Induction of Electrical Heterogeneity Impairs Ventricular Defibrillation
An Effect Specific to Regional Conduction Velocity Slowing

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Background—This study determined whether dispersion of conduction velocity, refractoriness, or excitability increases biphasic shock defibrillation energy requirements (DERs).

Methods and Results—Twenty-four swine were instrumented with a mid-LAD perfusion catheter for regional infusion of lidocaine 0.75 mg · kg⁻¹ · h⁻¹ (n=6), low-dose d-sotalol (0.16 mg · kg⁻¹ · h⁻¹) (n=4), high-dose d-sotalol (0.5 mg · kg⁻¹ · h⁻¹) (n=6), or saline (n=7). Effective refractory periods (ERPs) were determined at 5 myocardial sites, and regional conduction velocity was determined in LAD-perfused and -nonperfused regions. Regional lidocaine infusion increased DER values by 84% (P=0.008) and slowed conduction velocity by 23% to 35% (P<0.01) but did not affect ERP. Conversely, regional low- and high-dose d-sotalol infusion did not alter DER values or conduction velocity but increased regional ERP by 14% to 17% (P<0.001). Regional lidocaine increased conduction velocity dispersion by 100% to 200% (P=0.01) but did not change ERP dispersion, whereas d-sotalol increased ERP dispersion by 140% (P<0.001) without affecting conduction velocity dispersion. Lidocaine infusion induced ventricular fibrillation (VF) in 6 of 7 animals, whereas regional d-sotalol was not proarrhythmic. Regional infusion of lidocaine and d-sotalol prolonged VF cycle length by 23% to 41% (P<0.05) in the perfused region and increased VF cycle length dispersion by 85% to 240% (P<0.05). Both agents increased pacing threshold (excitability) in the perfused region by 93% to 116% (P<0.05).

Conclusions—Regional conduction velocity slowing increased DER values, which was probably a result of spatial dispersion of conduction velocity. Increasing refractory period dispersion without changing conduction velocity did not alter DFT values. Thus, dispersion of conduction velocity may be a more likely regulator of defibrillation efficacy than dispersion of refractoriness. (Circulation. 1999;100:2534-2540.)

Key Words: fibrillation ■ defibrillation ■ electrical stimulation ■ pharmacology ■ electrophysiology

Mapping studies demonstrate that nonuniform activation patterns occur after a defibrillation shock and are responsible for failed defibrillation.¹⁻² Whether the nonuniform propagation is due to postshock spatial dispersion of refractoriness or conduction velocity is unknown. Spatial dispersion of refractoriness can occur when the shock produces a graded tissue response such that a new action potential is elicited in excitable tissue and refractoriness is extended in relatively refractory tissue.³ Because the graded response is dependent on local voltage gradient, which can differ by >10-fold across the myocardium, there is dispersion of postshock refractoriness.⁴ Similarly, a shock may cause regional changes in conduction velocity, especially in high-voltage-gradient regions, thereby creating spatial dispersion of conduction velocity.⁵ Evidence suggests that spatial dispersion of refractoriness or conduction velocity can affect defibrillation efficacy.⁶ This is based on data demonstrating that biphasic shocks produce less spatial dispersion of postshock refractoriness, less regional conduction block, and lower defibrillation energy requirement (DER) values than monophasic shocks.⁷,⁸ Thus, biphasic shocks may defibrillate with greater efficacy by limiting postshock electrical heterogeneity.

Although these associations have been noted, no cause-and-effect relationship between electrical heterogeneity and defibrillation efficacy has been established.⁷ The purpose of this study was to establish cause and effect and determine which factor, refractory period or dispersion of conduction velocity, is a mechanism regulating defibrillation. The present study incorporated a model whereby electrical dispersion was created by infusing specific ion channel blockers into the mid left anterior descending coronary artery (LAD) that caused a regional reduction in conduction velocity (lidocaine) or regional increase in refractoriness (d-sotalol). This model has clinical implications for acute myocardial ischemia because acute ischemia can cause electrical heterogeneity and acutely elevate DER values.⁸

Methods

Animal Preparation and Surgical Instrumentation

Procedures were approved by the Animal Care and Use Committees. Domestic farm swine (25 to 30 kg) were premedicated with ketamine.

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15 mg/kg, anesthetized with pentobarbital 15 mg · kg⁻¹ · h⁻¹, and mechanically ventilated. Monophasic action potential catheters (EP Technologies) were placed into the right ventricular apex and the left ventricle lateral wall. Spring defibrillation coils were placed into the right ventricular apex (anode) and superior vena cava (cathode). Subcutaneous wire arrays (cathode) were placed within the lateral anterior chest wall. The defibrillation leads were interfaced with an external biphasic defibrillator using a truncated waveform (65% fixed tilt) and pulse duration between 8 and 14 ms. Device output was determined by preset voltage adjustments (Ventak ECD, CPI Guidant).

After a sternotomy, a small area (3 to 5 mm) on the LAD, just past the second diagonal branch, was isolated from surrounding myocardium. A 24-gauge plastic catheter was inserted into the LAD (Figure 1) and affixed to adjacent epicardium. A 2-mm ultrasonic flow probe (Crystal Biotech, VF-1) was placed distal to the catheter, which demonstrated that coronary flow was unaffected by the catheter. The perfusion solution contained normal saline, 100 U/mL heparin, and 0.5 mg/mL nitroglycerin infused at 10 mL/h to prevent clotting and vasospasm. After 30 minutes, the coronary infusion consisted of saline and heparin. Quadripolar (5-mm interpole distance) Ag-AgCl electrodes (In Vivo Metrics) were placed onto the epicardium of the left ventricular apex (LAD catheter perfused area), left ventricle base, and right ventricular outflow tract (Figure 1). Monophasic action potential probes were placed adjacent to these electrodes. An intramural temperature probe (Yellow Springs Inc) was placed in the perfused area. Myocardial temperature consistently remained 0.5°C above rectal temperature. The chest was draped to retain moisture and heat. Arterial blood gases (Corning 170, Ciba Corning) and sodium and potassium concentrations (Nova 1, Baxter) were measured every 20 to 30 minutes and maintained at physiological values.⁹

**Study Design**

Electrophysiology and DER values were measured at baseline. Subsequently, the coronary perfusion (10 mL/h) was changed to the randomly determined treatment group. The control group (n=7) received heparinized normal saline. The lidocaine group (n=7) received 0.75 mg · kg⁻¹ · h⁻¹ lidocaine in heparinized saline. The low-dose (n=4) and high-dose (n=6) d-sotalol groups received 0.166 or 0.5 mg · kg⁻¹ · h⁻¹ d-sotalol in heparinized saline, respectively. Lidocaine and low d-sotalol doses were 10-fold less than systemic doses that change DER values.⁹,¹⁰ A 30-minute period separated baseline and treatment periods to completely clear the infusion line.

**DER Testing**

Defibrillation shocks were applied ~8 seconds after induction of ventricular fibrillation (VF).² Defibrillation trials were repeated every 4 minutes but not until arterial blood pressure was within 10% of preshock value. DER was measured by a step-down–step-up method that incorporates 12 fibrillation-defibrillation trials per study phase.⁹ This estimates the energy response curve (20% to 80% successful response) that achieves 20% (ED₂₀), 50% (ED₅₀), and 80% (ED₈₀) successful response with an iterative computer program (MERFFIT, Guidant).⁹

**Conduction Velocity**

Regional changes in conduction velocity were evaluated in 5 additional animals. The animals were instrumented as described above except that two 16-pole electrode arrays were affixed to the epicardium. One array was located within the LAD-perfused region (left ventricular apex), and the other was affixed to a nonperfused region located at the right ventricular base. The electrodes were arranged in bipolar pairs in 2 perpendicular rows, with each row containing 4 bipolar Ag-AgCl electrodes (2-mm interbipole spacing), as depicted in Figure 2.¹¹ Conduction velocity was assessed by local cathode pacing at a 300-ms cycle length (CL) for 20 seconds. The anode was located on the right ventricular outflow tract. Fiber orientation was determined during cathode pacing and rotation of the electrode array until the differences in conduction times between the fourth and D electrodes were maximal. The signals were processed with a high-gain amplifier and filtered with a bandwidth of 0.1 to 1 kHz (Universal amplifier, Gould Instruments). Conduction velocity was the time required for the impulse from the first electrode of a row to reach the distal electrodes of the same row divided by distance traveled. Arrival time was the point of maximum dV/dt at each bipole. After baseline conduction velocity had been recorded, lidocaine (0.75 mg · kg⁻¹ · h⁻¹) was continuously infused into the LAD. Conduction velocity was assessed 45 minutes after the lidocaine infusion had been initiated. The lidocaine infusion was stopped, and a 30-minute washout phase ensued. Conduction velocity was measured at the end of the washout period. Then d-sotalol (0.166 mg · kg⁻¹ · h⁻¹) was continuously infused into the LAD. Conduction velocity was assessed...
velocity was assessed 45 minutes after the d-sotalol infusion had been initiated.

**Electrophysiological Parameters**

The electrophysiological variables (paced QRS duration and action potential duration) were measured during right ventricular pacing at a 300-ms CL and averaged from 5 consecutive beats. Ventricular pacing was continued for 15 to 20 seconds before measurement of these parameters to ensure a nearly steady-state level of ion channel conductance and ion channel block. Pacing threshold was measured at each stimulation site with an isolated constant-current unit (Bloom Associates, Fisher Imaging), and delivered current was measured with a digital multimeter (Fluke 867, Fluke Instruments).

Myocardial repolarization was assessed from the monophasic action potential duration at 90% complete repolarization. Local effective refractory period (ERP) was determined at a 300-ms CL by a premature-stimulus method as previously described. Each ventricular recording site was tested in random order. VFCL was measured before the defibrillation shock. VFCL was measured from monophasic action potentials recorded from 5 ventricular sites as previously described. Spatial heterogeneity (dispersion) between recording sites was evaluated for the electrophysiological parameters: action potential duration, ventricular refractoriness, pacing threshold, VFCL, and ventricular conduction velocity. Dispersion was calculated as the difference between the maximum and minimum values of the 5 (2 sites for conduction velocity) recording sites. All electrophysiological measurements were obtained at the start and end of the DER protocol at baseline and drug treatment phases. These values were averaged for each study phase. Electrophysiological and hemodynamic signals were processed with Gould Universal amplifiers, digitally acquired at 3000 Hz, and stored for offline analysis (Datawave). Monophasic action potentials were DC coupled, filtered at 300 Hz, amplified, and stored for offline analysis values were averaged for each study phase. Electrophysiological and hemodynamic signals were processed with Gould Universal amplifiers, digitally acquired at 3000 Hz, and stored for offline analysis (Datawave). Monophasic action potentials were DC coupled, filtered at 300 Hz, amplified, and stored.

**Local Voltage Gradients**

Epicardial potential gradients were measured from the quadripolar epicardial electrode array located in the LAD perfused region (left ventricular apex). The 4 electrodes formed 2 bipolar pairs at 90° angles to each other. Each bipolar was interfaced with a differential voltage probe (Tektronics) and a dual-channel digital oscilloscope (TDS-320, Tektronics Inc). The voltage gradient of a 400- and 500-V shock was the square root of the sum of the squares of the x and y bipolar values divided by the interpole distance (5 mm).

**Data Analysis**

Paired t test or 2-way ANOVA tested differences between parameters at baseline and treatment within group (animal as its own control). One-way ANOVA tested differences between groups. Fisher’s exact test compared frequency of VF induction during electrical pacing between treatment groups. All data and statistical analysis was performed with a personal computer using Sigma Stat 2.0 (Jandel Scientific). Statistical significance was a value of P<0.05 by a 2-tailed test. Data are presented as mean±SEM.

**Results**

**DERs and Voltage Gradients**

Mean baseline DER values between the 4 groups were not different (Figure 3). DER values for the control group during saline treatment did not differ from baseline (Figure 3A, P=NS). Baseline DER values in the low-dose d-sotalol group did not change during the treatment phase (Figure 3D). Because of these findings, the dose of d-sotalol was tripled (high-dose d-sotalol group) to ensure an effective dose. Similar to the low-dose d-sotalol group, DER values during high d-sotalol infusion did not change from baseline values (Figure 3C). Lidocaine, however, greatly increased baseline ED20, ED50, and ED80 DER values (Figure 3B: ED20=13.7±1.2 to 24.6±1.7 J, P<0.01). The DER values increased in a nonlinear manner such that ED20, ED50, and ED80 DER values increased by 58±12%, 84±12%, and 121±25% (P<0.025 ED50 versus ED20 and ED80), respectively. This indicates that regional lidocaine changes the probabilistic nature of defibrillation. Systemic lidocaine, on the other hand, increases DER values uniformly, suggesting that regional and systemically administered lidocaine may increase DER values by different mechanisms.13

The above findings cannot be attributed to changes in lead impedance or local voltage gradients. Lead impedance did not differ between groups, although there was a slight impedance drop in all groups, a common finding in this model.13 Neither lidocaine nor d-sotalol affected epicardial voltage gradients in

**Figure 3.** DERs achieving 20% (ED20), 50% (ED50), and 80% (ED80) success at baseline and treatment study phases for placebo (A), lidocaine (B), high-dose d-sotalol (C), and low-dose d-sotalol (D) groups. *P<0.05 baseline vs treatment phase.
the catheter-perfused region. Local voltage gradients at the left ventricular apex during baseline and local lidocaine were 17.6±1.2 and 18.0±1.9 V/cm, respectively, for the 400-V shocks (P=NS) and 22.6±1.8 and 21.8±2.1 V/cm, respectively, for the 500-V shocks (P=NS). Local voltage gradients during baseline and high-dose d-sotalol were 19.8±2.5 and 16.3±2.1 V/cm, respectively, for the 400-V shocks (P=NS) and 24.0±3.9 and 19.9±2.4 V/cm, respectively, for the 500-V shocks (P=NS). Similar findings occurred in the control and low-dose d-sotalol groups.

Conduction Velocity
Lidocaine significantly slowed longitudinal and transverse conduction velocity within the perfused region by 23% and 35%, respectively (P<0.001) (Figure 4). After a 30-minute washout phase, conduction velocity returned to baseline values. Lidocaine did not affect conduction velocity at the nonperfused right ventricular site, demonstrating a local effect. Moreover, QRS duration, a marker of global ventricular conduction velocity, was unaffected by regional lidocaine infusion (baseline, 88±3 ms; lidocaine, 88±4 ms), and myocardial spillover of lidocaine into the systemic circulation produced plasma concentrations of 1.1±0.2 µg/mL, values well below therapeutic values.13 Hence, regional lidocaine infusion created dispersion of conduction velocity between the left ventricular apex and right ventricular base (Figure 5) and probably other non–LAD-perfused regions. The d-sotalol infusion did not affect conduction velocity at either site.

Refractoriness and Excitability
Local lidocaine did not affect local ERP (Table). Low-dose d-sotalol, however, increased ERP in the perfused area by 17%, whereas ERP at other recording sites did not change (Table), demonstrating a local effect. Consequently, dispersion of ERP increased from 11±2 to 38±1 ms (P<0.001) (Figure 5). High-dose d-sotalol produced similar effects, although ERP increased slightly in some of the nonperfused regions (Table), indicating a mild systemic effect. Interestingly, the magnitude of ERP increase at the perfused site was similar between the low and high doses of d-sotalol (34 versus 30 ms, respectively). Action potential duration was affected by local infusions of lidocaine and d-sotalol in a manner similar to ERP (data not shown).

Local lidocaine and high-dose d-sotalol increased pacing threshold (decreased excitability) at the left ventricular apex from 0.29±0.06 to 0.56±0.10 mA (P<0.05) and 0.36±0.05 to 0.78±0.11 mA (P<0.05), respectively. Both drugs, however, did not affect pacing thresholds at the 4 nonperfused pacing sites, indicating a local effect. Hence, dispersion of pacing thresholds was increased by 52% and 120% for lidocaine (0.27±0.05 to 0.41±0.22 mA, P<0.01) and high-dose d-sotalol (0.24±0.05 to 0.53±0.12 mA, P<0.01), respectively. Pacing thresholds in the low-dose d-sotalol and control groups remained at baseline levels during the treatment phase at all pacing sites.

Ventricular Fibrillation
At baseline, VF could not be induced by continuous pacing or single premature stimulus. During saline and low- or high-dose d-sotalol treatments, VF also could not be induced. Local lidocaine, however, induced VF in 6 of 7 animals (P<0.01 control and d-sotalol) with either electrical pacing or a single premature stimulus.

VFCL was slowed by low- and high-dose d-sotalol and lidocaine, but VFCL remained stable during saline treatment (Table). Regional lidocaine infusion increased VFCL by 43% (P<0.01) in the locally perfused region. This effect increased spatial VFCL dispersion by 260% (P<0.01) (Figure 5). Similarly, low- and high-dose d-sotalol increased VFCL in the perfused region by 23% (P<0.01) and 30% (P<0.01), respectively. Consequently, low- and high-dose d-sotalol increased VFCL dispersion by 85% and 63%, respectively (Figure 5). Both d-sotalol and lidocaine altered epicardial action potential morphology during VF (Figure 6). Fibri lation action potentials during saline treatment (control group) were fractionated, had double potentials, and rarely reached diastolic potentials. Local lidocaine and d-sotalol decreased the number of action potentials at the perfused recording site, widened the action potential duration, and qualitatively changed action potential appearance such that double and fractionated potentials were less evident. This suggests that the myocardium in the lidocaine- and d-sotalol–perfused region was less likely to be excited by colliding wave fronts.
and/or there was less block of wave-front propagation in this region.\(^4,6\)

**Discussion**

Electrical heterogeneity can be increased by various perturbations, including high-energy field stimulation.\(^4,6\) High-energy field stimulation increases refractory period dispersion immediately after shock and may cause a spatial dispersion of conduction velocity. It is conceivable that increasing electrical heterogeneity could hinder defibrillation efficacy by promoting arrhythmic propagation after a therapeutic shock. The present study altered conduction velocity or tissue refractoriness in a small myocardial region, creating spatial dispersion of conduction velocity or refractoriness. These data demonstrate that regional conduction velocity slowing induced by lidocaine adversely affects defibrillation efficacy, increasing DER values by 84%. However, regional prolongation of refractoriness induced by \(d\)-sotalol did not affect defibrillation efficacy. These data indicate that conduction velocity dispersion may be a more prominent regulator of defibrillation efficacy than refractory period dispersion.

Postshock electrical heterogeneity may be a regulator of defibrillation.\(^7\) Dillon\(^15\) observed that successful defibrillation was associated with postshock synchronized repolarization. It was postulated that a shock that extends repolarization and refractoriness more uniformly would produce lower DER values. Data from Behrens et al\(^7\) and Sims et al\(^4\) support this postulate by associating lower DER values with less dispersion of postshock repolarization and refractoriness. Sims et al demonstrated that biphasic shocks produce less postshock dispersion of refractoriness than monophasic shocks, suggesting that this may be the mechanism by which biphasic shocks defibrillate with greater efficacy. However, biphasic shocks also produce less disturbance in postshock conduction velocity than monophasic shocks.\(^6\) Because these studies cannot prove causation, it is impossible to determine which of these factors, postshock conduction velocity or refractoriness, regulates defibrillation. The present study attempted to establish cause and effect by separately increasing dispersion of conduction velocity or refractoriness and assessing how these perturbations altered DER values.

**Figure 6.** Monophasic action potentials from left ventricular apex epicardium (LV Apex), left ventricular base epicardium (LV Base), and right ventricular base epicardium (RV Base) recorded during VF and treatment with placebo (top left), lidocaine (top right), high-dose \(d\)-sotalol (bottom left), and low-dose \(d\)-sotalol (bottom right) in a representative animal.
Regional Lidocaine
The present study indicates that increased dispersion of conduction velocity is more likely to hinder defibrillation efficacy than dispersion of postshock refractoriness. This conclusion is supported by high-density electrical mapping data, in which a uniform degree of refractoriness was not necessary for successful defibrillation, nor did it predict the likelihood that postshock activations would propagate and cause failed defibrillation. Another explanation of our data could be that lidocaine, whether administered regionally or systemically, increased DER values by slowing ventricular conduction velocity. If this possibility were true, then we would expect regional and systemic lidocaine infusions to increase DER values by similar magnitudes. However, this is not the case, given that systemic administration of lidocaine does not affect biphasic shock DER values, whereas local lidocaine significantly increases biphasic DER values (present study). Given this difference, it is not possible that the regional lidocaine infusion increased biphasic DER simply by slowing conduction velocity. Rather, it is more plausible that the regional lidocaine infusion impaired biphasic defibrillation by increasing dispersion of conduction velocity.

Because we did not map the myocardium, we cannot determine the mechanism by which regional lidocaine infusion and the resultant dispersion of conduction velocity impaired defibrillation. However, it is unlikely that the actions of regional lidocaine on defibrillation were due to changes in excitability or VFCL, because lidocaine and d-sotalol reduced pacing thresholds and slowed VFCL in the perfused region, but only lidocaine increased DER values. Therefore, we propose that regional lidocaine increased DER values via a postshock proarrhythmic mechanism induced by spatial dispersion of conduction velocity. Normally, conduction velocity is homogeneous across the myocardium, albeit anisotropic. This results in uniform propagation of an activation front. In the absence of a defibrillation shock, regional conduction velocity slowing creates a spatial dispersion of conduction velocity and can be highly proarrhythmic, increasing the probability of ventricular arrhythmias. In fact, VF induction is closely associated with slow conduction in local regions. Consistent with these reports, the present study demonstrated that slowing of regional conduction velocity induced by lidocaine was highly arrhythmogenic to point stimulation. Although the present study suggests that spatial dispersion of conduction velocity facilitates a proarrhythmic state after shock, direct data supporting this conclusion are not available. Evidence from computational and mapping studies, however, allows for speculation that conduction velocity dispersion can promote VF after shock by causing functional conduction block followed by wave break. Functional conduction block may occur because tissue in the slow-conduction region is out of phase with distant myocardial regions. As an activation front spreads, tissue in the slow-conduction region activates later in time, which will cause repolarization and refractoriness in this region to occur later in time. The resultant dispersion of activation and repolarization between the slow-conduction and normal-conduction regions may disrupt uniform propagation, creating postshock arrhythmias.

Regional d-Sotalol
It was surprising that increasing spatial dispersion of refractoriness did not affect defibrillation efficacy, because the magnitude of refractoriness after shock has been postulated to be a regulator of defibrillation success, and failed defibrillation has been correlated with spatial dispersion of postshock refractoriness. Hence, the association between increased postshock refractory period dispersion and failed defibrillation may not be causative.

It was believed that increasing refractory period dispersion would be highly proarrhythmic, because data suggest that d-sotalol induces torsades de pointes by prolonging refractoriness in a nonhomogeneous manner. In the present study, d-sotalol infusion did not elicit a proarrhythmic response. Regional d-sotalol infusion did not affect DER values, nor did it induce spontaneous or electrically provoked ectopic activity. The low proarrhythmic incidence might be due to the fast basal heart rate of the swine (400- to 550-ms CL), which limits refractory-period dispersion. The sinus CL and paced CL in the present study were much faster than heart rates (>500-ms CLs) associated with arrhythmias induced by refractory-period dispersion and Ina blockade. This may also be the case after a defibrillation shock, when the dispersion of postshock refractoriness is limited by the early occurrence of postshock activations (<300 ms). Thus, the level of refractory period dispersion after shock may not be of sufficient magnitude to be proarrhythmic.

Limitations
Electrophysiological perturbations were made in a single myocardial region. We cannot speculate whether numerous regions of electrical heterogeneity would affect defibrillation in a different manner. Second, electrical heterogeneity was induced with drugs that block specific ion channels. It is possible that other pharmacological probes that also change conduction velocity and refractoriness could effect defibrillation in a different manner. Last, we did not document that the interventions actually produced dispersion of conduction velocity or refractoriness after shock. We did document that during rapid ventricular pacing, lidocaine increased dispersion of conduction velocity and d-sotalol increased dispersion of refractoriness. The electrophysiological properties of d-sotalol appear to be similar between ventricular pacing and immediately after shock. In both circumstances, d-sotalol increases refractoriness. Therefore, regional infusion of d-sotalol probably increased postshock refractoriness in the perfused region and caused postshock dispersion of refractoriness. In contrast, the electrophysiological action of lidocaine differs between pacing and defibrillation. Lidocaine does not affect refractoriness during pacing, a well-documented finding, although lidocaine does increase postshock refractoriness. The reason for this difference is unknown, but it may relate to conduction velocity slowing. Whether lidocaine slows ventricular conduction velocity immediately after shock is unknown, although there is no reason to believe that this would not be the case.

Clinical Implications
The proposed model has relevance to patients with ischemic heart disease and implantable defibrillators. Regional slowing of
conduction velocity may occur in patients with severe coronary disease who receive systemically administered sodium channel-blocking drugs. Tightly stenosed coronary arteries are likely to have less drug distribution than nondiseased arteries, causing nonuniform drug delivery to the myocardium. This may be a contributing factor by which sodium channel blockers impair defibrillation in coronary artery disease patients regardless of defibrillation waveform.9,22

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