Peer Review File

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Reviewer A

1) First of all, my major concern is that the comparing the heart tissues between patients with dilated cardiomyopathy and heart failure and normal controls from the GSE29819 and GSE21610 cannot answer the research question of key genes associated with heart failure in dilated cardiomyopathy. The correct approach is to compare the heart tissues between dilated cardiomyopathy patients with and without heart failure. The authors need to reconsider the research question that is appropriate for the current data. The title should be diagnostic accuracy, not "diagnostic efficiency".
   Reply: Thank you for your comment. We agree with your point of view. We first checked the clinical diagnoses of two sets of samples and made modifications to the questions. Heart failure is an inevitable result of the progression of all cardiomyopathy. We believe that the focus of this study is dilated cardiomyopathy, rather than heart failure.
   Changes in the text: Paragraph 1/Title
2) Second, the abstract needs some revisions. The background did not explain why the current bioinformatics analysis can identify the mechanisms of heart failure in dilated cardiomyopathy and what the limitations are with respect to known biomarkers of heart failure in dilated cardiomyopathy. The methods need to describe how the heart failure and dilated cardiomyopathy were clinically diagnosed and clearly indicate the normal heart tissues were from healthy controls. The conclusion is misleading because of my above concern.
   Reply: Thank you for your comment. We strongly agree with your point of view. We have first added and modified the background section. We are very sorry that we were not careful enough in drafting the title of the article, which may have misled the readers. Heart failure is an inevitable outcome of the progression of all cardiomyopathy, a description of the state of cardiac function, and not a pathological diagnosis. In the selection of diagnostic markers, we should follow specific pathological diagnosis and not emphasize functional diagnosis. We have elaborated and revised in the article.
   Changes in the text: Paragraph 1-4/ abstract
3) Third, the introduction needs have a brief review on what has been known on the biomarkers associated with heart failure and dilated cardiomyopathy, biomarkers associated with failure in dilated cardiomyopathy, and have comments on the knowledge gaps and limitations of prior studies. The authors seems to be rather arbitrary to describe the significance of this study as "clarify the mechanisms of disease occurrence, and identify new biological markers

and potential therapeutic targets". Without external validation and further experimental studies, the authors should reconsider the purpose of this analysis.

Reply: Thank you for your comment. We are very sorry for the lack of caution in drafting the title of the article. Heart failure is an inevitable outcome of the progression of all cardiomyopathy, a description of the state of cardiac function, and not a pathological diagnosis. In the selection of diagnostic markers, we should follow specific pathological diagnosis and not emphasize functional diagnosis. We have elaborated and revised in the article.

Changes in the text: Paragraph 1-3/ introduction

4) Fourth, in the methodology of the main text, please review the clinical samples, healthy controls, and diagnoses of heart failure and dilated cardiomyopathy in the datasets in detail. The comparison between patient sample and healthy controls is not necessary since in clinical medicine, the clinical difficulty is the differential diagnosis within patients with heart failure and dilated cardiomyopathy and other diseases with similar clinical presentations.

Reply: Thank you for your comment. We partially agree with your point of view. Comparative analysis between patient samples and healthy controls has been used in a wide range of clinical studies. Its main significance lies in early diagnosis of diseases, screening of therapeutic targets, and elucidation of pathogenic mechanisms. Differential diagnosis is very important, but it is only one of the research directions. Research on differential diagnosis has limitations in elucidating pathogenic mechanisms and identifying potential therapeutic targets.

Changes in the text: Paragraph 1/ methods

5) Finally, please consider to review and cite several related papers to support the novelty of this research focus: 1. Su H, Hu K, Liu Z, Chen K, Xu J. Carbonic anhydrase 2 and 3 as risk biomarkers for dilated cardiomyopathy associated heart failure. Ann Palliat Med 2021;10(12):12554-12565. doi: 10.21037/apm-21-3561. 2. Dzudie A, Barche B, Nkoke C, Ngatchuesi VG, Ndom MS, Mouliom S, Ndjebet J, Nouko A, Fogue R, Abang S, Abah J, Djomou A, Nzali A, Sidikatou D, Menanga A, Kingue S, Kamdem F, Mbatchou BH, Luma HN. Survival rate and predictors of 36-month mortality in patients with heart failure in Sub Saharan Africa: insights from the Douala Heart Failure Registry (Do-HF). Cardiovasc Diagn Ther 2022;12(5):577-588. doi: 10.21037/cdt-22-166.

Reply: Thank you for your comment. We supplemented it in the article.

Changes in the text: Paragraph 1/ introduction, and Paragraph 1/ Discussion

Reviewer B

The paper titled “Selection of key genes for dilated cardiomyopathy with heart failure based on machine learning algorithms and assessment of diagnostic efficiency” is interesting. CCL5 and CTGF are key disease-causing genes in dilated cardiomyopathy with heart failure and have good diagnostic efficiency for the disease. CCL5 and CTGF may be related to immune cell enrichment and myocardial fibrosis, respectively. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) The description of some methods in this study is too simplistic, please describe in detail.

Reply: Thank you for your comment. We have supplemented the method section.

Changes in the text: Paragraph 1,4/ method

2) It is recommended to add in vivo and in vitro experimental validation of the results of this study.

Reply: Thank you for your comment. This is one of the shortcomings of this study. We elaborated during the discussion.

Changes in the text: Paragraph 4/ Discussion

3) Suggest integrating some figures according to magazine requirements. And some fonts are unclear and need to be enlarged.

Reply: Thank you for your comment. We have made modifications to the figures.

Changes in the text: Figure 7,8,9,10

4) What are the biggest strengths and weaknesses of this research model? What is the biggest problem faced? Suggest adding relevant content.

Reply: Thank you for your comment. We supplemented the discussion.

Changes in the text: Paragraph 4/ Discussion

5) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “Integrative bioinformatics analysis of potential therapeutic targets and immune infiltration characteristics in dilated cardiomyopathy, PMID: 35433958”. It is recommended to quote the article.

Reply: Thank you for your comment. We supplemented the reference in the discussion section of the article.

Changes in the text: Paragraph 2/ Discussion

6) It may be more meaningful to add functional research on key genes.

Reply: Thank you for your comment. We strongly agree with your viewpoint. We did not conduct research on gene function, which is one of the shortcomings of this study. We elaborated on the gene function during the discussion.

Changes in the text: Paragraph 4/ Discussion

7) How to analyze the immune infiltration pattern of dilated cardiomyopathy with heart failure? It is recommended to add relevant content.

Reply: Thank you for your comment. We supplemented the discussion.

Changes in the text: Paragraph 1/ Discussion