Response to Letter Regarding Article, “Clinical Presentation and Outcomes of Coronary In-Stent Restenosis Across 3-Stent Generations”

We appreciate the interest and comments from Drs De Rosa and Indolfi in regard to our article.1 As stated in our article, neoatherosclerosis, which leads to late neointima formation, is seen across all 3 generations of metallic stents. It is our impression that the neointima of second-generation drug-eluting stents (DES) is less vulnerable and, as a result, associated with fewer events when compared with first-generation DES. Although vessel caging is also common across the 3 generations of metal stents, it is only one component of the mechanism for restenosis. Neoatherosclerosis has been frequently implicated as the final pathway of late failure for both DES and bare-metal stents.2 This widespread occurrence of neoatherosclerosis across stent generations may in fact explain the similarities in clinical presentation of in-stent restenosis and lead to the vulnerable stent. It remains to be seen whether neoatherosclerosis is independently associated with stent type and whether it carries an equal risk of vulnerability across stent generations.

Imaging studies have shown that neoatherosclerosis occurs less frequently in second- than first-generation DES. Lee et al observed a lower rate of neoatherosclerosis in first- than second-generation DES,3 and Yonetsu et al also demonstrated by univariable analysis that first-generation DES were significantly associated with neoatherosclerosis, whereas second-generation devices were not.4 Furthermore, neointimal rupture is less likely to occur in patients with second- than first-generation DES.3 Notably, this in vivo finding was consistent with a postmortem study in which no unstable features of neoatherosclerosis were observed in second-generation DES.3 This differentiation can be explained by more biocompatible polymers of second-generation DES. Therefore, it is reasonable to hypothesize that not all neoatherosclerosis underlying stent neointimal tissue has the same risk and propensity to rupture.

We agree that biodegradable scaffold can potentially resolve the caging and the neoatherosclerosis. Biodegradable scaffold, however, also resulted in restenosis, some of which had neointima and led to local inflammation during scaffold degradation and the thick strut. Restenosis of biodegradable scaffold was beyond our article and should be a subject for future research.

Disclosures
Dr Waksman reports personal fees from Biosensors International, personal fees from Abbott Vascular, grants from The Medicines Company, and grants from Edwards Lifesciences. The other authors report no conflicts.

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