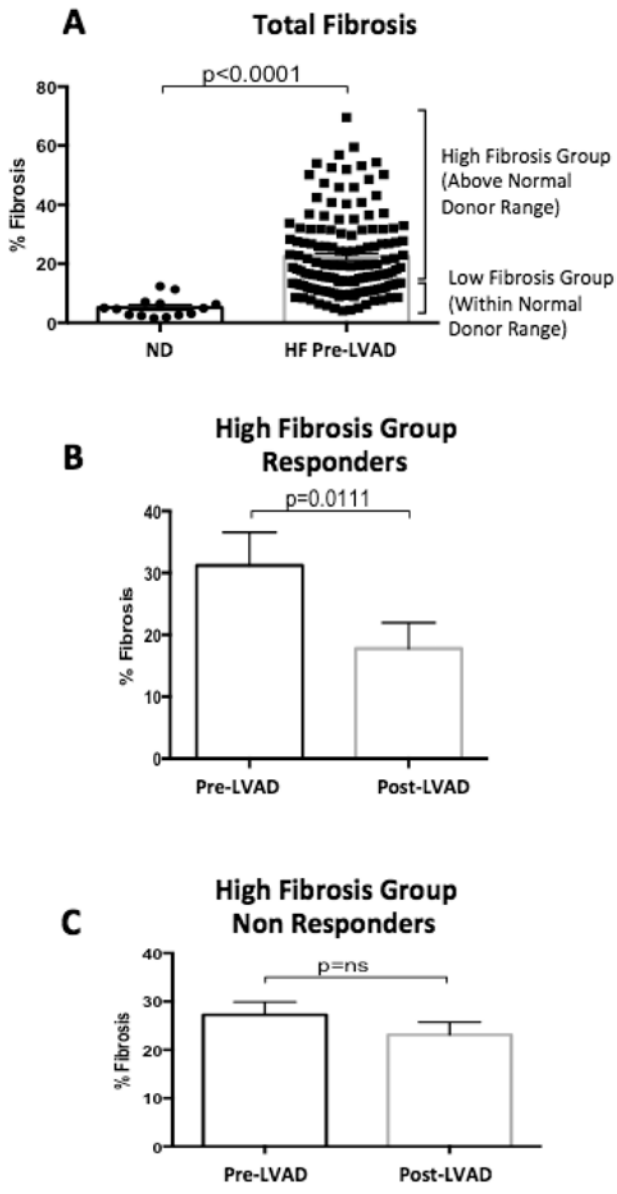

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Soluble ST2 Levels in End-Stage Heart Failure and during LVAD Support

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Purpose: The interleukin 33 (IL-33)/suppressor of tumorigenicity 2 (ST2) pathway might play an important role in the progression of heart failure (HF) and is related to cardiac fibrosis. Although the exact source of the ST2 protein is not clarified, increased serum levels (sST2) are associated with adverse outcome in HF. Left ventricular assist device (LVAD) patients offer a clinical model to investigate sST2 both during severe end-stage HF as well as after LV unloading. In this study sST2 measurements were performed sequentially before and after LVAD support in the same patients. Furthermore we analyzed which clinical factors were associated with sST2 levels during HF.
Methods: Serial serum measurements of sST2 were performed in EDTA plasma pre-implantation and 1, 3 and 6 months after LVAD-implantation in 38 patients, using the high-sensitive Presage ST2 assay. The overall effect of LVAD on sST2 levels was analyzed with the Friedman test. Comparison at different time points was done with Wilcoxon-signed-rank test, corrected for multiple testing. Several clinical factors were analyzed for their relation with sST2 levels using Mann Whitney U tests.
Results: sST2 levels were significantly elevated in end-stage HF just before LVAD implantation (74.2 ng/ml (IQR 54.7 -116.9; normal < 30 ng/ml) and decreased substantially during LVAD support, to 29.5 ng/ml (IQR 24.7-46.6) (p< 0.001), normalizing in most patients. This normalization was complete at 3 months post-LVAD. The variation in sST2 levels at baseline could not be correlated to any of the clinical factors tested (gender, HF etiology, duration of HF, right ventricular function and kidney function).
Conclusion: LVAD support results in a significant drop in sST2 levels with normalization within 3 months post implantation. This suggests that even in patients with end-stage HF, sST2 may be used as a biomarker to monitor therapy. The great variance in sST2 levels at baseline cannot be explained by differences in gender, HF etiology or duration, right ventricular function and kidney function.

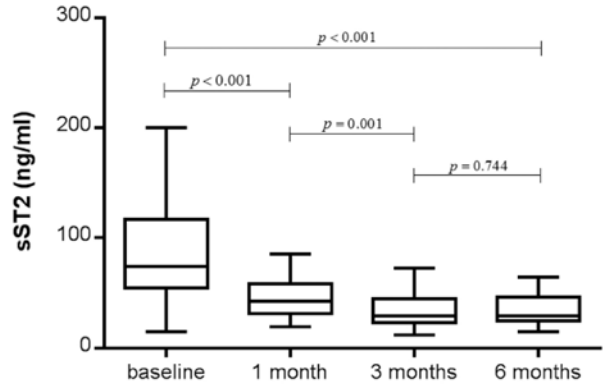

Figure 1. Boxplot showing median sST2 levels during LVAD support with IQR (25-75%), p <0.05 was considered significant.

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Interleukin-1 Receptor Antagonist for the Treatment of Heart Failure in Patients with Left Ventricular Assist Devices

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Purpose: Patients with left ventricular assist devices (LVADs) that experience sufficient myocardial recovery can become candidates for device explantation. Inflammation promotes adverse cardiac remodeling, and antagonism of the Interleukin-1 (IL-1) receptor using Anakinra has been shown to decrease inflammation and reduce adverse myocardial remodeling. We hypothesized that the incidence and magnitude of myocardial recovery in patients with LVADs can be significantly improved through the administration of Anakinra.
Methods: A prospective, pre-post design, pilot investigation of the use of Anakinra in patients with newly implanted LVADs was begun. Beginning four weeks after LVAD implant, patients received 100 mg of Anakinra daily for two weeks. Biologic efficacy was assessed through serial monitoring of C-reactive protein (CRP), tumor necrosis factor (TNF)-alpha, neutrophil counts, and interleukins 1-beta, 6, and 10. Clinical efficacy was assessed by echocardiographic evaluation of ejection fraction (EF), and left ventricular end diameter in diastole and systole (LVEDd and LVEDs, respectively). To maximize the opportunity for recovery, patients were followed for six months.
Results: Seven patients (of an intended 10) have been enrolled thus far, and five have completed the trial. Among patients completing the trial, CRP was 2.7 ± 0.7 mg/dL prior to Anakinra, which reduced to 1.0 ± 0.8 mg/dL ($p = 0.078$) after Anakinra and 1.0 ± 0.6 mg/dL at 6 months ($p = 0.042$). Neutrophil count was 6.7 ± 2.2 k/μL before Anakinra, compared to 5.1 ± 0.9 k/μL after Anakinra ($p = 0.043$) and 4.2 ± 0.8 k/μL at 6 months ($p = 0.043$). EF prior to Anakinra was 18 ± 7%, 21 ± 15% after Anakinra ($p = 0.317$), and 34 ± 11% at 6 months ($p = 0.068$). There were no significant differences over the course of the study with regard to LVEDd, LVEDs, TNF-alpha, or interleukins 1-beta, 6, or 10.
Conclusion: Anakinra use in newly implanted LVAD patients is associated with a reduction in inflammatory markers. Myocardial recovery, as measured by EF, trended towards significance over the course of the study. Additional