Author's response to reviews

Title: Predictive factors for pacemaker requirement after transcatheter aortic valve implantation

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Author's response to reviews: see over
Re: Revision of manuscript 1420323820760872

Dear Dr. Noutsias,

thank you so much for the careful review of our manuscript entitled „Predictive factors for pacemaker requirement after transcatheter aortic valve implantation“ (manuscript-number 1420323820760872) and the profound comments by the reviewers. We have addressed all comments by a point-point rebuttal. With profound and careful editing we hope to be accepted for publication in BMC Cardiovascular Disorders.

Looking forward to your support and advise.

Yours sincerely

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“Predictive factors for pacemaker requirement after transcatheter aortic valve implantation”

Comments to Reviewer 1:

Reviewer 1 welcomes the paper and qualified it as an article of importance on the field of TAVI. Our respond to the comments are listed.

The Reviewer is right by his comments. This study is a retrospective one and has the weakness of such a design as compared to prospective randomized trial. (See page 11, para 2) A prospective randomized trial with clinical endpoints would require a large number of patients, which is not really realistic due to the invasive nature of these required measurements during index procedure and during the follow-up in such severe ill patients. We tried to identify trends in predictive factors. The low number of patients is also a limitation of this analysis, but due to the invasive nature of measurements, which was by the way unique in literature, there was no possibility to measure all consecutive patients. (see page 11, para 2)

The Reviewer is right by his comment regarding the high rate of pacemaker requirement. Due to the novelty of the TAVI procedure and due to the high rate of frailty patients there were somewhat a “liberal” indication for pacemaker implantation (e.g. prolongation of HV time (>75msec) in combination of new LBBB). (see page 9, para 1) There are data from the literature that a HV prolongation to values of >75ms is associated with a progress to complete AV block (Scheinmann MM, et al. Circulation 1977;56:240-44). But to date we have no information about the transient nature of these ECG changes during a long-term follow up. Thus, for predictive analysis we only used hard endpoints like complete AV block and type II AV block. (see page 5 para 2 and page 6 para 1)

We revised our method section and stated that all patients received an intracardiac measurement during in-hospital follow-up (see page 5, para 1). Additionally, we have revised the labelling of the figures.
Comments to Reviewer 2:

Reviewer 2 also welcomes the paper and classified it as an important study, which adds more information on an emerging technique.

Ad 1: The Reviewer is right. There are several data from the literature dealing with predictive factors for pacing after surgical aortic valve replacement (page 8, para 3). We think that the differences might be due to the different procedure techniques. In surgical valve replacement there is a clear approach, which means the valve is taken and replaced by another valve. Thus, the amount of conduction damage is predictable because the local extent of trauma is nearly the same in all patients. However, in TAVI the self-expandable CoreValve presses the native valve against the aortic annulus (not only during the index-procedure but also during a follow-up due to the further expansion of the nitinol frame). Thus, the amount of local damage is dependent on local calcification, the height of implantation in LVOT, the extent of trauma during index-procedure (balloon valvuloplasty, diameter of balloon, balloon/aortic annulus relation, post-TAVI dilatation etc) and the further expansion of the nitinol frame during follow-up. (see page 9, para 2) Due to these differences it is difficult to determine predictive factors from baseline ECG and baseline clinical parameters. One of the major predictive factors in the literature is a pre-existing right-bundle branch block. This makes sense, due to the anatomic vicinity of the left bundle branch block to the aortic cusp and thus the risk of resulting complete heart block in case of new left bundle branch block. The Reviewer is also right by his comment that there might be limitation due to limited number of patients (we just had 2 patients with pre-existing right-bundle branch block). There might be a speculation that with more patients there would be a more accurate analysis showing predictive factors from baseline ECG and clinical parameters. (see page 11, para 2) But, like stated above, due the different parameters influencing the resulting clinical event there would be a need for a large number of patients.

Ad 2: The number of events is too low to make a breakdown in different regurgitation degrees and to perform a statistical analysis according to these different degrees. We do not believe that these factors would influence the need for a pacemaker, because the local trauma mechanisms during TAVI are not just dependent the aortic
valve but also from other variables (see point 1). Due to this we have not analysed
the aortic valve calcification, which is somewhat difficult as there is no evidenced and
widely accepted calc score in TAVI allowing a precise describing of local calc
deposition and calc composition. A descriptive analysis of chest x-ray and CT would
be not reliable enough to ensure adequate comparisons.

Ad 3: We are sorry, but we have no measurements of implantation height. (see point 1)

Ad 4: The Reviewer congratulates for the important study.

Ad 5: We have implanted since 2007 327 aortic valves. Our pacemaker rate was
initially nearly 45%. This was due to the novelty of this technique and lack of
information regarding the true indication for pacing. However, with further analysis of
patients and improving implanting techniques (e.g. high implantation technique, no
further post-TAVI balloon dilatation) our pacing rate decreased to 9-10%. Based on
our data we decided not to perform routinely intracardiac measurements. We see,
that there is a transient character of ECG changes (especially for left bundle branch
block). The presence of a new left bundle branch block in case of normal AV
conduction on surface ECG is not an indication for pacing.

Ad 6: The Reviewer is right. This is the reason, why we perform the predictive
analysis for the hard endpoint of type II second degree AV block and complete AV
block. A predictive analysis just for “pacemaker implantation” (including our liberal
indication) would not make sense. (see page 5, para 2 and page 6 para 1)

Ad 7: We are sorry, but there is no close follow-up with ECG, echocardiography and
pacemaker analysis of these patients (many of them being not from our region and
thus having different follow-up evaluations).

Ad 8: We have added an * on the bottom of table 3.