Commentary: The power of a patch: Utilizing exosome therapy to treat heart disease

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Ischemic heart disease presents as a spectrum of myocardial pathophysiology ranging from chronic contractile dysfunction to infarction of heart tissue. Literature on myocardial hibernation has shown that although revascularization strategies can induce myocardial functional improvement, incomplete revascularization can lead to persistent ischemia and abnormal myocardial function and decreased long-term survival. It is therefore important to explore adjunctive therapies that can be coupled with revascularization to improve outcomes.

The delivery of membrane-bound, microRNA-carrying extracellular vesicles termed exosomes that are secreted by mesenchymal stem cells appears to represent one means of enhancing ischemic myocardial function. Compared with “traditional” stem cell therapy, the potential benefit of exosome therapy is that it avoids the challenges in the retention and survival of exogenous stem cells delivery to ischemic or infarcted myocardium. In this issue of the Journal, Aggarwal and colleagues perform low-dose dobutamine magnetic resonance imaging experiments in chronically ischemic porcine models to demonstrate improved systolic function and diastolic relaxation in animals treated with exosome-laden patch onlays and coronary artery bypass grafting compared with animals treated with coronary artery bypass grafting alone or no-intervention control groups (Figure 1).

Aggarwal and colleagues further show that this improvement is associated with improved (in vitro) mitochondrial respiration and reduced in vivo inflammation and fibrosis. The authors conclude that these improvements may be induced via paracrine microRNA expression effects. These authors found that varying the environmental conditions of cardiomyocytes co-cultured with mesenchymal stem cells (eg, hypoxia vs normoxia) induced different exosomal microRNA transcriptomic signatures, which they theorized could provide differential paracrine effects when implanted into the cardiac patch. These variable transcriptomic signatures could provide an avenue for targeted acellular therapy to improve pathological processes (eg, ischemic injury).

The work of Aggarwal and colleagues advances the possibility for acellular therapy to become an important means to improve functionality of persistently ischemic myocardium. Their identification of specific microRNA exosomal mediators suggest the further possibility of using genetic engineering to generate exosomes providing tailored microRNA modifiers of myocardial function.
References


FIGURE 1. Exosome patches can increase systolic and diastolic heart function in hibernating myocardium. LAD, Left anterior descending; HIB, hibernating myocardium; CABG, coronary artery bypass grafting; PFR, peak filling rate; EDV, end diastolic volume; miRNA, microRNA.