Differences between Proximal Left and Right Bundle Branch Block Action Potential Durations and Refractoriness in the Dog Heart

JOHN C. BAILEY, DAVID A. LATHROP, AND DENNIS L. PIPPENGER

SUMMARY To date the electrophysiological mechanism responsible for aberrant intraventricular conduction of critically timed premature supraventricular impulses has not been documented. Microelectrode techniques were used to measure in vitro action potential and refractory period durations of the canine proximal right and left bundle branches equidistant from the distal bundle of His. Both measurements in the right bundle branch were statistically significantly longer than these parameters of the left bundle branch. Transection of the bundle branches immediately distal to the distalmost recording sites effected no change in the proximal right bundle action potential but caused marked prolongation of proximal left bundle branch action potential and refractory period durations. We conclude that functional right bundle branch aberrancy is most likely due to the longer proximal right bundle action potential duration and refractoriness. Our data also suggest that the shorter proximal left bundle branch action potential durations and refractory periods may be due to the proximol of the low ohmic resistance Purkinje fiber-muscle junctions on the left septal surface, effecting electrotonic foreshortening of these proximal left bundle branch parameters.

ALTHOUGH aberrancy of intraventricular conduction due to functional right bundle branch block is a well known phenomenon since first described by Sir Thomas Lewis,1,2 and in spite of the fact that a variety of explanations have been offered for the functional right bundle branch block, the responsible electrophysiological mechanism has not been documented. The purpose of this study was to record the behavior of the left and right bundle branches in vitro in an effort to determine whether electrotonic interactions between the bundle branches and septal muscle might account for the functional differences between the bundle branches.

Methods

Adult mongrel dogs of either sex, weighing 10-15 kg, were anesthetized with secobarbital (30 mg/kg, iv). Their hearts were removed rapidly through a lateral thoracotomy and immersed in cool oxygenated Tyrode’s solution. Initial experiments were performed on single bundle branches and their peripheral ramifications. The right bundle branch preparation (Fig. 1, lower left) consisted of the right half of the interventricular septum containing the septal portion of the right bundle branch, the major Purkinje false tendon coursing from the lower interventricular septum to the anterior papillary muscle, and a portion of the right ventricular free wall containing most of the peripheral ramifications of the right bundle branch. The left bundle branch preparation (Fig. 1, right half) included the left half of the interventricular septum containing the common left bundle branch, its anterior, septal, and posterior divisions and their peripheral ramifications, and the anterior and posterior papillary muscles. The thickness of these preparations was approximately 8-10 mm. Either the right or left bundle of a particular dog was used. A total of seven right and seven left bundle branch preparations were studied. The preparation was pinned to the floor of a 60-ml Lucite chamber that was continuously superfused at a rate of 20 ml/min with Tyrode’s solution maintained at 37 ± 0.5°C and gassed with 95% O2-5% CO2. Composition of the Tyrode’s solution, in mmol/liter, was: Na+, 150; K+, 4.0; Cl−, 147; Ca2+, 2.7; HCO3−, 12.0; H2PO4−, 0.9; Mg2+, 0.5; glucose, 5.5.

A bipolar, extracellular stimulating electrode was placed on the proximal portion of the bundle branch. Recording sites located 1 cm and 2 cm distal to the stimulating electrode were identified and marked with small stainless steel pins placed in the septal myocardium alongside the bundle branch. During constant stimulation at a...
was affixed to the floor of a 50-ml chamber in a two-dimensional fashion, facilitating simultaneous impalement of both bundle branches equidistant from their origins (Fig. 1). A bipolar, extracelular stimulating electrode was placed on the exposed distal His bundle. The distal recording site was the length of the subendocardial portion of the right bundle branch measured from the stimulating electrode. This distance was measured and marked on both right and left bundle branches. The proximal recording sites were one-half the distance to the distal marks. As in the previous experiments, action potential durations and refractory periods were measured before and after transection of the bundle branches immediately distal to the distal markers.

Conventional microelectrode techniques were used. Data were recorded on Polaroid films using a Tektronix C59 oscilloscope camera and stored on 1-inch magnetic tape. A stereomicroscope fitted with a graduated eyepiece allowed accurate location of recording microelectrodes. A t-test for two unpaired groups was used to analyze data statistically.

**Results**

Figure 2 (upper panel) summarizes all action potential duration data from both 1-cm and 2-cm recording sites in the right and left bundle branches before transection of the distal bundle branches. Mean action potential durations of the right bundle at 1 cm (336 ± 24 msec) and 2 cm (335 ± 17 msec) were statistically highly significantly longer (P < 0.01) than mean action potential durations of the left basic cycle length of 800 msec, action potential durations, measured at 100% repolarization, were recorded from these sites. Premature extracellular or intracellular stimuli (1.5 times diastolic threshold requirements) were introduced following a train of 10–15 basic stimuli. This maneuver allowed measurement of functional and effective refractory periods, respectively. The dots of Figure 1 indicate the 1-cm and 2-cm recording sites for the individual right bundle branch and left bundle branch preparations. Impalements of the left bundle branch included both major divisions as well as subendocardial Purkinje fibers. Similar measurements were made immediately distal to the 2-cm recording site. At least 1 hour was allowed for “healing over” of the cut ends of the bundle branch fibers. At a constant cycle length of 800 msec, or with intermittent premature stimulation, action potential durations and refractory periods at the 1-cm and 2-cm sites again were measured. Because there was no assurance of impaling the same cells before and after transection we randomly impaled numerous Purkinje cells at these two sites. To measure action potential durations immediately distal to the transection, it was necessary to move the stimulating electrode to a Purkinje fiber distal to the cut edge.

In five experiments we incorporated both bundle branches and a significant portion of their peripheral ramifications en bloc so that action potential durations and refractory periods could be measured simultaneously in both bundle branches, equidistant from their origins. In these studies the interventricular septum and portions of both ventricular free walls were removed, and the septum was split longitudinally from the apex to within 2 mm of the His bundle into right and left halves. The preparation was affixed to the floor of a 150-ml chamber in a two-dimensional fashion, facilitating simultaneous impalement of both bundle branches equidistant from their origins (Fig. 1). A bipolar, extracelular stimulating electrode was placed on the exposed distal His bundle. The distal recording site was the length of the subendocardial portion of the right bundle branch measured from the stimulating electrode. This distance was measured and marked on both right and left bundle branches. The proximal recording sites were one-half the distance to the distal marks. As in the previous experiments, action potential durations and refractory periods were measured before and after transection of the bundle branches immediately distal to the distal markers.

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bundle branch at 1 cm (291 ± 30 msec) and 2 cm (293 ± 17 msec). After transection of the distal bundle branches (Fig. 2, lower panel) action potential durations of the right bundle branch did not change significantly, whereas left bundle branch action potential durations markedly increased at both recording sites. Indeed, when the peripheral distribution of the left bundle was removed, there was no significant difference (P > 0.05) in action potential duration between right and left bundle branches at either recording site. Refractory period changes paralleled changes in action potential duration in a predictable fashion.

Action potential durations, recorded simultaneously from both bundle branches in continuity, are enumerated in Table 1. These measurements were obtained before transection of the distal bundle branches. It is clear that at basic cycle lengths of 500 msec and 800 msec at both proximal and distal recording sites, the left bundle branch action potential durations were significantly shorter than right bundle branch action potential durations. After transection, right bundle branch action potential duration and refractoriness did not change, whereas these parameters of the left bundle branch prolonged to equal the right bundle branch (Fig. 3).

The resting potential and action potential amplitude of the recorded cells immediately distal to the cuts were unchanged in all experiments following the transections, indicating that trauma as a result of the cut did not affect our results.

**Discussion**

A number of theories have been proffered regarding the electrophysiological mechanism(s) for functional right bundle branch block. Rosenbaum et al.3 postulated that an early atrial premature systole might be conducted equally slowly in both left and right bundle branches. Because of its longer length, the right bundle branch would require a longer depolarization time, causing sufficient delay of right ventricular activation to produce the QRS aberration of right bundle branch block. Myerburg et al.4 described a site of maximum action potential duration and refractoriness of Purkinje fibers located 2–3 mm proximal to Purkinje fiber-muscle junctions. In a majority of instances they found that action potential duration and refractoriness were longer in the peripheral distribution of the right bundle branch than the left. They suggested that functional block of the right bundle branch might occur at these peripheral sites.

Other investigators, however, have indicated that the site of functional right bundle branch block is located in the more proximal portion of the right bundle branch. Moe et al.5 reported, indirect evidence that the block occurred within the main right bundle, proximal to its peripheral ramifications. Damato et al.6 studying human subjects with an electrode catheter, recorded extracellular electrograms from the most proximal portion of the right bundle branch. During atrial premature stimulation resulting in functional right bundle branch block, the right bundle branch electrograms disappeared, indicating functional block in the proximal right bundle. Likewise, Rosen et al.7 concluded that, during normal intraventricular conduction, the proximal bundle branches are activated virtually simultaneously and that the site of functional right bundle branch block in humans is at or near the His bundle-right bundle branch junction. More recently Zipes et al.8 recording directly from the main false tendon of the canine right bundle branch (proximal to the peripheral "gates"), demonstrated that functional right bundle branch block occurred between the bundle of His and their false tendon recording site.

### Table 1 Summary of Right (RBB) and Left (LBB) Bundle Branch Action Potential Durations Recorded Simultaneously from the Split Septum Preparation Prior to Transection

<table>
<thead>
<tr>
<th>Total action potential duration (msec)</th>
<th>Proximal</th>
<th>Distal</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCL = 500</td>
<td>BCL = 800</td>
<td>BCL = 500</td>
</tr>
<tr>
<td>RBB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>303 ± 10</td>
<td>327 ± 12</td>
<td>305 ± 9</td>
</tr>
<tr>
<td>(9)</td>
<td>(9)</td>
<td>(10)</td>
</tr>
<tr>
<td>LBB</td>
<td>286 ± 21</td>
<td>300 ± 19</td>
</tr>
<tr>
<td>(10)</td>
<td>(10)</td>
<td>(10)</td>
</tr>
<tr>
<td>P &lt; 0.05</td>
<td>P &lt; 0.01</td>
<td>P &lt; 0.01</td>
</tr>
</tbody>
</table>

At both proximal and distal recording sites and at basic cycle length (BCL) of 500 and 800 msec, RBB action potential durations are significantly longer than LBB action potential durations. The mean value of action potential durations ± 1 so and the number of observations (in parentheses) are listed.
Recent microelectrode studies\(^9\) demonstrate that, following eccentric stimulation of single proximal His bundle cells, transverse activation of the His bundle is rapid, and longitudinal transmission occurs as a single uniformly advancing wavefront. Thus preferential intra-His conduction\(^8\) is a less likely mechanism for functional right bundle branch block.

Our data afford an explanation for functional right bundle branch block that is consistent with known clinical and experimental features of this phenomenon. The study indicates that the action potential duration of the proximal right bundle branch is significantly longer than that of the left bundle branch, and that the bundle branch block is required to effect the shorter proximal left bundle branch action potential duration and refractoriness.


Rosen KM, Rahimtoola SH, Sinno MZ, Gunnar RM: Bundle branch

Acknowledgments

We are grateful for the expert technical assistance of David L. Mendel and the secretarial assistance of Sharron Poole.

References

1. Lewis T: Paroxysmal tachycardia, the result of ectopic impulse formation. Heart 1: 262-282, 1910

2. Lewis T: Observations upon disorders of the heart's action. Heart 3: 279-300, 1911


7. Rosen KM, Rahimtoola SH, Sinno MZ, Gunnar RM: Bundle branch
Isolation and Characterization of Myosin from Subjects with Asymmetric Septal Hypertrophy

BARRY J. MARON, VICTOR J. FERRANS, AND ROBERT S. ADELSTEIN

SUMMARY Human cardiac myosin isolated from operatively obtained samples of ventricular septum and left ventricular free wall of subjects with asymmetric septal hypertrophy (ASH) was compared, with respect to structural and enzymatic properties, to myosin isolated from hearts of subjects without heart disease. The following parameters were studied: (1) activation of myosin ATPase activity by K\(^+\)-EDTA and Ca\(^{2+}\), (2) molecular weight of the heavy and light chains of myosin as determined by electrophoretic migration in polyacrylamide-sodium dodecyl sulfate (SDS) gels, and (3) ability to form bipolar aggregates at low ionic strength, as examined by electron microscopy. No difference was present in any of these parameters between human cardiac myosin from subjects with ASH and from subjects without heart disease. Thus, the genetic defect present in subjects with ASH is not expressed in the particular structural and functional characteristics of myosin evaluated in this study.

ASYMMETRIC septal hypertrophy (ASH) is a genetically determined cardiac disease that is transmitted as an autosomal dominant trait and is characterized by disproportionate thickening of the ventricular septum with respect to the left ventricular free wall. Hypertrophied and bizarrely shaped cardiac muscle cells arranged in a disorganized fashion are the characteristic histological feature of the ventricular septum of virtually all patients with ASH. These disorganized cardiac muscle cells presumably are a morphological expression of the genetic defect in ASH. Disorganized cardiac muscle cells are distributed widely in the left ventricular free wall of patients without outflow obstruction, but rarely are present in the ventricular free walls of patients with obstruction. With these morphological observations in mind, the present study was undertaken to determine whether the biochemical and structural characteristics of myosin isolated from the ventricular septum of subjects with obstructive ASH differ from the characteristics of myosin isolated from the left ventricular free wall of the same subjects or of subjects without heart disease.

Methods

PATIENT SELECTION AND CLINICAL DATA

The biochemical and ultrastructural studies reported in this communication are based on analyses of myocardium obtained from 14 patients with obstructive ASH and four patients without heart disease. The clinical diagnosis of ASH was confirmed in each of the 14 patients by cardiac catheterization, by echocardiography, and at operation. Each of the four patients used as controls in this study died of noncardiac diseases and had no evidence of heart disease at necropsy.

Patients with ASH were selected for operation if they had cardiac symptoms sufficient to produce severe functional limitation (New York Heart Association functional classes III or IV) and did not respond adequately to propranolol. The patients ranged in age from 20 to 71 years (average, 42); seven were men and seven were women. Thirteen patients had a significant obstruction to left ventricular outflow under basal conditions, with peak systolic pressure gradients between left ventricle and systemic artery in these patients ranging from 20 to 120 mm Hg. The other patient had only a 6-mm Hg gradient under basal conditions but a 70-mm Hg gradient after provocation with isoproterenol infusion.

SELECTION OF TISSUE

In each patient with ASH, myocardium was taken at the time of left ventricular myotomy-myectomy. The tissue studied are removed routinely at our institution from patients with ASH to determine the extent of the myopathic process. In keeping with institutional policy, informed consent was not required for performance of the additional studies done on these tissues. This tissue (0.5–2.7 g) was resected from the cephalad portion of the left side of the ventricular septum (12 patients) after 20–40 minutes of cardiopulmonary bypass and after a period of 10–12 minutes of cardiac arrest. During the latter period the
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Circ Res. 1977;40:464-468
doi: 10.1161/01.RES.40.5.464

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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