Adrenergic Effects on Reentrant Ventricular Rhythms in Subacute Myocardial Infarction

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Background. Reentry has been shown to be a mechanism of ventricular arrhythmias elicited by programmed premature stimulation in the subacute ischemic period of dogs subjected to myocardial infarction. The spatial distribution of refractoriness in these hearts has been shown to play an important part in the formation of functional arcs of conduction block during programmed ventricular stimulation. Because the adrenergic nervous system influences cardiac arrhythmias and myocardial infarction can directly affect sympathetic innervation in the heart, we investigated the role of the sympathetic nervous system on reentry in the canine heart 4 days after infarction.

Methods and Results. The influences of adrenergic stimuli on the initiation of reentrant ventricular excitation were studied using a 128-channel computerized recording system in the canine heart 4 days after ligation of the left anterior descending coronary artery. Bilateral stimulation of the ansae subclavia preferentially improved conduction of prematurity beats in the normal zones. This corresponded to an improvement in excitability, as measured by a decrease in stimulus strength at the same premature coupling interval as control. Consequently, the effective refractory period was preferentially shortened at normal sites but not at ischemic sites. Both of these changes contributed to a shift of the arc of functional conduction block toward more normal tissue. As a result, sites proximal to the arc of functional conduction block had more time to recover excitability and thereby were available to be reexcited by the distal activation wave front. Conversely, intravenous infusion of norepinephrine preferentially shortened the effective refractory period of sites in the ischemic zone, thereby indicating that denervation hypersensitivity had occurred at these sites. The spatial dispersion of refractoriness and the arc of functional conduction block were significantly reduced in size. As a consequence, previously inducible reentrant rhythms were no longer inducible.

Conclusions. Sympathetic stimulation can be considered an arrhythmogenic intervention, whereas norepinephrine infusion may be considered antiarrhythmic in this experimental model. (Circulation 1992;86:247–254)

KEY WORDS • nervous system, sympathetic • norepinephrine • hypersensitivity • arrhythmias

Reentry has been shown to be the mechanism by which a stimulated premature beat produces a nonstimulated ventricular rhythm in the subacute ischemic ventricular myocardium 4 days after infarction.1 Previous studies have shown that refractoriness is spatially distributed on the ventricular surface; refractoriness increases from the perimeter of the infarction toward the core of infarction. This spatial pattern of refractoriness has been shown to play an important part in the development and the location of the functional arc of conduction block during programmed ventricular stimulation.2 Subsequent reentrant activation is dependent on both the extent of the arc of block and the conduction delay incurred distal to the block.3

It is well known that adrenergic autonomic activity plays a role in the generation and perpetuation of cardiac arrhythmias.4–6 However, ischemia can directly affect the sympathetic innervation of the ventricles and thereby alter the effects of sympathetic tone on the ventricle.7 Transmural myocardial ischemia has been shown to disrupt sympathetic innervation of the ventricles and to cause denervation hypersensitivity.8,9 In this case, sympathetic stimulation would increase the dispersion or gradient of refractoriness between innervated and denervated regions.7,10,11

The adrenergic effects on reentry in the subacute ischemic ventricle 4 days after infarction has not been studied in detail. It was the purpose of this study to determine how sympathetic nerve stimulation and norepinephrine infusion affect reentry in the canine heart 4 days after infarction.

Methods

Surgical Preparation

Mongrel dogs weighting 13–20 kg were anesthetized with sodium pentobarbital (Nembutal) 30 mg/kg i.v., and supplemental anesthesia was administered through
a catheter placed in the cephalic vein. The dogs were ventilated with room air through a cuffed endotrachial tube using a Harvard Apparatus positive-pressure respirator. Using sterile techniques, the heart was exposed through a left thoracotomy at the fourth intercostal space, and the pericardium was incised. The left anterior descending (LAD) coronary artery was ligated distal to the anterior septal branch.

Four days after the ligation, the dog was reanesthetized as above and ventilated with room air through a cuffed endotrachial tube using a Harvard Apparatus positive-pressure respirator. ECG lead II and arterial blood pressure, measured from a femoral artery (Statham), were continuously monitored on an Electronics for Medicine DR12 physiological recorder. The right ansa subclavia and stellate ganglion were dissected through the first right intercostal space. The stellate ganglion was doubly ligated and transected to produce decentralization. Bipolar silver electrodes (Teflon coated, 0.010-in. diameter) were placed on the anterior and posterior ansae subclavia.

A left thoracotomy was then performed. The left ansa subclavia and stellate ganglion were dissected at the first left intercostal space through the thoracotomy. As above, the stellate ganglion was doubly ligated and transected to produce decentralization, and both the anterior and posterior ansae subclavia were prepared for stimulation.

The pericardium was opened, and a sock electrode array was placed on the ventricular surface for simultaneous recording at 126 epicardial sites. Each bipolar electrode consisted of a pair of silver wires (Teflon coated, 0.005-in. diameter) sutured to the sock with an interpolar distance of 1–2 mm. The electrode arrangement and recording technique have been detailed and described previously.1–3 A bipolar plunge electrode for control stimulation at the right ventricle, adjacent to the septal border of the infarct, consisted of two hooked stainless steel wires (enamel coated, 0.005-in. diameter). It was inserted using a 23-gauge hypodermic needle. An additional bipolar electrode was placed in the left atrial appendage to record atrial rhythm. Core temperature and intrathoracic temperature were monitored using two electronic telemeters (Yellow Spring Instruments). The thoracic temperature was maintained at 37±0.5°C using a heated blanket and heat lamp.

After surgical preparation, the ribs were approximated, and the chest cavity was closed. The right and left vagosympathetic trunks were dissected free and transected.

A USCI 6F bipolar pacing electrode catheter (inter-electrode distance of 10 mm) was introduced via the left carotid artery and was maneuvered into the aortic root, where a bundle of His electrogram was recorded. The anodal output paddle of a DC defibrillator (Hewlett-Packard) was placed under the left scapula, and the cathodal paddle was connected to the distal pole of the electrode catheter. A 100-J DC shock was delivered. When complete heart block was not achieved, a second shock was given. The ventricles were then paced at twice diastolic threshold at a constant rate through the plunge electrode described above.

**Cardiac Stimulation Techniques**

Ventricular programmed electrical stimulation was provided by a Bloom DTU-101 digital stimulator. The control stimulation sequence consisted of a train of eight basic driven beats (S1, S2 of 400 msec) at twice diastolic threshold followed by a premature stimulus, S3. The premature stimulus was introduced at decreasing coupling intervals, starting at 250 msec, until unstimulated ventricular responses were induced. Computer-generated electrode recordings were obtained and used to manually construct isochronal maps of epicardial activation.

Isochrones of activation were delineated by closed contours at 20-msec intervals, beginning with the earliest detected time of activation. A difference in activation time between adjacent recording sites of 40 msec or electrotonic deflections representing distant activation defined areas of functional unidirectional conduction block. A continuous line could be drawn through these regions and is defined as an arc of functional conduction block. The resultant isochronal activation maps revealed that the reentrant circuit could be bridged in both space and time on the ventricular epicardial surface.1–3

**Measurement of Ventricular Refractoriness**

Effective refractory periods (ERPs) at certain recording sites were determined (average, 30–40 sites). ERPs were measured at twice diastolic threshold after a train of eight basic driven beats (the cycle length was equal to the rate used to initiate reentry), using the extrastimulus method.

The ERP of the premature beat was determined at selected sites in the region of reactivation for the S1,S2 interval that resulted in an unstimulated reentrant response. It was measured at twice diastolic threshold after a train of eight basic driven beats and two extrastimuli. The coupling period of the first extrastimuli for each site was set equal to the measured response interval that resulted from the S1,S2 delivered at the control site.2

**Strength–Interval Curves**

The strength–interval relation was determined at selected nonischemic ventricular sites with a diastolic threshold <0.5 mA. Using bipole cathodal stimuli at twice diastolic threshold, an extrastimulus (S2) was introduced after a train of eight basic (S1) beats (400-msec drive cycle length). The threshold of the extrastimulus was measured for each S1,S2 coupling interval from <250 msec with a maximal current of 10 mA. The strength–interval curves were measured at intervals of 3–10 msec and current steps of 20–100 μA.

**Protocol**

The protocol was limited to the study of adrenergic influences on the initiation of reentrant rhythms. Therefore, the stimulation protocol was limited to the use of a single premature beat, S3, to initiate reentry.

The ansae subclavia were stimulated bilaterally using a Grass S88 stimulator (square pulses of 4 msec, 4 Hz). The voltage of stimulation was regulated to achieve 25–40% increase in sinus rhythm as measured from the atrial electrogram and 20–30% increase in systolic blood pressure: This averaged 4–8 V. During bilateral
ansae subclavia stimulation, programmed ventricular stimulation was performed. Similarly, the ERPs and strength–interval relations were determined during bilateral ansae subclavia stimulation.

Infusion of norepinephrine (0.1–0.5 μg/kg/min) was given. The rate of infusion was adjusted so that systolic blood pressure would increase by an equivalent amount that was elicited during bilateral ansae subclavia stimulation (an increase by 30–40%). Programmed ventricular stimulation and ERPs were recorded during these conditions.

Sham-Operated Dogs

Dogs were prepared with the same surgical procedure except that when the coronary artery was dissected free and a silk ligature was placed around the LAD coronary artery, it was not ligated. Four days later, the same experimental procedures were repeated.

Statistical Analysis

Mean±SD was used to assess the dispersion of the data. Student’s t test, a one-way ANOVA, or the Wilcoxon signed rank test was used, as appropriate, to interpret the data. A value of p<0.05 was considered significant.

Definitions

S1S2 is the interval between the last basic stimulus of a pacing drive (S1) and the first premature stimulus (S2). R1R2 is the interval between the ventricular response to S1 (R1) and the response to S2 (R2). ERP is the ERP of R1 (2) measured in 5-msec increments at twice diastolic threshold. The ERP1 was defined as the shortest S1S2 that produced a propagated local response, R2, after a train of eight basic S1 stimuli. ERP2 is the ERP of R2 and is defined as the shortest S2S2 that produced a propagated local response, R3, following a selected S1S2 interval.

Results

Twenty dogs were studied; 17 dogs had coronary artery ligation, and three dogs were sham operated. An arc of functional conduction block resulted after the shortest S1S2 interval in 12 of the 17 dogs; the remaining five dogs showed no arc of block. Postmortem examination of these five dogs showed that the LAD ligation had caused a subendocardial infarction with a relatively thick surviving epicardial layer (>5 mm). Similarly, the three sham-operated dogs showed no myocardial infarction and did not develop an arc of functional conduction block after the shortest S1S2 interval.

Effect of Sympathetic Stimulation

Reentrant ventricular rhythms were recorded in only four of the 12 dogs in which an arc of functional conduction block had formed after the shortest S1S2 interval. In these eight dogs that did not show reentry, bilateral ansae subclavia stimulation caused the development of reentrant ventricular beats in four of them. No reentrant beats occurred in the five dogs with a thick surviving epicardium or in the three sham-operated dogs.

Figure 1 shows the epicardial activation pattern and the respective electrograms of a heart in which no conduction block occurred after S1 during control or sympathetic stimulation. After basic pacing during control, an S2 at 160 msec blocked as it entered the ischemic zone. Conduction proceeded around this arc of functional conduction block (the thick line). Activation arrived on the distal side of the arc of functional conduction block but did not reexcite areas proximal to the arc, i.e., no reentrant beat occurred. During subsequent bilateral ansae subclavia stimulation, an S2 at 160 msec produced an arc of functional conduction block and a reentrant beat, V1. During the control S2, the arc of functional conduction block was located between sites b and c. During bilateral ansae subclavia stimulation, the arc of functional conduction block shifted toward the more normal myocardium (to between sites a and b, Figure 1). Conduction was improved proximal to the arc as evidenced by the reduction in response interval (R1R2). The R1R2 interval at site a shortened during sympathetic stimulation, but ERP1 and ERP2 at sites a, b, and c were not changed. Therefore, S2 arrived earlier at site a, and R2 was unable to propagate directly to site b because it was still refractory (Figure 1, electrograms). Consequently, the wave front conducted around the arc of functional conduction block and then excited site b. The conduction time from site a to site b provided sufficient time for site a to recover its excitability, and the wave front was then able to reexcite site a. Thus, a reentrant beat, V1, was initiated.

Figure 2 shows the pattern of epicardial activation in another heart. In this case, S2 at 160 msec produced an arc of functional conduction block. During control stimulation, a reentrant beat did not occur at this or at any shorter coupling interval. During bilateral ansae subclavia stimulation, the same S1S2 induced a prolongation in the arc of functional conduction block and reentry. As in the previous example, there was a reduced response time at sites proximal to the arc of functional conduction block during bilateral ansae subclavia stimulation. Consequently, at site c, the R1R2 was shortened by 20 msec, and the arc of functional conduction block extended to between sites c and d. The reentry occurred between sites b and a because the shorter R1R2 at site a permitted this site to recover relatively sooner and thereby be reexcited by the wave front coming from site b. Thus, sympathetic stimulation promoted reentry.

The average reduction of R1R2 during sympathetic stimulation in response to the same short S1S2 was measured from sites proximal and distal to the arc of functional conduction block. At an average S1S2 of 160±12 msec, there was a significant shortening of R1R2 by 9.1±5.7 msec (p<0.0001) at sites proximal to the arc of functional conduction block. In contrast, there was no significant change in the R1R2 at sites distal to the arc of functional conduction block.

Sympathetic stimulation induced shortening of the R1R2 at proximal sites suggested a possible shortening of the functional refractory period. To understand more completely the effects of sympathetic stimulation on excitability, strength–interval relations were measured at selected sites proximal to the arc of functional conduction block in six hearts. Figure 3 shows a representative example of one such strength–interval curve. Bilateral ansae subclavia stimulation did not affect diastolic threshold. However, there was a measurable shift to the left at shorter S1S2 intervals. Therefore, less current was needed to reexcite the tissue at a shorter
Epicardial activation map during control (left) and sympathetic stimulation (S.S., right). The top two maps represent the activation of R1. The bottom two maps represent the activation pattern of R2. The arc of functional conduction block is represented by the heavy line. The arc of functional block shifted during sympathetic stimulation. During sympathetic stimulation, a reentrant beat was also initiated (arrow in map). Electrograms of the selected sites are shown for each control and sympathetic stimulation under the respective maps. The upward arrows represent the respective effective refractory periods (values indicated) relative to the time of activation. Asterisks denote electrotonic potentials from adjacent sites on the opposite side of the arc of functional conduction block.

Control

S. S.

S1

S2

FIGURE 2. Epicardial activation maps of R2 during S1S2 of 160 msec. Left panel was during control and right panel was during sympathetic stimulation (S.S.). During control, site a was excited during the 60-msec isochron, and there was no functional block between sites c and d. During sympathetic stimulation, the same S1S2 of 160 msec resulted in a shortened R1R2 interval at site a (during the 40-msec isochron). Block developed between sites c and d, thereby extending the arc of functional conduction block. In addition, reentry occurred between sites b and a (at the site of the arrow). Because site a had been excited earlier than during control, it had a longer time in which to recover excitability.

Epicardial Activation During Norepinephrine Infusion

Norepinephrine infusion prevented the initiation of reentrant activation that had occurred during control or during sympathetic stimulation. Figure 5 presents one coupling interval near the ERP. This shift was measured at all six sites. Because of the different ERPs at each site, the data were normalized to the absolute refractory period of each site (absolute refractory period was measured as the S1S2 at 10 times diastolic threshold); thus, for each data set, the abscissa origin begins with absolute refractory period for that data set. Figure 4 presents the composite strength–interval curve from all six sites, and it, too, showed a significant shift to the left during bilateral ansae subclavia stimulation (p<0.05).
The total infusion, norepinephrine during 161 to 200 msec, was divided into two arcs. The total activation time shortened during norepinephrine infusion, and there was preferential shortening of the ERP at sites previously distal to the arc of functional conduction block. In this example, the average ERP, for all sites proximal to the arc of functional conduction block during control was 179±12 msec. It was shortened to 161±10 msec (an average shortening by 18 msec) during norepinephrine infusion. The average ERP, for all sites distal to the arc of functional conduction block during control was 249±15 msec. It was shortened to 195±18 msec (an average shortening by 54 msec) during norepinephrine infusion. Therefore, norepinephrine decreased the gradient of the refactoriness between the normal and ischemic sites. Consequently, the length of the arc of functional conduction block was reduced and shifted toward more ischemic tissue.

A dramatic example of this occurred in the same heart shown in Figure 1 and Figure 6. The arc of functional conduction block completely disappeared during norepinephrine infusion; no arrhythmia followed an S2 at 160 msec. The S2 activation pattern resembled the control S1 activation pattern (Figure 1). Examples are shown of how the ERPs (underlined numbers) were preferentially shortened at paired sites, one proximal and one distal to the control arc of functional conduction block.1

The average effects of sympathetic stimulation and norepinephrine infusion on ventricular ERPs were measured. The ventricular sites were organized into two primary groups: those proximal to the arc of functional conduction block and those distal to it. To compare the effects measured in hearts (n=12) that showed an arc of functional conduction block after the earliest S1S2 with the infarcted hearts (n=5) in which no arc of block was measured and the sham-operated hearts (n=3), epicardial sites on these latter two categories were organized as being either proximal (within 1–3 cm to right ventricular side) or distal (within 1–3 cm to left ventricular side) to the LAD coronary artery. These areas approximated the distribution of the respective sites to the arc of block.1 The ERP1 of proximal and distal sites were compared (Table 1).

Bilateral ansae subclavia stimulation significantly reduced the ERP1 at proximal sites in all hearts but only significantly reduced the ERP1 at distal sites in hearts in which no arc of functional conduction block was measured. The ERP2 was measured only at proximal sites in hearts with an arc of functional conduction block, and it did not significantly change (155±15 to 148±18 msec, n=22).

Norepinephrine infusion significantly shortened the ERP1 in all hearts at both proximal and distal sites. In hearts with an arc of functional conduction block, distal sites shortened (−53±28 msec) more than the proximal sites shortened (−27±12 msec, p<0.01). However, there was no differential shortening between proximal and distal sites in the sham-operated hearts of the ligated hearts with no arc of functional conduction block.

**Discussion**

The primary findings of this study are that sympathetic stimulation shortened conduction time in normal tissue and increased the dispersion or gradient of refractoriness between normal and ischemic regions and, thereby, facilitated the occurrence of reentrant rhythms. In contrast, norepinephrine infusion decreased the gradient of refractoriness between normal and ischemic regions and virtually abolished reentry.

**Sympathetic Stimulation**

In this study, we utilized the fact that reentry was not inducible in some hearts (4 days after infarction) that developed an arc of functional conduction block after a prematurely stimulated beat (S2). Sympathetic stimulation improved the likelihood that reentry would follow.
this same S₂ as a result of two mechanisms: 1) improved conduction in epicardium proximal to the arc of functional conduction block (as measured by a reduced conduction time between stimulus artifact and the activating electrogram) and 2) preferential reduction of the ERP at sites proximal to the arc of functional conduction block. As a consequence of both of these effects, the arc of functional conduction block shifted toward the more normal tissue, thereby making the sites proximal to the arc of functional conduction block available to be reactivated sooner and initiate reentry. Another effect of preferential shortening of the ERP in the normal zone was the extension of the arc of functional conduction block. Although not directly shown in the present study, the lengthening of the arc of functional conduction block and/or the de novo creation of an arc of functional conduction block in the ischemic zone can potentially facilitate the occurrence of reentrant excitation.¹³

The physiological results are consistent with the tenet that sympathetic denervation occurred in the ischemic area, where a thin epicardial layer of myocardium survived the infarction. Alternatively, the results could be interpreted to mean that the surviving epicardial tissue was less sensitive to the sympathetic neurotransmitter during sympathetic stimulation. This alternative is less plausible because intravenous norepinephrine shortened ERPs in the surviving epicardium to a greater extent than in the normal epicardium.

Barber et al.⁹ have shown that when a branch of the LAD coronary artery was ligated, the resulting infarction did not denervate areas distal to the infarction, whereas the creation of a transmural infarction with latex injection did produce denervation. One consequence of the ischemia-induced denervation was a hypersensitive response by the denervated myocardium to intravenous norepinephrine. Trautner et al.¹⁴ have

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**FIGURE 5.** Top: Epicardial activation map during control (left) and during norepinephrine infusion (right). The dotted line in the control map represents the area of earliest reentrant excitation. The enlarged section (bottom) is from the area of the arc of functional conduction block with the refractory period of each respective site noted. There was significant shortening of the effective refractory periods at sites distal to the arc of functional block during norepinephrine infusion. The dotted line in the norepinephrine maps represents the previous position of the arc of functional conduction block during control. Reentry did not occur during norepinephrine infusion.

**FIGURE 6.** Map of heart depicted in Figure 1: Norepinephrine can abolish the arc of functional conduction block. Left, control; right, norepinephrine infusion. Underlined numbers refer to the effective refractory period at the respective sites both during control and norepinephrine infusion.
shown, however, that ligation of the main LAD coronary artery, not just a branch, caused denervation in the ischemic/infarcted region. A reduced fluorescence of the sympathetic nerve terminals in the ischemic epicardium was similarly measured using histofluorescence techniques.9,14 These results suggest that although some fibers may be denervated, others may only have a reduced level of neurotransmitter. It has been shown that the efferent fibers from the stellate ganglion reach the anterior left ventricle by traveling through the epicardium along the coronary arteries in a base-to-apex direction.15,9 Our results agree with these findings, but they suggest that the sympathetic fibers were affected by ischemia/infarction to within 2–3 mm of the epicardial surface. The fibers were directly affected by such an infarct or indirectly affected by the diffusion of metabolites from the area of ischemia/infarction. The finding that a reduced R1R2 was measured at specific sites for the same S1S2 during sympathetic stimulation compared with control suggested an effect that could be the result of a reduced late diastolic threshold and/or a reduced relative refractory period. Therefore, the strength–interval relation was determined (Figures 3 and 4). These curves showed that the late diastolic threshold was not reduced. The strength–interval curve of nonischemic epicardium was shifted to the left, indicating a reduction in the absolute refractory period. In addition, the reduced amount of current (downward shift) at the same premature coupling interval that was required permitted 1) more rapid conduction of R2 from the same control, i.e., the action potential could bring a greater number of cells to threshold and thereby improve R2 conduction, and 2) successful reactivation of potentially reentrant sites proximal to the arc of functional conduction block by current flowing from sites distal to the arc. As a result of improved conduction of S2 at sites proximal to the arc of functional conduction block during sympathetic stimulation, two factors improved the likelihood for reentry to occur. First, conduction block occurred between sites that during control were both proximal to the arc of functional conduction block. The proximal site during sympathetic stimulation had a shorter ERP because of its more normal location along the ischemia-induced gradient of ERP2 and because of the direct effect of sympathetic stimulation (Figure 1). It could, therefore, be reexcited earlier than the corresponding site could during control. Second, the circulating wave front had to conduct a longer distance in the area distal to the arc of functional conduction block. As in Figure 2, an additional isochron of activation time occurred between sites proximal and distal to the arc of functional conduction block. This permitted additional time for the recovery of excitability at sites proximal to the arc of functional conduction block. As a result of these two changes, the sites just proximal to the arc of functional conduction block had a shorter ERP and a longer recovery time before the reactivating wave front arrived; therefore, reentrant reactivation was more likely to occur.

**Norepinephrine Infusion**

It has been previously reported that in the canine heart, normal myocardium apical to a transmural infarct was hypersensitive to intravenous norepinephrine,16 i.e., denervation hypersensitivity.17,18 The hypersensitive response to norepinephrine in this study occurred to such an extent that the gradient of effective refractoriness was reduced. Conduction block failed to occur during R2. In less severe examples, the arc of functional conduction block was reduced in size and did not provide an extensive barrier, as it had before norepinephrine infusion. The most dramatic manifestation of this was when the arc of functional conduction block failed to appear at all (Figure 6).

We did not observe extra beats elicited by premature stimulus during norepinephrine infusion. Any circuits measured were much larger than those described as micoreentrant by Zuanetti et al19 in isolated epicardium superfused with norepinephrine.

**Limitations**

Denervation has only been measured functionally in this study and, therefore, the extent to which it was present 4 days after ligation was underestimated. Denervated areas were those in which sympathetic stimulation did not shorten ERP, but intravenous norepinephrine elicited a hypersensitive response. However, its influence on the ability to initiate reentrant ventricular rhythms is clear. Sympathetic stimulation was measured to have a differential shortening effect on the ERP in normal epicardium, but the extent to which differential shortening occurred was underestimated. Sites proximal to the arc of functional conduction block were classified as normal but, in fact, they were in the border or transitional areas between the normal and ischemic epicardium.

Although damage to the sympathetic nerves cannot be ruled out as a direct result of the ligation of the LAD coronary artery, the results strongly argue that the ligation had a minimal effect. As in the study of Inoue et al,11 our sham-operated dogs demonstrated no arc of functional conduction block or any differential changes in ERP at sites proximal or distal to the arc of functional conduction block. Likewise, when the occlusive ligation
was performed but a thick (≥5 mm) epicardial layer survived the ligation, there was neither an arc of functional conduction block after the earliest premature S₂ nor was there a differential shortening of ERP. Only when the infarct reduced the surviving epicardium to 2–3 mm thick was there an arc of functional conduction block, differential shortening of the ERP during sympathetic stimulation, and denervation hypersensitivity after norepinephrine infusion.

Our observations can explain the influence of adrenergic stimuli on the initiation of reentrant rhythms but not on the perpetuation of reentrant rhythms as a tachyarrhythmia.

Conclusions

In this experimental model of ischemia-induced reentrant arrhythmias, sympathetic activity can be considered to be arrhythmogenic, whereas the infusion of catecholamine can be considered to be antiarrhythmic.

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