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Alternate Site Pacing and the Impact on Intracellular Calcium Handling During the Post-Extrasystolic Cardiac Cycle

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Abstract

Objective: Previous work has shown that alternate site (RV apex) results in myocardial dysfunction.6 With the development of tools to place endocardial pacing leads in locations that create physiological pacing activation, we sought to evaluate how ventricular trans-septal or left ventricular apical placement pacing differs from right atrial pacing. We will evaluate how these chronic pacing modes impact the PR and RF at baseline, 0, and 16 weeks in the canine heart.

Methods: Quantitative analysis will be performed on previously generated data. The data set includes pacing of 15 dogs total (8 with trans-septal leads & 7 with left ventricular apical leads). GraphPad Prism software will be used for the statistical analysis of the data. The recirculation fraction value will be calculated as the slope of dP/dtmax following the extra-systole. The potentiation ratio will be calculated by normalizing dP/dtmax from the first beat following extrasystole to the steady state dP/dtmax. From these values we will uncover any changes in the force interval relationship which can be attributed to differences in calcium handling associated with different pacing sites.

Results / Conclusions: The results of this study are expected to demonstrate how alternate site pacing impacts intracellular calcium handling using the post-extrasystolic cardiac cycles. We expect some loss in the force interval relationship following the 16 weeks of alternant site pacing due to the alterations in Ca+2 handling that accompanies the post-extrasystolic beat. Through this project we hope to gain a deeper understanding of cardiac function while simultaneously hoping to provide evidence for the reintroduction of the RF and PR parameters into the clinical space.

Expected Results

The results of this study are expected to demonstrate how alternate site pacing impacts intracellular calcium handling using the post-extrasystolic cardiac cycles. We expect some loss in the force interval relationship following the 16 weeks of alternant site pacing due to the alterations in Ca+2 handling that accompanies the post-extrasystolic beat.

Methods

Adult mongrel dogs (28±3.5 kg) of either sex were premedicated, anesthetized, and treated after surgery as described before. All received a transvenous lead in the right atrium (Medtronic 5568) and were randomized to receive either an epicardial lead at the LV apex (n=7; Medtronic 5071) via a limited thoracotomy or a transvenous lead in either the RV apex (n=9; Medtronic 3830 or 5076), RV midseptum (n=7; Medtronic 3830), or the LV midseptum (n=8). The latter received a custom pacing lead (Medtronic 3830 lead) with extended helix that was introduced transvenously and, after positioning against the RV septum using a preshaped guiding catheter, driven through the interventricular septum with the screw-in tip until the LV endocardium was reached. All leads were positioned according to the prescribed anatomic location; no attempt was made to search for sites resulting in narrower paced QRS complexes. After creation of total AV block by radiofrequency ablation, the animal was paced for 16 weeks in VDD mode (Medtronic Sigma, Kappa, or Enpulse series). AV delay (110±20 ms) was set to maintain P-Q segment length on ECG lead II as measured just before creation of AV block. Under all conditions, pacing was performed at about twice the stimulation threshold.

After finishing the temporal measurements at 16 weeks, the thorax was opened and epicardial leads were placed at the RV apex, LV apex (in nonchronically LV-apical paced animals), and LV lateral wall. The same measurements described above were repeated during DOO pacing at 110 bpm in 4 modes: implant site (IS) pacing, RV apical pacing, LV apical pacing, and RV apical/LV lateral pacing (BiV). In this way, each chronic implant site could be compared with 3 reference sites/combinations within each animal.

The RF value will be calculated as the slope of dP/dtmax following the extra-systole and PR will be calculated by normalizing dP/dtmax from the first beat following extrasystole to the steady state dP/dtmax. GraphPad Prism software will be used for the statistical analysis of the data.

Background

Post-extrasystolic potentiation (PESP) is defined as an increase in contractility of cardiac muscle during the beat that follows extrasystole. It has often been debated as a potential diagnostic and therapeutic tool for patients exhibiting heart failure.1 PESP along with mechanical restitution make up the force interval relationship, which accounts for changes in contractility caused by alterations in stimulation patterns.2 PESP is linked to calcium homeostasis and heart failure, and while heart failure is associated with abnormal calcium homeostasis, PESP appears to be influences differently than the fundamental force-frequency principal of the heart.3 Both the recirculation fraction (RF) and potentiation ratio (PR) can be used to evaluate calcium handling and provide additional insight for the assessment of cardiac performance. Seed et al. has shown patients with heart failure have a lower RF which can be attributed to a decrease in calcium reuptake.4 Ahlberg et al. asserts an inverse relationship exists between RF (decrease) and PR (increase) as heart failure progresses which is a trend that can be used for diagnostic purposes.5

Previous work has shown that alternate site (RV apex) results in myocardial dysfunction.6 With the development of tools to place endocardial pacing leads in locations that create physiological pacing activation, we sought to evaluate how ventricular trans-septal or left ventricular apical placement pacing differs from right atrial pacing. We will evaluate how these chronic pacing modes impact the PR and RF at baseline, 0, and 16 weeks in the canine heart. The data set contains 8 canine hearts with trans-septal leads and 7 with left ventricular apical leads for a total of 15 canine models.

Expected Conclusion

The force interval relationship can be used to evaluate Ca+2 handling at chronic non physiologic pacing sites. This type of cardiac pacing provides insight into lead placement within patients acutely at baseline, 0, and 16 weeks. Through this project we hope to gain a deeper understanding of cardiac function while simultaneously hoping to provide evidence for the reintroduction of the RF and PR parameters into the clinical space.

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