Reviewer’s report

Title: Integrative model of leukocyte genomics and organ dysfunction in heart failure patients requiring mechanical circulatory support: A prospective observational study

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Reviewer: Robert M. Blanton

Reviewer's report:

In the current manuscript Wisniewski and colleagues characterize the time-dependent changes in clinical parameters and whole-genome mRNA expression changes in circulating leukocytes in order to attempt to create a testable model for organ dysfunction and gene expression after mechanical support surgery in heart failure patients. The authors use a sophisticated statistical analysis to identify a time-dependent relationship between mononuclear cell transcriptional changes and organ dysfunction.

The strengths of the study include the clinical relevance of understanding the mechanisms predicting death or organ dysfunction after mechanical support. The main concern is that the study does not identify how the findings after mechanical support surgery differ, or not, from those after other types of surgeries. See individual comments below.

Major Comments:

1. Ideally the study would contain control, non-MCS patients, and more importantly would perform a similar analysis on patients receiving other types of cardiac surgery or non-cardiac surgery. This would help answer the question of what gene expression patterns are unique to the MCS population.

This limitation is of course difficult to address experimentally in the present study. However, increased discussion of this in the manuscript, particularly in the Discussion section, would be useful.

2. The detailed model outlined in paragraph 2 of the Background section and in Figure 1 would benefit from more citations of the literature.

3. The n's of the study are relatively small. However, this is acknowledged appropriately in the discussion.
Minor comments

1. The italicized sections in the discussion distract the reader and should be removed.

2. Figures 1 and 6 could be laid out more clearly.

3. Figure 1. The "A," "B," "C" in the legends are confusing.

4. Any biological data to support the gene expression changes would be useful. For example, measures of mitochondrial function in leukocytes, etc would be useful if they correlated with the gene expression patterns.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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