Influence of Postshock Epicardial Activation Patterns on Initiation of Ventricular Fibrillation by Upper Limit of Vulnerability Shocks

Nipon Chattipakorn, MD, PhD; Jack M. Rogers, PhD; Raymond E. Ideker, MD, PhD

**Background**—Shocks of identical strength and timing sometimes induce ventricular fibrillation (VFI) and other times do not (NoVFI). To investigate this probabilistic behavior, a shock strength near the upper limit of vulnerability, ULV_{50}, was delivered to yield equal numbers of VFI and NoVFI episodes.

**Methods and Results**—In 6 pigs, a 504-electrode sock was pulled over the ventricles. ULV_{50} was determined by scanning the T wave. S_1 pacing was from the right ventricular apex. Ten S_2 shocks of approximate ULV_{50} strength were delivered at the same S_1-S_2 coupling interval. Intercycle interval (ICI) and wave front conduction time (WCT) were determined for the first 5 postshock cycles. ICI and the WCT of cycle 1 were not different for VFI versus NoVFI episodes (P=0.3). Beginning at cycle 2, ICI was shorter and WCT was longer for VFI than NoVFI episodes (P<0.05).

**Conclusions**—The first cycle after shocks of the same strength (ULV_{50}) delivered at the same time has the same activation pattern regardless of shock outcome. During successive cycles, however, a progressive decrease in ICI and increase in WCT occur during VFI but not NoVFI episodes. These findings suggest shock outcome is (1) deterministic but exquisitely sensitive to differences in electrophysiological state at the time of the shock that are too small to detect or (2) probabilistic and not determined until after the first postshock cycle. (Circulation. 2000;101:1329-1336.)

**Key Words:** electrophysiology • fibrillation • shock

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**Results**

Thirty of the 60 shocks in the 6 pigs were VFI episodes. One VFI episode was excluded because the last S_1 stimulus did not capture. A shock at ULV_{50} produced a shock voltage of 498±112 V. The mean coupling interval (CI) at which VF was induced with ULV_{50} shocks was used as the S_1-ULV_{50} CI (sCI); the sCI was 214±14 ms. To determine ULV_{50}, 15±11 shocks were required. The diastolic pacing threshold (DPT) was 0.2±0.1 mA. Heart weight was 154±45 g. For each animal, delivered shock voltage for the 10 ULV_{50} shocks was nearly constant (%SD of 0.1 to 0.3). Repeatability of the shock potential distribution at the 504 electrodes was measured in 1 pig. The mean correlation coefficient of the potentials was 0.995±0.004 for all 10 shocks.

The preshock interval and wave front conduction time (WCT) of the last paced cycle before the shock was not different between VFI and NoVFI episodes (Table 1). The similarity of the last paced cycle before the shock (Table 2) was not different, which suggests that the activation sequence of the last paced cycle was constant for all 10 shock episodes.

**Cycle 1 Site of Earliest Activation**

Cycle 1 sites of earliest activation (SEAs) were always at the anteroapical left ventricle (LV). While the cycle 1 SEA varied slightly between animals, it was highly repeatable for each animal (Table 3), showing that the first postshock cycle varied in the same epicardial region regardless of shock outcome.
Maximum first derivative (dV/dt) of activation at the cycle 1 SEA was not different for VFI and NoVFI episodes (Table 3). Mean dV/dt at the SEA of cycles 2 to 5 was less negative than that of cycle 1 for VFI episodes (P<0.01). However, no dV/dt differences were found among the first 5 postshock cycles in NoVFI episodes. For VFI episodes, SEA repeatability for cycles 2 to 5 (Table 3) was slightly lower than for cycle 1 because the SEA of cycles 2 to 5 moved a short distance (2±3 electrodes) away from the cycle 1 region of earliest activation (REA). However, the SEA of cycles 2 to 5 in NoVFI episodes moved a much greater distance away from the cycle 1 REA, 9±4 electrodes (P<0.002 vs VFI episodes).

### Propagation Pattern in VFI Episodes

A typical VFI episode is shown in Figure 1A (first cycle) and Figure 2A (subsequent cycles). All 5 cycles began in the anteroapical LV 36, 140, 229, 320.5, and 430 ms after the shock, respectively. Cycle 1 initially propagated toward the LV base, blocking at the right ventricular (RV) apex. It continued bilaterally around the apex, rejoining on the posterior RV to complete activation. Subsequent cycles did not block at the RV apex and activated both ventricles in a more radial pattern from apex to base. WCTs increased progressively up to cycle 3, then slightly decreased (89, 161, 215, 170, and 160 ms, respectively). Cycle 2 did not overlap temporally with cycle 1; however, subsequent cycles all overlapped with their immediate predecessor.

### Propagation Pattern in NoVFI Episodes

Cycle 1 after a NoVFI shock in the same animal (Figure 1B) was nearly identical to cycle 1 of the VFI episode. This first-cycle similarity is also apparent in the electrograms (Figure 3). Because cycle 1 for both episodes blocked at the RV apex, we paced from the anterobasal LV in the absence of shocks to establish there were no anatomic or functional barriers at the apex to cause the block (Figure 1C).

![Figure 1](http://circ.ahajournals.org/)

**Figure 1.** Examples from same animal of postshock cycle 1 for VFI (A) and NoVFI episodes (B) and of paced cycle (C). Electrode sites at which dV/dt was ≤−0.5 V/s at any time during a 10-ms interval are black. Numbers above frames indicate start of each interval in milliseconds relative to start of shock. Sock orientation is shown in Figure 7D. Arrows indicate SEA for each cycle. A, Cycle 1 arose at anteroapical LV, propagated toward anterobasal LV, and blocked over RV apex. B, Cycle 1 arose in same region as in A and propagated similarly. C, Activation initiated by pacing from anterobasal epicardial LV propagated without slowing across apex.
Cycle 2 from this NoVFI episode (Figure 2, B1) followed a pathway similar to the VFI cycle 2 but began later and conducted faster. Overlapping cycles were absent. Cycles 3 (B2) and 4 (B3) arose after long delays from different SEAs and had fast WCTs (73 and 38 ms, respectively). Cycle 4 was sinus and not analyzed.

### Postshock Intercycle Intervals

The mean intercycle interval (ICI) (Figure 4A) of cycle 1 did not differ between VFI (51±23 ms) and NoVFI episodes (n=24, 68±78 ms). The SD of NoVFI episodes was high because of 1 episode with an extremely long postshock interval (461.5 ms). This episode had its SEA near the posterobasal LV, whereas the SEAs from other episodes in this animal were at the anteroapical LV. If this NoVFI episode is excluded, the mean postshock interval for NoVFI episodes becomes 54±23 ms (P=0.6 vs VFI). ICIs for VFI episodes were significantly shorter than for NoVFI episodes for cycle 2 (138±38 vs 387±312 ms) and cycle 3 (132±31 vs 389±193 ms) (n=12 and 10, respectively). For cycle 4, the mean ICI for VFI (126±40 ms) was shorter than for NoVFI (484±182 ms) episodes; however, the difference was not significant, probably because there were only 5 NoVFI episodes with a fourth ectopic cycle. ICIs of cycle 5 were not compared because only 1 NoVFI episode had a cycle 5 (537 ms). ICIs of cycle 5 for VFI episodes were 128±41 ms.

### Postshock WCTs

The WCT (Figure 4B) of cycle 1 did not differ between VFI (116±19 ms) and NoVFI episodes (113±16 ms). The mean WCTs of cycles 2 (172±51 vs 99±44 ms), 3 (203±51 vs 83±18 ms), and 4 (197±55 vs 59±25 ms) were significantly longer for VFI than for NoVFI episodes (P<0.01). WCT of the single cycle 5 for NoVFI episodes was 58 ms. WCT of cycle 5 for VFI episodes was 210±53 ms. In all VFI episodes, overlap occurred during cycles 2 to 3, 3 to 4, and 4 to 5 (overlapping index >1) but not cycles 1 to 2 (overlapping index <1) (Figure 4C). In contrast, there was no overlap among the first 5 ectopic cycles in any NoVFI episode.

### Correlation of 504 Electrograms of Cycle 1

The similarity function, \( s_p \), and temporal lag, \( \tau_m \), were compared for all possible combinations of first cycles in each animal and divided into 3 groups: VFI versus VFI, VFI versus NoVFI, and NoVFI versus NoVFI episodes (Table 4). There were no differences in any group for either variable. The very
Figure 3. Selected electrograms from episodes shown in Figure 1. A, Polar map with numbers 1 through 5 representing sites where 5 electrograms shown in B through D were recorded. Arrows represent direction of propagation of activation. B, Electrograms from NoVF episode. Multiple vertical lines are shock artifact. Activation was earliest in electrogram 1 and latest in electrogram 5. Second deflection in electrogram 1 was an activation in cycle 2. C, Electrograms from VF episode. Second deflection in electrogram 1 was activation during cycle 2. D, Electrograms from B (dotted) and C (solid) superimposed.
high similarity and short temporal lag among different episodes indicate that first postshock cycles were nearly identical whether or not VF was initiated.

Cycle 2 in NoVFI Episodes
In NoVFI episodes, cycle 2 could be divided into 2 distinct subgroups. Subgroup 1 (n=7) had a short ICI, long WCT, and same REA as cycle 1. Subgroup 2 (n=6) had a long ICI, short WCT, and different REA than cycle 1.

ICIs in subgroup 1 were all <200 ms (142±27 ms) but were all >400 ms (672±228 ms) in subgroup 2 (P<0.002). Although the cycle 2 ICI of subgroup 1 was not different from that in the VFI episodes, in subgroup 2 it was significantly longer than in the VFI episodes (P<0.002). Subgroup 1 all had WCTs >100 ms (135±21 ms), whereas subgroup 2 all had WCTs <80 ms (56±12 ms, P<0.01). WCTs of both subgroups were significantly shorter than WCTs of cycle 2 in VFI episodes (P<0.004).

Cycle 2 SEA repeatability in subgroup 1 (63±48%) was different (P<0.04) from subgroup 2 (0±0%) in NoVFI episodes. Cycle 2 SEA repeatability in VFI episodes (60±33%) was different from that of subgroup 2 (P<0.007) but not subgroup 1. Thus, cycle 2 SEAs in the No-VFI subgroup with longer ICIs (subgroup 2) moved to a different site, whereas in the NoVFI subgroup with shorter ICIs (subgroup 1), as well as in VFI episodes, they mostly remained in the REA of cycle 1. The mean dV/dt for cycle 2 in VFI episodes also differed from that of subgroup 2 (−3.2±1.7 V/s) but not of subgroup 1 (−2.2±0.6 V/s) in the NoVFI episodes.

Thus, episodes could be distinctly divided into 3 groups: (1) VFI, (2) NoVFI subgroup 1, and (3) NoVFI subgroup 2. The propagation patterns (Figure 5) as well as electrograms (Figure 6) of cycle 1 from these 3 groups were nearly identical. Cycle 2 for groups 1 and 2 were also similar but not quite identical (Figure 5). Group 3 had a different REA and shorter WCT than did groups 1 and 2.

TABLE 4. Mean Correlation and Temporal Lag of Postshock First Cycles

<table>
<thead>
<tr>
<th></th>
<th>Correlation of Potential</th>
<th>Temporal Lag, ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>VFI-VFI</td>
<td>0.9987±0.0019</td>
<td>1±4</td>
</tr>
<tr>
<td>VFI-NoVFI</td>
<td>0.9989±0.0017</td>
<td>1±3</td>
</tr>
<tr>
<td>NoVFI-NoVFI</td>
<td>0.9993±0.0011</td>
<td>0.4±2</td>
</tr>
</tbody>
</table>
Discussion

Similarity of First Postshock Cycle Regardless of Shock Outcome

Our major finding is that the first cycle after a ULV \textsubscript{50} shock that induces VF cannot be distinguished from that after a shock of identical strength and timing that does not induce VF. This finding was apparent in the activation sequence animations and in the similarity of the following first-cycle variables: (1) SEA repeatability, (2) postshock interval, (3) WCT, (4) \(dV/dt\) at the SEA, (5) similarity function, and (6) temporal lag.

Most studies reporting differences of activation sequences and dispersion of refractoriness between VFI and NoVFI episodes used multiple shock strengths and coupling intervals.\textsuperscript{6,7} Those studies found that NoVFI episodes correlated with a lower dispersion of refractoriness immediately after the shock, whereas VFI episodes correlated with a greater dispersion of refractoriness. However, in those studies the shock strengths of NoVFI episodes were higher than those of VFI episodes. Thus, absence of VF induction may not have been secondary to a lower dispersion of refractoriness; rather, both lack of VF induction and a lower dispersion of refractoriness could have been
secondary to higher shock strength. To evaluate this possibility, we kept shock strength and timing constant. Our results suggest that when shock strength and timing are constant, differences in the dispersion of refractoriness are not large enough to cause measurable differences in postshock activation sequences and potentials. However, differences may exist immediately after the shock that are too small to be detected. These very small differences, according to the Chaos theory, could cause prominent differences after several cycles.

**Association of Overlapping Cycles With VFI**
Although differences between VFI and NoVFI episodes were first seen at cycle 2, a prominent distinction was not universally seen until cycle 3. This is because cycle 2 in 1 NoVFI subgroup behaved similarly to cycle 2 in the VFI episodes. However, no overlapping cycles were present in either NoVFI subgroup, whereas they were always present in the VFI group. Overlapping cycles may not be the direct cause of VF induction but may be a marker for short ICIs and long WCTs that are responsible for unstable reentry and VF induction. However, these results imply that at least 3 ectopic cycles with overlap by the third cycle may be required to initiate VF. If so, a method to halt the initiation of ectopic cycles in the REA could prevent VF even if it is applied as late as the third postshock cycle. Recent defibrillation and VF induction studies support this hypothesis.

**Implications for Mechanism of VF Induction**
It has been proposed that VF occurs by 2 mechanisms, an initiating mechanism that may involve ectopic unifocal impulses and a maintaining mechanism that involves reentry. Our results are consistent with reentry as a consequence of the initial accelerating, overlapping cycles observed in the VFI episodes. The rapid activation rate that led to the overlap of wave fronts also probably caused action potential duration to shorten and dV/dt to slow in the second to fifth cycles, possibly leading to unidirectional block, wave front fractionation, and reentry. In addition, the degeneration from the first postshock activation to VF could also be due to the nonuniform recovery of excitability of cardiac muscle after the premature stimulation of the first few postshock cycles.

**Study Limitations**
Although we did not observe epicardial reentry, intramural reentry cannot be ruled out because we did not record transmurally. The similarity of the first postshock cycle was based on epicardial recordings; therefore differences may have existed intramurally. The first postshock cycles could have differed in ways too small to be detected in our maps. Epicardial reentry may have been missed because it was too small to be detected by electrodes 4 mm apart or because part of the pathway consisted of activations that were so slow and small that the recordings did not meet our activation criterion.

**Conclusions**
The first postshock cycle has the same epicardial activation sequence regardless of shock outcome (VFI vs NoVFI), which suggests that large global differences in conduction or tissue refractoriness caused by the shock are not always the primary factors determining VF induction. Unidirectionally propagating epicardial activation followed by several ectopic, radially spreading impulses precedes VF. A progressive decrease in ICI and increase in WCT, resulting in overlapping cycles, heralds VF initiation.

**Acknowledgments**
This study was supported in part by National Institutes of Health research grants HL-28429 and HL-42760.

**References**


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Circulation. 2000;101:1329-1336
doi: 10.1161/01.CIR.101.11.1329

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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