

regulation in the context of the heart-to-brain connection in patients with AD.

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## Cardiac Recovery During Long-Term LVAD



### Is There an Interaction Between Beta-Blockers and Cardiac Progenitor Cells?

We welcome the paper by Wever-Pinzon et al. (1) who investigated the longitudinal effects of left ventricular assist device (LVAD) unloading on cardiac function. Notably, subjects who experienced cardiac recovery more frequently took beta-blockers (BBs), which have an established cardioprotective effect in heart failure (2) and leads to a 250% higher probability of recovery with the concomitant use of BB and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (1).

The report raises some interesting issues. First, it is well established that several pathophysiological mechanisms interplay in a complex, yet not

completely clarified, fashion regarding the benefits of LVADs. Specifically, important mediators on the way to cardiac recovery include apoptotic pathways, microRNAs, and growth factors (3). Furthermore, the increased abundance of an undifferentiated stem side population in the heart after unloading (3) strongly suggests that the magnitude of the regenerative reservoir in the heart might be involved in determining whether patients respond favorably to LVAD therapy.

We recently reported that BB treatment in cardiac surgery patients positively affected isolation efficiency and phenotype of resident cardiac progenitors in the form of cardiosphere-derived cells (CDCs) (4). Beta-blocked CDCs have distinctive immunophenotypic and microRNA and/or gene expression profiles, consistent with reduced pro-fibrotic and enhanced regenerative features versus CDCs that are not beta blocked. Therefore, it could be speculated that beta-blockade and LVAD may have additive and/or synergistic benefits on the biological potentiation of resident progenitors in the failing heart.

Because features of enhanced cardiac regenerative function have been reported as positive prognostic indexes after coronary bypass (5), it will be crucial to further investigate the biology of progenitors in patients with LVADs, which may provide further diagnostic and/or prognostic parameters to improve clinical predictive models, such as INTERMACS Cardiac Recovery Score (1), which would allow optimal patient stratification and boost the probability of cardiac recovery.

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Please note: Dr. Frati holds a patent concerning stem cells in cardiovascular medicine (WO2005012510) and a patent concerning platelet lysate in regenerative medicine (WO2013042095). Dr. Biondi-Zoccai has served as a consultant for Abbott Vascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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