Myocardial ischemia-reperfusion damage impacts occurrence of ventricular fibrillation in dogs

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METHODS

Twenty-three healthy adult mongrel dogs of either sex weighing 10–20 kg were studied. This protocol was approved by the Animal Care and Use Review Board at the University of Iowa, and is consistent with the US Animal Welfare Act and other applicable federal, state, and local laws and regulations. The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Xing, Dezhi, and James B. Martins. Myocardial ischemia-reperfusion damage impacts occurrence of ventricular fibrillation in dogs. Am J Physiol Heart Circ Physiol 280: H684–H692, 2001.—To define the relationship between ischemia-reperfusion-induced myocardial damage (IRD) and the occurrence of ventricular tachycardia (VT) and fibrillation (VF), we studied 23 dogs with a three-dimensional activation mapping system. Left anterior descending (LAD) coronary artery occlusion and reperfusion were performed while recording electrograms during VF and atrial pacing. Prior nonischemic sites showing IRD, defined as at least 10% loss of electrogram voltage after reperfusion, had the longest ventricular effective refractory periods (ERPs). IRD sites also occurred more frequently in dogs with reperfusion VF (44 ± 2 sites, P < 0.01) compared with dogs with VT (18 ± 5 sites) and no VT (16 ± 3 sites). In dogs (n = 3) with 3 h of reperfusion, 95% of IRD sites still had lower voltage than those recorded during occlusion. Activation mapping of the first eight complexes of VF had Purkinje or endocardial focal origin in 57%, and complexes originated from IRD sites in 28%. In contrast, dogs with only reperfusion VT also had Purkinje or endocardial focal origin in 79%, but only 5% (P < 0.01 vs. VF dogs) of the sites of origin had IRD. Therefore, dogs with reperfusion VF had more IRD sites where the ERP was longest, and more focal ventricular complexes originated from IRD sites, indicating that IRD may be one important factor in the occurrence of VF during reperfusion.

Reperfusion therapy resulting from thrombolytic or percutaneous transluminal coronary angioplasty has been commonly performed as a logical maneuver in the saving of myocardium undergoing necrosis (19). Investigators have demonstrated that reperfusion therapy could substantially improve left ventricular systolic and diastolic function and reduce overall mortality both in experimental and clinical studies (1, 15). However, although beneficial in terms of overall ventricular salvage, the process of reperfusion may cause deleterious consequences known as reperfusion injury and life-threatening ventricular arrhythmias such as ventricular tachycardia (VT) or ventricular fibrillation (VF) (2, 11, 15).

Kloner (15) has summarized four types of reperfusion injury that have been observed in experimental animals: 1) lethal reperfusion injury, 2) vascular reperfusion injury, 3) stunned myocardium, and 4) reperfusion arrhythmia. So far the lethal reperfusion injury or damage of otherwise potentially salvageable myocardium remains controversial (2, 11, 15).

Although reentry is generally considered to be the mechanism for the early ischemic arrhythmias with nonreentry mechanisms also operative (3, 4, 8), the mechanisms of VT and VF occurring with reperfusion are not clearly known (20). Vera and colleagues (24) recorded early afterdepolarizations (EADs) both during ischemia and during reperfusion and postulated that EADs participated in the genesis of reperfusion VT and VF. Murdock and co-workers (18) demonstrated that the conduction delay resulting from myocardial ischemia rapidly returned to control times with reperfusion providing evidence against reentry. Kappel and colleagues (13) speculated that reperfusion VT and VF are not associated with a single mechanism. Using three-dimensional mapping, Pogwizd and Corr found that 75% of reperfusion ventricular complexes originated from endocardial foci without enough evidence of reentry (21). There is, of course, no known relationship between postulated reperfusion damage and reperfusion-induced VT and VF. Understanding the mechanisms of VT and VF and the relationships with ischemia-reperfusion injury or damage may lead to life-saving treatments especially if spontaneous reperfusion is common (16).

Recently, we observed a link between the number of nonischemic sites with voltage loss observed only after reperfusion with occurrence of VF upon reperfusion (27). This study was undertaken to identify the potential relationship between the presence of ischemia-reperfusion damage (IRD) and the mechanisms of reperfusion-induced VT or VF.

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of Iowa and conformed to all regulations for animal use including the Guidelines of the American Physiological Society.

General preparation. Dogs were pretreated with ketamine (5 mg/kg im) and anesthetized with α-chloralose (150 mg/kg iv). They were then intubated and mechanically ventilated on a volume-cycled respirator (Harvard) to maintain a PaO₂ of 80–110 Torr, a PCO₂ of 35–45 Torr, and a pH of 7.35–7.45. Fluid-filled cannulas were inserted in the femoral artery to continuously measure arterial pressure and in the femoral vein to infuse fluid and drugs. Anesthesia was maintained with continuous infusion of α-chloralose dissolved in polyethylene glycol (mol wt 200) at 8 mg·kg⁻¹·h⁻¹. Arterial pressure, surface electrocardiographic (limb) leads, and precordial lead V5R were monitored throughout the entire experiment.

The pericardium was incised through a midline sternotomy approach and sutured to the wounded edges forming a pericardial support for the heart. A 3-0 polyester suture was placed around the left anterior descending (LAD) coronary artery including the adjacent myocardium just distal to the first diagonal, and a snare was put around the suture to produce a reversible occlusion. Temperature was maintained at ~37°C by an infrared heating lamp positioned over the incision, and a plastic sheet was draped over the sternotomy to prevent desiccation and heat loss. Warm saline was applied to the heart intermittently to prevent surface cooling and drying.

Electrophysiological study. After the region of the sinus node was permanently clamped to control the rate, atrial pacing at a cycle length of 300 ms was performed with a bipolar pacing electrode at twice the diastolic threshold with pulses of 2-ms duration. To record transmural signals, 23 bipolar pacing electrode at twice the diastolic threshold with pacing at a cycle length of 300 ms was performed with a custom-built system consisting of a 266 MHz Pentium II G6 computer coupled with a DAP 2400/6 (Microstar Laboratories) high-speed acquisition board, an analog signal multiplexer, and 64 independent amplifier circuits, band-pass filtered from 3–1,300 Hz and digitized with a 12-bit analog-to-digital converter at 3.2 kHz per channel. Presampling of all of the data allowed for acquisition of electrograms for 4 s before an event with both systems. Three-dimensional activation maps were constructed from multiplexed signals ±14 s with data from both acquisition systems. Data from the two computers were synchronized on an atrial pacing spike.

After instrumentation of the myocardium with multipolar plunge electrodes, dogs were observed for 40–60 min before LAD occlusion to exclude ventricular arrhythmias due to mechanical artifact. The LAD was then occluded by tightening of the snare. After 20 min, the myocardium was reperfused by loosening the snare, which was accompanied by an abrupt epicardial color change from blue to pink and usually a prominent rhythm change (see Fig. 5; pH 4.0) from atrial pacing to VT and VF.

To determine the effect of defibrillation on myocardial damage and electrode dislodgement, three dogs had electrically induced VF and defibrillation (20 J) without LAD occlusion. In this latter group the mean voltage dropped <10% at 5 min after defibrillation compared with the values at baseline. Nearly all VTs or VF’s that occurred at the time of LAD occlusion and reperfusion were recorded and stored on both computers and then mapped using the three-dimensional computer-activation mapping system to locate the origins. Voltage amplitude was recorded as the magnitude of peak positive to peak negative for each electrogram; measurements were made on one complex because there was no complex-to-complex voltage change.

Definitions. VT was defined as a least three premature ventricular complexes in a sequence. Focal origin of a VT complex was defined when no electrical activity could be recorded on all adjacent sites in three dimensions spanning the latest activation of the previous QRS interval to the earliest of the QRS complex in question.

Purkinje origin of a complex of VT was defined as a focal endocardial mechanism with recording of a Purkinje potential occurring before the QRS on the lead recording the earliest site of activity (3).

Mechanisms were defined as reentrant when the earliest activation site was located immediately adjacent to the site of the latest activation from the previous complex and continuous diastolic activation was recorded between complexes.
We specifically searched for conduction delay from one site of earliest activity to the adjacent electrodes where late activity might be recorded which might account for a majority of the cycle length of a VT complex. In such a case, the mechanism might be recorded which might account for a majority of the earliest activity to the adjacent electrodes where late activity was also termed reentrant (3).

To account for this reentry, we specifically searched for conduction delay from one site of earliest activity to the adjacent electrodes. The voltage loss at the IRD site persisted through 90 min of reperfusion. In contrast, the voltage of the IRD site did not show enough decrease to indicate ischemia during occlusion, but further dropped after reperfusion instead of returning toward baseline. The voltage loss at the IRD site persisted through 90 min of reperfusion.

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Ischemia was defined as a reduction in voltage amplitude of electrograms of 45% from preocclusion baseline for the mid-myocardium and epicardium (22, 27). The usual response to reperfusion is return of ischemic voltages toward preocclusion values (Fig. 2, Table 1). In ischemic sites, the voltage did not decrease enough to meet the ischemic definition. In contrast, sites with IRD were less ischemic. Therefore, to clearly identify reperfusion damage and to exclude sites that may not have been reperfused, we further restricted our definition of IRD to sites that did not show an ischemic voltage drop during LAD occlusion. This definition may exclude some sites with reperfusion damage that were also ischemic; however, such sites that may not have been reperfused, we further restricted our definition of IRD to sites that did not show an ischemic voltage drop during LAD occlusion. This definition may exclude some sites with reperfusion damage that were also ischemic; however, such

Table 1. Values of voltage measurement in sites with ischemia and IRD

<table>
<thead>
<tr>
<th></th>
<th>Preocclusion, mV</th>
<th>20-min Occlusion, mV</th>
<th>5-min Postreperfusion, mV</th>
</tr>
</thead>
<tbody>
<tr>
<td>VF alone</td>
<td>1.4 ± 0.2</td>
<td>ND</td>
<td>1.3 ± 0.2 (defibrillation)</td>
</tr>
<tr>
<td>Reperfusion, no VT or VF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With ischemia</td>
<td>1.7 ± 0.2</td>
<td>0.8 ± 0.1*</td>
<td>1.3 ± 0.1*</td>
</tr>
<tr>
<td>With IRD</td>
<td>1.2 ± 0.1</td>
<td>1.1 ± 0.1</td>
<td>0.8 ± 0.1*</td>
</tr>
<tr>
<td>Reperfusion, VT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With ischemia</td>
<td>1.8 ± 0.1</td>
<td>0.7 ± 0.1*</td>
<td>1.2 ± 0.2*</td>
</tr>
<tr>
<td>With IRD</td>
<td>1.4 ± 0.2</td>
<td>1.2 ± 0.1</td>
<td>0.9 ± 0.1*</td>
</tr>
<tr>
<td>Reperfusion, VF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With ischemia</td>
<td>1.7 ± 0.2</td>
<td>0.4 ± 0.1*</td>
<td>0.9 ± 0.1*</td>
</tr>
<tr>
<td>With IRD</td>
<td>1.5 ± 0.1</td>
<td>1.1 ± 0.1</td>
<td>0.7 ± 0.1*</td>
</tr>
</tbody>
</table>

Values are means ± SE. IRD, ischemia-reperfusion-induced damage; VF, ventricular fibrillation; VT, ventricular tachycardia; ND, not determined; *P < 0.01 vs. previous intervention.

Fig. 3. Effective refractory period (ERP) in normal, ischemic, and IRD sites measured at least 30 min after reperfusion. ERP was prolonged in sites with IRD compared with prior ischemic sites and normal sites. There was no difference between normal and former ischemic sites.
sites may not have been reperfused and instead simply had further ischemia. Another methodology such as myocardial blood flow measurement (which was not employed in this study) must clarify this question. Thus we believe our IRD designation in sites that did not meet criteria for ischemia were likely damaged by reperfusion alone (Fig. 2).

To further investigate the electrophysiology of IRD sites, we examined durations of electrograms recorded in normal, ischemic, and IRD sites. IRD and normal sites did not prolong during LAD occlusion as did the ischemic sites. However, ERP was determined with programmed electrical stimulation at normal, ischemic, and IRD sites as defined by voltage measurements at 5 min of reperfusion. The ERP at previously ischemic sites (155 ± 4 ms) was not significantly different compared with nonischemic sites (157 ± 3 ms). In contrast, ERP was prolonged in sites with IRD (169 ± 4 ms) (Fig. 3). In three dogs, we also found that 95% of the IRD sites had continuously decreased voltages that were less than those recorded during occlusion even though the reperfusion was maintained ≥180 min (Fig. 4).

The number of sites with IRD was different according to arrhythmia occurrence: the number was higher in dogs with VF (mean per dog, 44 ± 2 sites; P < 0.01) compared with dogs with VT (18 ± 5 sites) or no VT (16 ± 3 sites). Because these data suggest that IRD may be arrhythmogenic, we examined the relationship between IRD and the mechanisms of VT and VF (Table 2). The first 8 ventricular complexes were analyzed.

![Figure 4](http://example.com/figure4.png)

**Baseline Occlusion 5 mins 180 mins**

Fig. 4. Voltage measurements at IRD sites during various time periods including 5 and 180 min after reperfusion. The greatest drop occurred 5 min after reperfusion but continued at 180 min to be less than that recorded during coronary artery occlusion.

![Figure 5](http://example.com/figure5.png)

**Fig. 5.** Electrograms of an atrial-paced complex followed by three complexes of ventricular tachycardia (VT) recorded during reperfusion in the same experiment as Fig. 2. Purkinje recordings are indicated (down arrows). Shown are surface electrocardiogram (ECG) lead, V5R, and electrograms from Purkinje (P) or endocardial (E) recording sites at focus of origin (-F3) and from immediately surrounding areas north (-N), west (-W), south (-S), overlying (-O), northeast (-NE), and southeast (-SE) of the F3 area. Vertical lines indicate onset of surface ECG of VT complexes. The first VT complex originates near epicardium of SE-F2 (not shown). The second VT complex originates in the subendocardium (up arrow) underlying Purkinje (P-F2). The third VT complex originates in a Purkinje focus (P-F3, up arrow), which is the IRD site depicted in Fig. 2. There is not enough conduction delay in the surrounding sites to suggest reentry of any complex of VT.

### Table 2. Sites of earliest activity of first eight ventricular complexes during reperfusion after coronary artery occlusion

<table>
<thead>
<tr>
<th>Dog</th>
<th>VT1</th>
<th>VT2</th>
<th>VT3</th>
<th>VT4</th>
<th>VT5</th>
<th>VT6</th>
<th>VT7</th>
<th>VT8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EPI</td>
<td>ENDO</td>
<td>ENDO</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>EPI</td>
</tr>
<tr>
<td>2</td>
<td>EPI</td>
<td>M</td>
<td>P</td>
<td>ENDO</td>
<td>P</td>
<td>EPI</td>
<td>ENDO</td>
<td>P</td>
</tr>
<tr>
<td>3</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
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<tr>
<td>4</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
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<td>P</td>
<td>P</td>
</tr>
<tr>
<td>5</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>6</td>
<td>ENDO</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>ENDO</td>
<td>EPI</td>
</tr>
<tr>
<td>7</td>
<td>P</td>
<td>ENDO</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>8</td>
<td>EPI</td>
<td>ENDO</td>
<td>P</td>
<td>P</td>
<td>EPI</td>
<td>P</td>
<td>EPI</td>
<td>P</td>
</tr>
<tr>
<td>9</td>
<td>EPI</td>
<td>EPRE</td>
<td>P</td>
<td>P</td>
<td>EPI</td>
<td>P</td>
<td>EPI</td>
<td>P</td>
</tr>
<tr>
<td>10</td>
<td>P</td>
<td>EPRE</td>
<td>P</td>
<td>P</td>
<td>EPI</td>
<td>P</td>
<td>EPI</td>
<td>P</td>
</tr>
<tr>
<td>11</td>
<td>ENDO</td>
<td>EPI</td>
<td>P</td>
<td>P</td>
<td>EPI</td>
<td>P</td>
<td>EPI</td>
<td>P</td>
</tr>
<tr>
<td>12</td>
<td>ENDO</td>
<td>ENDO</td>
<td>P</td>
<td>P</td>
<td>ENDO</td>
<td>EPI</td>
<td>EPI</td>
<td>P</td>
</tr>
<tr>
<td>13</td>
<td>EPRE</td>
<td>EPRE</td>
<td>SRE</td>
<td>EPI</td>
<td>EPRE</td>
<td>EPRE</td>
<td>EPRE</td>
<td>EPRE</td>
</tr>
<tr>
<td>14</td>
<td>EPI</td>
<td>EPI</td>
<td>ENDO</td>
<td>ENDO</td>
<td>EPI</td>
<td>EPRE</td>
<td>EPRE</td>
<td>ENDO</td>
</tr>
</tbody>
</table>

_Dogs 1–6 had reperfusion VT and dogs 7–14 had reperfusion VF. Bold type, sites with IRD; underlined type, sites with ischemia; italic type, adjacent ischemia. P, Purkinje focal; ENDO, endocardial focal; M, midwall focal; EPI, epicardial focal; SRE, septal reentry; EPRE, epicardial reentry._
with three-dimensional activation mapping in 14 dogs of which 8 degenerated to VF. In the VT group with 38 ventricular complexes analyzed (owing to cessation of VT in some dogs before 8 complexes), 30 (79%) had endocardial or Purkinje focal VT, but only 2 (5%) VT complexes originated from the IRD sites (Table 2). In contrast, in the VF group with 61 ventricular complexes analyzed, 35 (57%) had endocardial or Purkinje focal origin (Figs. 5–7); however, 17 (28%) complexes took origin from sites with IRD ($P < 0.01$ vs. VT group; Table 2). Of interest, dog 7, with the highest number of IRD sites as foci of VT and VF, had the smallest ischemic zone, which suggests no simple relationship between ischemic zone size and arrhythmogenicity due to IRD. The total numbers of endocardial focal sites in VT and VF groups are consistent with the results of Pogwizd and Corr (21).

Figure 8 shows the distribution of IRD sites in this study. Although IRD occurred in sites bordering the ischemic zone, a greater frequency occurred in endocardial and Purkinje layers, and two-thirds of the foci of VT with IRD were located in endocardial or Purkinje layers.

**DISCUSSION**

This study demonstrated that dogs with reperfusion VF had more sites with IRD than dogs with nonsustained reperfusion VT or no VT. The ERP was also prolonged in IRD sites after reperfusion, and the low voltage persisted after reperfusion at least 3 h. Three-dimensional activation mapping showed that more than one-fourth (28%) of the first ventricular complexes of VF originated from IRD sites. In contrast, only 5% of sites of origin had IRD in reperfusion VT; therefore, IRD may be an important factor in the mechanism of reperfusion VF.

In our experiments, we put a higher density of plunge needles in the ischemic zone surrounded by
fewer electrodes in normal zone. Previous studies did not show any important changes of ventricular activation or blood flow with this instrumentation (22, 26). We also observed that our multipolar needles stayed in their original places for the duration of the experiment even after application of defibrillation energy. Therefore, the transmural signals could be utilized to compare changes with duration of ischemia and reperfusion in the same tissue sites and locate sites with IRD or ischemia.

It is known that duration of ischemia predicts whether myocardial cells are injured either reversibly or irreversibly (9). Reperfusion of reversibly injured myocardial cells results in salvage of ischemic tissue (6, 15, 25). Reperfusion arrhythmias during the first minutes of reperfusion and stunned myocardium probably represent a functional component of reperfusion injury (5, 10). However, it is still controversial whether a certain population of cells that were reversibly injured at the end of a period of ischemia would go on to die only because of reperfusion itself (2, 11, 15). We found that IRD sites, which by definition did not suffer voltage loss as severe as to be called ischemic during LAD occlusion, occur in dogs with or without ventricular arrhythmias, which means IRD was ubiquitous after reperfusion. Regardless of arrhythmia occurrence, the ERP measured in sites with IRD is significantly prolonged compared with the sites with ischemia and restoration of voltage as well as with normal sites. This injury marked by voltage reduction persists for hours after reperfusion. Therefore, our data support the notion of reperfusion damage separate (at least anatomically and in time) from the ischemic process itself (Fig. 8). We must point out, however, that it is not clear what the basis of this damage may be. It may in fact result from cell death but it may also be due to intercellular edema or uncoupling of normal cells from ischemic cells.

Shinohara and colleagues (23) demonstrated that the ERP was shortened during ischemia and rapidly decreased.
shortened further immediately after reperfusion, but was slightly prolonged 10 min after reperfusion. The differences in these two studies are probably owing to the facts that: 1) we measured the ERP only after 30 min of reperfusion (time to measure voltages could take up to 30 min) rather than immediately after reperfusion, and 2) we utilized high-density plunge-needle electrodes to locate the IRD sites on 1-mm separated bipoles to accurately measure the ERP only in sites with IRD or ischemia, and we compared results with normal sites.

Reperfusion may salvage the ischemic myocytes causing the voltages to return toward preocclusion values in sites with reversible ischemia. Such areas had postreperfusion ERP measurements no different than normal, because these sites may not have had as intense damage as ischemic sites with further voltage reduction after reperfusion. In these latter sites, we did not measure ERPs, because they may reflect damage from both ischemia and reperfusion.

The prolonged ERP in IRD sites may interfere with the electrophysiological stability of the myocardium (7, 14, 23), which may lead to life-threatening ventricular arrhythmias during reperfusion after LAD occlusion. The resulting mechanisms of VT and VF may be multifactorial involving IRD sites. Such sites may predispose to reentry by blocking propagation owing to refractoriness, yet other sites may not, promoting micro- or macroreentry. Alternatively, prolonged ERP is associated with triggered early or delayed after depolarizations (26), which is consistent with the focal origin of the first complexes of VT. We did not measure ERPs in IRD sites at the time of VT or VF, and thus these possibilities are speculative; nevertheless, further studies may be designed that could allow testing of such possibilities.

The detailed relationship of IRD to occurrence of ventricular arrhythmias has not been studied heretofore. Our detailed analysis in 14 dogs of the first 8 ventricular complexes after reperfusion demonstrated that the origin of complexes leading to VF is from an endocardial focus in 57% of cases, and 28% of the complexes originated from the IRD sites, which was almost sixfold greater than the VT group (5%). This suggests that myocardial IRD may be an important factor in the occurrence of reperfusion VF.

Fig. 8. Schematic map of sites in three dimensions (similar to Fig. 6) with most common areas of IRD in at least 50% of VF dogs (i). Ischemic sites tended to be in center of electrode array.
We also found the voltage of the electrograms returning toward the baseline in some IRD sites with longer reperfusion, but it remained lower than that measured during LAD occlusion (Fig. 4). This suggests that the IRD was not always equal to reperfusion lethal injury, because in some IRD sites the damage was at least partly reversible. However, the prolonged voltage abnormality produced by reperfusion may be more severe than ischemia alone and allows for further study. In any event, our results suggest that reperfusion is a complicated pathophysiological process.

Regarding potential limitations of this work, it is theoretically possible that we could miss some VTs originating from sites outside the area covered by the electrodes because signals were not recorded from the whole heart. These sites are not likely to suffer from ischemia or reperfusion damage because they would be remote from the risk zone. But each of the complexes analyzed in Table 2 originated from sites that were surrounded on all sides by later activation; therefore, sites outside the electrode array played no role in our results. Moreover, we cannot exclude microreentry with our electrode density, although even in such small circuits the surrounding tissues show conduction delay (20), which may be suggested by our electrode density; we did not find evidence of such conduction delay in the focal sites of origin.

In these preliminary observations of IRD leading to VF, we did not plan additional studies to characterize the IRD sites. Such studies could include measurement of myocardial blood flow which would clarify whether the IRD sites did not indeed have as severe ischemia as the ischemic sites shown in Table 1. Preliminary studies suggest no differences in blood flow in IRD sites compared with normal sites during coronary occlusion as is predicted by our voltage measurements. The loss of voltage after reperfusion may also indicate the no-reflow phenomenon making milder ischemia worse. This possibility awaits further study, although preliminary study suggests blood flow to IRD sites after reperfusion is also no different than that measured in normal sites. We also plan to perform histological evaluation of IRD by several techniques including standard hematoxylin and eosin stains, which preliminarily show no contraction-band necrosis. Despite the lack of these studies, our present observations that voltage loss in sites only after reperfusion plays a role in occurrence of VF remain novel.

In summary, IRD sites, where the ERP is prolonged after reperfusion, are much more frequently observed in dogs with reperfusion-induced VF than with or without nonsustained VT. Three-dimensional activation mapping showed that 28% of the first eight ventricular complexes in dogs with reperfusion VF originated from the sites with IRD, which is almost sixfold greater than in dogs with VT. Our study demonstrated that IRD is a major factor in the occurrence of VF during reperfusion after coronary artery occlusion.

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REFERENCES


