

Can GDF-15 be used to Assess Ventricular Recovery Following Left Ventricular Assist Device Therapy?

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Opinion

With the rising incidence of end stage heart failure and the stagnating pool of donors, left ventricular assist device (LVAD) therapy has emerged as a bridge to recovery/transplant or as destination therapy. However, the number of patients who actually undergo device explant as a result of ventricular recovery happens to be highly variable at the present time [1,2]. Ventricular recovery is a complex phenomenon influenced by several factors such as the etiology/duration of heart failure, extent of scarring and fibrosis of the myocardium at the time of implantation and adjunct medical management protocol tailored for recovery immediately post device implantation. The identification of biomarkers would open up avenues to tailor diagnosis and therapy leading to better understanding of ventricular recovery and guiding therapies.

Growth and differentiation factor 15 (GDF-15) is known by a number of different names such as macrophage inhibitory cytokine-1, placental bone morphogenetic protein, nonsteroidal anti-inflammatory drug-activated gene 1 (NAG-1), prostate-derived factor and placental transforming growth factor-beta. GDF-15 was first identified in the murine system as a transforming growth factor beta super family member that was induced in liver injury and inflammation [3]. Zimmers et al. showed that in the murine system, this protein is an early mediator of response to injury and is upregulated in hepatic and renal injury [4]. Its role in cardiovascular physiology was demonstrated in 2006 ascribing a potential cardioprotective role in stress and hypertrophy as well as ischemia/reperfusion injury in murine models [5-7].

Recent studies have shown reduction of a number of biomarkers such as NT-proBNP, ST2, galectin-3, GDF-15, hs-CRP, and copeptin post LVAD placement suggesting that multiple pathways are affected in ventricular remodeling. None of these markers were reduced to normal levels post LVAD implantation [8] indicating residual ventricular dysfunction. Lok et al showed that decrease in GDF-15 in non-ischemic cardiomyopathy correlates significantly with myocardial fibrosis [9]. This is a characteristic that could be helpful in monitoring ventricular recovery. However, the fact that none of the studies show complete

resolution of any of these biomarkers demonstrate that existing medical therapies added to mechanical unloading is still insufficient for complete ventricular recovery affording device explant. Extensive research is still warranted on the use of biomarkers for precisely following ventricular remodeling which in turn will pave the way for development of targeted therapeutics. A panel of biomarkers would probably be the answer for this very complicated process. A combined strategy of mechanical unloading added to aggressive/appropriate medical therapy may be the road to complete ventricular recovery.

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