Reviewer’s report

Title: Analysis of Cardiovascular Mortality, Bleeding, Vascular and Cerebrovascular Events in Patients with Atrial Fibrillation vs. Sinus Rhythm Undergoing Transfemoral Transcatheter Aortic Valve Implantation (TAVR)

Version: 2 Date: 12 Oct 2017

Reviewer: Umberto Barbero

Reviewer's report:

Herold et al. presented an interesting paper on TAVR in patients with and without AF. They showed that Patients with AF had significantly more severe bleeding complications after TAVR, which significantly determined mortality, without difference in the rate of cerebrovascular complications. This is a registered study in the German Clinical Trial Register, and highlights how therapy's management in patients with AF undergoing TAVR is of extremely importance in order to reach the best performances. 148 patients with SR vs. 109 with AF who underwent TAVR via transfemoral access were included in this study. Significantly, more patients in the AF group than in the SR group had PAD, an issue that could be related to access-related bleeding and complications. Indeed, almost three times as many major vascular complications occurred in patients with AF than in patients with sinus rhythm (AF 14.7% vs. SR 5.4%, p = 0.016). Patients with pre-interventional AF had near three times as many of life-threatening secondary bleeding events as patients with SR (AF 11.9% vs. SR 4.1%, p = 0.028). This result corresponds to the rates and the temporal development of major vascular complications. Thus, most of the life-threatening bleeding occurred around the time of implantation and the changeover to OAC (NOAC or VKA) and Dual Antiplatelet Therapy (DAPT). The authors concluded AF should be added to future risk score for TAVI due to these data.

I think the paper is really well written, with a simple idea (dividing patients with SR to AF) from which important conclusion were drawn. Statistics are correct and the conclusion interesting. Nevertheless some questions should be answered before considering it for publication.

First off, the authors claim AF as related to greater mortality because of the significant amount of vascular complications and bleeding: this conclusion should be strengthened by a multivariate analysis in which these factor appear significantly related, but i don't see it in the table 7. Furthermore anemia intended as <6.5 g/dL is not useful as a clinical predictor, given that no one would bring a patients in the cath lab with such a hemoglobin level and should be removed. Please explain better this analysis and eventually change abstract and text accordingly.

In discussion, page 14 line 39, please add a paragraph regarding the current EBM evidence of the use of anticoagulant and/or anti platelet therapy after either coronary percutaneous intervention
(see for example the paper by D'Ascenzo F, et al. Meta-analysis of randomized controlled trials and adjusted observational results of use of clopidogrel, aspirin, and oral anticoagulants in patients undergoing percutaneous coronary intervention. Am J Cardiol. 2015 May 1;115(9):1185-93.) and TAVR (see the recently published paper by D'Ascenzo F et al. Which is the best anti-aggregant or anti-coagulant therapy after TAVI? A propensity matched analysis from the ITER registry. The management of DAPT after TAVI. EuroIntervention. 2017 Sep 5.), adding adequate references. Furthermore the authors should explain the choice of three months therapy with clopidogrel + NOAC or clopidogrel plus OAK at the light of these recently published data (see citation above) and discuss the role of single anticoagulant therapy in patients with AF receiving TAVR: there are studies confirming that in patients undergoing TAVR, AF was associated with a significantly higher rate of all-cause mortality throughout 12 months follow-up, but for example in the paper by Seeger J et al Apixaban in Patients With Atrial Fibrillation After Transfemoral Aortic Valve Replacement. JACC Cardiovasc Interv. 2017 Jan 9;10(1):66-74.) the early safety endpoint in patients with AF on apixaban was significantly less frequent compared with patients receiving a VKA. In the recently published BRAVO-3 trial instead despite greater baseline comorbidities than non-AF patients, AF was not associated with significantly higher risk of adjusted 30-day outcomes. In the BRAVO 3 trial, early outcomes were similar regardless of anticoagulant strategy in each group (see Hengstenberg C, et al. Impact of pre-existing or new-onset atrial fibrillation on 30-day clinical outcomes following transcatheter aortic valve replacement: Results from the BRAVO 3 randomized trial. Catheter Cardiovasc Interv. 2017 May 11.) and discuss that for example in page 21, discussion section.

Figure 5 correct the title (… at AF) and change germsn terms (i.e. Monate, etc)

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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