Peer Review File

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Reviewer comments

Reviewer A

wish to congratulate with the authors for their well written and comprehensive review. The manuscript reads well and gives all the relevant information. I would recommend few changes before accepting it for publication.

Comment 1: In line 108 there is mention of "IDE group" but meaning of acronym is not explained. This needs to be addressed to improve clarity for the reader.

Reply 1: Thanks for pointing this out. Updated the manuscript.

Changes in the text: Acronym spelled out – Investigational Device Exemption [IDE] (see Page 7, line 115-116)

Comment 2: At page 4, I would expand the "Current outcomes" section regarding the use of pulsatile flow device. It is significantly shorter than the "Early experience" section but more relevant to the reader.

Reply 2: That is a good point. The current outcomes section was updated including the latest results from the FDA post-marketing approval surveillance study published this year.

Changes in the text: The FDA post-approval surveillance study report published this year shows how far the field has come. Despite significantly more risk factors such as being younger, smaller, and more likely to have congenital heart disease, the post-marketing approval surveillance study group had an 86% 6-month success rate (transplant, explant with recovery or still on device) compared to 76% for previously reported Berlin Heart study group. (28) All adverse events improved including stroke (11.5 vs 3.99 events per 100 patient months), major bleeding (33.9 vs 6 events per 100 patient months), and major infection (40.36 vs 10.39 events per 100 patient months). Frequency of pump exchanges also decreased 40%. Similarly, (see Page 8, line 135-142).

Comment 3: Similarly, I would expand more the "Discussion" session and rephrase lines 218-222.

Reply 3: Discussion expanded as requested and lines 218-222 were rephrased.

Changes in the text: While single-center studies and small case series have been helpful to introduce novel management strategies and surgical techniques, the small number of patients are insufficient to create evidence-based recommendations. Because individual centers all have relatively few pediatric patients, registries such as Pedimacs and Euromacs have helped create larger data repositories that have helped further define complications and morbidities with pediatric VAD use including stroke rate, infection, bleeding, and inpatient length of stay (see Page 12, lines 237-244). Additional changes were made to the discussion as detailed in Comment/Reply 4.

Reviewer B

This is a well written, succinct review of VAD management in pediatric patients on the wait list for heart transplantation.

Comment 4: I have no major suggestions to improve the VAD portion of the manuscript, other than perhaps adding a table or something else summarizing the review (i.e. VAD options in a list), or a figure showing some of the devices.

Reply 4: I agree that it is reasonable to add a table outlining devices mentioned.

Changes in the text: Table 1 shows many of the VADs that are used in the pediatric population. (see page 6, lines 91-92). Table 1 included in the submission.

Comment 5: The one major flaw in this reviewer's mind is the limited information on everything that isn't a VAD. The title of the document refers to MCS supporting pediatric pts on the waitlist, but only about 4 lines each are given to ECMO and percutaneous devices. It would seem like there is considerably more complexity in many of these management decisions while on the waitlist. For instance, what to do with the patient who can't be on a VAD? Who can and can't get a VAD (another potential table?)? In what situations is other support reasonable? Does expectations of recovery change the modality chosen? Based on this review, we should only use VADs and never use ECMO in any situation where transplant is a possibility, but that is clearly missing the nuances of how we make these decisions. I think if a little more is added, it will read much less like a VAD review paper and more like a broader MCS paper. If meant to be only a VAD paper, then the cursory yet dismissive paragraphs about ECMO and percutaneous devices aren't needed.

Reply 5: The reviewer's point is well taken. One of the challenges is that many of the temporary devices including ECMO, IABP and Impella are used as a bridge to bridge, as opposed to a direct bridge to transplant in the current era. That said, there have and will continue to be need for these other devices as part of the MCS in transplant. This concept of bridge to bridge was expanded on in the conclusion.

Changes in the text: Bridge to bridge management is idea that before a patient is deemed stable enough for a durable ventricular assist device such as a Berlin Heart, HeartWare or HeartMate 3, that a temporizing form of mechanical support may be necessary and could potentially improve outcomes. VA-ECMO remains the gold-standard for temporizing MCS in pediatric patients with cardiogenic shock in part because of the ease and rapidity of deployment as well as full cardiopulmonary support. Other temporary paracorporeal devices that are implanted surgically include Rotaflow (Maquet, Rastatt, Germany) and Pedimag/Centrimag (Abbott Laboratories, Abbott Park, IL, US). These devices can be placed with ECMO cannulae, or have been used with Berlin Heart cannulae, thereby simplifying conversion to the EXCOR (59, 60). Some centers have use these devices longer-term as a bridge to transplant as well with mixed success, although often in the setting of the sickest patients (61). Finally, more interest has been shown in recent years for percutaneous bridge to bridge options such as the TandemHeart (CardiacAssist, Pittsburgh, PA, US) or Impella (Abiomed, Danvers,

MA, US) devices, which are inserted across the aortic valve into the left ventricle either via femoral or left axillary artery access (62). There is limited adult data of Impella use as direct bridge to transplant in settings where waitlist times are expected to be very short (63). Ultimately, these strategies have come about due to the unacceptably high morbidity and mortality among children presenting with acute cardiogenic shock. (see Pages 13-14, lines 253-169)