Conclusion: In an ovine model of chronic AV block, true dual-chamber (DDD) leadless pacing was achieved with ~99% rate of beat-by-beat AV synchrony.

CI-525-04

A NEW CRITERIA TO DETERMINE LEFT BUNDLE BRANCH CAPTURE BASED ON TEMPORARY HIS BUNDLE OR RIGHT VENTRICULAR SEPTAL PACING

Fengwei Zou MD; Zhiyong Qian MD, PhD; Siyuan XUE MD; Xiaofeng Hou MD and Jiangang Zou MD, PhD, FHRS

Background: How to differentiate left bundle branch pacing (LBBP) from left ventricular septal pacing (LVSP) still remains challenging, especially in patients who do not present with generally-accepted criteria.

Objective: We aimed to develop a new criteria to confirm left bundle branch (LBB) capture in patients with both normal cardiac function or heart failure (HF), using temporary His bundle pacing (HBP) or right ventricular septal pacing (RVSP) as references.

Methods: Patients were included if surface ECGs of HBP or RVSP were recorded during procedure. Δsti-LVAT1 was defined as the difference of Sti-LVAT between HBP and LBBP/LVSP. Δsti-LVAT2 was defined as the difference of Sti-LVAT between RVSP and LBBP/LVSP.

Results: A total of 80 patients with normal cardiac function (65 LBBP and 15 LVSP) and 23 patients with HF were enrolled. Among 23 patients with HF who were corrected by LBBP, surface ECGs of LVSP were also recorded in 11 patients during procedure. Patients with LBBP showed significantly shorter Δsti-LVAT than those with LVSP. The cut-off value of 12.5 ms for Δsti-LVAT1 showed 73.9% sensitivity and 93.3% specificity to confirm LBB capture in patients with normal cardiac function. Δsti-LVAT2 > 31.0 ms was also useful to determine LBB capture with a specificity of 93.3%. For patients with HF, the cut-off value of 9.0 ms for Δsti-LVAT1 exhibited the greatest accuracy to confirm LBB capture with a sensitivity of 91.3% and a specificity of 100%.

Conclusion: Utilizing temporary HBP and RVSP as references during procedure could help determine LBB capture in patients with normal cardiac function or HF with great sensitivity and specificity.
arrhythmias including SVT, AF, flutter, and AV block. Cardiac MRI was available for 21,222 of the WES individuals. We extracted the LV ejection fraction (LVEF), end-systolic (LVESV) and end-diastolic volumes (LVEDV). We removed outliers > 7 SD from the mean and normalized volumes (LVEDV, LVESV) by body surface area (BSA), age and sex. For each of the gene groups, we compared those with rare variants to the rest.

Results: We validated that nonsense variants in genes of the definitive and strong evidence group were associated with both adverse cardiovascular outcomes, LV dilation and ventricular/SV arrhythmia. Importantly, we found that genes in the “moderate” evidence group (ACTC1, ACTN2, JPH2, NEXN, TNNI3, TPM1, VCL) with ClinVar annotations were associated with increased cardiac morbidity (OR 3.6, 95% CI 1.7-7.6), and variants with SIFT or nonsynonymous annotations were associated with increased LVESV (+3.94 ml vs control, p<0.001) and LVEDV (+4.45 ml vs control, p=0.03), and decreased LVEF (-0.65% vs control, p=0.03), as well as with SV arrhythmia (OR 5.1, 95% CI 2.2-11.6).

Conclusion: We provide evidence to support the interaction of genes previously classified as “moderate” with DCM, arrhythmia and adverse cardiovascular outcomes.

HF-566-02
Predicted Risk of Ventricular Arrhythmia in Individuals with Desmosome Gene Variants Identified via Population Genomic Screening

Eric Carruth PhD; Amro Alsaid MD; Brittnay Murray MS, CGC; Crystal Tichnell MGC, RN; Amy C. Sturm MS, CGC; Cynthia A. James PhD, CGC and Christopher M. Haggerty PhD

Background: Population genomic screening for desmosomal variants associated with arrhythmogenic right ventricular cardiomyopathy (ARVC) may help facilitate early detection of disease and protective intervention. However, early studies have shown that disease penetrance in this setting is low. The ARVC risk calculator offers a novel means to risk stratify individuals who present with variants identified via population genomic screening.

Objective: Quantify the risk of arrhythmic events in individuals with ARVC-associated variants ascertained “genome first” from a general population.

Methods: Individuals harboring a pathogenic/likely pathogenic (P/LP) variant in a desmosome gene (PKP2, DSP, DSG2, or DSC2) were identified through the Geisinger MyCode Genomic Screening and Counseling program. The ARVC risk calculator was applied to all patients with a subsequent evaluation of RV function. Missing 24-hour PVC counts (i.e. no rhythm monitoring study or PVC count not quantified), were imputed with the group median.

Results: Of 184 individuals with a clinically confirmed P/LP desmosome variant, 80 (median age 57 [IQR 44-68]; 71% female) had cardiac imaging in follow-up. Fifty-eight (72%) had no ARVC task force criteria (TFC) besides the P/LP variant (possible diagnosis), 11 (14%) had a single minor criterion (borderline diagnosis), and 11 (14%) met criteria for definite diagnosis. The overall median 5-year predicted VA risk was 5.2% (risk of fast VA 2.0%), notably much lower than median risk in the calculator’s derivation cohort (20.6%). The predicted risk was modestly higher in individuals with any TFC (10.1 [4.5-17.0]% versus those with none (4.5 [2.8-7.1%]; p<0.01). The risk was also higher in those with left ventricular dysfunction and arrhythmia (i.e. "ALVC" 13.7 [8.2-18.5]% vs. non-ALVC 4.9 [2.9-7.9]%);

Conclusion: The predicted 5-year risk of VA in individuals ascertained via population genomic screening with ARVC risk is relatively low (5.2%; 2% for "fast" VA) but may vary by gene, having any TFC, and affected ventricle.

HF-566-03
EMD Missense Variants Are Associated with a Dilated Cardiomyopathy and Conduction System Disease/ATL

Ahmed Alsalem MD; Renae Judy; Erica S. Zado PAC, FHRS; Gustavo S. Guandalini MD; Rajat Deo MD; Jeffrey Arkles MA, MD; Robert D. Schaller DO, FHRS; Pasquale Santangeli MD, PhD; Saman Nazarian MD, PhD, FHRS; David S. Frankel MD, FHRS; Michael P. Riley MD, PhD; Sanjay Dixit MD, FHRS; Fermin C. Garcia MD; Andrew E. Epstein MD, FHRS; David J. Callans MD, FHRS, CCDS; Francis E. Marchlinski MD, FHRS; Scott Damrauer and Matthew Craig Hyman MD, PhD

Background: Emerin (EMD) is an essential inner nuclear envelope protein encoded by EMD. Loss of function (LoF) variants in EMD result in Emery-Dreifuss muscular dystrophy type 1 (EDMD1). Cardiac involvement in EDMD1 is characterized by sinus node dysfunction (SND), atrial fibrillation (AF) and dilated cardiomyopathy (DCM). Recently a non-syndromic cardiac phenotype termed cardiac emerinopathy was recognized in patients with predominantly LoF variants in EMD. The contribution of EMD missense variants to cardiac disease is unknown.

Objective: To characterize the impact of EMD missense variants and delineate the associated cardiac phenotypes.

Methods: We surveyed exome sequencing data in the Penn Medicine Biobank (PMBB) for all coding variants identified in EMD. The medical record of male individuals with non-synonymous EMD variants (given an X-linked inheritance pattern) were reviewed to characterize cardiac and musculoskeletal pathology. Male individuals with synonymous EMD variants with no predicted effect on mRNA splicing were used as a reference group.

Results: A total of 28 EMD missense variants and a single frameshift insertion were identified in 68 male individuals (mean age 68±14). Seventy-seven patients with synonymous variants