

## LETTERS TO THE EDITOR

# Paclitaxel-Eluting Balloons for Sirolimus-Eluting Stent Restenosis

We read with interest the randomized study by Habara et al. (1) comparing paclitaxel-eluting balloon (PB) (n = 25) with conventional balloon (BA) (n = 25) in patients suffering from sirolimus-eluting stent (SES) in-stent restenosis (ISR). In these patients, PB provided a dramatic improvement in angiographic parameters at late follow-up, compared with BA. This information is timely, because ISR after drug-eluting stent (DES) implantation is becoming a growing concern due to the widespread use of DES in increasingly complex anatomic scenarios (2). This study nicely complements a pioneer randomized trial where PB were also strikingly superior to BA in patients with bare-metal ISR (3). Actually, in-segment late angiographic loss after PB (0.03 mm) was even lower than that found in the present study in SES ISR (0.18 mm) (3). Considering the clinical implications of this small yet provocative study, clarifying some methodological issues would be of major practical value.

First, SES ISR frequently locates at the stent edges (4). In this regard, data on the presence and implications of edge ISR with respect to the relative efficacy of PB over BA would be of major interest (5). Second, SES underexpansion remains a frequent trigger for subsequent ISR (6). Therefore, if available, intravascular ultrasound data on the degree of stent expansion in these patients would be also of value. Likewise, information on inflation pressures, both during pre-dilation and especially at final optimization, would be of great practical value, especially considering that relatively low pressures are recommended with PB. Third, after DES implantation, late angiographic findings (late loss, minimal lumen diameter, percentage diameter stenosis) usually do not follow a normal distribution (7). It would be of interest to know whether similar angiographic distribution patterns are seen after PB.

The excellent results obtained with PB in the current study are reassuring and open new venues in the management of patients with DES ISR. We fully agree (2) with the suggestion that further studies are warranted to confirm the efficacy of PB in ISR affecting other DES types and also to assess the relative value of PB versus repeat DES implantation (i.e., RIBS IV [Restenosis Intrastent in drug-eluting stents: paclitaxel-eluting Balloon versus everolimus-eluting Stent] randomized study) in this challenging anatomic setting.

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## Reply

We thank Dr. Alfonso and colleagues for their concern and suggestions based on our recent publication (1). We appreciate their suggestions and have performed the following analysis.

Focal restenosis occurs frequently at stent edges after drug-eluting stent (DES) implantation (2). In the paclitaxel-eluting balloon (PEB) group of our study, stent edge restenosis affected 3 of the 13 focal restenotic lesions. No recurrent restenosis occurred in this group. We cannot conclude that PEB was effective for stent edge restenosis, because of the small sample size in this study. We believe stent edge restenosis should be handled carefully to not cause coronary dissection.

Stent underexpansion is considered the cause of recurrent restenosis (3). We did not have adequate intravascular ultrasound data that could assess DES restenosis at the time of PEB use. In our study, pre-dilation was performed with a noncompliant balloon in all lesions. Pre-dilation pressure was higher in the conventional balloon angioplasty group than in the PEB group ( $21.4 \pm 3.7$  atm vs.  $19.2 \pm 6.4$  atm;  $p = 0.001$ ). Balloon artery ratio was similar ( $1.08 \pm 0.07$  vs.  $1.10 \pm 0.08$ ;  $p = 0.3$ ) between the groups. In the PEB group, inflation pressure for the SeQuent Please balloon catheter (B. Braun Melsungen AG, Vascular Systems, Berlin, Germany) was  $13.0 \pm 2.4$  atm. We believe that obtaining a high acute gain and avoiding stent underexpansion by

high-pressure pre-dilation are essential for minimizing the risk of recurrent restenosis and target lesion revascularization in patients with in-stent restenosis lesions. We used PEB with relatively high pressure, because we believed that it might be more effective for drug delivery into the vascular wall. In our study, we had no major dissection after PEB use.

Late loss is used as an important endpoint to compare interventional therapy. In our study, late loss had a normal distribution between the PEB and balloon angioplasty groups ( $p = 0.31$  and  $p = 0.22$ , respectively). Thus, late loss might be a reliable marker of the true efficacy of PEB.

Our study was a single-center randomized trial with a relatively small sample size. Further studies with a larger sample size are required for studying the management of DES restenosis.

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