Letters to the Editor
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**LDL-cholesterol predicts negative coronary artery remodelling in diabetic patients: an intravascular ultrasound study**

We read with great interest the article entitled 'LDL-cholesterol predicts negative coronary artery remodelling in diabetic patients: an intravascular ultrasound study',

A major finding of this study is the high frequency (72%) of negative remodelling (i.e., a decrease in total vessel cross-sectional area in response to development of an atherosclerotic plaque) in their cohort of diabetic patients. We think that several shortcomings in the methods could have contributed to this finding.

In this study, all of the lesions used in the remodelling analyses were located in a coronary artery that had undergone stenting right before intravascular ultrasound imaging. These lesions had to be at least 10 mm distal or proximal to the stented segment. Negative remodelling was defined as a lesion external elastic membrane (EEM) area less than proximal reference EEM area, and the proximal reference site was chosen within 10 mm proximal to the lesion. Thus, in the case of lesions that were about 10 mm distal to the stented segment, the reference site would be very close (and possibly within) to the distal edge of the stent, which could be artificially dilated due to pre-dilatations, stent implantation, and post-dilatations. This would lead to an overestimation in the frequency of negative remodelling. Moreover, defining remodelling using only a proximal reference does not take the normal vessel tapering into account and can also overestimate negative remodelling. However, using a definition of remodelling that includes not only the proximal but also the distal reference site, the frequency of negative remodelling in diabetic patients was reported to be <30%.

Similarly, using another definition of remodelling that does not incorporate any measurements of the reference sites, positive remodelling was found to be the predominant remodelling behaviour in diabetics. According to the methods of the current report, the investigators measured EEM areas of not only the proximal, but also of the distal reference sites. However, data regarding the distal references are not reported. Additionally, the slopes of the regression lines of the second and third panels of Figure 3 should have negative values due to the inverse relationship between the parameters.

References


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**LDL-cholesterol predicts negative coronary artery remodelling in diabetic patients: an intravascular ultrasound study: reply**

Sipahi et al. address the issue of the high incidence of negative remodelling that was observed in our study and suggest the possibility that this phenomenon might be overestimated because of the methodology used. The following considerations may clarify this concern.

First, we are well aware of the concept of geographic miss as we described it first in the brachytherapy era and later on after drug-eluting stent implantation. In this regard, in the design of the DIABETES trial, we seriously took into consideration the judicious stent implantation technique. Therefore, as stated in the protocol, all balloon inflations had to be filmed and the stent had to cover the entire injured segment. As a result, the incidence of edge effect in the entire DIABETES trial was very low (2% in the conventional stent arm and 3.9% in the sirolimus group) when compared with diabetics included in other large-scale trials (i.e., SIRIUS). However, to ensure that evaluated segments were not previously injured, we excluded from the analysis those lesions that were close to segments in which some doubts existed about the location of the balloons used during angioplasty. Besides, all lesions included in this intravascular ultrasound study were exclusively located proximal to the stent, ruling out the possibility raised by Sipahi et al.

We believe that the cut-off value used to categorically define the type of remodelling, rather than the location of the reference segment, is the main influencing factor on the incidence of negative remodelling. In addition, normal vessel tapering may overestimate this incidence. In this regard, Mintz et al. defined lesion/proximal reference EEM CSA <0.78 as inadequate arterial remodelling in order to avoid the effect of arterial tapering (an average of 10% per 10 mm of arterial length). Among all the reported definitions of remodelling, we finally used the one proposed by the American College of Cardiology Clinical Expert Consensus document, which dichotomizes remodelling in <1 or >1 without any other recommendation on which reference has to be used for remodelling index calculation. In contradiction to Sipahi’s comments, a recent article coming from the same centre reported a 60% incidence of negative remodelling in lesions of patients with stable angina. Interestingly, remodelling index was also calculated using only the proximal reference.

Sipahi et al. also referenced a manuscript of Weissman et al. to support the concept of higher than expected incidence of negative remodelling in diabetics. However, although the overall incidence of negative remodelling was rather low (24%), only one-third of the patients included in that analysis were diabetics. Besides, as opposed...