

(BMI), NRI and all lipid parameters during the period of LVAD support. These lipid increases did not correlate with time since LVAD implantation, or change in albumin or BMI. However the degree of HDL increase correlated with BNP decrease ($r=-0.47$, $p=0.0001$), and triglyceride increase correlated with the improvement in NRI ($r=0.34$, $p=0.002$).

Conclusion: Pre-LVAD mean lipid parameters were at the lower limits of normal. At a mean of 13 months' LVAD support, all lipid parameters in our cohort had significantly increased. These lipid panel changes may be related to both improved nutritional status and reduced circulatory congestion.

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Persistent Hyperbilirubinemia Following LVAD Implantation Predicts Postoperative Multisystem Organ Failure and Mortality

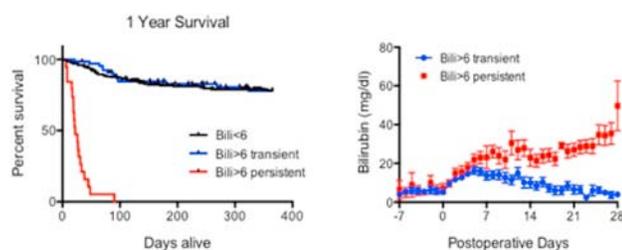
K.J. Lavine,¹ J. Vader,¹ S. Larue,¹ M. Nassif,¹ D. Raymer,¹ A. Tibrewala,¹ S. Prasad,² S. Silvestry.² ¹Cardiology, Washington University School of Medicine, St Louis, MO; ²Cardiac Surgery, Washington University School of Medicine, St Louis, MO.

Purpose: Multisystem organ failure (MSOF) remains an important cause of early mortality following LVAD implantation. Postoperative hyperbilirubinemia has previously been associated with hepatic failure and MSOF in small case series, however, the clinical importance of hyperbilirubinemia following implantation of modern continuous flow devices remains unexplored.

Methods: To define predictors and clinical outcomes associated with postoperative hyperbilirubinemia we performed a retrospective analysis of 286 patients who underwent LVAD implantation at a high volume center between 2009 and 2013.

Results: Based on a bilirubin level >6 mg/dL, we identified 84 patients with postoperative hyperbilirubinemia and demonstrated that patients with a peak bilirubin >6 mg/dL have increased in-hospital (RR 3.06, 95% CI 1.71-5.47) and 1 year mortality (RR 1.88, 95% CI 1.26- 2.80) compared to patients with a peak bilirubin <6 mg/dL. Hyperbilirubinemia was associated with postoperative RV failure, vasopressor requirement, renal failure, and ongoing hepatic injury. Among patients with a peak bilirubin >6 mg/dL, persistent hyperbilirubinemia (defined by failure to decrease bilirubin 50% by postoperative day 10) was independently associated with MSOF, bacteremia, and 100% mortality. Clinical predictors of persistent hyperbilirubinemia included preoperative hepatic injury, RV dysfunction, and need for temporary mechanical support. Pathologically, patients with persistent hyperbilirubinemia demonstrated hepatic necrosis, neutrophilic inflammation, and sinusoidal loss.

Conclusion: Together, these findings define persistent postoperative hyperbilirubinemia as a biomarker predicting MSOF and mortality following LVAD implantation.



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Systemic Inflammation in End-Stage Heart Failure Patients Undergoing Different Axial-Flow Left Ventricular Assist Devices

L. Botta, R. Caruso, A. Cannata, G. Bruschi, F. Milazzo, S. Nonini, J. Campolo, M. Lanfranconi, C.F. Russo, P. Marraccini, M. Frigerio, O. Parodi, L. Martinelli. Niguarda Hospital, Milano, Italy.

Purpose: The impact of different axial-flow devices on systemic inflammation and early outcomes was investigated in end-stage heart failure (ESHF) patients.

Methods: From 2005 to 2012, 70 ESHF-patients received a VAD at our department. Biochemical analysis was performed preoperatively, at 1, 3, 7 and 30 days post-LVAD for assessment of plasma interleukin (IL)-6, IL-8, sICAM-1, sP-Selectin, and urinary neopterin levels. The following clinical outcomes were considered: multi-organ failure, evaluated by total sequential organ failure assessment (tSOFA) score, ICU stay, hospitalization and 1-month survival.

Results: Following matching for pre-implant clinical and inflammatory characteristics, 35 patients were included into the study and divided in two groups (A-Group, 14 patients: 6 Incor and 8 DeBakey; B-Group, 21 HeartMate II). In-hospital mortality was 21% in A- vs. 19% in B-group ($p=1.000$). Hospitalization was shorter in B- than in A-group ($p=0.040$). Total-SOFA score at 3 days was higher in A- than in B-group ($p=0.019$), and at 1 week was still higher than baseline only in A-group ($p=0.002$). At 1 day, IL-6 levels were higher in A-group; IL-6 and IL-8 levels were still higher in A- than in B-group at 7 and 30 days. During the first post-LVAD week, neopterin levels increased more in A-group, while sICAM-1 and sPSelectin levels remained higher in A- than in B-group, even at 30 days.

Conclusion: HeartMate II implantation is associated with reduced systemic inflammation, particularly a minor expression of monocyte-attracting chemokines and attenuated activation of monocytes and endothelium. Further investigations are needed in the prolonged phase of LVAD support.

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Stabilin-1: A Possible Functional Biomarker for Pro-Fibrotic Alternative Macrophage Activation in Dilatative Cardiomyopathy Patients With Left Ventricular Assist Device Implantation

K. Wassilew,¹ E. Potapov,² C. Schmuttermaier,³ A. Gratchev,³ R. Hetzer,² J. Kzhyshkowska.³ ¹Cardiac Pathology, Deutsches Herzzentrum Berlin, Berlin, Germany; ²Cardiothoracic and Vascular Surgery, Deutsches Herzzentrum Berlin, Berlin, Germany; ³Innate Immunity and Tolerance, Institute of Transfusion Medicine and Immunology, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany.

Purpose: Mechanical circulatory support (MCS) is now widely used as a destination therapy in terminal heart failure patients. After mechanical unloading only a small percentage of mainly dilatative cardiomyopathy (DCM) patients could be weaned from the device. Inflammatory reactions are thought to trigger progression or cardiac remodeling through the activation of alternatively activated macrophages (M2), which support ongoing chronic inflammation. The aim of the current retrospective study was to investigate the effect of M2 activation by use of a specific M2 marker (stabilin-1) on the development of interstitial fibrosis (IF) and outcome of MCS.

Methods: Patients were separated in 2 groups according to outcome of MCS (13 pts underwent heart transplantation, 7 were weaned from the device). Paraffin sections of myocardium from the MCS implantation site at the LV apex were examined for expression of CD68 and stabilin-1 using double immunofluorescence/confocal microscopy. The level of IF was assessed on Sirius Red stained slides using a specific software. Human monocytes were isolated from buffy coats using CD14-positive MACS. Quantitative RT-PCR was performed on primary human monocyte-derived macrophages differentiated in vitro under stimulation of cytokines and corticoids.

Results: On confocal microscopy no M2s were detected in patients weaned from MCS but were present in 7 of 13 HTx patients. A higher percentage of CD68+/stabilin-1+ cells in the myocardium was associated with a higher grade of fibrosis in most patients. Total IF was elevated in the HTx group (3-24%, mean 12.7%) in comparison to the myocardial recovery group (8%) in all but one patient (normal $<9%$). Our data indicate that high expression of stabilin-1 is associated with ongoing chronic localized inflammation and scarring. Results from a model of human primary monocyte-derived macrophages demonstrate that TGF-beta stimulates stabilin-1 independently of IL-4 and stabilin-1 in TGF-beta stimulated macrophages mediates endocytosis of SPARC.

Conclusion: Our results confirm our hypothesis that stabilin-1 can be used as a prognostic functional biomarker for the M2-coordinated chronic ongoing inflammation resulting in continuous remodeling of the myocardium in MCS patients. *shared first authorship.

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Interstitial Fibrosis of the Lungs and the Heart in the Goat Following Prolonged VA-ECMO

T. Mizuno, T. Tsukiya, Y. Takewa, E. Tatsumi. Dept. of Artificial Organs, National Cerebral and Cardiovascular Center Institute, Suita, Japan.

Purpose: A venoarterial bypass ECMO is becoming a potent therapeutic option in treating the patients with severe respiratory and circulatory failure. The ECMO cases have been limited to short-term use up to several days, however, recent progresses in devices and materials seem to enable a longer time use without an exchange of devices. However, the chronic effect of this modality