Prediction of ARrhythmic Events with Positron Emission Tomography – PAREPET

Objective. Left ventricular ejection fraction (LVEF) is the only parameter currently used to prospectively identify patients at high risk of sudden cardiac arrest (SCA) who would benefit from an implantable cardiac defibrillator (ICD). Unfortunately, this approach is inefficient and expensive, with only 25% of ICD implants delivering therapy within 5 years. Our single-center, NIH-sponsored Prediction of ARrhythmic Events with Positron Emission Tomography (PAREPET) study tested the hypothesis that quantifying cardiac sympathetic denervation could identify patients at highest risk for SCA.

Methods. We prospectively enrolled 204 subjects with ischemic cardiomyopathy (LVEF less than 35%) eligible for primary prevention ICDs. PET was used to quantify myocardial sympathetic denervation (11C-metahydroxyephedrine, 11C-HED), perfusion (13N-ammonia) and viability (insulin-stimulated 18F-2-deoxyglucose). The primary end-point was SCA defined as arrhythmic death or ICD discharge for life-threatening ventricular arrhythmias (ventricular fibrillation or ventricular tachycardia greater than 240 bpm). Results. After 4.1 years follow-up, SCA occurred in 16.2%. Infarct volume and LVEF were not predictors of SCA. In contrast, patients developing SCA had greater extent of sympathetic denervation reflecting viable, denervated myocardium. Denervated myocardium remained a significant predictor of SCA by multivariate analysis (along with LV end-diastolic volume index, B-type natriuretic peptide level and angiotensin inhibition therapy). Favorable values for these four variables identified 44% of the cohort with a very low risk of SCA (less than 1% per year), while greater than 1 unfavorable values identified high risk (20% of cohort; SCA-11.7%/year).

Conclusions. In subjects with ischemic cardiomyopathy, sympathetic denervation assessed with PET predicts SCA independently of other clinical variables. Potential clinical translation includes identification of: a) sufficiently low risk of SCA in patients with ischemic cardiomyopathy to withhold ICD therapy, and b) high risk of SCA among patients with more preserved LVEF who are not currently considered ICD candidates.