Reviewer's report

Title: Sequencing of NOTCH1, GATA5, TGFBRI AND TGFBRII genes in familial cases of Bicuspid Aortic Valve

Version: 1 Date: 3 January 2013

Reviewer: Muhammad Hassan

Reviewer's report:

Dear Editor

Thank you for selecting me as a reviewer for manuscript SEQUENCING OF NOTCH1, GATA5, TGFBRI AND TGFBRII GENES IN FAMILIAL CASES OF BICUSPID AORTIC VALVE by Ilenia Foffa et al.

My comments and suggestions are given below.

Major Compulsory Revisions:

1- Introduction is precise, but the word COHORT is not suitable for a group of 11 patients...
2- In methods section, there should be MIM codes for respective gene sequences. It will facilitate the reader to exactly identify the sequence which was used as control.
3- In methods section, authors mentioned use of cDNA sequence from genbank for primer construction of GATA5 gene, which seems contradictory to previous statement in same section about sequencing of coding and flanking intronic and un-translated regions.
4- Again in methods, authors mentioned 3 sofware for prediction of functional consequences of mutations but very little is discussed in results/discussion about them. Also, it would be better to precisely describe results obtained by any one software. I would delete the sentence after these software names in methods section (we confirm the presence or absence of mutation).
5- In results section, my suggestion is that authors should focus on novel mutations and on considerably important polymorphisms only. Mutations and important polymorphisms (found present in 45% affected individuals etc) can be added for each affected individual in table 1 as well. However, a table can be added about all polymorphisms detected in all four genes, as a supplementary material. There is no need to mention about novel variants which are also present in controls.
6- Thr67Pro variant in GATA5 gene seems interesting. Authors should check conservation of this variant with the help of bioinformatics in different related species. A figure can be added in this regard.
7- Presence of a premature stop codon in exon 4 of TGFBRII gene in 73% of
patients and 60% of controls is surprising...authors mentioned that it was
designated as framshift mutation in previous studies, but no reference is given
May be the previous studies were using an older version of the reference
sequence...Clinical testing results of controls should be reassessed, just to be on
safe side.

8- Discussion section should add a paragraph about homology
conservation/otherwise of GATA5 variant and also some words about TGFBRII
variant.

best regards

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a
statistician.

Declaration of competing interests:

I declare that I have no competing interests