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Transseptal Dispersion of Repolarization and Its Role in the Development of Torsade de Pointes Arrhythmias

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Abstract

Objective—This study was designed to quantitate transseptal dispersion of repolarization (DR) and delineate its role in arrhythmogenesis using the calcium agonist BayK 8644 to mimic the gain of function of calcium channel current responsible for Timothy syndrome.

Background—Amplification of transmural dispersion of repolarization (TDR) has been shown to contribute to development of Torsade de Pointes (TdP) arrhythmias under long-QT conditions.

Methods—An arterially-perfused septal wedge preparation was developed via cannulation of the septal artery. Action potentials (APs) were recorded using floating microelectrodes together with a transseptal electrocardiogram (ECG). These data were compared to those recorded from arterially-perfused canine left ventricular (LV) wedge preparations.

Results—Under control conditions, the shortest AP duration measured at 90% repolarization (APD_{90}) was observed in right ventricular (RV) endocardium (181.8±15 ms), APD_{90} peaked close to mid-septum (278.0±32 ms), and abbreviated again as LV endocardium was approached (207.3±9 ms). Transseptal DR averaged 106±24 ms and T_{peak}-T_{end} 84±7 ms (n=6). TDR and T_{peak}-T_{end} recorded from LV wedge were 36±9 ms and 34±19 ms, respectively (n=30). BayK 8644 increased transseptal DR to 123.2±35 ms (n=5) and induced early and delayed afterdepolarizations (3/5), rate-dependent ST-T-wave alternans (5/5), and TdP arrhythmias (3/5).

Conclusions—Our data indicate that dispersion of repolarization across the interventricular septum is twice that of the LV free wall, predisposing to development of TdP under long-QT conditions. Our findings suggest that the coronary-perfused ventricular septal preparation may be a sensitive model in which to assess the potential arrhythmogenic effects of drugs and pathophysiological conditions.

Keywords

Interventricular Septum; Dispersion of Repolarization; Sudden Cardiac Death; Arrhythmias; Long-QT Syndrome

INTRODUCTION

Arterially-perfused right and left ventricular wedge preparations have proved valuable in the elucidation of the cellular basis for the electrocardiogram (ECG) and the mechanisms underlying a variety of arrhythmogenic syndromes, including the Brugada, long-QT, and

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short-QT syndromes 1 as well as conduction disease, catecholaminergic VT 2, and ischemia-related arrhythmias.3, 4 In all cases, transmural heterogeneities, or differences in the action potential duration and morphology across the ventricular wall, have been shown to contribute prominently to arrhythmogenesis attending these syndromes.

Timothy syndrome, also referred to as syndactyly-associated long-QT syndrome (LQTS) or LQT8, is a multisystem disorder characterized by developmental defects causing dysmorphic facial features including round face, flat nasal bridge, receding upper jaw, thin upper lip and webbing of the toes and fingers (syndactyly). 5 The disorder is also associated with prolongation of the QT interval, development of ventricular arrhythmias, and sudden cardiac death. The syndrome has recently been linked to a missense mutation in the $Ca_V1.2$, which encodes the α subunit of the L-type calcium channel, resulting in a gain of function of the L-type calcium current ($I_{Ca,L}$). 5: A LV wedge model of long-QT syndrome created with use of BayK 8644 to augment $I_{Ca,L}$, has been shown to recapitulate the electrocardiographic and arrhythmic manifestations of Timothy syndrome. 6.

Although the interventricular (IV) septum is known to play an important role in clinical arrhythmias (ischemia 7, hypertrophic cardiomyopathy 8, outflow tract arrhythmia 9, and long-QT syndrome 10 (LQTS), the electrophysiological characteristics of the IV septum are poorly defined. For technical reasons, an arterially-perfused septal preparation has been out of reach. The present study used a canine ventricular septal preparation developed by perfusion of the septal artery 11¯13 to assess the heterogeneity of action potential characteristics across the IV septum, to quantitate the transseptal gradient of repolarization and to delineate its role in arrhythmogenesis using the calcium agonist BayK 8644 to mimic the gain of function of calcium channel current responsible for Timothy syndrome

METHODS

Dogs weighing 20-35 kg were anticoagulated with heparin (180 IU/kg) and anesthetized with sodium pentobarbital (35 mg/kg, IV). The chest was opened via a left-thoracotomy and the heart excised and placed in a cold cardioplegic solution ($[K^+]_0$ = 8 mmol/L, 4°C). All protocols were in conformance with guidelines established by the Institutional Animal Care and Use Committee.

The arterially perfused septal preparation

An arterially-perfused septal preparation was developed via cannulation of the septal artery, a branch of the left anterior descending (LAD) coronary artery. After removal of the anterior aorta, just below the opening of the LAD, both the LAD and its septal branch were visible. The cannula was placed in the opening of the septal branch and sutured in place. The most anterior and posterior portions of the septum, shown by dye studies with Evans Blue (Sigma-Aldrich, St. Louis, MO, USA) to be poorly perfused, were excised in order to remove areas of potential ischemia. Cut branches of the septal artery were sealed using electrocautery or ligated using sutures.

The composition of the Tyrode's solution was (in mM): NaCl 129, KCl 4, NaH_2PO_4 0.9, $NaHCO_3$ 20, $CaCl_2$ 1.8, $MgSO_4$ 0.5, and D-glucose 5.5. Action potential (AP) recordings were obtained using floating glass microelectrodes. A transseptal ECG was recorded using 2 Ag/AgCl half cells (2 mm diameter × 4 mm) placed approximately 1 cm from the right ventricular (RV) endocardial and left ventricular (LV) endocardial septal surfaces of the preparation and along the same axis as the intracellular recordings. Stimuli were applied to the RV or LV endocardium. Action potentials (APs) were recorded from the right and left endocardial (Endo) surfaces as well as across the septal wall. Arterially-perfused septal preparations were allowed to equilibrate in the chamber for 2 hours while paced at a basic

cycle length (BCL) of 2000 ms using silver bipolar electrodes placed in contact with the RV Endo surface. Perfusion pressure was maintained at 40-50 mmHg and temperature at 37±0.5°C. The preparations were fully immersed in the extracellular solution throughout the course of the experiment.

We performed experiments in 6 arterially-perfused septal preparations. Transseptal dispersion of repolarization (DR) was defined as the difference between the longest and the shortest repolarization times (activation time plus action potential duration measured at 90% repolarization, (APD_{90})) of transmembrane APs recorded across the septum. The QT interval was defined as the time interval between QRS onset, and the point that the line of maximal downslope of the T wave crossed the base line. T_{peak}-T_{end} was defined as the difference between the peak and the end of the T wave of the transseptal ECG. Data obtained from the arterially-perfused septal preparation were compared with data obtained over the same time period by the same investigator, using the arterially-perfused LV wedge. 14

Arterially-Perfused Canine Left Ventricular Wedge Preparations

Transmural LV wedge preparations with dimensions of approximately 12 mm × 35 mm × 12 mm were dissected from the mid-to-basal anterior region of the LV wall and a diagonal branch of the left anterior descending coronary artery was cannulated to deliver the perfusate (Tyrode's solution). Intracellular action potentials were recorded from epicardial and subendocardial M cell regions using floating microelectrodes. A transmural pseudo-ECG was recorded as for the septal preparation. Transmural dispersion of repolarization (TDR) was defined as the difference between the longest and the shortest repolarization times (activation time plus action potential duration (APD) measured at 90% repolarization, APD_{90}) of intracellular APs recorded across the wall (typically M-cell minus epicardial cell repolarization time). The QT interval was defined as the time interval between QRS onset and the point at which the line of maximal downslope of the T wave crossed the isoelectric line.

Programmed electrical stimulation (PES)

Induction of arrhythmias was tested by premature stimulation (PS). PS was applied to the RV or LV endocardial surface before and after each concentration of drug in an attempt to induce arrhythmias. Single pulses (S2) were delivered once after every tenth basic beat (S1) at cycle lengths of 2000 ms. The S1-S2 coupling interval was progressively reduced until refractoriness was encountered (S2 stimuli were of 2-3 ms duration with an intensity equal to 3 to 5 times the diastolic threshold).

Drugs—BayK 8644 was prepared as a 1 mM stock in 100% Dimethylsulfoxide (DMSO) and diluted to 1 μM in external solution.

Statistics—Statistical analysis was performed using one-way repeated measures analysis of variance (ANOVA) followed by Bonferoni's test. Mean values were considered to be different when $p < 0.05$.

RESULTS

In a previous study, we examined the deteminants of adequate perfusion and electrical stability of the septal preparation following cannulation of the septal artery. 11 We demonstrated that no significant changes in QT and Tpeak-Tend intervals are observed over a 4-hour period.

Action potential characteristics in the arterially-perfused septal preparation

In an initial series of experiments in the present study, we recorded APs from discrete sites spanning the interventricular septum. Fig. 1 shows APs simulatenously recorded from 3 locations across the septum together with an action potential recorded from a subendocardial Purkinje fiber on the RV Endo surface. Marked difference in action potential duration and morphology were observed. The briefest AP, found in the RV Endo, is coincident with the peak of the electrocardiographic T wave, while the ventricular AP found in the mid-septum coincides with the end of the T wave. The AP recording obtained from PF from the endocardial surface of the RV displayed the longest APD, but this activity did not register in the transseptal ECG. We identified PF action potentials on the basis of their longer action potentials, more negative plateau, slower phase 3 of repolarization, and their localization within conduction tissue strands stained with Lugol's solution administered via coronary perfusion at the end of the experiment. Stained Purkinje fibers were observed only at right and left endocardial surfaces but not in the mid septal regions of the preparations. These APDs were not included in the determination of the transseptal dispersion of repolarization.

Distribution of action potential duration and transseptal dispersion of repolarization

The distribution of action potential duration measured at 90% repolarization (APD_{90}) across the interventricular (IV) septum is illustrated in Fig. 2. Fig. 2A shows the distribution of AP morphologies across an arterially-perfused septal preparation. APD_{90} is shortest in RV Endo increase until reaching a maximum beyond mid-septum, abbreviating near the LV Endo. The Purkinje fiber AP recorded from the RV Endo surface displayed the longest APD. The middle panel (B) shows the distribution of APD_{90} in each individual experiment, and the lower panel (C) shows composite data from 6 experiments. Fig. 2 B shows that APD_{90}, was shortest in RV Endo in 5 of 6 experiments, increases until reaching a maximum just beyond mid-septum, once again abbreviating near LV Endo. The spike and dome morphology of the AP was generally most accentuated in the deep subendocardium on both sides of the septum, and least accentuated at the surface and in the mid-septum. Composite data graphed in Fig. 2C highlights the biphasic distribution of APD_{90} across the septum. APD_{90} increases progressively as the position of the roving floating microelectrode shifts away from RV Endo, reaches a maximum near mid-septum, and abbreviates again as we approach LV Endo.

Table 1 shows maximum and minimum APD_{90}, transseptal dispersion of repolarization (DR) and T_{peak}-T_{end} values recorded from 6 septal preparations. Mean transseptal DR was 106 ± 24 ms, and mean T_{peak}-T_{end} was 84 ± 7 ms (mean ± SD). The mean transseptal dispersion of repolarization is nearly double of the TDR and T_{peak}-T_{end} values observed in experiments performed in the LV wedge preparations ($p<0.05$) (Table 2).

Effects of BayK 8644

In another series of experiments, the calcium agonist BayK 8644 (1 μM) was introduced to the coronary perfusate to accentuate transseptal DR and mimic the gain of function recently described in a variant of the long-QT syndrome (LQT8) known as Timothy syndrome (TS). With the addition of the calcium agonist, T_{peak}-T_{end} increased significantly from 85±6 to 121 ± 32 ms (n=5). At a basic cycle length (BCL) of 300 ms, BayK 8644 induced rate-dependent ST-T-wave alternans in 5 of 5 preparations, mainly due to alternans of action potential duration, particularly in the mid-septal region (Fig. 3). BayK 8644 induced delayed and early afterdepolarizations (DADs and EADs), in 3 out of 5 preparations that led to the development of spontaneous extrasystoles (Fig. 4). The extrasystoles served as a trigger for the initiation of TdP arrhythmias in the septal preparation (Fig. 5). The ST segment depression observed in the beats preceding the TdP episode and its accentuation following TdP appears to be a consequence of multiple previous episodes of TdP that may have

induced some ischemia in the preparation. Previous traces of TdP in the preparation showed little or no ST segment depression in the transmural ECG. DADs and EADs, together with the presence of an amplified dispersion of repolarization provided the trigger and substrate for the development of reentry, which has been shown to underlie the development of TdP. In all cases, the arrhythmias self-terminated after a period of 10 seconds to a minute. None of the preparations developed arrhythmias under control conditions. Following administration of 1 μM BayK 8644, 5 of 5 preparations displayed triggered activity, and TdP arrhythmias developed in 3 of these 5 preparations. In all cases TdP occurred spontaneously.

DISCUSSION

Canine ventricular septal preparation perfused via the septal artery are shown in the present study to display marked transseptal heterogeneity of action potential characteristics and transseptal DR, more than double that observed in wedge preparation isolated from the LV wall. The LV wedge data reported in the present study are similar to those previously reported. 14, 15

The calcium agonist BayK 8644 is shown to further accentuate trans-septal DR and induce DADs and EADs, thus providing the substrate and trigger for the development of TdP. Our data suggest that the arterially-perfused ventricular septal preparation is a sensitive model with which to assess the potential arrhythmogenic effects of drugs and pathophysiological conditions.

Electrical heterogeneity within the ventricular wall and interventricular septum: the role of M cells

Numerous studies have highlighted regional differences in electrical properties of ventricular cells as well as well as differences in the response of the diverse cell types to pharmacological agents and pathophysiological states (for review 16, 17).

Ventricular myocardium is comprised of at least 3 electrophysiologically distinct cell types: epicardial, M, and endocardial. The 3 ventricular myocardial cell types differ principally with respect to phase 1 and phase 3 repolarization characteristics.

M cells are distinguished by the ability of their action potential to prolong disproportionately relative to the action potential of other ventricular myocardial cell types in response to a slowing of rate and/or in response to drugs with QT-prolonging actions. 18 The ionic basis for these features include the presence of a smaller slowly activating delayed rectifier current (I_{Ks}) 19, a larger late sodium current (late I_{Na}) 20, and a larger electrogenic sodium-calcium exchange current ($I_{Na\text{-}Ca}$). These ionic distinctions also sensitize the M cells to a variety of pharmacological agents or genetic mutations that reduce the delayed rectifier current (I_{Kr}), I_{Ks} or increase late I_{Na} or I_{Ca}.

Previous studies have described M cells not only within the ventricular wall, but also in tissues isolated form deep subendocardial structures, including trabeculae, papillary muscles and interventricular septum. 21 Heterogeneity of action potential characteristics has also been observed in cells isolated from the canine interventricular septum. 22 Tissue slices isolated from the canine IV septum have been shown to possess cells with M cell characteristics, including a steep APD-rate relationship and sensitivity to APD prolonging agents. 21 The present study defines the transseptal distribution of APD across the interventricular septum, defines the location of cells with M cell characteristics and delineates their contribution to the development of TdP. M cells with the longest APD_{90} reside near the mid-septum and display a steep APD-rate relationship and heightened sensitivity to APD prolonging drugs, such as BayK 8644, typical of this cell type.

Our observation of a marked transseptal gradient in the arterially-perfused septal preparation is in sharp contrast to those reported by Morita et al 12 in a similar preparation. The authors found no repolarization gradients across the septum. Differences in methodology may account for the disparate results. Morita's study employed optical mapping techniques that require use of voltage sensitive dyes and electrical-mechanical uncoupling agents, which were not used in our study. Optical recording techniques do not permit recording of responses from discrete cells, but rather from groups of cells. It is also noteworthy that the action potentials recorded by Morita and co-workers did not display an I_{to}-mediated spike and dome morphology, which we observed and which have been reported in previous studies.21¯24 It is noteworthy that the same group failed to observe significant dispersion of repolarization in canine LV wedge preparations under baseline conditions.25

The arterially-perfused septal wedge preparation vs the arterially-perfused wedge preparation

The newly developed arterially–perfused septal preparation confirms the existence of M cells in the interventricular septum, delineates the transseptal distribution of action potential characteristics, defines the transseptal gradients of repolarization, and demonstrates a correlation between transseptal APs and the transseptal ECG. Like the arterially-perfused ventricular wedge preparation, a marked heterogeneity of action potential characteristics is observed in the arterially-perfused septal preparation. The spike and dome morphology of the AP is most accentuated in the deep subendocardium and longer action potentials (M cells) are observed in the mid-septal regions. The transseptal DR, defined as the difference between the shortest (RV endocardial) and the longest (M cell) repolarization times was nearly twice that recorded from the LV free wall, where maximal transmural dispersion is typically delineated by the difference in repolarization time of epicardium and the M region. In both preparations, the end of the transmural T wave is approximated by repolarization of the M cell with the longest action potential. The peak of the T wave, however, is coincident with full repolarization of the RV endocardial action potential in the case of the septal preparation, but with full repolarization of the epicardial action potential in the case of the LV free wall.

The APD of Purkinje fibers recorded from both the right or left endocardial surfaces was always longer than that of the longest transseptal action potential. It is noteworthy that the delayed repolarization of the Purkinje system fails to register on the transseptal ECG (Figure 1). This is likely due to the relatively low mass of Purkinje tissue coursing through the septum. These findings are similar to those previously reported in the LV wedge preparation, where subendocardial Purkinje fibers display APDs longer than those of the M cells, but do not register on the transmural ECG. 26

In both cases, T_{peak}-T_{end} provides a global measure of the transmural dispersion of repolarization, which may prove to be a valuable index of spatial dispersion of repolarization across the septum when measured using transseptal leads. It would be of interest to determine to what extent T_{peak}-T_{end} measured in the mid-precordial leads of the 12-lead ECG reflect increases in transseptal dispersion of repolarization. The much steeper gradient of repolarization found across the interventricular septum suggests that this structure likely plays an important role in the development of arrhythmias, particularly under long-QT conditions.

The arterially-perfused septal preparation recapitulates the electrocardiographic and arrhythmic manifestations of the long-QT syndrome

LQTS is characterized by the appearance of long-QT intervals in the ECG, an atypical polymorphic ventricular tachycardia known as Torsade de Pointes (TdP), and a high risk for

sudden cardiac death. 27 Models of the LQT1, LQT2, LQT3, LQT7 and LQT8 forms of the long-QT syndrome have been developed using the canine arterially-perfused left ventricular wedge preparation. 6, 28, 29 The recently developed Timothy syndrome model (LQT8) 6 involves a gain of function of the L-type calcium current ($I_{Ca,L}$) and can be mimicked using the calcium channel agonist BayK 8644. In the LQT1, 2, 3 and 8 models of LQTS, preferential prolongation of the M cell action potential leads to an increase in the QT interval, as well as an increase in transmural dispersion of repolarization, which provide the substrate for the development of spontaneous as well as stimulation-induced TdP. 1, 30

In the present study, we used the calcium channel agonist BayK 8644 in the arterially-perfused septal preparation to mimic the Timothy syndrome (LQT8) model. BayK 8644 was found to accentuate transseptal DR and induce DADs and EADs, thus providing the substrate and trigger for the development of TdP arrhythmias. In both the arterially-perfused LV free wall and septal preparations, the addition of BayK 8644 reproduces the electrocardiographic and arrhythmogenic manifestations of Timothy syndrome including prolongation of the QT interval, ST-T alternans, and polymorphic ventricular tachycardia. The coronary-perfused septal preparation, however, was found to be more sensitive to the effects of BayK 8644; transseptal DR was significantly larger than the LV free wall transmural dispersion of repolarization, both before and after BayK 8644. TdP was observed in 3 of 5 (60%) septal preparations but in only 2 of 9 (22.2%) LV wedge preparations. 6 These findings suggest that the arterially-perfused septal preparation may be a more sensitive model to study the effects of QT prolonging agents.

Occurrence of T wave alternans (TWA)

TWA is an electrical phenomena characterized by beat-to-beat alternation of the morphology, amplitude, and/or polarity of the T wave. TWA often is associated with acquired as well as congenital LQTS and is considered an important prognostic indicator in that it is commonly observed just before episodes of TdP. TWA as well as ST-T segment alternans have been described clinically in Timothy syndrome 31 as well as in the LV wedge model of Timothy syndrome. 6 BayK 8644-induced ST-segment alternans in the septal preparation is due largely to beat-to-beat alternation of plateau voltage and APD of the mid-septal cells (Figure 3).

In vivo models of LQTS

Vos and colleagues have used dogs with biventricular hypertrophy secondary to chronic complete A-V block (CAVB) to test the potential of drugs to precipitate TdP. 32–34 Torsadogenic agents were generally those exhibiting larger interventricular dispersion of repolarization recorded using monophasic action potentials electrodes placed on either side of the septum.35 These data are consistent with our observations of an association of TdP with a large transseptal dispersion of repolarization in our model of Timothy syndrome.

Limitations of the study

Our results are based on measurements made in a limited portion of the interventricular septum perfused by the septal artery. It remains to be determined whether other parts of the septum have similar characteristics.

The greater sensitivity of the arterially-perfused septal preparation to unmask the arrhythmogenic potential of the calcium agonist when compared with the arterially-perfused LV wedge is indeed a desirable feature in safety pharmacology. The extent to which the model may be overly sensitive, sacrificing sensitivity for specificity, remains to be established. Moreover, the extent to which this enhanced sensitivity applies to other APD prolonging agents remains to be probed.

As with most experimental studies, extrapolation to the clinic must be done with great care. Further studies are warranted to determine the role of the septum in the generation of ventricular arrhythmias.

CONCLUSION

The available data suggest that the coronary-perfused ventricular septal preparation may be a sensitive model in which to assess the potential arrhythmogenic effects of drugs and pathophysiological conditions.

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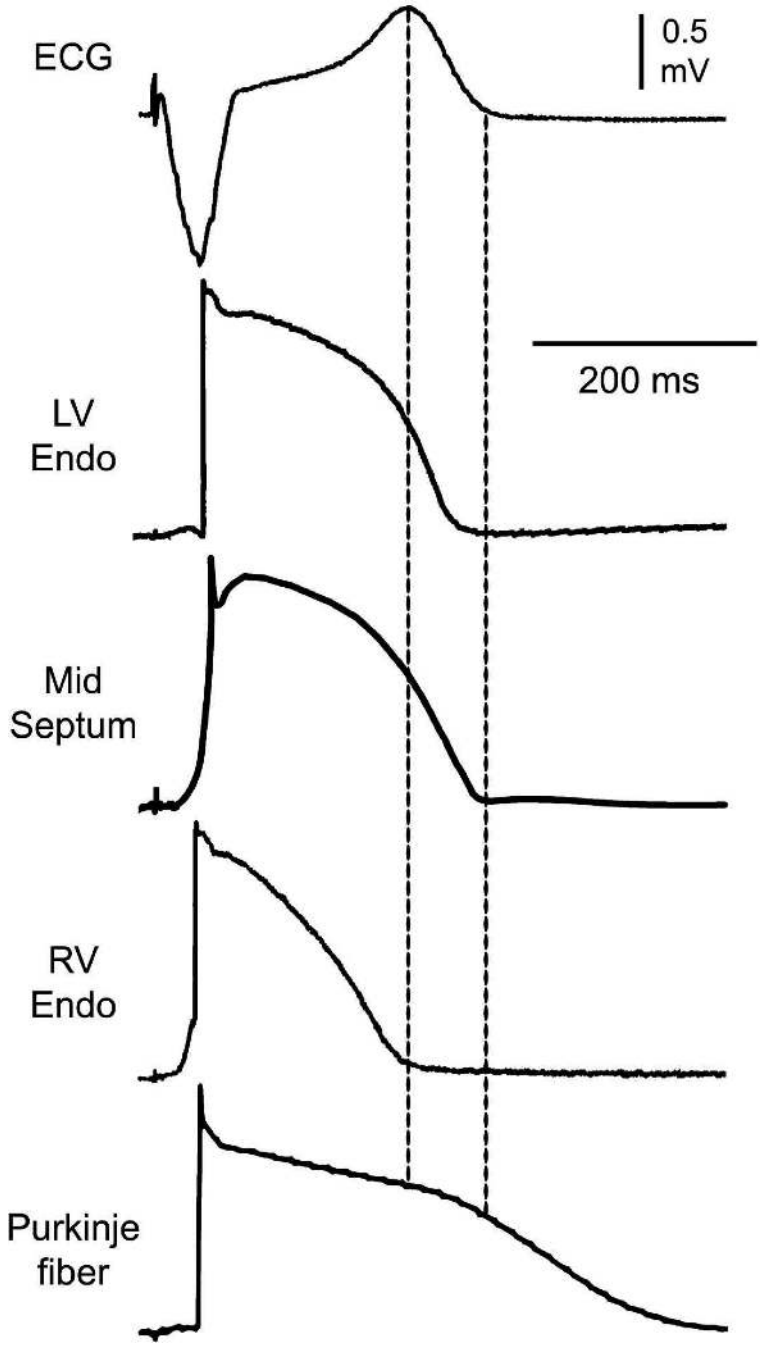

Figure 1.

Electrical activity recorded from an arterially-perfused septal preparation. Simultaneous recordings from 3 sites across the interventricular (IV) septum, a subendocardial Purkinje fiber (PF) from the right ventricular endocardial (RV endo) surface and a transseptal electrocardiogram (ECG). Marked differences in action potential (AP) morphology and duration were observed. The briefest AP was found in RV Endo, coinciding with the peak of the T wave of the ECG. The transseptal AP, observed near mid-septum, coincides with the end of the T-wave. AP recording obtained from PF displayed the longest APD but this activity did not register in the transseptal ECG. RV Endo stimulation. Basic cycle length (BCL) = 2000 ms.

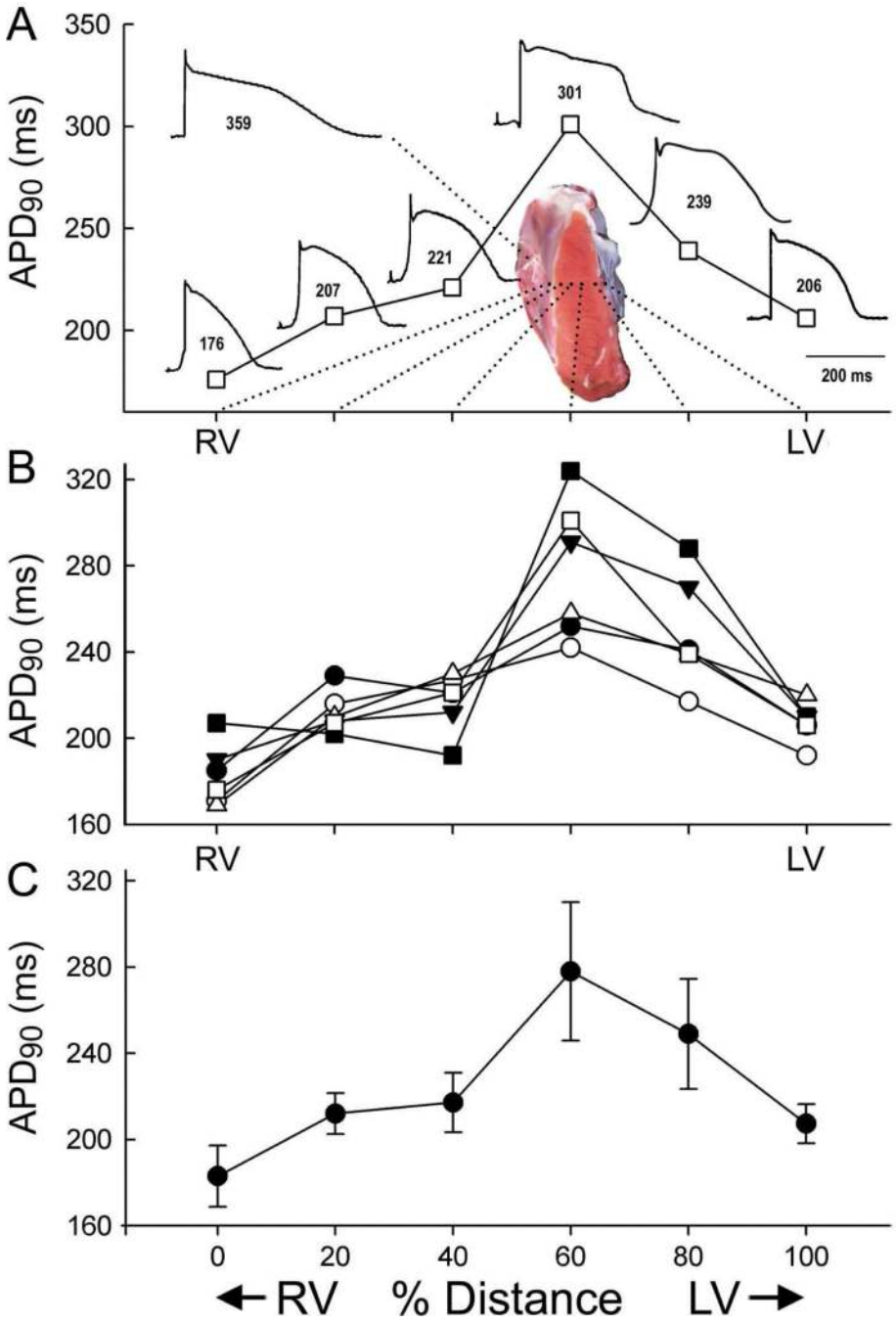

Figure 2.

Distribution of action potential duration (APD) across the interventricular (IV) septum in arterially-perfused septal preparations. **A:** Distribution of action potential morphologies and APD at 90% repolarization (APD_{90}) as a function of the transseptal distance, expressed as percent from right ventricular endocardium (RV Endo) to left ventricular endocardium (LV Endo) **B:** Graph of APD_{90} as a function of the transseptal distance in 6 distinct septal preparations. **C:** Graph of composite data from the 6 septal preparations shown in middle panel. The shortest AP are found in RV endocardial sites in 5 of 6 preparations and the longest APs are found in the mid-septum (6 of 6 preparations) Each point represents mean ±

SD. Basic cycle length (BCL) = 2000 ms, RV Endo stimulation. * $p<0.05$ 60% vs 0%, 20%, 40%, 100%. # $p<0.05$ 80% vs 0%, 100%.

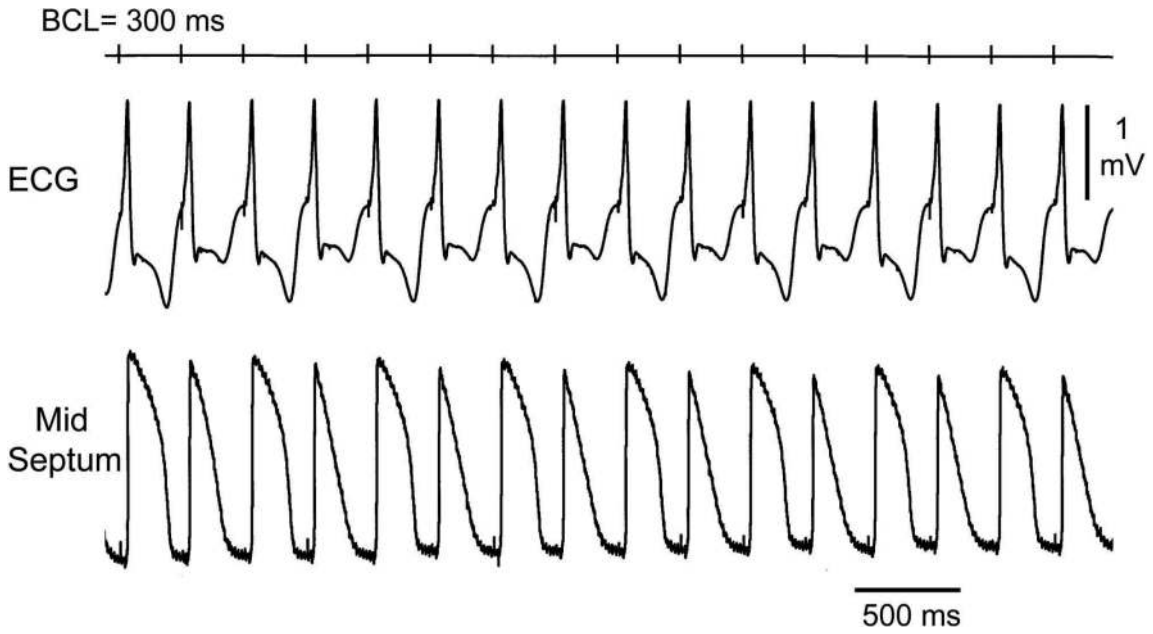

Figure 3.
BayK 8644-induced T wave alternans in an arterially perfused septal preparation. BayK 8644 (1μM) induced T wave alternans, consistent with the alternans observed in the action potential duration of a mid-septal cell. Left ventricular endocardium (LV Endo) stimulation. Sti: stimulus marker. Basic cycle length (BCL) = 300 ms.

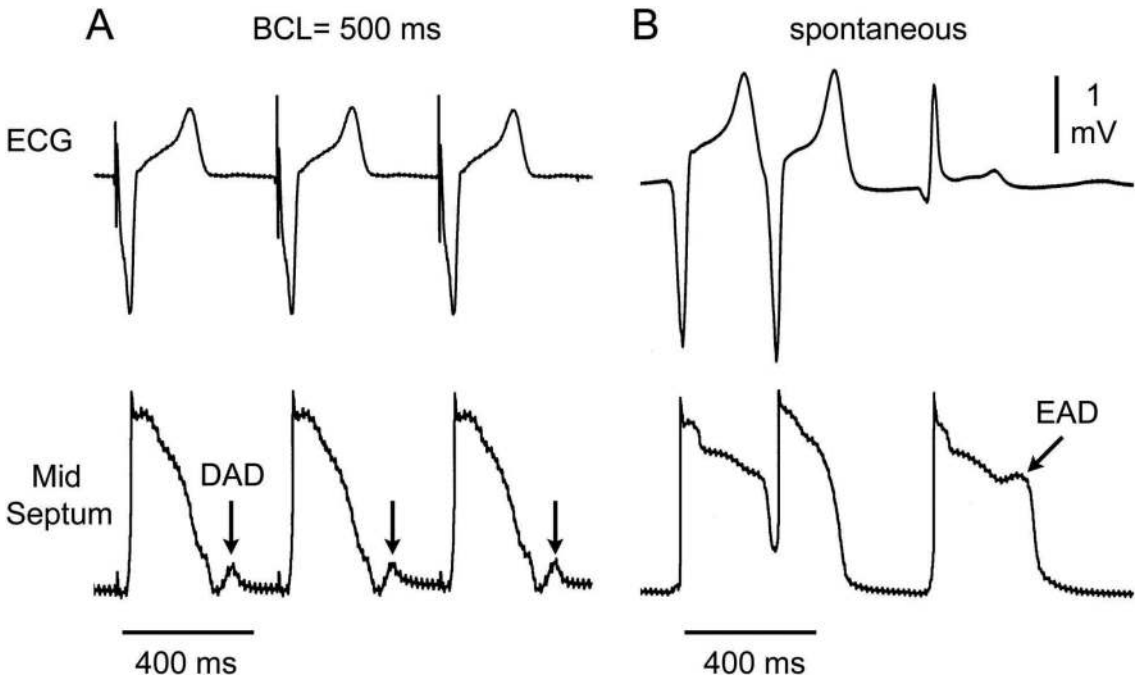

Figure 4.

BayK 8644 (1 μM)-induced early and delayed afterdepolarizations (EADs and DADs) in an arterially-perfused septal preparation. **A:** DADs are observed in a mid-septal cell. Right ventricular endocardium (RV Endo) stimulation, basic cycle length (BCL) = 500 ms. **B:** DADs and EADs recorded from a mid-septal cell. RV Endo stimulation.

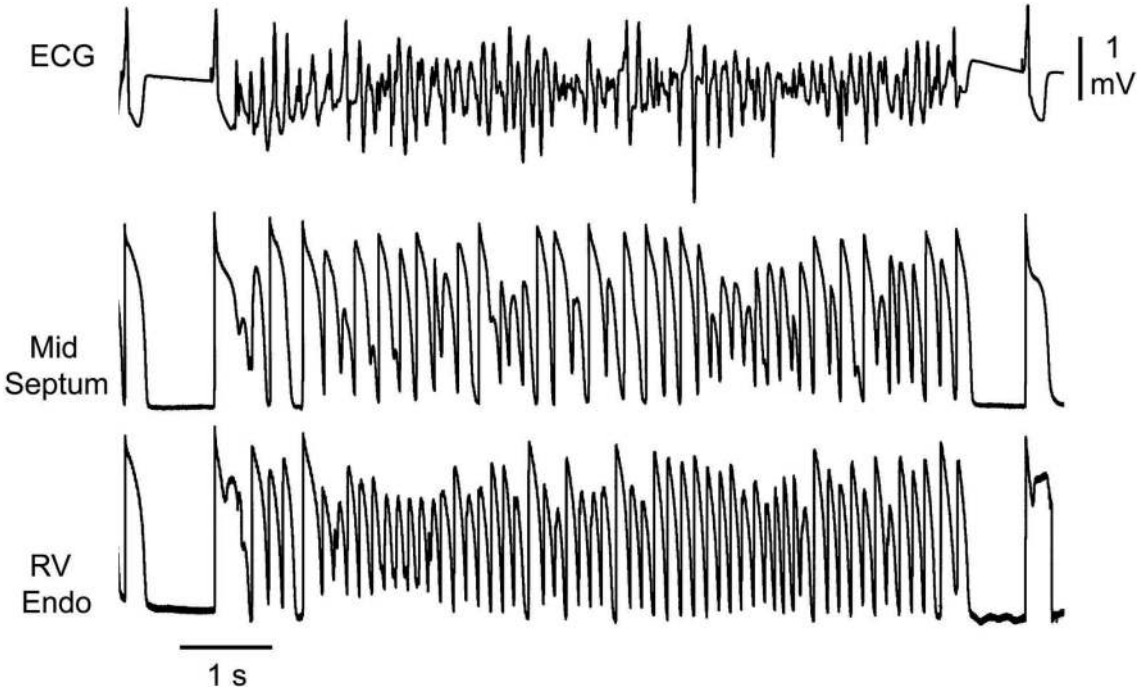

Figure 5.
BayK 8644 (1 μM)-induced Torsade de Pointes (TdP) arrhythmia in an arterially-perfused septal preparation. Spontaneous TdP episode develops following a 2 sec pause. Left ventricular Endo stimulation. The arrhythmia self-terminated after 10 sec.

Table 1

Electrophysiological characteristics of arterially-perfused septal preparations (n=6). Maximum action potential measured at 90% repolarization (Max APD_{90}), minimum APD_{90} (Min APD_{90}), transseptal dispersion of repolarization (DR) and T_{peak}-T_{end} values recorded from 6 septal preparations (A to F).

Exp	Max APD_{90} (ms)	Min APD_{90} (ms)	TDR (ms)	Tp-Te (ms)
A	252	185	81	78
B	242	171	84	88
C	291	190	107	90
D	258	169	96	76
E	324	201	128	81
F	301	176	141	92
Mean ± SD	278±32	182±12	106±24	84±7

Table 2

Maximum action potential measured at 90% repolarization (Max APD_{90}), minimum APD_{90} (Min APD_{90}), transmural or transseptal dispersion of repolarization (TDR or trans-septal DR) and T_{peak}-T_{end} from left ventricular (LV) wedge (n=30) and septal preparations (n=6).RV= right ventricular.

	LV Wedge	**Septal Preparation**
	Endocardial Stimulation (n=30)	**RV Endocardial Stimulation (n=6)**
Max APD_{90} (ms)	280±26	278±32
Min APD_{90} (ms)	241±25	182±12
TDR (ms) or Transseptal DR (ms)	36±9	106±24
T_{peak}-T_{end} (ms)	34±19	84±7