

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8193-review.doc).

Title: Arrhythmogenic Ventricular Cardiomyopathy:
A Paradigm Shift from Right to Biventricular Disease

Author: Ardan Muammer Saguner, Corinna Brunckhorst, Firat Duru

Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 8193

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 and the editor

Reviewer No. 1: 02565578

1. This manuscript constitutes an updated overview of arrhythmogenic ventricular cardiomyopathy and describes the paradigm shift in the understanding of AVC from an isolated right sided entity to biventricular disease, as described in 2010 task force criteria. I would just like to point out that the term "arrhythmogenic cardiomyopathy" is used by the authors when they introduce the acronym AVC. This acronym corresponds to "arrhythmogenic ventricular cardiomyopathy", as correctly acknowledged in the abstract, hence this term should be also used in the first sentence of introduction.

Authors's response: done as suggested

2. Pathogenesis section could be better organized and follow a more logical order, starting from "genetically-determined disruption of intercalated disc integrity", followed by "loss of desmosomal integrity can substantially affect gap junctions... in the absence of overt structural damage" (this part is included in Genetics section) and ending with "the theories for progressive fibro-fatty replacement of the myocardium". As regards the latter, point 2: hypothesis of transdifferentiation of myocytes into fibroblasts and adipocytes has been already rejected and should be abandoned.

Authors's response: We thank the reviewer for this important comment. We have re-structured the pathogenesis section as suggested by the reviewer. We agree with the reviewer that the hypothesis of transdifferentiation of myocytes into fibroblasts and adipocytes has recently been rejected. Thus, we have deleted this part.

3. Few grammar mistakes and typos should be corrected

Authors's response: We thank the reviewer for this important advice, and have checked the whole manuscript for grammatical mistakes and typos, and have corrected them.

Reviewer No. 2: 02565578

In this review the authors described the epidemiology, pathogenesis, clinical presentation, diagnosis, prognosis and risk stratification of arrhythmogenic ventricular cardiomyopathy. The

paper is very interesting and clearly written. There are some suggestions: 1. The authors should report the role of the 3D echocardiography in the diagnosis and prognosis of arrhythmogenic ventricular cardiomyopathy, as well as the new technology, in particular 2D strain.

Authors's response: We thank the reviewer for these important suggestions. We have modified the manuscript in accordance with these suggestions, and have included the role of 3D echocardiography, as well as 2D strain in the current version of the manuscript (subheadings: pathology, diagnosis, and risk stratification).

Reviewer No. 3: 02565578

The authors present a comprehensive review of arrhythmogenic ventricular cardiomyopathy and point out the need for a paradigm shift to realize the diverse clinical picture of the disease with involvement of both ventricles in many cases.

Authors's response: no modifications suggested

Editor's comments:

1. We now provide the revised manuscript in word format.
2. All changes suggested by the reviewers were highlighted in yellow.
3. We have checked the whole manuscript for grammatical mistakes and typos, and have corrected them. We believe that after these corrections, this manuscript now has reached Grade A. All three authors of this manuscript lived in the United States of America for a long period of time, and have worked in an academic environment. We thus feel that copyediting by professional English language editing countries may not be necessary.
4. We now provide main title of figure 1A and B, and decomposable figures as ppt format, whose parts are movable and words can be edited.

3. References and typesetting were corrected

We have revised the manuscript in accordance with your and the reviewers' comments. We sincerely hope that the revised version is now suitable for publication in the *World Journal of Cardiology*.

Sincerely yours,



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