Canadian Cardiovascular Society (CCS) Abstracts — Electrophysiology

P064
ATOMOXETINE FOR SUPPRESSION OF VASOVAGAL SYNCOPE: A CLINICAL CASE SERIES

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BACKGROUND: Vasovagal syncope (VVS) is a common clinical condition that lacks effective medical therapies despite being associated with significant morbidity. The norepinephrine transport inhibitors reboxetine, sibutramine, and atomoxetine (Strattera) all prevent the induction of vasovagal syncope on tilt table testing. We hypothesized that atomoxetine would be effective in suppressing syncope in patients with recurrent VVS.

METHODS AND RESULTS: This was a retrospective, open-label, observational case series of 12 patients taking atomoxetine for compassionate-use suppression of recurrent vasovagal syncope. We compared syncope frequency in the periods 1 year before atomoxetine and while subjects were taking atomoxetine. We used novel applications of the Poisson distribution to describe the results as a collection of n=1 studies. The Poisson distribution is ideal for assessing the significance of distributions with few events per subject. There were 12 subjects, 8 female, with mean age 47+/-22 years and a mean Calgary Syncope Score of 2. The dose of atomoxetine that the patients received was 66+/-16 mg (1.06+/-0.21 mg/kg). In the preceding year they had had a mean 9.5+/-11.1 syncopes and a median 5.5 (IQR 4, 6.75) syncopes. While taking atomoxetine all patients appeared to improve and 8/12 had no syncope in followup ($p = 0.0013$). The mean syncopes per year decreased from 9.5+/-11.1 to 0.51+/-0.92 ($p=0.019$, T test). Syncope frequency decreased from a median 5.5 (IQR 4, 6.75) syncope per year to 0 (IQR 0, 0.88) syncope per year ($p=0.0015$, Wilcoxon test). All 4 patients who fainted in follow-up improved from a previous year count of 5.75+/-1.26 syncopes to 1.52+/-1.03 syncopes per year on atomoxetine ($p=0.0006$). According to the Poisson distribution 7/12 subjects were each significantly improved with p values of $<$ 0.0001 to 0.023, and an eighth subject had borderline significant improvement ($p=0.082$). Of the 5 subjects who did not improve significantly one fainted once and 4 did not faint but lacked a significantly long follow-up duration. Therefore, in total 8/12 subjects were significantly or nearly significantly improved ($p=0.005$, T test), and 4/12 subjects had insignificantly long follow-up times to test whether they responded significantly to atomoxetine.

CONCLUSION: In this case series atomoxetine was effective in preventing vasovagal syncope. The novel use of the Poisson distribution permits per patient assessment of improvement and detects insufficient followup despite apparent improvement. Atomoxetine merits a formal randomized trial. The Poisson distribution merits further study for n=1 clinical trials.

P065
BI-ATRIAL MAPPING AND ELEVATED HEART RATES IDENTIFY ABNORMAL ATRIAL SUBSTRATE IN ATRIAL FIBRILLATION PATIENTS WITHOUT LOW-VOLTAGE AREAS IN THE LEFT ATRIUM

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BACKGROUND: Low-voltage areas (LVA) provide the substrate for AF. In AF patients without left atrial (LA) LVA, the presence of abnormal atrial substrate has not been well defined. Our aim was to identify abnormal atrial substrate in AF patients without LA LVA using bi-atrial mapping and elevated heart rates.

METHODS AND RESULTS: Patients with AF undergoing first-time pulmonary vein isolation were prospectively enrolled. High-resolution bi-atrial electroanatomic mapping was performed during right atrial (RA) pacing at 750 and 400ms. LVA (bipolar voltage $<$ 0.5mV) and the slowest conduction velocity (CV) were defined globally and regionally in the RA and LA. Only patients without LA LVA (-LVA), defined as $<$ 5% LA LVA of total LA surface area, were included (n=52). This cohort was compared to prospectively enrolled controls without AF, who underwent bi-atrial electroanatomic mapping during RA pacing (n=10). -LVA had AF for 2(1-5)yr (79% paroxysmal AF). -LVA were older (56$\pm$11 vs. 37$\pm$10yr, $p< 0.001$) and predominantly male (94 vs. 40%, $p< 0.001$) compared to controls. -LVA had larger LA (36$\pm$10 vs. 28$\pm$4ml/m2, $p=0.013$) and RA (19$\pm$4 vs. 15$\pm$3cm2, $p=0.022$) compared to controls. At 750ms pacing, -LVA had more global LA LVA than controls (1.4(0.5-3.6)% vs. 0.4(0.2-0.4)%, $p=0.01$), which was most evident in the septum (3.1(0.7-7.4)% vs. 0%, $p< 0.01$) and PV antra (0.7(0-5.7)% vs. 0%, $p=0.02$). -LVA also had greater global RA LVA than global LA LVA (3.7(2.2-6.0)% vs. 1.4(0.5-3.6)%, $p< 0.001$). Regional LA CV was similar between -LVA and controls. Regional RA LVA and CV were also similar between -LVA and controls. At 400ms pacing, -LVA had greater global LA LVA (3.5(1.0-5.8)% vs. 1.4(0.5-3.6)%, $p=0.001$) and slower global CV (0.74$\pm$0.11 vs. 0.83$\pm$0.17m/s, $p< 0.001$) compared to 750ms pacing. These changes were most evident in the septum and PV antra. In contrast, controls had similar LA LVA and CV at 400ms compared to 750ms pacing.

CONCLUSION: AF patients without LVA in the LA still have bi-atrial structural remodeling as evidenced by (i) greater bi-atrial size, (ii) greater RA LVA, and (iii) greater rate-dependent LA LVA and CV slowing compared to controls without AF. The septum and PV antra are most affected in -LVA. Although