Association between Left Ventricle Sympathetic Innervation and Torsion in Patients with Type 1 Diabetes

S. D. Swanson[1], G. C. Mueller[1], D. Raffel[1], D. Happ[1], C. S. Duvernoy[2,3], and R. Pop-Busui[4]
[1]Department of Radiology, University of Michigan, Ann Arbor, MI, United States, [2]Cardiology Section, VA Ann Arbor Health Care System, United States, [3]Department of Internal Medicine, University of Michigan, [4]Department of Internal Medicine; Division of Metabolism, Endocrinology and Diabetes, University of Michigan

Introduction

In type 1 diabetes (T1DM), left ventricular (LV) dysfunction often precedes significant coronary artery disease or hypertension. Cardiac autonomic neuropathy (CAN) is associated with an increased prevalence of silent myocardial ischemia and is an independent risk factor for cardiac mortality. Longitudinal studies of CAN subjects have shown 5 year mortality rates between 16-50% (1), particularly in patients with sympathetic CAN. Sympathetic imbalance associated with CAN may critically influence myocardial glucose utilization and contribute to regional ventricular wall motion abnormalities and functional deficits.

We have developed the use of positron emission tomography (PET) with [^{11}C]*meta*-hydroxyephedrine ([^{11}C]HED) as a sensitive technique to explore the integrity of the LV sympathetic innervation (Figure 1). We observed that [^{11}C]HED tracer retention deficits affected 36-40% of the LV in early-stage T1DM patients, despite normal cardiovascular reflex testing, consistent with sympathetic neuronal dysfunction (2).

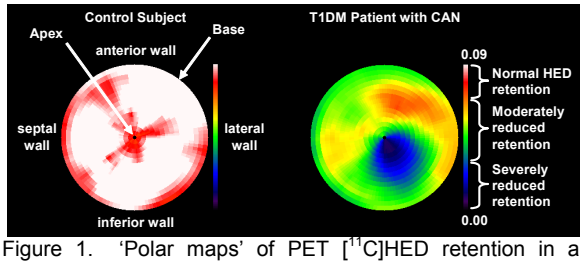

Figure 1. 'Polar maps' of PET [^{11}C]HED retention in a normal control (left) and a T1DM patient with CAN+ (right). The color table is set to a maximum HED RI value of 0.09 mL blood/min/mL tissue. Reduced [^{11}C]HED tracer retention in T1DM indicates sympathetic dysfunction.

MRI tagging techniques allow assessment of regional and global cardiac tissue deformations such as torsion and strain. MRI tagging techniques have been used to detect early contractile dysfunction in diabetics with normal LV ejection fraction and mass, normal blood pressure, and tight glycemic control (3). In this study we examine the relationship between sympathetic innervation and LV torsion in patients with T1DM.

Methods

Cardiac MRI with tagging was used to assess LV torsion in 3 subjects with T1DM and CAN (CAN+), mean age 45±7 years, HbA1c 8.8±1.1% and in 4 subjects with T1DM without CAN (CAN–), mean age 41±4 years, HbA1c 8.5 ±1. 7%. All subjects had normal LV ejection fraction. Tagged MR images were acquired using a SPAMM sequence on a Philips Achieva 1.5 T unit (Philips Medical Systems, Best, The Netherlands) with a sixteen-element phased-array coil dedicated to cardiac imaging. Torsion (angular difference between basal slice and apical slice divided by slice distance) was measured using harmonic phase software (4) developed in-house (Matlab, The MathWorks, Natick, MA). In one patient with T1DM and CAN+, both the regional LV sympathetic innervation as assessed by [^{11}C]HED PET and regional LV torsion and as assessed by cardiac MRI with tagging were obtained and the results compared by linear regression.

Results

Figure 2 demonstrates that CAN+ subjects have significantly increased peak LV torsion (12.57±2.70 deg/cm) compared with CAN- subjects (3.26±0.96 deg/cm, P=0.0013). Figures 3A-C show that the PET map of sympathetic innervation is inversely related to the regional amount of LV torsion generated in the midline (outer circle) and the apex (inner circle) in one CAN+ patient.

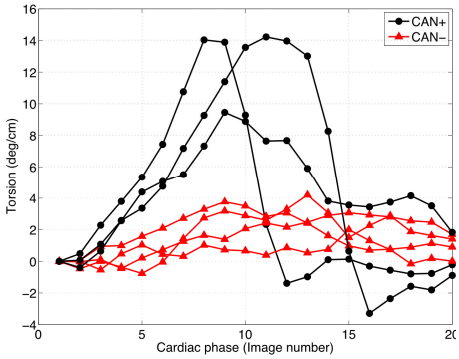

Figure 2. Torsion (degrees/cm) in apical slice as a function of cardiac phase for CAN+ and CAN- subjects.

Conclusion

These preliminary results suggest that subjects with T1DM without coronary artery disease or heart failure may present with abnormal LV torsion and that increased torsion is related to sympathetic dysfunction. These findings are illustrated by the significantly higher torsion rates in CAN+ subjects and by the high degree of correlation of LV rotation in the distal apical regions with regions of sympathetic denervation.

References

1. O'Brien IA et al. Q J Med 79:495-502, 1991. 2. Pop-Busui R et al. J Am Coll Cardiol 44:2368-2374, 2004. 3. Chung J et al. J Am Coll Cardiol 47:384-390, 2006. 4. Osman NF et al. Magn Reson Med 42:1048-1060, 1999.

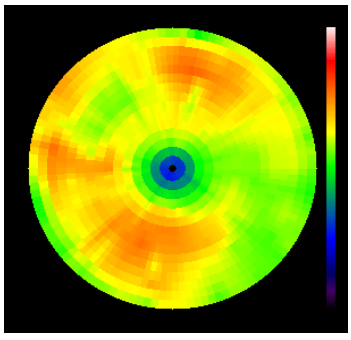

Figure. 3A. Polar map of PET [^{11}C] HED retention in LV of CAN+ patient. Green represents areas of severe denervation.

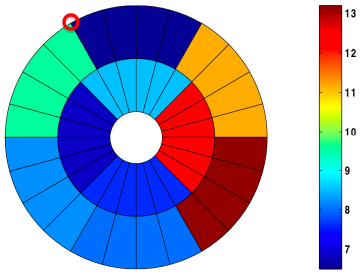

Figure. 3B. Polar map of LV Torsion (degree/cm) in same patient as Fig. 3A. Red represents areas of high torsion. (Red circle represents the RV insertion point.)

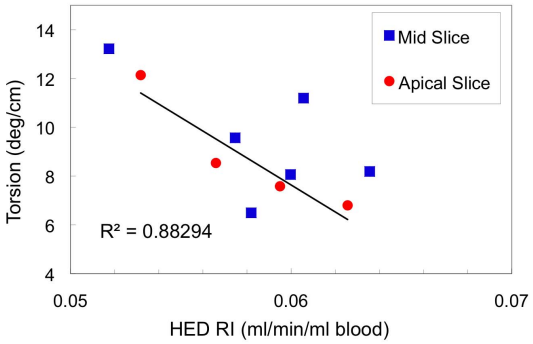

Figure. 3C. LV Torsion vs. HED retention. The r^2 coefficient between LV Torsion and HED retention is 0.883 in the apical slice. Decreased HED retention correlates with increased LV torsion.