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Dear Editor,

We greatly appreciate the reviewers' comments which we feel strengthen our manuscript. We hope you will now find the manuscript suitable for publication. Please find our point by point response below:

Reviewer ***03497352***

1) Provide a reference for the line: "While use of echocardiography has proven useful for optimization of HeartMate II (Pleasanton, CA) CF-LVAD pump speed, this has not proven helpful for other CF-LVADs"

   This reference is now provided: Uriel N, Levin AP, Sayer GT, Mody KP, Thomas SS, Adatya S, Yuzefpolskaya M, Garan AR, Breskin A, Takayama H, Colombo PC, Naka Y,Burkhoff D, Jorde UP. Left Ventricular Decompression During Speed Optimization Ramps in Patients Supported by Continuous-Flow Left Ventricular Assist Devices: Device-Specific Performance Characteristics and Impact on Diagnostic Algorithms. J Card Fail. 2015;21:785-91. PMID:26117282 DOI: 10.1016/j.cardfail.2015.06.010]

2) For the line: "This flow increased to a range of 8-9 liters/minute on post operative day #8...", what does 'this' flow mean? The Fick CO? Kindly clarify.

   Thank you, we have clarified:
   '**The flow through the CF-LVAD as measured by the flow probe** increased to a range of 8-9 liters/minute'

3) Methods, 1st para: Provide an abbreviation for revolutions per minute in parenthesis i.e. revolutions per minute (rpm).

Thank you, we have done.

4) Discussion, 3rd para: "Loss of the V-wave on the PCWP tracing, coupled with aortic valve closure by echocardiogram, argued against the presence of a high cardiac output state", please add: with increasing rpm after Loss of the V-wave on the PCWP tracing, coupled with aortic valve closure by echocardiogram. Also I have difficulty understanding this sentence. How does that mean that it argues against a high output state. Kindly clarify

   We have amended:
   'After increasing the RPM, the loss of the V-wave on the PCWP tracing, coupled with aortic valve closure by echocardiogram, also argued against the presence of a high cardiac output state, as these suggest further unloading by the CF-LVAD. '

   'with increasing rpm after Loss of the V-wave on the PCWP tracing, coupled with aortic valve closure by echocardiogram

5) If the ultrasound flow probe measurements are inaccurate after the immediate postop period, why would we use those? Thank you for an opportunity to review.

   Thank you for the comment. If the ultrasound flow probe measurements are inaccurate, we should not use those , hence our caution:

   'Clinicians should use corroborative techniques (such as RHC) to confirm abnormal changes in CF-LVAD flows before acting on that data, both for CF-LVADs that estimate flows and those that directly measure flows.'

   Reviewer ***03493210***

   The manuscript is a case report involving a single patient with documentation of hemodynamic and echocardiographic changes during a ramp right heart catheterization/echocardiogram, in a patient with a continuous flow left ventricular assist device with comparison of cardiac output by catheterization to that measured via flow probe on the outflow graft to the left ventricular assist device. Obviously, this is a single patient and RAMP catheterization and echocardiograms have been previously published in continuous flow left ventricular assist devices, so there is nothing novel about this aspect of the case.

Indeed, the only really novel aspect of this case is the comparison of cardiac output by catheterization to that by the flow probe.

We thank you for your constructive comments.

1. I think the manuscript could be made stronger with a clear delineation of how the ramp catheterization was actually used in this patient; he authors do not describe what the baseline speed actually was and what the final set speed was at the end of the ramp study. Similarly, they do not determine what parameters they actually used to set the final speed. This is one of the major purposes of a RAMP study so it needs to be better delineated in the text.

   We agree, and have amended the manuscript accordingly:

   'The baseline speed was 9100 RPM. We changed speed by 400 RPM increments to determine the best hemodynamics (normal biventricular filling pressures with normal cardiac output), as well as optimal aortic valve opening (aortic valve opening frequency of at least 1:3 cardiac cycles).'

   As a result, given acceptable hemodynamics at 8700 RPM and intermittent aortic valve opening with optimal position of the IVS, the speed was changed to 8700 RPM at the conclusion of the study.

2. Similarly, the echocardiographic portion of the ramp study was not really described in much detail at all. They mention that the aortic valve opening and the mitral regurgitation decreased as pump speed increased. However there was no note of change in the left ventricular dimensions or septal position.

   Thank you, we have amended accordingly:

   '**At baseline RPM the left ventricular end diastolic dimension (LVIDd) was 8.0 cm and the interventricular septum (IVS) bowed mildly toward the LV.** As pump speed increased, the degree of mitral regurgitation decreased**, the LVIDd decreased further to 7.8 cm but the IVS shifted even more toward the LV. At lower speeds the IVS was midline, and at 8300 RPM the LVIDd was 8.3 cm.**

3. With regards to the observation that the measured flow through the graft was higher than the Fick cardiac output, I think a major limitation of their

conclusions is that there are using an assumed Fick for estimated O2 consumption. In the postoperative state, or in sepsis, it seems quite reasonable/likely that the patient might have a significantly higher O2 consumption than that estimated by K x BSA. The K they use is 125 but in our center, we will often use a K of 133. I suspect that this is part of the reason why there was a difference between the assumed Fick cardiac output and that via the flow probe.

Thank you for this comment. We have addressed the limitation of using an assumed Fick:

'One limitation of our study was the use of an assumed Fick calculation. We felt that was mitigated somewhat by the comcomitant thermodilution data in the intensive care unit, which closely correlated with the Fick cardiac output. Simultaneous measurement of Fick and thermodilution cardiac outputs in the catheterization laboratory, as well as the use of metabolic cart to calculate peak oxygen consumption would more directly address this limitation.'

When using a K of 133 there was not a substantial change in measured Fick cardiac output, and the result was still markedly discrepant from the flow measured by the flow probe.

4. It seems unlikely that there would be a lot of sensor 'drift' this soon after the LVAd and probe were implanted. It would be interesting and would have been easy for the authors to obtain thermodilution cardiac output readings - this is commonly done in surgical intensive care units. Can they comment on why this was not done?

   We agree that it would be surprising that sensor drift would occur so early, but find that a plausible explanation. We did obtain thermodilution cardiac output readings, which are now incorporated in the manuscript:

   'In the intensive care unit his flow through the CF-LVAD as measured by the flow probe ranged between 5 and 6 liters/minute, with cardiac output measured via the Fick principle in the 7-8 L/min range, **and cardiac output by thermodilution in the 7-8 L.min range as well**.'