Format for ANSWERING REVIEWERS

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 14873-review.doc).

Title: Percutaneous closure of secundum type atrial septal defects: more than 5-year follow-up

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Name of Journal: *World Journal of Cardiology*

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer:

Reviewer comments:

We would like to thank the reviewers for reading our manuscript and help to improve it for publication.

Reviewer 1:
I read with great interest the paper submitted to the journal for his team. However, some considerations must be taken into account to clarify some aspects of the paper.

(1) I'm agree with the limitations proposed by the authors, but I think that the main limitations of the study are the small sample size and the single-centre design. These should be added in the limitation section.

We agree with the reviewer that the main limitations of the study are the small sample size and the single-centre design. We added this to the limitation section (page 11).

(2) In the methods section, it would be nice to specify the cath-lab experience with the implantation of both device, number of physicians involved in the procedure and to explain the

preference for the Amplatzer device (almost 3 to 1 proportion compared with Cardioseal/Starflex device).

In total, two interventional cardiologists performed the percutaneous closure procedure.
As previously described by Post MC et al. (Catheterization and Cardiovascular Interventions 2006;67:438-443), the type of device was chosen by the interventional cardiologist.
Because of a relatively high dislocation rate in the CS/SF group within the first 6 months after the initial percutaneous closure procedure, both interventional cardiologists decided not to use the CS/SF device anymore.

(3) In the statistical analysis, the authors comment the implementation of a
univariate analysis to find predictors of residual shunt in the methods description, but all results shown are descriptive variables. Probably the authors did not find predictors of residual shunt, but they don't specify. Please clarify this item in the results section.

Thank you for noticing the absence of the univariate analysis in our results. Our analyses showed no significant differences in the diameters of the ASD or the device used between the patients with or without a residual shunt. Secondly, no predictors for a right-to-left shunt at long-term follow-up could be found using univariate analysis. We added this information to the Results section (page 8).

(4) In the table 1: Baseline characteristics, authors don't mention patients treatment. Specially the antithrombotic treatment of the patients would be of interest if is available.

We fully agree with the reviewer and added this information to table 1 (page 20).

(5) In the table 1: Baseline characteristics, the indication for closure in percentage was RV volume overload (69.2%) and cryptogenic TIA/stroke (20.2%). What about the other 10.6% of indications? I think is important to mention if available.

We fully agree with the reviewer. In 10.6% of the patients, the ASD was found by coincidence. All patients were asymptomatic without signs of right ventricular dilatation on transthoracic echocardiogram but with a significant shunt. This information was added to table 1 (page 20).

(6) What was the diagnostic method for new-onset supraventricular tachycardia? Routine ECG? Emergency visit? 24 hours ECG monitoring? Patient-related symptoms?

New-onset supraventricular tachycardia's were diagnosed by routine ECG when patients visited the outpatient clinic or when patients visited the emergency department because of symptoms. No regular 24-hours ECG monitoring was performed. We added this information to the Methods section (page 5).

Reviewer 2:

The paper by dr. Snijder et al. reports the experience in percutaneous closure of atrial septal defects in 104 patients using two devices. Interestingly, in a long-term follow-up (transthoracic echocardiographic data are available in only 54.8% of the cases) a residual left-to-right shunt is absent, although the rate of a residual right-to-left shunt is relatively high. In the present version of the manuscript there are some points which require revision and improvement.

(1) This cohort is large enough to analyze and report the reasons and/or the risk factors for device embolization. Was it dependent on anatomy, operator's experience, other procedure variables?

The answer of this question was previously reported by Post MC et al. (Catheterization and Cardiovascular Interventions 2006;67:438-443) who described the short term follow up of ASD closure using both devices. Because device embolization occurred more often in patients with a Cardioseal/Startflex device, we analysed potential reasons/risk factors only for this device. Post et al. showed that the initial ASD and the device diameter were significantly higher in the patients in whom the device was embolized. However, due to the small sample size of this study it is difficult to make any conclusions. Therefore, we did not include this analysis in the manuscript. This study was added to the Discussion section on page 9.

(2) Similarly, it would be interesting to analyze and report the reasons and/or the risk factors for residual right to left shunt observed during follow-up.

We could not find significant differences in the diameters of the ASD or the device used between the patients with or without a residual shunt. Secondly, no predictors for a right-to-left shunt at long-term follow-up could be found using univariate analysis. We added this information to the Results section as also suggested by the first reviewer (page 8).

(3) The study design (retrospective, non-randomized) does not allow conclusions on the comparison between the two devices used. Therefore, all the statement on the superiority/inferiority of one device as compared to the other should be deleted in the discussion and in the conclusions.

We agree with the reviewer. Therefore we deleted the statements about superiority/inferiority.

(4) In the limitation section, it is stated that the echocardiographic data were not analyzed by an independent core lab. However, it would be interesting to report if they were analyzed by a single or by multiple operators. In case of multiple operators, the agreement among operators should be reported.

All echocardiograms were analysed by two experienced cardiologists. In 53 patients both reviewers fully agree about the shunt grade. In four patients there was a difference of one grade between the two cardiologists. They discuss the shunt grade in those patients and came to an agreement.

(5) The last limitation on the patients lost at long-term follow-up should be more clear. Moreover, the number of patients lost at long-term follow-up should be clearly reported in the result section.

The number of patients lost at follow-up is already mentioned in the result section.
In total 13 patients were lost to follow-up because of different reasons. We incorporated this information into the flowchart of the study population (new Figure 2). See next comment.

(6) In the manuscript, a wide body of acute and follow-up data are presented. A figure showing the flowchart and the results of the study would help the reader in understanding quickly the study and its results.

As mentioned above we incorporated a flowchart showing the results and follow-up data. The flowchart was named Figure 2 and was added to the Figures section (page 19).

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Cardiology*.