What's New in MCS

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Nandini Nair, MD, PhD
Providence Sacred Heart Medical Center
Spokane, Washington, USA
Nandini.nair@gmail.com

July Reviews

Sato T, Seguchi O, Iwashima Y et al (2015) Serum Brain Natriuretic Peptide Concentration 60 Days After Surgery as a Predictor of Long-Term Prognosis in Patients Implanted With a Left Ventricular Assist Device ASAIO J 61; 373-378

The role of biomarkers in the unloaded ventricle continues to be an active area of research in the era of mechanical circulatory support. Brain Natriuretic Peptide (BNP) levels are up regulated in chronic volume overload/myocardial stretching and tend to decrease post-LVAD implantation with reduction in wall stress.

In a retrospective analysis Sato T et al (ASAIO J 2015: 61; 373-378) studied 83 patients placed on LVAD support between May 2001 and July 2012 to assess clinical markers associated with all - cause mortality. Of all clinical markers studied BNP was the only marker that showed a prognostic value. The study population predominantly consisted of patients on paracorporeal support (Nipro-Toyobo). Log BNP levels appeared to decrease status post VAD implantation and stabilized at 60 days post implant in multivariate analyses. No statistically significant decrease in BNP levels was noted at 90 days post VAD implant. Receiver-operating-characteristic curve analysis of BNP levels at 60 days post implant revealed an area under the curve of 0.779 with a sensitivity of 71.4% and specificity of 79.8 %. Kaplan–Meier curves showed that survival had significantly decreased by 2 years in the patients with >322pg/ml at 60 days post implantation suggesting a prognostic value for BNP.

Analysis:

The role of serum BNP levels in predicting clinical outcomes of patients supported on VADS has been investigated in the past. In 2001 Sodian et al (JACC 38; 1942-49) noted a decrease in BNP levels in patients supported on VADs (Berlin Heart and Novacor) in a small retrospective analysis. They hypothesized that such reductions in BNP levels were suggestive of recovery of ventricular function. In the same year Milting et al (J Heart Lung Transplant 20; 949-955) observed differences in the time courses of ANP and BNP depending on the type of VAD used for support suggesting that the pump mechanics would have a significant role to play. In 2011 Kato et al (Circ Heart Failure 4; 546-553) showed significant differences in BNP levels in pulsatile vs continuous flow VADS with lower levels noted in pulsatile VADS again suggestive of differences depending on the type of VAD used.

The retrospective study discussed here by Sato T et al showed that serum BNP levels could predict survival but the study population is largely composed of the Nipro-Toyobo paracorporeal pulsatile-flow VAD which is different from the present day population of continuous flow LVADS. Additionally the study population appears to be younger (39 +/- 12 years) with an essentially close to normal BMI (19.8 +/-3.5) and dilated cardiomyopathy as the predominant etiology. Though the study by Sato et al has its limitations it would help pave the way for more definitive biomarker studies for

prognostication in patients supported on CF-LVADS used today and may facilitate further comparisons between axial and centrifugal pumps.

Awad M, Czer LCS, Soliman C et al (2015) Prevalence of Warfarin Genotype Polymorphisms in Patients with Mechanical Circulatory Support ASAIO J 61; 391-396

The fine line between adequate anticoagulation and bleeding complications is an ongoing problem in patients who require chronic anticoagulation due to the narrow therapeutic index of warfarin. With the discovery of genetic polymorphisms in the ***VKORC1*** **and** ***CYP2C9*** genes a genotypic approach to warfarin dosing continues to be an area of active investigation.

The single center retrospective analysis by Awad et al (ASAIO J 61; 391-396) is the first report on this approach in the mechanical circulatory support (MCS) population. Awad et al studied polymorphisms for ***VKORC1*** and ***CYP2C9*** in 65 patients who had MCS surgery. Approximately 67.7% had at least one polymorphism. ***VKORC1*** constituted 44.6 % followed by ***CYP2C*9*** at 7.7% and other groups with polymorphisms on both genes. The parameters assessed in this study were post implant warfarin dose, international normalized ratio (INR), and bleeding events until discharge, at 6 months post implant, or composite end point (in-hospital MCS recovery, heart transplant, or death). The authors noted no significant difference in bleeding but patients with any polymorphism received a lower mean warfarin dosage at discharge or before composite end point to achieve the same INR. These results suggest that a genotype-driven anticoagulation regimen helps avoid excessive therapy and the complications that result from it.

Analysis

Genotype driven management of anticoagulation is a valuable approach. There are many factors that influence this type of management. Racial differences in genetic polymorphisms have an important role to play. Composition of study populations therefore influences results. The two randomized clinical trials EU-PACT and COAG published in NEJM 2013 studied the utility of pharmacogenetic versus standard dosing of warfarin and arrived at interestingly different results. Another EU-PACT randomized clinical trial also published in NEJM 2013 compared acenocoumarol and phenprocoumon which failed to show any significant difference in the average percentage of time in the therapeutic INR range between genotype based dosing versus clinical dosing in the study period of 12 weeks. However, these study populations did not include patients on MCS support.

The MCS population differs from those reported in these trials because of additional effects of sheer stress, the acquired von Willebrand syndrome and prior surgical procedures on bleeding tendencies. Hence genotype-guided tailored anticoagulation protocols may be appropriate in the MCS population due to the inherent complexity in the MCS population. Despite the limitations of this study such as being small and retrospective, it opens the doors for designing larger controlled double blinded clinical trials to definitively investigate the utility of genotype driven anticoagulation protocols in MCS patients.

ASAIO J July /Aug 2015

1. **Moazami N, Anandamurthy B (2015) Acute Circulatory Support with ECMO: Great Achievements but Still a Long Road Ahead ASAIO J 61; 371-372
2. ***Sato T, Seguchi, O, Iwashima Y et al (2015) Serum Brain Natriuretic Peptide Concentration 60 Days After Surgery as a Predictor of Long-Term Prognosis in Patients Implanted With a Left Ventricular Assist Device ASAIO J 61; 373-378
3. ***Truby L, Mundy L, Kalesan B et al (2015) Contemporary Outcomes of Venoarterial Extracorporeal Membrane Oxygenation for Refractory Cardiogenic Shock at a Large Tertiary Care Center ASAIO J 61; 403-409

4. ***Haglund NA, Davis ME, Tricarico NM et al (2015) Readmissions After Continuous Flow Left Ventricular Assist Device Implantation: Differences Observed Between Two Contemporary Device Types ASAIO J 61; 410-416
5. *Lovich MA,Pezone MJ, Wakim MG et al (2015) Inhaled Nitric Oxide Augments Left Ventricular Assist Device Capacity by Ameliorating Secondary Right Ventricular Failure ASAIO J 61;379-385
6. **Dionizovik-Dimanovski M, Levin AP, Fried J et al (2015) Correlation Between Home INR and Core Laboratory INR in Patients Supported with Continuous-Flow Left Ventricular Assist Devices ASAIO J 61; 386-390
7. ***Awad M, Czer LCS, Soliman C et al (2015) Prevalence of Warfarin Genotype Polymorphisms in Patients with Mechanical Circulatory Support ASAIO J 61; 391-396
8. *Wang D, Jones C, Ballard-Croft Cherr et al (2015) Development of a Double-Lumen Cannula for a Percutaneous RVAD ASAIO J 61; 397-402
9. **Nielsen VG, Sobieski MA II, Slaughter, MS et al (2015) Left Ventricular Assist Device–Associated Carbon Monoxide and Iron-Enhanced Hypercoagulation: Impact of Concurrent Disease ASAIO J 61; 417-423
10. *Karimov JH, Steffen RJ.; Byram N et al (2015) Human Fitting Studies of Cleveland Clinic Continuous-Flow Total Artificial Heart ASAIO J 61; 424-428
11. *Rhodes LA, Sasser WC, Mcmahon WS et al (2015) Transhepatic Cannulation for Venovenous Extracorporeal Membrane Oxygenation ASAIO J 61; e29-e30

Journal of Thoracic and Cardiovascular Surgery July 2015

1. **Smedira NG (2015) Adding a new dimension to our understanding of continuous-flow physiology J Thorac Cardiovasc Surg. 150:207-8
2. **Mallidi HR, Anand J, Singh SK (2015) Long-term mechanical circulatory support: A new disease state? J Thorac Cardiovasc Surg. 150: e13–e14

Circulation Heart Failure July 2015

1. *Sperry BW, Jacob MS, Menon V et al (2015) Defying Dogma: Recovery After Left Ventricular Assist Device Implantation and Aortic Valve Replacement for Bicuspid Aortic Valve Circ Heart Fail. 2015;8:832-835

Journal of the American College of Cardiology July 2015

No articles pertaining to MCS

Journal of Cardiac Failure July 2015

No articles pertaining to MCS

European Journal of Heart Failure July 2015

No articles pertaining to MCS