiographic pattern of in-stent restenosis is a powerful predictor of future TLR; as the 1-year rate of TLR increases in parallel with increasing severity of angiographic in-stent restenosis, ranging from 19% for patients with focal in-stent restenosis to 83% for patients with total occlusions.5

Finally, registry data on sirolimus-eluting stents for the treatment of in-stent restenosis have also become recently available, and thus far 41 patients (16 in Rotterdam, The Netherlands and 25 in Sao Paulo, Brazil) were treated with a sirolimus-eluting stent for in-stent restenosis. The 1-year MACE rate in these patients was 9.8%. These results, although based on a small number of patients, are extremely encouraging and should pave the way for randomized clinical trials of drug-eluting stents for the treatment of in-stent restenosis, which perhaps will be its most important and ultimate challenge.

References