Background. Continuous-flow left ventricular assist devices (LVADs) are used in heart failure (HF) patients either as a bridge to transplantation or as a permanent (destination) therapy. HF is precipitated by myocardial infarction (MI) in most (ischemic; I) but not all (non-ischemic; NI) patients. We hypothesized that coronary vascular dysfunction is greater in I (63±2 y; n=14) vs. NI (51± y; n=23) HF patients, and that dysfunction is attenuated by LVAD support.

Methods and Results. Arteries from a transmural biopsy of the left-ventricle were obtained, and concentration-response curves to bradykinin (BK, 10^{-6} to 10^{-10} M) and sodium nitroprusside (SNP, 10^{-4} to 10^{-9} M) were completed after vessels were precontracted to ~65% of maximal tension development. Maximal BK-induced vasorelaxation was less (p<0.05) in arteries from I (72±7%; n=24 arteries, 215±19 μm i.d.) vs. NI (90±4%; n=48 arteries, 205±13 μm i.d.) patients, while responses to SNP (~90%) were similar between groups. These findings indicate endothelial dysfunction is greater in I vs. NI patients at the time of LVAD implant. Next we assessed vascular reactivity in 6 I (56±2 y) and 6 NI (51±7 y) patients wherein samples were obtained at implant and 226±47 days later at explant. Maximal BK-induced vasorelaxation was greater (p<0.05) in coronary arteries from I patients at explant (87±6%, n=15 arteries, 260±34 μm i.d.) vs. implant (54±14%, n=11 arteries, 237±37 μm i.d.). Maximal BK-induced vasorelaxation was similar in coronary arteries from NI patients obtained at explant (61±11%, n=14 arteries, 328±48 μm i.d.) and implant (76±9%, n=11 arteries, 154±16 μm i.d.). Responses to SNP were similar (~93%) at implant and explant for I and NI patients. Total collagen content (“total fibrosis;” TF) was assessed in a subset of patients from both paired groups, by quantifying whole-field stained tissue without excluding any areas. TF (%) was 12±2 and 9±2 at implant and explant, respectively, in 3 NI patients. TF (%) was 23±5 and 13±3 at implant and explant, respectively, in 5 I patients.

Conclusion. These preliminary findings indicate that endothelial dysfunction and tissue fibrosis in patients with advanced ischemic cardiomyopathy is improved through LVAD support.