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Abnormal Restitutional Dynamics Cause Unidirectional Block in Canine Postinfarction Ventricular Tachycardia

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The emergence of unidirectional conduction block is a prerequisite for initiation of reentrant monomorphic ventricular tachycardia (MVT) after myocardial infarction (MI). Abnormal restitution of action potential duration (APD) increases spatial dispersion of repolarization and has been shown to cause excitation wave break-up during ventricular fibrillation. Using optical mapping in isolated canine left ventricular epicardial preparations, we characterized repolarization restitution dynamics within the reentrant circuit of post MI MVTs. Methods: In mongrel dogs (n = 7) MI was created percutaneously by injecting embolization foam selectively into the posterolateral branches of the left circumflex artery (LCX). Optical mapping was performed 14 ± 1 days after MI. Isolated preparations were perfused with Tyrode×s solution through cannulation of the LCX. Excitation-contraction uncoupling was achieved with cytochalasin-D. Results: Continuous pacing (600 to 250 ms) showed monotonic decreasing APD restitution curves with decreasing local diastolic interval (DI). Sustained and non-sustained MVTs (cycle lengths of 297 ± 14 ms (n = 4 out of 7 dogs)) were induced by 2 or 3 extrastimuli. In all MVTs, lines of conduction block were located near the MI border zone and appeared to be functional: continuous pacing after termination of MVT showed slow, but continuous activation in these same areas. APD restitution curves of MVT induction showed 2 types of response to decreasing local DIs, depending on local conduction velocity: (1) monotonic decreasing (normal conduction) and (2) monotonic increasing (site with conduction block). Mean APD at shortest local DI (105 ± 20 ms vs. 133 ± 18 ms) in these 2 response types were significantly different ($P < 0.005$) Conclusion: The complex non-linear interplay between abnormal APD restitution and abnormal conduction velocity restitution results in dynamic large spatial dispersion in refractoriness. This favors the emergence of lines of conduction block and subsequent reentry, also in relatively less complex reentrant arrhythmias that arise from single reentrant circuits such as post infarction MVT.

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A Relationship Between DFT, Arrhythmia Complexity, and the Isoelectric Window

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It is unclear why the defibrillation threshold increases with the complexity of reentrant activity. The difference in behavior may be due to transmural electrical events that remain inaccessible to the current optical mapping techniques. The goal of this simulation study is to provide mechanistic insight into the role of the pre-shock tissue state (simple vs. complex reentry) in defibrillation. Methods: We assess shock efficacy in a bidomain model of a 4 mm thick transverse section through the canine ventricles immersed in a perfusing bath. A shock is applied between a RV cathode and a distant anode to terminate one of two types of arrhythmias: VT (single scroll wave) or VF (multiple scroll waves). Results: The ED50 for VT was found to be 13% less than that for VF. We observe an isoelectric window after successful shocks at ED50 shock strength with a duration of approximately 40% APD that is unrelated to the type of arrhythmia. Unsuccessful shocks near ED50 have a shorter isoelectric window compared to successful ones. Analysis of the results demonstrates that the shock induces strong virtual electrode polarization (VEP) on the myocardial surfaces that rapidly decreases in magnitude in the transmural direction. For failed shocks, reentrant wavefronts on the surfaces are terminated by strong VEP, however dispersion of refractoriness is not reduced within the tissue volume. Shock-induced wavefronts propagate slowly through partially recovered tissue in the midmyocardium and eventually emerge into recovered tissue on the myocardial surface completing a reentrant pathway. Delaying the time to breakthrough reduces the remaining dispersion of refractoriness and thus, the likelihood of reentry. In the midmyocardium, which is marginally affected by the shock, dispersion of refractoriness is related to the preshock tissue state. There is less organization of activity in VF compared to VT and therefore more dispersion of refractoriness in the myocardium before the shock. The lack of preshock organization leads directly to increased probability of shock failure. Conclusions: This study reveals the reasons that an elevated defibrillation threshold is associated with VF as compared to VT.

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Capacitance, Coupling Conductance and the Heterogeneity Are Key to Maintaining Sinus Node Activity

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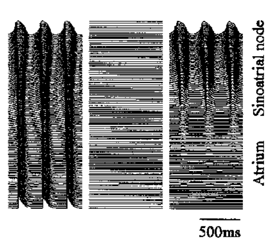
Introduction: The sinoatrial node (SAN) is a heterogeneous structure and activation patterns in the sinoatrial node vary dynamically as a consequence of various physiological and pathophysiological interventions. We hypothesized that characteristics and electrotonic interaction has an important role in maintaining spontaneous activity. Method: One dimensional model of 50 SAN cells and 50 atrial muscle cells is created as a string of tissue with a length of 1.0 mm. Distribution of cell capacitance wad designed from 20pF to 65pF proportional and power functional pattern. Ionic current conductance was proportional to cell capacitance. Electrotonic interaction within the tissue was set to be changed from 25nS to 1000nS. The location of the leading pacemaker site and conduction pattern of the spontaneous activity was observed. Result: Three patterns of activation of SAN was presented from various cell capacitance and coupling conductances. Pattern A, excitation is initiated from the SAN and propagated to atrium. Pattern B, excitation is not generated from the SAN. Pattern C, excitation is initiated from the SAN and propagated to atrium, but excitation could not drive atrium. In pattern A, leading pacemaker site was center or periphery of the SAN. Conclusion: Both heterogeneous distribution of cell characteristics of the SAN and the cell to cell coupling are important in maintaining sinus node spontaneous activity.



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Effects of Wall Heterogeneity in an Anatomically Realistic Model of Canine Ventricles: A Simulation Study

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Background. To date, simulations of cardiac tissue in anatomically realistic structures have assumed homogeneous cell types. However, variations in cell properties through the ventricular wall are essential for reproducing ECGs without inverted T-waves. Methods. Using published experimental data, variations in action potential (AP) shape and rate adaptation, including LV vs. RV, were developed for an ionic cell model and incorporated for the first time into a computer model of the canine ventricles (see figure) that includes fiber orientations. Results. Simulated activation and recovery patterns matched experiments, allowing normal ECGs with regular T-waves to be generated. Varying the relative thicknesses of the epicardial, midmyocardial, and endocardial layers resulted in different variations of the ECG. These variations are likely related to the anatomic and cell type distributions found clinically. Conclusions. Incorporating transmural and left-right heterogeneities in simulated canine ventricles resulted in ECGs similar to those observed clinically and may have implications for future risk stratification of patients.