Letter by Brugaletta et al Regarding Article, “Interference of Drug-Eluting Stents and Endothelium-Dependent Coronary Vasomotion: Evidence for Device-Specific Responses”

To the Editor:

We read with interest the article by Hamilos et al, demonstrating a variable endothelium-dependent coronary vasomotor response at coronary segments adjacent to different drug-eluting stents (DES) and bare metal stents. In particular, a better coronary vasodilatation induced by pacing was observed in patients receiving zotarolimus-eluting or bioresorbable A9–eluting stents when compared with patients receiving paclitaxel- or sirolimus-eluting stents. As discussed by the authors, endothelial dysfunction after first-generation DES may be induced by the effect of the drug, its release kinetics, the proinflammatory effect of the polymer, or the combination of these factors. However, before drawing easy conclusions, several methodological considerations should be, in our opinion, clarified.

What to measure and how to measure it: The study was based on the assessment of the endothelial function by means of the endothelium-dependent coronary vasomotion induced by atrial pacing. This method, already used in other studies, is based on the fact that exercise secondary to atrial pacing basically causes coronary vasodilatation of microcirculation through adenosine release, which, in normal conditions, causes an endothelial-independent vasodilatation of microvessels. In patients with coronary artery disease, atrial pacing increased stenosis and microvasculature resistance, which may be reverted by revascularization. Thus, atrial pacing may induce both endothelium-dependent coronary vasodilatation of epicardial vessels and endothelium-independent vasodilatation of microcirculation; the balance between both components of the vasomotor response may influence the results. A more specific method to evaluate endothelial function is the assessment of coronary blood flow and coronary diameter by quantitative coronary angiography after infusion of specific endothelium-dependent, such as acetylcholine, and endothelium-independent, such as adenosine or substance P, coronary vasodilators. Anyway, it is hard to demonstrate the true endothelial dysfunction at the site of the stent implantation, as this segment cannot be dilated or constricted under any vasomotor drug. The way that any stent, if it remains patent, may influence distal vasomotion is intriguing and difficult to demonstrate, especially when the functional assessment was performed only at follow-up. Thus, the knowledge of the preexisting vasomotor response at those segments is relevant to determine whether endothelial dysfunction is related to a certain type of stent.

When to measure it: In vivo human model, the actual times in which different DES are completely recovered by endothelium functional restoration are not defined. As described in pathologic studies, sirolimus- and paclitaxel-eluting stents exhibit a delayed endothelialization when compared with conventional and new-generation DES. Thus, one important finding of this study is the fact that different functional behavior may be related to different stages of endothelialization of different stents. Potentially, endothelial function of sirolimus- and paclitaxel-eluting stents may require longer follow-up to be restored than another DES with faster endothelialization. This hypothesis, however, remains to be demonstrated in serial functional analysis.

To minimize the amount of confounding variables involved in functional studies, a consensus on what, how, and when to measure is essential to demonstrate the differential pattern of endothelialization of a new generation of stent.

Disclosures

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References

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