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“Can Ventricular Assist Devices Reverse the Frailty Phenotype” (1 R21 AG046703-01A1)

Persons over the age of 65 years are the fastest growing segment of the population. Heart failure (HF) incidence is highest in this age group. The increasingly older HF population will require specific management, sometimes beyond the best available medical treatment. The use of a ventricular assist device (VAD) as a permanent solution for end-stage HF has been applied more widely recently. For the correctly chosen patient population, LVADs restore hemodynamics in failing hearts, extend lives and improve QOL. However, the mortality and morbidity of LVAD therapy can be substantial especially in older adults (OA) who often have concomitant co-morbidities and reduced functional capacity that impairs their ability to tolerate the surgical procedure and comply with the post LVAD implant care. Given the estimated 5 year cost of mechanical assist device at > \$350,000, appropriate selection of candidates for destination LVAD is imperative. Frailty is a geriatric syndrome characterized by decreased physiologic reserves and is strongly associated with increased vulnerability to functional decline and complications from interventions. However, the systematic measurement of frailty is not part of routine cardiovascular practice, despite its potential utility as a risk factor to guide selection of candidates for circulatory support. Also, frailty is not clinically employed serially to evaluate the impact of interventions. While no single therapeutic intervention has been shown to consistently reverse the frailty phenotype, clinical evidence suggests that placement of a LVAD may reverse several features of the frailty phenotype. The underlying hypothesis guiding this proposal is that by restoring a normal cardiac output and adequate organ perfusion, LVADs are capable of reversing the catabolic state associated with the advanced stage of HF and can result in a reversal of sarcopenia, impaired cognition and altered mood which are the hallmarks of the frailty phenotype. We propose a multi-disciplinary, collaborative, multi-center pilot study which will be executed through the Greater New York Geriatric Cardiology Consortium (www.gnygcc.org). While the frailty and HF phenotypes coalesce, this exploratory study will facilitate identification of those who have VAD-responsive frailty and those who have frailty that is independent of a VAD and thus could suffer adverse consequences from this intervention. This pilot, multi-center cohort study of frail OA (n=40, 10 at each site) receiving VADs for clinical indications and 10 controls (eligible to receive a VAD but do not) will evaluate the impact of mechanical circulatory support on the frailty phenotype. The primary hypothesis to be tested is elective implantation of an LVAD in frail older adults with advanced HF will reverse the frailty phenotype. This will be an initial step in strengthening collaborations between academic sites that constitute the GNYGCC, so it can serve as a platform for future multi-center investigations. These pilot data will inform future trials in which comprehensive geriatric assessment can be integrated into the preoperative assessment and care of older adults in order to enhance selection of candidates for DT VAD, risk prediction and optimize outcomes.