Inferences in QTc intervals between M and F OHT recipients were also compared. RESULTS: In the early post OHT period, there was a significant decrease in the QTc interval for the F to M transplantation subgroup which persisted throughout follow-up. QTc Changes Following Transplantation

<table>
<thead>
<tr>
<th>Group (Donor to Recipient)</th>
<th>2 days</th>
<th>1 week</th>
<th>1 month</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>M to M</td>
<td>-15.66</td>
<td>2.36</td>
<td>-6.46</td>
<td>1.40</td>
</tr>
<tr>
<td>M to F</td>
<td>2.92</td>
<td>-4.27</td>
<td>0.76</td>
<td>8.29</td>
</tr>
<tr>
<td>F to F</td>
<td>-15.49</td>
<td>-6.33</td>
<td>-37.17</td>
<td>8.31</td>
</tr>
<tr>
<td>F to M</td>
<td>-42.58</td>
<td>-23.18</td>
<td>-16.12</td>
<td>-24.22</td>
</tr>
</tbody>
</table>

When comparing the QTc among M and F recipients, there was no gender difference in the QTc interval at early follow-up (419.27 ± 420.23 mm/s for M vs F at 1 week; 416.31 ± 415.63 mm/s at 1 month). Gender differences were significant (p < 0.05 for change in QTc interval). In the early post OHT period, there was a significant decrease in the QTc interval for the F to M transplantation subgroup which persisted throughout follow-up. CONCLUSIONS: Gender-related QTc changes are evident both immediately and late after OHT. These effects are most consistent with a hormonal etiology and probably not due to autonomic influences.

2:30 p.m.

SCNSA Mutations in the S5-S6 Region Cause Brugada Syndrome and Cardiac Conduction Disturbances
Hidetaka Ito, Masami Shimizu, Hiroshi Mabuchi, Graduate School of Medical Science, Kanazawa University, Kanazawa, Japan

Background: The SCNSA gene encoding the alpha subunit of the human cardiac sodium channel plays a key role in cardiac electrophysiology. Mutations in SCNSA lead to a wide variety of phenotypes, including long QT syndrome, Brugada syndrome, and isolated progressive cardiac conduction defects. Clinically, there appears to be some overlap among these syndromes, as all are associated with a relatively high incidence of nocturnal sudden cardiac death without prior symptoms.

Methods: DNA was isolated from peripheral white blood cells of 40 patients with Brugada syndrome in Japan and analyzed SCNSA mutations by PCR-SSCP and direct sequence methods.

Results: We detected 2 point mutations in the SCNSA gene (Arg282His and Asn406Ser). These mutations were not detected in 200 chromosomes of normal controls and suggested disease causing mutations. In a 51-year-old man with frequent nocturnal polymorphic ventricular tachycardia, we found the Arg282His mutation in the S6 pore region of domain I. He had a 36-year-old brother who suffered sudden death. We analyzed 5 family members and detected 3 of the Arg282His mutation carriers and 2 noncarriers. The 2 noncarriers had neither aborted sudden death nor electrocardiographic changes. Two of the mutation carriers, excluding the proband, had no syncope or ventilatory fertilizer. All 3 mutation carriers had ST-segment elevations in leads V1 to V2/V3. Two of the mutation carriers, excluding the proband, had ST-segment elevations and a widened QRS complex. The PQ and QT intervals in all of the patients with the Arg282His mutation were normal. In a 67-year-old man with asymptomatic Brugada syndrome, we found the Asn406Ser mutation in the S6 segment of domain I. He had 21-year-old father and 27-year-old cousin who suffered sudden death. Proband with the Asn406Ser mutation had not only ST-segment elevation but bradycardia, first degree of atrioventricular block, and prolongation of the QRS width.

Conclusions: We suggested SCNSA mutations in the S5-S6 region cause both Brugada syndrome and cardiac conduction disturbances. Both mutations are located in important sites in the S5-S6 segment of domain I that confer ion selectivity and mutations might cause serious clinical phenotypes.

2:45 p.m.

Cardiac Autonomic Modulation by Estrogen in Female Mice Undergoing Ambulatory Monitoring and In Vivo Electrophysiologic Testing
Samir Saba, Vladimir Shusterman, Irmute Usiene, Barry London, University of Pittsburgh, Pittsburgh, PA

Introduction: Estrogen is an important modulator of cardiovascular risk, but its mechanism of action is not fully understood. In this study, we investigated the effect of ovarianectomy and its timing on the cardiac electrophysiology (EP) in female mice, with and without autonomic blockade. Methods: Thirty female mice (age 16.6 ± 3.1 weeks) under a single large bolus injection of anesthetics and atropine (0.5 mg/kg, IP) and propranolol (1 mg/kg, IP). Fifteen mice were ovariolectomized prepuberally (PRE) and 10 postpuberally (POST), 2 weeks prior to EP testing. Fifteen sham-operated female mice (F) served as controls. A subset of 13 mice (5 PRE, 3 POST, and 5 F) underwent 24-hour ambulatory monitoring prior to the EP testing. Ultras from all mice were automatically acquired and weighed. Results: With ambulatory monitoring, the average decrease in ventricular rate was 0.01 ± 0.02 heart rates were significantly slower in the ovariolectomized mice (PRE and POST groups) compared to the F group. At baseline EP testing, there were no significant differences between the ovariolectomized and intact mice in any of the measured parameters. With autonomic blockade, the F group had a significantly larger change (Δ) in the intraventricular (AV) nodal Wenckebach (AVW) period (Δ AVW = 11.3 ± 2.9 vs 2.1 ± 3.7 ms, p = 0.03) and functional refractory period (Δ FPRP = 11.3 ± 2.1 vs 1.22 ± 6.8 ms, p = 0.00) compared to the ovariolectomized mice. These results were not altered by the time of ovarioectomy (PRE versus POST groups). The weights of the uteri were significantly different among the 3 groups (14.3 ± 6.7 mg, 23.5 ± 10.5 mg, and 68.5 ± 17.7 mg for the PRE, POST and F groups respectively, p < 0.05 for all comparisons). Conclusion: Our results suggest that estrogen modulates the autonomic inputs into the cardiac sinoatrial and AV nodes. Low estrogen levels, regardless of the time of ovarioectomy, decrease the autonomic influence on the heart. These findings, if replicated in humans, might underlie the observed clustering of certain arrhythmias around menstruation and their higher incidence in men and postmenopausal women.

3:00 p.m.

Validation of Electrocardiogram Criteria for Pulmonary Hypertension
Khalid Al-Naamani, Thao Huynh, S. Andrews, McGill University Health Center, Montreal, PQ, Canada

Background: Measurements of right ventricular systolic pressure (RVSP) by 2D-echocardiography (echo) had been shown to have good correlation with that obtained by cardiac catheterization. We aimed to validate the sensitivity, specificity and predictive values of electrocardiography in patients with elevated RVSP diagnosed by 2D-echocardiography.

Methods: We analyzed all patients who had echo and EKG, with a 1-month interval, at our institution during 2000-2001. The following criteria were studied: 1) R wave in V1>17mm or 2) R wave in V5>55mm or 3) R wave in lead aVR 4) R/S in V1 >0.10mm or 5) S wave in V6<20mm or 6) R/S in V1>1.0 or 7) R/S in V6>1.0 or 8) RV1+SV5+10mm or 9) RV=110 or 9 R/S in V6>1.0 or 9 R/S in V6>1.0 or 9 R/S in V6>1.0 or 9 R/S in V6>1.0 or 9 R/S in V6>1.0 or 9 R/S in V6>1.0 or 9 R/S in V6>1.0. Significant pulmonary hypertension was defined as RVSP>40 mm Hg by 2D echo and no pulmonary stenosis.

Results: There were 365 patients with EKG and echo in a 1-month interval. We excluded patients with pacemaker rhythm and poor EKG quality. The above criteria had very poor sensitivity (0.0% to 13%), negative predictive values (24% to 36%). They had excellent specificity (92% to 100%) with positive predictive values ranging from 64% to 100%.

Although highly specific, these criteria have poor sensitivity and negative predictive values.

Conclusion: The currently available EKG criteria are poorly sensitive for significant pulmonary hypertension. New EKG criteria with better sensitivity should be developed.

3:15 p.m.

Increased Levels of High-Sensitivity C-Reactive Protein Are Associated with a Longer QTc Interval in Apparently Healthy Subjects
Anna P. Yazdanbakhsh, Bojan Vrtovec, Branimir Radovancevic, Todd T. Schlegel. NASA Johnson Space Center, Houston, TX

Background: QTc interval prolongation is associated with an increased risk of cardiovascular mortality in apparently healthy individuals. Furthermore, healthy subjects with increased levels of high-sensitivity C-reactive protein (hsCRP) see a rise in the risk of cardiovascular disease. Whether increased levels of hsCRP are associated with a longer QTc interval has not yet been studied. Methods: In 110 (56 male/54 female) healthy volunteers with a mean age of 36 ± 11 (range 20-65) years, mean QT interval was measured from a standard 12-lead ECG and QTc interval duration was calculated with the Bazett formula. At the time of ECG recordings, plasma levels of hsCRP were measured using the Kallesty assay. Cardiovascular risk stratification included assessment for the presence of hypertension, smoking, and diabetes mellitus, and measurement of serum cholesterol, LDL, and HDL levels. The 10-year coronary disease risk was calculated according to Framingham risk estimates. Results: The overall mean QTc interval was 0.40 ± 0.06 ms (range: 0.31 - 0.42 ms), and the mean hsCRP level was 1.05 ± 0.34 mg/dl (range: 0.002 - 2.517 mg/dl). Out of 110 subjects, 48 (43%) had an hsCRP level > 0.12 mg/dl, and 62 (57%) had an hsCRP level < 0.12 mg/dl. The subjects with hsCRP > 0.12 mg/dl had a significantly longer QTc interval than those with hsCRP < 0.12 mg/dl (405 ± 23 ms vs. 392 ± 25 ms, p=0.018). In multivariate analysis, hsCRP level > 0.12 mg/dl was associated with significantly longer QTc interval (p=0.047). No other differences in cardiovascular risk factors between the high-hsCRP and low-hsCRP groups were found.