



## Intracoronary Ultrasound-Guided Stenting: Is it Really Beneficial?

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### Dear Editor,

We would like to congratulate the authors of the study: "Intracoronary ultrasound-guided stenting improves outcomes: a meta-analysis of randomized trials"<sup>1</sup> and make the following comments:

1. There is significant heterogeneity among the meta-analysis studies, which includes both studies with provisional stenting technique, now in disuse, as well as a study with drug-eluting stent. Three studies excluded patients with long lesions and one of them did not use IVUS for lesion analysis prior to stent implantation.

2. Although there was no significant reduction in major cardiovascular events (MACE) and myocardial infarction, the number of deaths was higher in the intervention group guided by IVUS. Thus, there is an interpretation bias by the authors, who suggest that "with more studies and a larger number of

patients, IVUS-guided stenting can significantly reduce MACE cases," when in fact the number of deaths could also increase.

3. The authors conclude on the benefit of IVUS, based on analysis of surrogate outcomes: angiographic restenosis and target vessel revascularization, for which blinding is difficult. Only 62% of the studies reported blinding of outcome examiners. The use of surrogate outcomes should be viewed with caution, as it does not always relate to the clinical events of interest<sup>2</sup>.

We point out the existence of publication bias in this meta-analysis, a hypothesis reinforced by applying the test of Egger<sup>3</sup> to the data on restenosis ( $p = 0.037$ ) and MACE ( $p = 0.023$ ). Considering the figures presented by the authors, it is clear that the smaller studies had "more positive" results and the "trim and fill"<sup>4</sup> test was also positive in our analysis.

Thus, we believe that the main conclusion of the study is the absence of evidence of clinical benefit from the use of IVUS to guide stent implantation.

Conclusions based on meta-analyses of surrogate endpoints, especially when there is heterogeneity of the studies and suspected publication bias should be assessed with caution.

### Keywords

Ultrasound; interventional; coronary artery disease; meta-analysis.

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### References

1. Sbruzzi G, Quadros AS, Ribeiro RA, Abelin AP, Berwanger O, Plentz RD, et al. Intracoronary ultrasound-guided stenting improves outcomes: a meta-analysis of randomized trials. *Arq Bras Cardiol.* 2012;98(1):35-44.
2. la Cour JL, Brok J, Gotzsche PC. Inconsistent reporting of surrogate outcomes in randomised clinical trials: cohort study. *BMJ.* 2010;341:c3653.
3. Egger M, Smith GD. Bias in location and selection of studies. *BMJ.* 1998;316(7124):61-6.
4. Sutton AJ, Duval SJ, Tweedie RL, Abrams KR, Jones DR. Empirical assessment of effect of publication bias on meta-analyses. *BMJ.* 2000;320(7249):1574-7.

## Response Letter

We would like to thank you for the comments regarding our article: "Intracoronary ultrasound-guided stenting improves outcomes: a meta-analysis of randomized trial"<sup>1</sup> and would like to clarify some questions raised by our colleagues:

Our article aimed to systematically review the impact of adding the IVUS angiography for optimal stent implantation on clinical and angiographic outcomes, and for this purpose, we included eight randomized clinical trials: seven studies using conventional stents and one that used drug-eluting stent (DES)<sup>2</sup>. For the outcome 'major cardiovascular events' (MACE), when analyzing all the studies together, it was shown that there was no significant reduction for it by adding IVUS to the angiography, which did not change even when the study that used DES was excluded, both regarding the main outcome, and the heterogeneity. The same was observed in the study using the provisional stenting technique<sup>3</sup>: the exclusion of this study from the meta-analysis did not change either the overall result or the heterogeneity.

It is important to stress that although DES are preferably used in current practice, this approach is associated with higher costs and not all patients are good candidates to receive such devices, such as, for instance, those with contraindications or low adherence to long-term double antiplatelet therapy, planned non-cardiac surgery and comorbidities associated with increased risk of bleeding<sup>4</sup>.

Regarding the meta-analysis that assessed mortality individually, we observed an increase in this outcome that was not statistically significant, i.e., no significant difference between the IVUS group and the ANGIO group. In fact, as the quality of this evidence was moderate for this outcome and the optimal size of the information was not reached, further clinical trials may alter this result, to increase, reduce or even maintain the association with no difference in the use of IVUS with this outcome.

The comment about the appraisal of surrogate outcomes merely reiterates what has already been addressed in the discussion, as follows: "This systematic review and meta-analysis demonstrates that IVUS-guided stenting reduces angiographic restenosis and target-lesion revascularization when compared with stenting guided by angiography, but does not reduce MACE cases. These data may provide further support to the use of IVUS, but further randomized larger-scale and high-quality clinical trials are needed to elucidate the possible benefit of IVUS in relation to hard outcomes. Furthermore, although target-vessel revascularization can be considered a surrogate endpoint, it is associated with decreased quality of life and increased follow-up costs<sup>5</sup>.

The publication bias identified by the authors is probably due to the inclusion of studies in English, Portuguese and Spanish only and because a literature search for unpublished studies was not carried out. The decision to not include this type of study was due to the fact that they do not go through the peer-review process, and may have worse methodological quality.

Therefore, we believe in the benefits of IVUS-guided stenting in reducing angiographic restenosis and target-lesion revascularization when compared to stenting guided by angiography, which did not lead to reduction in hard endpoints. We believe that carrying out new larger-scale and high-quality randomized controlled trials is crucial in order to elucidate the possible benefit of IVUS in relation to hard outcomes.

We appreciate the comments of the author and hope to have clarified their questions.

Sincerely,

**Graciele Sbruzzi**

**Alexandre Schaan de Quadros**

**Beatriz D'Agord Schaan**

## References

1. Sbruzzi G, Quadros AS, Ribeiro RA, Abelin AP, Berwanger O, Plentz RD, et al. Intracoronary ultrasound-guided stenting improves outcomes: a meta-analysis of randomized trials. *Arq Bras Cardiol.* 2012;98(1):35-44.
2. Jakabcin J, Spacek R, Bystron M, Kvasnák M, Jager J, Veselka J, et al. Long-term health outcome and mortality evaluation after invasive coronary treatment using drug eluting stents with or without the IVUS guidance. Randomized control trial. *HOME DES IVUS. Catheter Cardiovasc Interv.* 2010;75(4):578-83.
3. Frey AW, Hodgson JM, Muller C, Bestehorn HP, Roskamm H. Ultrasound-guided strategy for provisional stenting with focal balloon combination catheter: results from the randomized Strategy for Intracoronary Ultrasound-guided PTCA and Stenting (SIPS) trial. *Circulation.* 2000;102(20):2497-502.
4. Daemen J, Simoons ML, Wijns W, Bagust A, Bos G, Bowen JM, et al. ESC Forum on Drug Eluting Stents European Heart House, Nice, 27-28 September 2007. *Eur Heart J.* 2009;30(2):152-61.
5. Rinfret S, Grines CL, Cosgrove RS, Ho KK, Cox DA, Brodie BR, et al. Quality of life after balloon angioplasty or stenting for acute myocardial infarction. One-year results from the Stent-PAMI trial. *J Am Coll Cardiol.* 2001;38(6):1614-21.