Reviewer’s report

Title: Enhanced expression of ROCK2 in left atrial myocytes of mitral regurgitation: A potential mechanism of myolysis

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Reviewer: Ana Savic-Radojevic

Reviewer’s report:

This manuscript by Chen et al, investigated the relationship between the activity and expression of Rho-associated kinase 2 (ROCK2) and myolysis in patients with mitral regurgitation. The authors speculated that increased ROCK2 activity is associated with a myolysis. This is a carefully conducted study. Although the results are not entirely novel, the data, which is obtained from the tissue of a chosen subgroup of patients add strength to the study. There are some major concerns.

Major Compulsory Revisions:

1. Authors defined the role of caspase-3 in apoptosis execution only. However, the evidence on the role of caspase-3 in activation of ROCK proteins by removing the ROCK autoinhibitory C-terminal domain is missing. Because this process occurs in early phase of apoptosis, and considering the fact that activation of ROCK might be caspase-independent, this matter must be clarified. I believe addressing this issue would significantly improve the obtained data on colocalization between ROCK2 and caspase-3.

The data of colocalization between these molecules missing in the abstract.

The explanation for results of colocalization (The paragraph 1: page 16, lines 233-239) must be rewritten, since those results don’t represent the “correlation analysis”, but the existence of potential protein:protein interaction between these two molecules. Also, the last sentence of this paragraph should be explained as confirmation of caspase-dependent activation of ROCK2 in myocytes of patients with mitral regurgitation.

2. Authors determined both the expression and activity of ROCK2 protein.

In the results section, expression of ROCK2 protein is expressed as “integrated intensity”. This phrase is confusing. I suggest that this term would be replaced with “expression” in abstract and results and the calculation would be explained under the Table 3.

Also, authors have chosen to study the activity of ROCK2 expressed as a relative ratio of the phosphorylated and total myosin-binding subunit of myosin light chain phosphatase. However, this information is missing in results section (the only explanation is under the Table 3). Considering the fact that ROCK2 has the other targets, this information must be clearly stated in results section. The result of ROCK2 activity is missing in the abstract.
3. Since the number of patients was small, the conclusions must be rewritten. In the abstract, “..significantly associated…” should be replaced with “might be involved”.

Minor Essential Revisions:

1. In the introduction section, authors stated that “ROCKs play a crucial role in apoptosis” (page 6, line 44). Since the both propaoptotic and antiapoptotic roles of RhoA/ROCK have been reported in cardiomyocytes (review article of Surma and Shi, Future Cardiology, 2011), this part of introduction needs to be rewriting, with more precise explanation of molecular mechanisms involved in ROCK2 mediated roles in apoptosis.

2. Since the definition of apoptosis is a well-known fact, it is not necessary to explain it (background: page 5, line 32). Please delete “.... Programmed cell death pathway activation” and “....is a morphologically distinct form of death in most physiological cells” (page 5, line 34).

3. In Table 1, p value obtained for dyslipidemia didn’t match the value in results section (page 12, line 156).

4. Delete “... although the difference did not reach statistical significance” page 14 line 194.

5. The word “a crucial” (Discussion: page 17, line 255) should be replaced with “important”.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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