October 30, 2018
Ying Dou
Science Editor, Editorial Office, World Journal of Cardiology

Re: Revise submission, Original Manuscript Number: **41662**, revised title "**Contemporary Characteristics and Outcomes of Familial Dilated Cardiomyopathy Adults Listed for Heart Transplantation**"

Dear respected reviewers,

Please find the paper previously entitled "**Contemporary Characteristics and Outcomes of Familial Cardiomyopathy Adults Listed for Heart Transplantation**" for consideration for publication in the World Journal of Cardiology (Original Manuscript Number: **41662**), and we were offered the re-submission as a revised manuscript to the World Journal of Cardiology. The manuscript has been revised as recommended by the reviewers. We are providing point-by-point answers to reviewers' comments.

This manuscript is not under consideration by another journal and has not been previously published. All authors have read and approved the manuscript. There is no conflict of interest with regard to this manuscript.

Familial dilated cardiomyopathy (FDCM) is a sub-type of non-ischemic cardiomyopathy (NICM) that may lead to end-stage heart failure (HF) requiring heart transplantation (HT). Previous studies described FDCM, however, it was not studied in patients with end-stage HF who are listed for HT. In our study, we presented the largest contemporary analysis that compares FDCM to ischemic cardiomyopathy, and NICM patients with end-stage HF who are listed for HT. We also described patients' outcomes before and after HT. Our study may help providers in making clinical decisions when managing FDCM patients with end-stage HF who are listed for HT.

We thank you for reviewing our manuscript and we hope that you find the revised manuscript suitable for publication in the *World Journal of Cardiology*

Sincerely,

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Reviewer 1 (03723709)

the authors presented an interesting retrospective study about Characteristics and Outcomes of Familial Cardiomyopathy Adults Listed for Heart Transplantation between January 2008 and September 2015 and compared them to non-ischemic cardiomyopathy (NICM) and ischemic cardiomyopathy (ICM) patients. the study is ell designed but i have few comments:

1- the manuscript needs good English editing.
- **Thank you. The manuscript has been revised for English clarity.**

2- There is major fault in the statistical analysis as we have three groups here so the recommended test for comparing continuous variables would be ANOVA with post hoc analysis not student t test. please correct that.
- **Thank you. We actually performed pairwise comparisons (FCM vs DCM, and FCM vs ICM) using student t-test and chi square.**

3- What were the primary and secondary outcomes of this study?
- **Thank you. These were added to the methods section as follows: "The primary outcomes of this study were waitlist mortality/delisting for clinical deterioration, and post-transplantation mortality among patients who undergo transplantation". The secondary outcomes were also added to the methods as follows: "Secondary outcomes were as follows: delisting due to improvement, transplant, post-transplantation stroke, post-transplantation permanent pacemaker implantation, post-transplantation acute rejection, post-transplantation dialysis, and length of stay for index transplant hospitalization"**

Reviewer 2 (03846820)

Dear authors, This paper represents results of the retrospective observational study (N=677) of patients with familial dilated cardiomyopathy and indications for heart transplantation which is aiming to better define the characteristics and clinical outcomes of that disorder. The article is written with the good English-speaking adduction of the arguments. The article is sufficiently novel and very interesting to warrant publication. All the key elements are presented and described clearly. The most discussable options in the article are:

1) Would you please kindly clarify what do you mean by"familial cardyomyopathy" - please, correct it to "familial dilated cardiomyopathy" with an abbreviation like Familial DCM or whatever.

- **Thank you. "familial cardiomyopathy" with the abbreviation "FCM" was updated to**

"familial dilated cardiomyopathy" with the abbreviation "FDCM", respectively. That also included the title which was updated from "Contemporary Characteristics and Outcomes of Familial Cardiomyopathy Adults Listed for Heart Transplantation to "Contemporary Characteristics and Outcomes of Familial Dilated Cardiomyopathy Adults Listed for Heart Transplantation"

2) Please, provide the definitions for your clinical outcomes. Here is a point of the quality for the patient data. Please, elaborate this point.

- **Thank you. Clinical outcomes were added to the methods as follows: "The primary outcomes of this study were waitlist mortality/delisting for clinical deterioration, and post-transplantation mortality among patients who undergo transplantation. Secondary outcomes were as follows: delisting due to improvement, transplant, post-transplantation stroke, post-transplantation permanent pacemaker implantation, post-transplantation acute rejection, post-transplantation dialysis, and length of stay for index transplant hospitalization."**

3) There must be a sort of the characteritics of the Registry in Methods because it's not something clear what UNOS Registry in case of your study truly means (with a number of patients).

- **Thank you. We have added details to the data source section in methods. We also added the number of patients in the database as follows: "At the time of analysis, the database included 99,177 patients listed for heart transplantation (1985-2015)."**

4) Statistical value - there are many options which must be discussed in the Discussion. The statistical power is one of them. You have a solution for any troubles with your statistical analysis - you can elaborate your analysis with more sophisticated approach, with more plots even. Your data look sometimes contradictory if compare with the previous smaller studies like from 00s. The quality of your Registry is low, but your paper can survive in case of more exciting performance with the elegant statistical approach.

- **Thank you. This is a retrospective exploratory analysis of a registry data, that includes all patients who were transplanted with FDCM. Given this is a national dataset that is inclusive, we believe that power analysis is not warranted. The discrepancies with previous studies in the 2000s are reflective of the small sample size in the previous reports. We have included statements in the discussion section on the limitation/shortcomings of the UNOS dataset. Additional figures will not add significant information beyond what is presented in text/tables. We would welcome suggestions for specific piece of data that may be better presented in figure form.**

Review 3 (03493974)

Khayata et al. present an interesting study on the characteristics and outcomes of adults with familial cardiomyopathy listed in for heart transplantation. The manuscript describes the largest series of patients (N=677) diagnosed with familial cardiomyopathy. These patients are compared with two other cohorts of CMP patients - those with non-ischemic and ischemic CMP. Data are derived from a registry which represents the major weakness of the study due to its retrospective design. However, this limitation s quite acceptable given the difficulties in running a study with a prospective design in this field. The

manuscript is well written and understandable by the reader. The results are presented in a straightforward manner and illustrated abundantly with tables and a figure. Conclusions drawn from them are clearcut and concise. I do not have specific comments and would recommend to accept this manuscript for publication.

- **Thank you.**

Reviewer 4 (00214240)

this article is a retrospective analysis of a large database of patients on a waiting list for heart transplantation the group of familial cardiomyopathy is compared to others groups messages are clear , limitations are described limitations are retrospective character and the definition of familial cardiomyopathy

- **Thank you.**