The Role of Canine Superficial Ventricular Muscle Fibers in Endocardial Impulse Distribution


SUMMARY Thin sections of canine right and left ventricular endocardium and myocardium were studied in a tissue bath to compare conduction properties of intraventricular specialized conducting tissue [Purkinje fibers (PF), the superficial layers of subendocardial ventricular muscle (SVM), and the deeper ventricular muscle (DVM)] below this level. The study was carried out because of observations that some areas of the endocardium, which are devoid of either specialized conducting tissue or of PF-VM junctions between specialized conducting tissue and ventricular muscle, conduct relatively rapidly, favoring specific orientations of propagation. Preparations containing PF, SVM, and DVM were studied electrophysiologically and histologically. A technique of stripping limited areas of endocardium was used to expose DVM in order to determine its intrinsic calculated conduction velocity. In 12 preparations, the average calculated conduction velocity in PF was 1.62 m/sec, and the average in DVM was 0.26 m/sec. The SVM conduction velocity was intermediate between the two, averaging 0.98 m/sec when propagation was parallel to SVM fiber orientation. Conduction velocity transverse to SVM fiber orientation was not significantly different from DVM conduction velocity. Histologically, the most superficial layers of VM were oriented uniformly in the direction of rapid subendocardial conduction, in contrast to DVM fibers in which orientation varied. It is concluded that the geometric arrangement of SVM fibers may provide a means for rapid subendocardial conduction and impulse distribution at a conduction velocity intermediate between PF and DVM in areas devoid of specialized conducting tissue.

RECENT observations in this laboratory have suggested the possibility of preferential orientation of impulse spread through endocardial muscle in regions of the ventricles devoid of specialized conducting tissue or functional junctions between specialized conducting tissue and surrounding muscle. The present investigation was carried out: (1) to determine the relationship between the defined role of the specialized conducting tissue and that of subendocardial muscle in impulse distribution through ventricular endocardium, (2) to determine whether the most superficial endocardial muscle plays a unique role in impulse distribution to intramural ventricular muscle, and (3) to determine whether there is an anatomic basis for such a relationship as might be inferred from the earlier studies of Pruitt et al.

Methods

Studies were performed on thin preparations of endocardium and myocardium dissected from the hearts of adult mongrel dogs weighing 5-25 kg. The dogs were anesthetized with sodium pentobarbital, 30 mg/kg, intravenously, and the hearts were removed rapidly through a right thoracotomy and placed in cool oxygenated Tyrode's solution, composed of (millimolar): NaCl = 137, NaHCO3 = 12, dextrose = 5.5, NaH2PO4 = 1.8, MgCl2 = 0.5, CaCl2 = 2.7, and KCl = 3.0.

Preparations to be studied were mounted with small steel pins in a wax-bottomed tissue bath. The tissue bath had an effective volume of 20 ml and a surface area of approximately 25 cm². Modified Tyrode's solution, equilibrated with 95% O2-5% CO2, perfused the tissue chamber at a rate of 8-10 ml/min. Temperature in the chamber was maintained between 36°C and 37°C.

Electrical activity was recorded from the surface of the tissue preparations by both surface electrogram and transmembrane action potential recording techniques. Bipolar surface electrograms were recorded with small (0.01 inch in diameter) contiguous bipolar silver electrodes, triple Teflon-coated except at their tips. Signals were amplified through a high gain differential amplifier (Tektronix, model 3A3) and were displayed on oscilloscopes for
monitoring, measuring intervals and durations, and recording electrograms (Tektronix, models 5030, 564, and 565). The response characteristics of this system have been reported previously. Transmembrane action potentials were recorded through machine-pulled glass microelectrodes filled with 3 M KCl and having resistances between 15 and 30 MΩ. Ag-AgCl junctions were used to connect the microelectrodes to amplifiers with input impedances of 100 MΩ, and input capacity neutralization (Bio-Electric Instruments, model NF-1). The outputs of these amplifiers were displayed on the oscilloscope screens, using a technique for on-line measurement of intervals described in detail elsewhere. Inter-electrode distances on the surfaces of the preparations were measured through the calibrated eyepiece of the dissecting microscope mounted above the bath. Whenever possible, inter-electrode distances for action potential and surface electrogram recordings were kept 1 mm because of the pitfalls inherent in calculating conduction velocities on uneven surfaces using widely spaced points. In many experiments, it was possible to use inter-electrode distances of 0.5 mm. The resolution of the microscope system over the tissue bath allows measurements of inter-electrode distances to ±60 μm.

**Tissue Preparations**

The general technique for identification, dissection, and isolation of the preparations of endocardium and myocardium, which include both specialized conducting tissue (PF) and ventricular muscle (VM), has been reported in detail in other publications. Most of the preparations used in the present study were rectangular, 2-5 cm long, 1-2 cm wide, and 2-4 mm thick. Preparations were obtained from the following areas: (1) the upper half of the right ventricular septum excluding the right bundle branch (devoid of PF); (2) the upper-third of the midportion of the left ventricular septum and the right bundle branch (devoid of PF); (3) areas containing junctions between PF and VM cells, such as the right ventricular free wall. In many of the experiments in this study, the continuity of the most superficial subendocardial VM cells was disrupted intentionally by gently stripping a section of the endocardial surface from the preparation. The purpose of this procedure was to allow a study of conduction velocity in VM 200-600 μm below the subendocardial PF and VM cells. In one group of experiments, each preparation was used as its own control: after the preparation had stabilized in the tissue bath, control recordings were obtained and the endocardial surface then was stripped. With the second technique, endocardial stripping was performed immediately after obtaining the preparation, before mounting it in the tissue bath; an adjacent preparation of endocardium, which was not stripped of endocardium, was used as the control. For both groups of experiments, the endocardial stripping was performed by making superficial incisions with a sharp scalpel blade at a depth just sufficient to result in retraction of the superficial edges (see below). A corner of the endocardium to be stripped was picked up with forceps, and gentle pressure resulted in separation of a plane between the endocardial surface and the deeper muscle. The thickness of the stripped endocardium ranged from 200 to 600 μm. In this report the term “superficial ventricular muscle” (SVM) refers to the layers of ventricular muscle cells (by electrophysiological and anatomic criteria) on the endocardial surface which are superficial to the plane of stripped endocardium. The term “deep ventricular muscle” (DVM) refers to those true ventricular muscle cells below the stripped endocardium. Transmembrane action potential characteristics of DVM cells were studied after allowing 15-45 minutes for healing of stripped surfaces. Resting potential, upstroke amplitude, dV/dt, and action potential configurations returned to normal before the stripped preparations were studied.

**Stimulation of Tissue**

The preparations were stimulated by the use of the same bipolar, Teflon-coated silver wire electrode described above for surface electrode recordings. To achieve simultaneous stimulation of specialized conducting tissue (PF) and surrounding VM, stimulus strength in excess of 3.0 times threshold was used. When specific stimulation of specialized conducting tissue was necessary, stimulus strength was maintained below 1.2 times threshold. Intracellular stimulation through a recording microelectrode and reed-relay system was used in those experiments in which it was necessary to ensure specific activation of ventricular muscle cells or specialized conducting cells. Preparations were driven at basic cycle lengths of 1000 msec, using pulse durations of 0.5-1.0 msec. When intracellular stimulation was used, pulse durations of 1.0-5.0 msec were required.

**Histology**

Immediately after completion of the electrophysiological studies, preparations were fixed for at least 72 hours in neutral-buffered 10% formalin. Blocks of tissue were cut in an orientation dictated by the electrophysiological observations and were embedded in paraffin by standard histological techniques. The paraffin blocks were cut in the appropriate orientation (see Results) and stained by both hematoxylin and eosin and Gomori one-step trichrome techniques.

**Results**

**The Endocardium of the Right Ventricle**

To determine whether superficial endocardial fiber orientation plays a role in the pattern of right septal endocardial excitation, nine right septal preparations were mounted in a tissue bath and stimulated in the mid-septal
region. Stimulating electrodes were positioned lateral to the right bundle branch over an area of muscle devoid of specialized conducting tissue. In all preparations, the functional connections between specialized conducting tissue and muscle were at the apical end of the preparations well beyond the site of the stimulating electrodes. Stimuli were delivered at 1.5 times threshold at a cycle length of 1000 msec, and the sequence of excitation was mapped with both microelectrode and surface electrogram recordings. The time from the onset of the stimulus to arrival of excitation at each point was recorded and isochronic lines were constructed. Mapping was carried out at 0.5-mm intervals across the entire preparation and from apex to base, and the isochrones were constructed from these maps. The left panel of Figure 1 shows the results of a representative experiment in which conduction velocity in the apicobasal orientation (parallel to the orientation of the right bundle branch) is approximately twice that of the anteroposterior orientation (perpendicular to the orientation of the bundle branch). In nine such preparations, apicobasal conduction velocity exceeded anteroposterior velocity by factors ranging from 1.9:1 to 3.7:1, with an average of 2.65:1. The right panel of Figure 1 demonstrates the isochrones recorded by a similar technique on five right ventricular free-wall preparations. In contrast to the right septal preparations, this region has dense interconnections within the specialized conducting system and between specialized conducting tissue and endocardial muscle. Surface electrode stimulation resulted in simultaneous excitation of Purkinje fibers and ventricular muscle. Intracellular stimulation of endocardial muscle fibers was used to study the effect of initiation of impulses in this specific tissue. No preferential orientation of conduction was recorded in any of these five experiments, whether excitation was initiated by surface or intracellular stimulation techniques. Histological studies, in which the right ventricular septal endocardium was sectioned in an orientation parallel to the direction of most rapid propagation (see below), demonstrated that rapid endocardial muscle conduction uniformly paralleled the direction of superficial endocardial muscle fiber orientation. This uniformity of fiber orientation did not persist in the deeper layers of septal myocardium.

The Left Septal Endocardium

The normal sequence of excitation of a left septal endocardial preparation containing the main left bundle branch and the septal subendocardial specialized conducting tissue, as well as endocardial muscle, is demonstrated in Figure 2. Eight bipolar surface electrograms were recorded from the level of the bundle branch at the base of the heart to the left ventricular apical endocardium. The sequence of activation is from the left bundle branch to the mid-septum (electrogram no. 5), at which point specialized conducting tissue engages septal endocardial muscle, and activation of the two types of tissue remains in a fixed relationship to the left ventricular apex (electrograms no. 5-8). However, conduction through muscle back to the base of the left septum occurs independently of the specialized conducting system in a retrograde direction. In the experiment shown, the conduction time in the specialized conducting tissue from the level of the left bundle branch (electrogram no. 1) to the point at
Eight bipolar surface electrograms were recorded from the base of the left ventricular septum to the apex of the left ventricular septum. The left bundle branch was stimulated at a cycle length of 1000 msec by impulses at 1.2 times threshold strength, and surface electrograms were used to record specialized conducting system (PF) activity, and ventricular muscle activity following the PF activation. See text for discussion.

Retrograde conduction through subendocardial VM from the level of electrogram no. 5 to electrogram no. 1 requires 19 msec. The calculated conduction velocity through PF (electrogram no. 1 to electrogram no. 5) is 2.00 m/sec, while the calculated conduction velocity for retrograde conduction through VM (level 5 to level 1) is 1.16 m/sec. This latter figure is considerably faster than data previously reported for conduction velocity through VM.

To determine whether features unique to superficial endocardial muscle played a specific role in LV subendocardial VM conduction, several types of experiments were carried out. In the first series of experiments, the apical end of a preparation was stimulated at 3 times threshold strength in order to activate subendocardial VM and PF simultaneously (Fig. 3). Electrograms were recorded to determine the site on the apicobasal axis at which the earliest engagement of ventricular muscle occurred (as in Fig. 2), and the recordings were made on the portion of the preparation extending from this region retrogradely to the level of the left bundle branch. Since the propagating retrograde wavefront in the subendocardial VM was

\[
\begin{array}{cccccc}
\text{APEX} & \text{PF, SVM} & \text{BASE} \\
\hline
\text{APEX} & \text{PF, SVM} & \text{BASE} \\
\hline
5.6 & 9.4 & 9.6 \\
7.2 & 11.6 & 13.0 \\
0.78 & 0.81 & 0.74 \\
\end{array}
\]

Conduction velocity differences between superficial ventricular muscle (SVM) and deep ventricular muscle (DVM). The preparation consists of the upper portion of the left ventricular septum from the level of the left bundle branch (right side of the illustration) to the mid-portion of the septal endocardium. The left side of the preparation extended further toward the apex than demonstrated in the illustration. The illustration is restricted to the portion of the preparation in which functional connections between Purkinje fibers (PF) and ventricular muscle (VM) are absent. In panel A (control), each circle represents a site at which a surface electrogram (SE) was recorded. Each column of five recordings was averaged because of minor variation in arrival times of the propagating impulse across the transverse axis of the preparation following stimulation of the apical end of the preparation at 3.0 times threshold with subsequent impulse propagation from apex to base. The variations in conduction times between each set of points was small enough that isochrones formed nearly straight lines across the transverse axis of the preparation. The top row of numbers indicate the measured distances between columns of SE recording sites between arrows in millimeters (mm), the second row is the average conduction time between arrows in milliseconds (msec), and the bottom row is the calculated conduction velocity between arrows in meters/second (m/s). The mean conduction times and standard deviations were 7.2 \pm 0.21 msec, 11.6 \pm 0.49 msec, and 13.0 \pm 1.56 msec, respectively. In panel B, the superficial endocardial muscle was stripped from the preparation following shallow incisions between columns 2 and 3 and between 4 and 5. Conduction time between columns 1 and 2, and between columns 5 and 6 were unchanged, but it was distinctly slowed between columns 3 and 4 to 0.31 msec. Mean conduction times and standard deviations were 7.0 \pm 0.33, 30.0 \pm 2.04, and 12.8 \pm 1.01 msec, respectively. The data have been superimposed on photographs of preparations from the same location of a different heart for the purpose of illustration. The PF are stained with Lugol's solution.
never precisely uniform across the transverse axis of these preparations, five surface electrograms equally spaced across the width of the preparation were recorded at each apicobasal level as indicated by the circles in panel A of Figure 3. The time from the onset of the stimulus to the arrival of the propagating wavefront is endocardial muscle at each of the five locations was averaged for each of the six levels shown in Figure 3, and conduction velocity was calculated. The calculated conduction velocity between the two most apical sets of electrogram recordings was 0.78 m/sec, between the third and fourth sets was 0.81 m/sec, and between the fifth and sixth sets was 0.74 m/sec. The isochrones constructed from the data points available were nearly straight lines across the transverse axes of the preparations. After these recordings had been obtained, shallow incisions were made transversely across the preparations between the second and third and between the fourth and fifth sets of electrogram recording sites, and the endocardium was stripped from this area. Repeat measurements after stabilization of the DVM revealed no significant difference in SVM conduction velocity between the first and second and between the fifth and sixth sets of electrogram recordings, compared to control. However, conduction between the third and fourth sets of electrograms, which now represented conduction through the DVM, was considerably slowed. This slowing occurred in all experiments in this series, and ranged from a 42% to 70% decrease in conduction velocity across the area stripped of SVM.

Similar results were observed in a second series of experiments, in which parallel strips of septum served as simultaneous control and experimental preparations, and SVM from the experimental strip was removed immediately after the tissue was obtained. This procedure was used as a control for the possibility that delayed stripping of endocardium, despite the thin layer, could have allowed anoxic damage to DVM in experiments such as that shown in Figure 3. In Figure 4, panel A, a control preparation is demonstrated. Retrograde conduction from level A to level B occurred at a rate of 1.94 m/sec in specialized conducting tissue (PF) and 0.90 m/sec in VM. The recordings obtained between electrograms at levels C and D indicated a conduction velocity of 1.59 m/sec in PF, and 0.88 m/sec in superficial VM. Panel B of Figure 4 demonstrates similar recordings obtained from the parallel experimental preparation in which a 4.5-mm strip of endocardium had been removed from the preparation surface immediately after isolation. Conduction velocity
in superficial VM between levels A and B was unchanged (0.97 m/sec), but was considerably slower through the deeper ventricular muscle between levels C and D (0.32 m/sec). No PF activity is recorded on the surface endocardium basal to the stripped area because of the lack of junctions through which excitation could reenter this tissue from VM in the upper half of the preparation. The slowing of conduction across areas stripped of subendocar-

Figure 6 Summary of a total of 29 experiments in which conduction velocity through PF, superficial ventricular muscle in the orientation of most rapid muscle conduction velocity (SVM-longitudinal), conduction velocity in deep ventricular muscle (DVM), and conduction velocity in superficial ventricular muscle cut transverse to the orientation of rapid muscle conduction velocity (SVM-transverse) are compared. See text.

dial SVM in this series of experiments was the same both qualitatively and quantitatively as that observed in the first series of experiments.

A third series of experiments was carried out on preparations from the upper third of both the right and left septum which were dissected in a manner such that the long axes of the preparations were perpendicular to the apicobasal axis of the ventricular septum. Without stripping a portion of the endocardium, it was observed in a series of 17 such preparations (10 left septal and seven right septal), that the conduction velocity in the transverse (i.e., anteroposterior) orientation through SVM was considerably slower (mean = 0.25 ± 0.13 m/sec) than conduction through SVM in the apicobasal orientation in the left ventricular and the right septal studies (mean = 0.98 ± 0.25 m/sec). The dV/dt recorded from SVM cells during longitudinal impulse spread, from SVM cells during transverse impulse spread, and from DVM cells were not significantly different (208 ± 22 V/sec, 199 ± 33 V/sec, and 216 ± 45 V/sec, respectively).

Histology

Figure 5A and B shows microscopic sections through the SVM and DVM in the preparation illustrated in Figure 4. The SVM (Fig 5A), sectioned along the apicobasal axis, reveals uniformly oriented muscle fibers, whereas the DVM (Fig. 5B) demonstrates changes in muscle fiber orientation at various levels. The section in Figure 5B was photographed 500 µm below the surface of the tissue. Uniformity of the SVM fiber orientation relative to the direction of rapid muscle conduction was observed in the six left septal and three right septal
preparations so studied. The width of the SVM layer ranged from 200 to 600 μm, mean = 475 μm.

Cumulative Data on Septal Preparations

Figure 6 demonstrates a comparison of the calculated conduction velocity in specialized conducting tissue, superficial endocardial muscle in the orientation of its axis of rapid conduction, and deep ventricular muscle recorded after stripping of the superficial endocardium in 12 experiments. The mean calculated conduction velocity in PF was 1.62 m/sec (sd = ±0.24), the mean velocity in SVM-longitudinal was 0.98 m/sec (sd = ±0.25 m/sec), and the mean for DVM in any orientation was 0.26 m/sec (sd = ±0.06 m/sec). The fourth column in Figure 6 shows data from the 17 experiments performed on SVM in preparations designed to study conduction perpendicular to the longitudinal axis of fiber orientation (SVM-transverse). Conduction velocity under these circumstances averaged 0.25 m/sec (sd = ±0.13) in the 17 experiments. These figures were not significantly different from the DVM conduction velocity measurements. Statistical analysis revealed significant differences between the observations for Purkinje fibers (PF) and superficial ventricular muscle fibers in longitudinal fiber orientation (SVM-longitudinal) (P < 0.001), and between the SVM and DVM fibers in any orientation (P < .001). There was no significant difference between conduction velocity through DVM and through superficial ventricular muscle transverse (SVM-transverse) to the direction of fiber orientation.

Superficial Endocardial Conduction in Papillary Muscle Preparations

The apices of the papillary muscles are devoid of functional connections between specialized conducting tissue and adjacent ventricular muscle.1,2 However there are dense connections between specialized conducting fibers and ventricular muscle at the bases of the papillary muscles. Thus, one pathway for distribution of propagating impulses from VM cells at the base of the papillary muscles to those at their apices may be through SVM, by a process analogous to that described above for septal muscle propagation. Figure 7, panel A, demonstrates the relationship between arrival of excitation in PF and VM at the apical and basal ends of a papillary muscle preparation. A propagating impulse is delivered through the posterior radiation of the left bundle branch system. Specific stimulation of the left bundle branch (beyond the edge of the illustration) was achieved by stimulating the bundle branch surface at 1.1 times threshold strength. Bipolar surface electrodes were positioned as shown on the figure in order to record PF and VM activity at both the apical and basal ends of the papillary muscle. The sequence of arrival of excitation is from the PF at the apex of the papillary muscle (stimulus-to-PF interval = 13 msec) to the PF at the base of the structure (stimulus-to-PF interval = 23 msec), followed by activation of VM at the base (PF-VM base = 3 msec), and finally to VM at the apex of the structure 19 msec after basal VM. In three experiments of this type, control recordings, (panel A) were followed by a superficial incision approximately midway between the apex and base of the papillary muscle, as shown in panel B. As a consequence of interrupting the superficial VM fibers along the longitudinal axis of this structure, there is a significant change in the arrival time in VM activation only at the apex of the papillary muscle. The apical VM activation time is delayed by 35 msec, compared to control. The interconnections within the posterior radiation account for the lack of a delay in PF activation at the base, despite the fact that the PF along the longitudinal axis of the papillary muscle

![Figure 7](image-url)
have been cut. Similar results were observed in the other two experiments, with a 38.3-msec average delay in SVM activation at the papillary muscle apex. In panel C of Figure 7, the apical end of the papillary muscle is totally transected, and there is no VM activation despite activation of regional PF. Histological sections through the long axis of the superficial endocardium of the papillary muscle reveal a VM fiber orientation concordant with this axis of rapid SVM propagation (Fig. 5C). The SVM fibers in the papillary muscle studies were more uniformly oriented than the general longitudinal orientation of VM fibers in papillary muscles.10

Discussion

The primary conclusion that we draw from these studies is that there appear to be three functional populations of cells in close proximity to one another in the subendocardium. These include (1) the true specialized conducting tissue (PF), (2) the deep ventricular muscle cells (DVM), and (3) the superficial subendocardial muscle cells (SVM). The calculated conduction velocity between two points in the latter plane of cells (SVM) is intermediate between that for similar measurements carried out in PF and DVM when conduction times are measured in the orientation of most rapid conduction. This orientation is parallel to the orientation of the superficial ventricular muscle fibers (SVM) in regions devoid of PF-VM junctions. However, when conduction occurs perpendicular to the orientation of the SVM fibers, the measured conduction time between two points is not significantly different from conduction through DVM fibers.

The anatomic and physiological interrelationships between PF, SVM, and DVM result in the superficial 200–600 μm of endocardial ventricular muscle fibers having a special role in endocardial impulse distribution. Rapid conduction is favored along the longitudinal axis of SVM fiber orientation, and even though these fibers are not specialized in a cellular electrophysiological or anatomic sense, they appear to play a specialized role in impulse distribution and velocity of impulse spread on the endocardial surface, presumably related in some way to their geometric arrangement. These results parallel the recent studies of Clerc11 who applied cable analyses to data acquired as a result of transverse and longitudinal currents applied to isolated right ventricular trabeculae of calf hearts. According to this study, the conduction velocity pattern observed can result from differences in resistivity of intra- and extracellular pathways of current flow in the longitudinal and transverse directions.11

Our present observations are in concert with the earlier studies of Pruitt et al.4 who suggested in 1951 that fiber orientation may be a determinant of the velocity of impulse spread, based on experiments involving both epicardium and endocardium. Their experiments were prompted by a conflict at the time between the concepts of Lewis and Rothschild12 which attributed rapid endocardial impulse spread virtually exclusively to properties of the Purkinje network, the challenge by the Glomsets13 of the very existence of a Purkinje network in man, and their own observations14 which were not consistent with either extreme. Within the limits of the technology available to them at the time, Pruitt et al. were able to develop data to support a concept that both the Purkinje system and endocardial muscle might be involved in experimental processes which delayed intraventricular conduction.4 There followed a period of more than 20 years of intense interest in the characteristics and pathophysiology of the then clearly established Purkinje network, and of interest in the cellular electrophysiological properties of cardiac tissue. Questions concerning the role of normal and abnormal subendocardial VM fibers in patterns of impulse distribution remain in abeyance. During this time, several investigators studying small isolated strips of cardiac tissue,15–17 or mathematical models based on known properties of cardiac tissue,17,20 developed a body of information supporting the general concept of fiber orientation as a contributing factor in conduction velocity. Our present observations now provide direct support from the study of large endocardial preparations for the earlier considerations of Pruitt et al.4 In our study, the role of SVM fibers, and their orientations, in the determination of patterns and velocity of impulse distribution was demonstrated in three areas of the endocardium devoid of functional connections between specialized conducting tissue and ordinary ventricular muscle—the right septum, the upper left septum, and the papillary muscles. Whether superficial muscle fiber orientation plays a role in areas in which there are dense connections between specialized conducting fibers and ventricular muscle has not been determined.

The observations presented necessarily raise questions concerning the mechanism(s) of intraventricular conduction abnormalities. The role of the proximal specialized conduction system (His Bundle and bundle branches) in normal impulse distribution, and the effect of disease processes on its function, have been studied intensively. However, it is likely that some specific patterns of abnormal intraventricular conduction result from disease in other tissues. Distal specialized conducting tissue disease may play a role in some of these abnormalities,18 but the role of abnormal function of superficial subendocardial VM also must be given attention. The role of abnormal SVM in "hemiblocks," and in older descriptions such as "arborization blocks" and "parietal blocks," appears worthy of reevaluation and of further study.

References


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The Mechanism of K⁺-Induced Vasodilation of the Coronary Vascular Bed of the Dog

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SUMMARY We tested a number of hypotheses concerning the mechanism of K⁺-induced vasodilation of the coronary vascular bed. Blood flow in the circumflex artery was measured in pentobarbital-anesthetized, open-chest dogs. Intracircumflex artery bolus injections of 40 μmol of isosmotic KCl produced decreases in coronary vascular resistance ranging from 34% to 48%, depending on the initial resistance of the vascular bed. K⁺ administration had no effect on heart rate and produced a 4 mm Hg decrease in mean arterial pressure. K⁺ injection caused a 0.2 vol% increase in coronary sinus O₂ content in a preparation in which left common coronary flow was held constant. The magnitude of K⁺-induced vasodilation was not significantly affected by the administration of propranolol, atropine, phentolamine, or lidocaine. K⁺-induced vasodilation was attenuated (50%) by ouabain plus lidocaine. Acetylcholine from parasympathetic nerve terminals in the heart, (2) an increased release of norepinephrine from sympathetic nerve terminals in the heart, (3) an increased release of acetylcholine from parasympathetic nerve terminals in the heart, (4) a withdrawal of α-adrenergic-mediated coronary vascular smooth muscle tone, or (5) an activation of the electrogenic Na⁺-K⁺ transport system of coronary vascular smooth muscle.

K⁺ IS RELEASED from myocardial cells under a variety of circumstances that are associated with decreased coronary vascular resistance. Moreover, K⁺ is a vasodilator of both the intact coronary bed and isolated coronary vascular architecture. For these reasons it has been proposed that K⁺ may be one mediator of the coronary vasodilation associated with increases in the metabolic activity of the heart. The mechanism of K⁺-induced vasodilation of the coronary vascular bed has not been fully investigated. Evidence gained from isolated vessel and heart preparations has largely supported the hypothesis that changes in vascular reactivity produced by small increases in extracellular K⁺ concentration are the result of a K⁺-stimulated increase in the activity of the electrogenic Na⁺-K⁺ transport system of coronary smooth muscle. However, other possible mechanisms of K⁺-induced vasodilation have not been excluded. It is possible that in intact systems, in which the level of coronary blood flow is determined by a number of factors, small increases in extracellular K⁺ concentration may produce increases in coronary blood flow not only through a direct effect of K⁺ on coronary vascular smooth muscle, but also indirectly by affecting other determinants of coronary blood flow. In this study we have investigated these possibilities. More specifically, we have attempted to determine whether the mechanism of K⁺-induced coronary vasodilation involves: (1) a primary increase in the metabolic activity of the heart, (2) an increased release of norepinephrine from sympathetic nerve terminals in the heart, (3) an increased release of acetylcholine from parasympathetic nerve terminals in the heart, (4) a withdrawal of α-adrenergic-mediated coronary vascular smooth muscle tone, or (5) an activation of the electrogenic Na⁺-K⁺ transport system of coronary vascular smooth muscle.

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