Reviewer’s report

Title: Right Ventricular Failure Following Left Ventricular Assist Device Implantation is Associated with a Preoperative Pro-Inflammatory Response

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Reviewer: Maziar Khorsandi

Reviewer’s report:

I would like to congratulate the authors on this great work. Much is lacking in the literature regarding aetiology of RHF following durable LVAD implantation. There are several questions that needs to be addressed

- Given that heart failure is a pro inflammatory state it is difficult to quantify in these group of patients how much of the raised inflammatory markers come from the "state of heart failure" itself vs. invasive procedures e.g. IABP etc. Therefore this invariably leads to great heterogeneity in the study population.

-While previous studies (by Anker et al and Mann et al) have linked inflammatory mediators being associated with heart failure (not necessarily in the setting of LVAD implantation), here many patients had antecedent devices such as IABP etc that could have accounted for raised inflammatory markers hence I am not certain that such a comparison is still valid. Can you please elaborate?

-I believe that the aim of the study may not necessarily be valid. There are plenty of mitigating factors leading to raised WCC and CRP as well as survival/mortality following MCS and I do not think that raised WCC and CRP can be looked as prognostic indicators?

-How did the investigators differentiate between active infection e.g. from a central venous line, leading to raised WCC and CRP (as sepsis increases mortality rate by itself) vs. raised WCC and CRP as a result of the organ system duress from the state of heart failure itself and patients on steroids with falsely elevated inflammatory markers?

-Patients with high CRP and WCC are clearly sicker (perhaps from other causes) and will naturally have higher risk of mortality than patients with normal inflammatory parameters. I therefore think this comparison is confounded as there are other mitigating factors in play here. The study findings would have been more valid if the investigators had performed propensity matching. How did the authors take confounding variables into consideration in their study please?

-Again it is difficult to know if the raised WCC and CRP are cause or the effect here... how was this addressed please?
- Perhaps my most important query is; How can the authors please explain how their finding is likely to impact clinical practice? i.e. how are they and the wider readership are going to benefit from their findings in terms of patient management? Are the authors suggesting that if the inflammatory mediators are corrected this might reduce the risk of need for an RVAD in heart failure patients receiving a cFLVAD? This needs to be clarified in the discussion and the discussion needs to be expanded. They are not adding any new information or claims in their discussion!

- The authors need to acknowledge significant heterogeneity in their study in the study limitations.

- It is not clear to me why there had to be 6 tables? Can you please make an effort to merge some of these please?

- Authors have not detailed anything regarding what constituted infection e.g. device infection... was this on the basis of the wound appearance, culture bacteriology swabs, blood cultures or both? The authors need to give this issue significant clarification in the methods section!

- The authors need to significantly expand on their methods and patient selection

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