The bigger, the better: true also for in-stent restenosis?

Stent implantation has become the most frequent percutaneous coronary intervention in Europe, with stents implanted in more than 60% of all patients treated with catheter-based interventions (Berhard Meier, PTCA Registry Working Group of Coronary Circulation, personal communication). The dark side of this treatment, in-stent restenosis, grows at the same pace or even at a faster pace as longer and more complex lesions are treated with stents. Unlike restenosis after balloon angioplasty, in-stent restenosis is a challenge to the interventionist because it consists of an exuberant intimal growth inside a rigid metallic cage, and responds poorly to conventional balloon dilatation with a risk of recurrent restenosis as high as 42%[2] and 63%[3] when diffuse proliferation along the stented segment is present.

Many studies have examined the predictors and mechanisms of in-stent restenosis and patient as well as lesion related factors have been established[4–6]. Schiele et al.[7] have the merit to be one of the first groups to study the predictors of clinical outcome after treatment of in-stent restenosis using intracoronary ultrasound, an imaging modality which allows precise evaluation of neointimal growth and stent expansion. The conclusion of this study is as simple as provocative: the only predictive factor for a new late clinical event after treatment of in-stent restenosis is the presence of a small lumen area at the end of the procedure. As suggested for all percutaneous coronary interventions[8], and stent implantation in particular[4–6], a large final lumen offers the best chance of a good late clinical outcome, irrespective of the mechanism of that lumen gain (tissue ablation or extrusion, further stent expansion).

The most logical approach to a proliferative process induced by wall stretching and intimal injury would be to remove as much intimal tissue as possible and avoid further injury with aggressive balloon dilatation and wall overstretch.

Unfortunately, nature rarely follows our logic, as shown by this study and confirmed in a careful European randomized trial, which compared balloon angioplasty alone vs aggressive rotational atherectomy followed by low pressure balloon angioplasty for treatment of in-stent restenosis (ARTIST trial, Angioplasty versus Rotablation for Treatment of Intra-STent Stenosis). This study included more than 300 patients with diffuse (>10 mm) in-stent restenosis, restudied angiographically at 6 months and its final results, presented by Dr vom Dahl at the last European Society of Cardiology Congress in Barcelona, showed a similar final lumen gain with the two treatment modalities and a restenosis rate of 51% and 70%, respectively.

Better results have been reported in other consecutive series with rotational atherectomy, but the persistence of relatively high restenosis rates (49% and 34%)[9,10] suggests a limited benefit of plaque removal for the treatment of in-stent restenosis.

Three possible criticisms can be made to the conclusion of this study:

1. Since even the largest burr available for coronary use (2·50 mm) can remove only a small fraction of the neointimal growth observed inside a stent expanded to 3·5–4·0 mm, you may argue that a more complete shaving of the plaque up to the stent surface can be more effective. In this study the intimal reduction of 2·1 mm² after rotational atherectomy with large burrs (burr to artery ratio=0·75) and further balloon dilatation is equal to 38% of the pre-treatment stent area, with an additional lumen gain in comparison with PTCA alone of 0·15 mm² when assessed by angiography and 0·50 mm² by intravascular ultrasound. This criticism has limited practical interest for the time being, since directional atherectomy is applicable only in a minority of restenotic lesions after stent placement[11] and none of the other devices applied clinically (excimer laser[12], pull-back atherectomy, X-Sizer) appears to achieve complete and safe removal of the neointimal growth.

2. The second criticism concerns the patient and lesion characteristics in this study, which were not representative of an aggressive process of in-stent restenosis, with an average lesion length of 10·0 ± 6·0 mm and the absence of total occlusions or fibro-proliferative restenoses, but with involvement of stent margins.

3. In this study measurements were performed immediately after treatment, but there is evidence of progressive plaque prolapse through the stent struts starting immediately after treatment of in-stent restenosis, a phenomenon named ‘instant’ in-stent restenosis. This phenomenon has been shown to induce a 20% reduction in immediate lumen gain 42 min after treatment and is observed also in patients treated with aggressive atheroablation[13].

The practical message of this study is that we should use the simplest, cheapest and most efficient technique to achieve the largest possible lumen within
the stent. This goal is not easy to achieve, as shown by the final lumen area (4.9 mm²) reported in this study, 32% smaller than the lumen area obtained immediately after stent implantation (7.2 mm²). This study certainly does not discourage the use of ablative techniques, provided that they can significantly improve lumen gain and it does not offer elements to judge whether the implantation of a second stent is beneficial to reduce the restenosis rate by restoring a large final lumen or detrimental by eliciting a further hyperplastic response.

Today, the impetus for treatment of in-stent restenosis is not in employment of more efficient mechanical interventions, but in the development of techniques to inhibit the proliferative response (radiation therapy[14,15], gene therapy). As long as this treatment does not become widely available, long-term efficacy and safety will not be proven. We have to work for in-stent restenosis in the same way as we work for all other percutaneous interventions: go for the bigger and hope for the better.

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References