Abstract:
Increasing numbers of patients with advanced coronary artery disease have limited options for percutaneous and/or surgical revascularization. A prospective, randomized, phase I clinical multicenter trial was performed to assess the feasibility and safety of delivering a pro-angiogenic transcription factor termed "hypoxia inducible factor-1alpha", delivered to ischemic cardiac muscle via a type 2 adenoviral (Ad2HIF) vector. The 13 patients were included under the following criteria: 1 hypoperfused area of viable ventricular muscle without options for revascularization and left ventricular ejection fraction \( \geq 30\% \). After coronary artery bypass grafting was completed, 10 injections of the study drug \( (n=10) \), in 3 escalating doses up to \( 1 \times 10^{11} \) viral particles or saline \( (n=3) \) as a placebo control, were injected intramyocardially. After completion of the 1-year follow-up, all patients had uncomplicated postoperative courses, are alive and feeling well; 1 patient had a self-limited run of tachycardia postoperatively and at 6 months, 1 patient developed recurrent angina. Positron emission tomography perfusion analysis revealed improvement in the Ad2HIF injected areas in selected patients. These data support the feasibility and preliminary safety of adenoviral transfection with Ad2HIF in regions of viable myocardium.
myocardium. Additional studies will be required to determine the efficacy and safety of Ad2HIF.