

differences in haemodynamic response to active leg raise test between LVAD and CHF patients ( $p > 0.05$  for all variables of interests). Peak O<sub>2</sub> consumption in LVAD and CHF patients was  $12.2 \pm 4.8$  and  $11.0 \pm 3.5$  mL/kg/min respectively,  $p = 0.54$ . There was a positive moderate relationship between  $\Delta$ cardiac index and peak O<sub>2</sub> consumption in LVAD ( $r = 0.68$ ,  $p = 0.06$ ) and CHF patients ( $r = 0.66$ ,  $p < 0.04$ ), Figure 1.

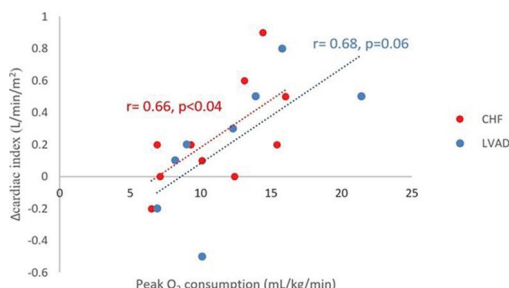


Figure 1 – Relationship between cardiac index change in response to active leg raise ( $\Delta$ cardiac index) and peak O<sub>2</sub> consumption in LVAD and chronic heart failure patients.

**Conclusion:** There is a significant positive relationship between cardiac index response to physiological stress and peak O<sub>2</sub> consumption. This suggests that haemodynamic response to stress can be used to predict functional capacity and potentially indicate cardiac reverse remodelling and recovery during mechanical circulatory support.

## P5122

### A novel method for early identification of cardiac tamponade in patients with continuous flow left ventricular assist devices by use of sublingual microcirculatory imaging

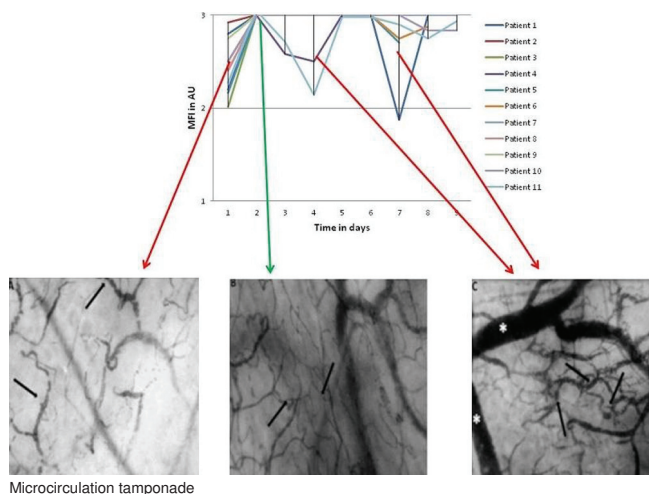
S. Akin<sup>1</sup>, C. Ince<sup>1</sup>, C.A. Den Uil<sup>1</sup>, A. Struijs<sup>2</sup>, R. Muslem<sup>3</sup>, I. Ocak<sup>2</sup>, G. Guven<sup>2</sup>, A.A. Constantinescu<sup>3</sup>, O.I. Soliman<sup>3</sup>, F. Zijlstra<sup>3</sup>, A.J.J.C. Bogers<sup>4</sup>, K. Caliskan<sup>4</sup>.  
<sup>1</sup>Erasmus Medical Center, Thoraxcenter, Department of Cardiology and Intensive Care, Rotterdam, Netherlands; <sup>2</sup>Erasmus Medical Center, Intensive Care, Rotterdam, Netherlands; <sup>3</sup>Erasmus Medical Center, Thoraxcenter, Department of Cardiology, Rotterdam, Netherlands; <sup>4</sup>Erasmus Medical Center, Thoraxcenter, Department of Cardiothoracic Surgery, Rotterdam, Netherlands

**Background:** Diagnosis of cardiac tamponade post continuous-flow left ventricle assist devices (cf-LVADs) is challenging due to missing pulsatility. Recent case studies of sublingually microcirculation with incident dark-field imaging (IDF) provide a new improved imaging for clinical assessment of cardiac tamponade in patients with cf-LVAD.

**Purpose:** We sought to examine the changes in microvascular flow index (MFI) as a sign of cardiac tamponade following LVAD implantation.

**Methods:** Off-site quantitative analysis of sublingual microcirculation clips with Automated Vascular Analyses software, and the velocity distributions followed during admission till discharge in patients with end-stage heart failure treated with cf-LVAD complicated by cardiac tamponade.

**Results:** Eleven out of thirty LVAD implantations, 9 males, mean age  $58 \pm 10$  years, April 2015 to January 2017, 8 Heart Mate 3 and 3 HeartMate II, were complicated by rethoracotomy due to early postoperative cardiac tamponade within 1 week. Their sublingual microcirculation was examined by a novel incident dark-field imaging (IDF) before and daily post-LVAD implantation. Pre-LVAD microcirculation was typical for heart failure, characterized by slowly, sludging movement of red blood cells (RBCs), (Figure 1A arrows). Directly after implantation, a normal microcirculatory flow was seen with a high RBCs velocity (Figure 1B). On the day



Microcirculation tamponade

of tamponade, patients were stable except for severe failure of microcirculation as reflected by drop in MFI (Figure 1C) and congestion in venules (\* in figure 1C). In 8 out of 11 patients there was a significant drop in MFI before tamponade was clinically recognized ( $p < 0.05$ ). Shortly after rethoracotomy a quick restoration of microcirculatory flow has been found.

**Conclusion:** Sublingual microcirculation imaging is a simple and sensitive non-invasive tool in early detection of cardiac tamponade.

## HEART VALVES: FROM DEVELOPMENT TO DISEASE

### P5123

#### Aldosterone effects in mitral valve cells could contribute to the development of mitral valve prolapse

A. Garcia De La Pena Urtasun, J. Ibarrola, V. Arrieta, R. Sadaba, V. Alvarez, A. Fernandez-Celis, A. Gainza, N. Lopez-Andres. Miguel Servet Foundation, Translational Cardiology, Pamplona, Spain

**Introduction:** Mitral valve prolapse (MVP) is one of the most common cardiac valvular abnormalities, with an estimated prevalence of over 176 million people worldwide. It is characterized by typical fibromyxomatous changes in the mitral leaflet tissue. However, little is known about the molecular and cellular mechanisms involved in the development and progression of the disease. Aldosterone (Aldo) induces myocardial and vascular fibrosis, but its effects in human valve tissue have not been studied. Mineralocorticoid receptor antagonists (MRA) reduce myocardial fibrosis in animal models of MVP. However, the impact of the drug on the specific alterations in the mitral valve has not been defined. In this study we investigated the effects of aldosterone (Aldo) in valvular interstitial cells (VICs) and valvular endothelial cells (VECs) extracted from patients with mitral valve prolapse.

**Methods:** Blood samples and mitral valves from 70 patients undergoing valve replacement for MVP were analyzed. VECs and VICs were isolated from mitral valve leaflets. VECs and VICs were cultured and transwell co-cultured. Cells were treated with Aldo ( $10^{-10}$  to  $10^{-8}$  M) +/- MRA (Spironolactone,  $10^{-6}$  M). Aldosterone synthesis enzymes (Aldosterone synthase, 11 $\beta$ -hydroxylase and 11 $\beta$ -hydroxysteroid dehydrogenase), mineralocorticoid receptor (MR) expression, proteoglycans (lumican, biglycan, versican aggrecan and decorin) and VICs activation markers/endothelial-mesenchymal transition markers ( $\alpha$ -smooth muscle actin, vimentin, metalloproteinase-2, VE-cadherin, CD31 and Von Willebrand factor) were measured by RT-PCR, Western Blot and ELISA. A cytokine array was used in cell supernatants of single cultures or co-cultures treated with Aldo to determine 54 secreted molecules. Aldo and proteoglycans levels were measured in serum and valves from MVP patients.

**Results:** Both VICs and VECs expressed 11 $\beta$ -hydroxylase and MR. In VICs, Aldo treatment enhanced VICs activation markers and proteoglycans synthesis. MRA blocked all the above effects. In VECs, Aldo induced endothelial-mesenchymal transition. MRA also blocked Aldo effects in VECs. In transwell co-culture of VICs and VECs, Aldo promoted a modest increase in VICs activation markers or endothelial-mesenchymal transition molecules. Interestingly, in transwell co-culture of VICs and VECs, Aldo increased proteoglycans secretion and metalloproteinase activities. Positive correlations were found between circulating Aldo levels and valvular proteoglycan expression in MVP patients.

**Conclusion:** Our data demonstrate that Aldo induces VICs activation, endothelial-mesenchymal transition and proteoglycans accumulation in human mitral valve cells from patients with mitral valve prolapse. Spironolactone blocked all these effects. These results suggest that Aldo could play a role in myxomatous degeneration of the mitral valve, thus potentially becoming a new therapeutic target.

### P5124

#### Therapeutic inhibition of microRNA-34a ameliorates aortic valve calcification via modulation of Notch1-Runx2 signaling in calcific aortic valve stenosis model mice by direct wire injury

T. Toshima, T. Watanabe, T. Shishido, T. Miyamoto, T. Takahashi, T. Sugai, K. Watanabe, J. Goto, I. Kubota, M. Watanabe. Yamagata University, Department of Cardiology, Pulmonology, and Nephrology, Yamagata, Japan

**Introduction:** Calcific aortic valve stenosis (CAVS) is increased in elderly population, whereas the effective medication has not been established yet. MicroRNAs (miRs) are expected to be therapeutic options in cancer and liver diseases. However, it remains unknown the impact of miRs on CAVS.

**Purpose:** We investigated whether miRs influence aortic valve calcification.

**Methods:** We measured 10 miRs expression which were reportedly involved in mineralization using aortic valve tissue from patients with CAVS or aortic regurgitation (AR) who underwent aortic valve replacement. Porcine aortic valve interstitial cells (AVICs) were harvested and treated with osteogenic medium (OM). C57BL/6 mice aged 8–10 weeks with normal diet were performed direct wire injury (WI) to the aortic valve as previously reported. Locked nucleic acid (LNA) miR inhibitor were delivered every two weeks for 8 weeks after WI.

**Results:** Expression of miR-23a, miR-34a, miR-34c, miR-133a, miR-146a, and miR-155 was increased, and contrarily expression of miR-27a and miR-204 was decreased in aortic valves of patients with CAVS compared to those with AR. OM treatment increased expression of miR-34a, miR-34c, miR-133a, miR-146a,