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Reviews:

A fully magnetically levitated circulatory pump for advanced heart failure,

Mehra MR, Naka Y, Uriel N, et al. NEJM Nov 16th 2016
<https://www.ncbi.nlm.nih.gov/pubmed/27959709>

Left ventricular assist devices (LVAD) improve survival and quality of life in patients with end stage heart disease. The morbidity associated with LVAD implantation improved as we moved from pulsatile flow into continuous flow devices. As a result, in the United States the HM-II (axial flow) was approved for implantation as bridge to transplant (BTT) and destination therapy (DT). The heart failure community was hopeful that implantation of LVAD at earlier stages of advanced heart failure would lead to further improvement of survival. Unfortunately, reports of increased frequency of LVAD thrombosis in patients who had received a HM-II device led to the halt of the REVIVE-IT clinical trial. The HM-III LVAD (continuous flow centrifugal pump) was designed to decrease the stasis of blood within the pump and hence decrease the chances of LVAD thrombosis.

This publication reports the short-term (6 months) outcomes of patients who received a HM-III device in comparison with those who received an HM-II device. The Momentum 3 trial was a randomized, non-blinded clinical trial. The trial was designed to test for non-inferiority of the HM-III device but it was also powered to test for superiority. A total of 294 Patients were randomized into the trial, HM-III (152) and HM-II (142) LVADs. The primary endpoint of this trial was a composite of **survival free of disabling stroke** (modified Rankin score >3) and **survival free of re-operation to replace or remove the device after implantation**. A total of 140 (92.7%) HM-III and 126 (91.3%) HM-II patients were discharged from the hospital after LVAD implantation. Among those discharged the length of stay was 19.5 d HM-III and 17.5 d (HM-II, p=0.23). There were a total of 27 deaths during the trial 13 in the HM-III and 14 in the HM-II groups respectively.

In an intention to treat analysis, the primary end point occurred in 131 patients (86.2%) in HM-III and 109 (76.8%) in the HM-II (absolute difference 9.4%, p<0.001 for non-inferiority. P=0.04 for superiority (HR 0.55 (0.32-0.95)). There were no differences in the frequency of disabling strokes between the groups, 6 in the HM-III and 4 in the HM-II groups. The frequency of any stroke was also similar, 12 (7.9%, HM-III) and 15 (10.9%, HM-II). Thus, the main driver in the difference in primary endpoint in this trial was the rate of re-operation due to pump malfunction. Only 1 patient in the HM-III group underwent device exchange due to driveline electrical fault, whereas 9 patients in the HM-II group had device exchange and 2 had urgent heart transplantation (p=0.002). There were no device thrombosis episodes in the HM-III groups, whereas there were 14 cases of suspected/confirmed device thrombosis in the HM-II group. The QoL in both groups was similar. Although there were no interactions noted between the primary endpoint and variables such as age, sex, race, device strategy and INTERMACS profile at the time of implantation, it was reported that patients older than 70 years old had worse overall survival in both groups. In fact, the 6 months survival in patients who received a HM-III were: 94.7±3% (18-59 years old), 89.9±3.9% (60-69 years old), and 76.5±7.3% (older than

70 years) ($p=0.0259$). The survival in patients who received a HM-II pump had similar distribution according to age. The frequency of GIB and other adverse events were similar within both groups. The authors concluded that HM-III had incremental improvement in clinical outcomes compared to HM-II due to a lower rate of re-operation due to pump malfunction. This is an important finding and a step forward in decreasing the morbidity associated with pump thrombosis in patients who receive an LVAD as treatment for end stage heart disease. However, the fact that complications, such as stroke or gastro-intestinal bleeding, were not affected by the HM-III device underscores that the challenges facing LVAD therapy still remain significant.

Prevention of HeartMate II Pump Thrombosis Through Clinical Management: The PREVENT multi-center study

Maltais S, Kilic A, Nathan S, et al. JHLT Nov 2016.

<https://www.ncbi.nlm.nih.gov/pubmed/27836022>

Pump thrombosis (PT) is a serious complication in patients supported by left ventricular assist devices (LVAD). In 2014, a report showed that the frequency of PT had increased significantly to 8.4%. The explanation for the increased PT rate was multifactorial. As LVAD therapy became spread in the US we recognized that bleeding was a frequent cause of morbidity in this population. As a result, publications suggested that we could safely manage these patients with lower INR goals or without the use of heparin bridging in the early postoperative period. In addition, implanting centers may have used lower LVAD speeds in order to prevent RV failure, aortic insufficiency and/or gastrointestinal bleeding.

Maltais et al present the results of the PREVENT trial, which was a prospective, multi-center, single arm, non-randomized study of 300 patients. The objective of this trial was to evaluate if adherence with a strict surgical/medical management would prevent or decrease the frequency of PT. The primary outcome was the frequency of PT at 3 months post implantation and secondary outcomes were the frequency of adverse events, survival and adherence of practices through 6 months. The authors hypothesized that at 3 months the confirmed rate of PT would be lower than 4% at 3 months (frequency of PT previously reported).

In order to minimize PT center were asked to comply with the following directions

Surgical -Adequate size of pump pocket, located inferiorly deep and lateral.

-Inflow cannula parallel to the septum, oriented to the central LV.

-Position of the outflow graft right to the sternal midline to avoid compression of the RV.

-Position of the pump below the diaphragm.

-Fixate the pump (to the diaphragm or the chest wall) to prevent migration.

Medical: -Begin heparin bridging with heparin or LMWH within 48 hrs. of implantation (goals 40-45 APTT for 48hrs and 50-60 APTT by 96hrs).

-Initiate warfarin within 48 hrs., INR goal 2-2.5 by 5-7 days.

-Initiate aspirin 81-325 mg daily by day 2-5.

-Maintenance treatment with aspirin & warfarin (INR 2-2.5).

-HM-II speed \geq 9000 rpm and avoid speeds $<$ 8600 rpm.

-Keep mean arterial pressures $<$ 90 mmHg.

The population enrolled in this study was predominantly male (83%) with a mean age of 57 yo. Seventy eight percent received LVAD as DT and 83% INTERMACS 1-3. Confirmed PT occurred in 9 patients (2.9%) and 12 patients had confirmed and suspected PT (3.6%). At 6 months there were a total of 20 confirmed and suspected (4.8%). Overall survival at 6 months was 89% and survival free of PT was 84%. The overall incidence of bleeding was 45% at 6 months 21% GIB, Early bleeding 34%, bleeding requiring surgery happened in 16%. Full adherence to recommendations was accomplished in 78% of patients. When comparison were performed between patients who had 100% compliance with the recommendations to prevent PT and those who had not. There was a lower risk for PT thrombosis

at 6 months (1.9% vs. 8.9%, $p < 0.01$) and lower composite risk of suspected thrombosis, hemolysis and ischemic stroke (2.7% vs. 17.7%, $p < 0.01$) in favor of patients who met the recommendations.

This report underlines how careful implantation technique and adherence to anticoagulation/medical recommendations can keep the frequency of PT at the reasonably low levels. However, It also shows how in routine clinical practice we may be able to adhere to these recommendations in approximately 78% of the patients.

Other Publications:

Journal of Heart and Lung Transplantation

Coagulation factor abnormalities related to discordance between anti-factor Xa and activated partial thromboplastin time in patients supported with continuous-flow left ventricular assist devices. [Adatya S, Sunny R, Fitzpatrick MJ et al. JHLT 2016;35:1311-20. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27836023>](#)

The NHLBI REVIVE-IT study: Understanding its discontinuation in the context of current left ventricular assist device therapy.

[Pagani FD, Aaronson KD, Kormos R et al. JHLT 2016;35:1277-1283. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27836022>](#)

Circulation: Heart Failure

[INTERMACS \(Interagency Registry for Mechanically Assisted Circulatory Support\) Profiling Identifies Ambulatory Patients at High Risk on Medical Therapy After Hospitalizations for Heart Failure. Stewart GC, Kittleson MM, Patel PC, et al. Circulation : Heart Failure Nov 2016. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27834198>](#)

Annals of Thoracic Surgery

Impact of Preoperative Atrial Fibrillation on Postoperative Thromboembolic Events After Left Ventricular Assist Device Implantation.

[Xuereb L1, Go PH1, Kaur B1 et al. Ann Thorac Surg, Nov 2016;102:1543-1549. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27469338>](#)