

CORONARY VASCULAR FUNCTION IS IMPROVED IN ISCHEMIC PATIENTS AFTER CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICE (LVAD) IMPLANTATION

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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 ± 5 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 $\sim 65\%$ of maximal tension development. Maximal BK-induced vasorelaxation was less ($p < 0.05$) in arteries from I ($72 \pm 7\%$; $n=24$ arteries, $215 \pm 19 \mu\text{m i.d.}$) vs. NI ($90 \pm 4\%$; $n=48$ arteries, $205 \pm 13 \mu\text{m i.d.}$) patients, while responses to SNP ($\sim 90\%$) 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 \pm 47 days later at explant. Maximal BK-induced vasorelaxation was greater ($p < 0.05$) in coronary arteries from I patients at explant ($87 \pm 6\%$, $n=15$ arteries, $260 \pm 34 \mu\text{m i.d.}$) vs. implant ($54 \pm 14\%$, $n=11$ arteries, $237 \pm 37 \mu\text{m i.d.}$). Maximal BK-induced vasorelaxation was similar in coronary arteries from NI patients obtained at explant ($61 \pm 11\%$, $n=14$ arteries, $328 \pm 48 \mu\text{m i.d.}$) and implant ($76 \pm 9\%$, $n=11$ arteries, $154 \pm 16 \mu\text{m i.d.}$). Responses to SNP were similar ($\sim 93\%$) 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.

