

Subclinical Autonomic Neuropathy in Type 2 Diabetes

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People with type 2 diabetes (T2D) develop excess cardiovascular disease and decreased cardiorespiratory fitness (CRF), a predictor of premature mortality. T2D includes impaired insulin sensitivity, vasodilation, and mitochondrial function. These cardiac and systemic abnormalities may contribute to impaired CRF. Cardiac autonomic neuropathy (CAN) is a common complication of T2D that is often not detected until late in disease progression. Because autonomic nerves (ANS) innervate the heart and vasculature, dysfunction impairs control of both heart rate and vascular dynamics. ANS dysfunction can manifest with decreased heart rate variability (HRV), prolonged QT, impaired exercise tolerance, and impaired blood pressure regulation which can result in arrhythmia, ischemia, and sudden death.

To characterize ANS function in T2D, we evaluated ANS function by measuring HRV during cycled breathing and Valsalva, and postural heart rate and blood pressure. We hypothesized that ANS function would be decreased in participants with uncomplicated T2D and would correlate with cardiac measures.

Data from subjects ages 22-70 with (N=53) and without (N=56) uncomplicated diabetes were included. In participants with diabetes, both HRV with cycled breathing and with Valsalva decreased in T2D. HRV with respiration decreased with age >50. Decreased HRV with respiration correlated with increased age in T2D but not in OWC. There were no significant changes in postural BP or HR with age >50 or T2D. Notably, Valsalva ratio was significantly positively correlated with end-diastolic volume (EDV) (Pearson's $r = 0.58$, $p=0.02$) and stroke volume (SV) (Pearson's $r = 0.55$, $p=0.03$); HRV with respiration was significantly positively correlated with longitudinal, diastolic peak strain rate (SR) (Pearson's $r = 0.68$, $p=0.007$) and postural BP was significantly positively correlated with circumferential and longitudinal, systolic peak SR (Pearson's $r = 0.45$ and 0.48 and p -value= 0.05 and 0.04 , respectively) and significantly negatively correlated with radial and circumferential peak strain (Pearson's $r = -0.49$ and -0.48 and p -value= 0.03 and 0.03 , respectively).

These data suggest development of subclinical cardiovascular autonomic neuropathy associated with cardiac dysfunction is present in people with otherwise uncomplicated T2D prior to development of symptoms and it is exacerbated with age. Detecting these changes early may offer opportunities for intervention to restore cardiometabolic health.