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# First in Man: Adipose-derived Stromal Vascular Fraction Cells May Promote Restorative Cardiac Function

*To the Editor:*

Despite advances in clinical intervention, heart disease remains a causation of mortality in the world. Research demonstrates that the adipose-derived stromal vascular fraction of cells contains multi-potent cells that exhibit mesodermal and ectodermal capacity and contain $CD44^+$, $CD90^+$, $CD73^+$, $CD105^+$, $CD34^+$, and $CD31^+$ cells, which act in tissue regeneration and vascular stabilization.[1] We discuss a patient who underwent such cell administration as rescue therapy for failing cardiac function, despite conventional interventions.

## CASE SUMMARY

The patient is a 73-year-old white man with a history of hyperlipidemia who presented with recurrent angina pectoris, for which he had undergone multiple angioplasties and 9 coronary stents (right posterior descending and distal right coronary beyond a saphenous vein graft to right coronary artery). He had further percutaneous coronary intervention to the distal right coronary artery and proximal posterior descending branch. His prior coronary bypass artery graft of 3 vessels had been redone. Robotic-assisted transmyocardial revascularization for angina was performed in the patient 2 months before cell delivery. He had significant left ventricular systolic dysfunction (ejection fraction, 20%) with a thinned, akinetic inferolateral segment. To evaluate left ventricular function, transesophageal echocardiography was performed in the patient.

As a last resort intervention for the patient's dysfunctional heart, 100 million adipose-derived stromal vascular fraction cells were delivered via localized intramyocardial injection (left apex), and 200 million adipose-derived stromal vascular fraction cells were delivered systemically via intravenous injection. The intracoronary delivery of freshly isolated autologous cells consisted of a complex cell composition. This uncultured population taken from lipoaspirate, which had an approximately 86% viability, consisted of $CD34^+$ cells.

Within 7 days of the procedure, transesophageal echocardiography was performed to evaluate recovery of the patient's left ventricular function. His ejection fraction improved to 35% with recovery in the contractility of the previously akinetic inferolateral segment. This confirmed the effectiveness of cell delivery in improving regional and global left ventricular systolic function.

## DISCUSSION

Spontaneous recovery of the damaged myocardium occurred. The effective delivery of the stromal vascular fraction cell population, which contained stem cells, may have improved regional and global left ventricular systolic function, aiding recovery. Adipose-derived stromal vascular fraction cells may have cardiomyogenic potential. Cellular composition of cells administered included endothelial progenitor cells, vascular smooth muscle cells, mesenchymal stem cells, fibroblasts, growth factors, and pericytes. This complex population has shown efficacy in repairing damaged tissue to partial restoration of functional normalcy.[2]

Angiogenesis may contribute to restoration of cardiac function through preservation of remaining viable and hibernating cardiomyocytes. This salvaging effect might be maintenance of border zone cells through stem cell–mediated anti-apoptotic and neoangiogenic effects, which are causative of stem cell–produced paracrine factors.[1] This cell population has a high expression in DKK-1 and ID proteins, which are associated with regulation of stem cell proliferation and differentiation.[2]

## CONCLUSIONS

We postulate that the intramyocardial administration of multi-potent adipose-derived stromal vascular fraction cells and their diverse composition guided engraftment in the damaged area, facilitated the cardiomyocyte regenerative properties, and helped improve cardiac function. Because subcutaneous adipose tissue is readily available in most patients, adipose-derived stromal vascular fraction cells present a feasible clinical intervention for cardiac dysfunction. The population complexity, which includes stromal vascular fraction and growth factors, likely promotes repair by recruiting cardiomyocytes. The autologous nature and multi-potency of these cells may contribute to them being ideal for cardiac function restoration.

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## References

1. Alt E, Pinkernell K, Scharalau M, et al. Effect of freshly isolated autologous tissue resident stromal cells on cardiac function and perfusion following acute myocardial infarction. *Int J Cardiol*. 2009;144:26-35.
2. Lin K, Matsubara, Masuda Y, et al. Characterization of adipose tissue-derived cells isolated with Celution™ system. *Cytotherapy*. 2008;10:417-426.