Telomere Length as a Biomarker and Potential Contributor of Heart Failure Progression

Background: Telomere length (TL) is a novel biological marker of aging, where telomere shortening is associated with senescence and shorter life. HF and its severity are known to inversely correlate with telomere length potentially triggered by inflammation and oxidative stress associated with the disease. However, it remains unknown whether telomere attrition and premature biological aging are causally intertwined with the progression of HF or vice versa. We hypothesize that effective aggressive HF therapy promoting hemodynamic and symptomatic improvement of the acute HF syndrome might stall the process of senescence and telomere attrition supporting the notion of refractory HF induced premature aging. Methods: Blood samples and demographic data were collected prospectively from consecutive patients before and 1 year after initiation of aggressive outpatient HF therapy in an outpatient Infusion Center setting. TL was measured in leukocytes using both Southern Blot and quantitative PCR. Response to therapy was assessed based on weight change, New York Heart Association (NYHA) class and number of hospitalizations. Statistical analysis was performed using paired and unpaired t-tests. Results: Thirty-five patients (28 males, 18 HFpEF) were enrolled, mean age 67.5 ± 10.7 years. Average treatment duration of 13.39 ± 1.9 months, they made an average of 18.25 infusion center visits (range 3-53). Weight significantly decreased at 1 year of treatment in those that demonstrated an improved NYHA class versus those that did not improve NYHA class (98.4 ± 21.3 vs 94.7 ± 19.4 kg, p = 0.003; 105.8 ± 25.0 vs 104.1 ± 25.6 kg, p = 0.33). TL is shown in the graph. TL was maintained in patients that were successfully treated leading to improved NYHA Class (0.48 vs 0.51; p = 0.55). In contrast, refractory severe HF showed persistent NYHA III/IV symptoms, worsening NYHA class (0.59 vs 0.53; p = 0.05), and/or increased HF admissions (0.56 vs 0.48; p = 0.01). Results were observed irrespective of systolic function; HFrEF or HfPEF. Conclusions: Effective treatment of HF symptoms with aggressive outpatient therapies provided by HF specialists prevents the progression of telomere shortening and premature senescence. Untreated or refractory HF, however, results in progressive telomere attrition and disease severity. These results suggest that TL could potentially be used as a biomarker for progressive heart failure and may be used to study the effectiveness of other HF therapies. Furthermore, refractory HF might be the cause for senescence rather than the other way around.

Minute Ventilation-Targeted Adaptive Servo Ventilation Reduces Kidney Injury in Patients With Acute Decompensated Heart Failure

Introduction: Acute kidney injury (AKI) is a frequent comorbidity in patients admitted for acute decompensated heart failure (ADHF). Minute ventilation targeted adaptive servo ventilation (MV-ASV) relieves apneas, pulmonary congestion, and renal hypoxia. Kidney injury molecule (KIM-1) is a marker of AKI and could be used to detect early injury and the improvement of kidney function. Hypothesis: MV-ASV may mitigate AKI in patients admitted of ADHF compared to standard care. Methods: This is a pilot study in which twenty-one consecutive patients with ADHF were randomized to receive either MV-ASV therapy (S9 VPAP Adapt, ResMed Corp.) with standard care, or standard care alone. MV-ASV therapy was administered for a minimum of six hours per day for up to 5 days, or until discharge. Daily measurements of plasma KIM-1 were obtained with SMC™ technology (Singulex). Daily serum creatinine levels were measured and used to calculate eGFR. Results: Median baseline KIM-1 levels in the MV-ASV and standard groups were 312µg/mL and 361µg/mL, respectively. In the control group KIM-1 increased 18% to 426µg/mL while the group with MV-ASV demonstrated a mitigation of kidney injury with a 7% decrease to 290µg/mL. These changes correlated with subsequent changes in serum creatinine and eGFR. Conclusions: The use of MV-ASV therapy resulted in mitigation of kidney injury typically seen in patients with ADHF during hospitalization.