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# Rapid Assessment of Ventricular Fibrillation Thresholds During Experimental Infarction in the Canine Heart[1] (38936)

JOSEPH R. LOGIC

*Division of Circulatory Diseases University of Tennessee Medical Units Memphis, Tennessee 38163*

The pathogenesis and optimal management of the ventricular tachyarrhythmias remain major unsolved problems in acute myocardial infarction. Due to the well-known clinical significance of certain types of premature ventricular extrasystoles, the measurement of multiple ventricular response thresholds (MVRT) and ventricular fibrillation thresholds (VFT) seem especially pertinent in experimental myocardial infarction, even though the duration of the threshold decreases may persist for only a short period of time (1). The classical method of assessing VFT utilizing extrasystoles in the vulnerable period (VP) introduced by Wiggers and Wegria (2) was thought too time consuming and inappropriate for repeated assessments within minutes of experimental coronary occlusion by Burgess and associates (3). Indeed, these later authors, in addition to others (4, 5), have more recently utilized trains of high frequency pulses to obviate the apparent technical difficulties involved in the classical experimental technique.

Since the single stimulus exploration of the VP would appear to be highly relevant to the "R on T" type of ventricular extrasystole and its clinical consequences (6), we report here the instrumentation which makes such threshold measurements in the classical manner rapidly and easily repeatable using a constant-current generator with a dc current probe and amplifier. In addition, we analyzed the time course of changes in vulnerability to fibrillation during the early stages of experimental infarction in the canine heart using these techniques.

*Materials and Methods.* A schematic of the instrumentation used to measure thresholds of vulnerability to tachyarrhythmia during experimental myocardial infarction is shown in Fig. 1. A dual-output multifunction solid-state stimulator[2] provided square wave dc pulses of variable intensity and duration to each of two isolation transformers.[3] The output of the first isolation unit (S1) was connected to stainless steel clip electrodes positioned for bipolar right atrial pacing. The second output (S2) delivered a 150-V source to the constant current unit,[4] which delivered constant current dc pulses of up to 50 mA intensity at selected time intervals from S1. On one of the Teflon-coated wires leading to a set of hook type stimulating electrodes, we positioned a dc current probe which was connected to its amplifier.[5] The output of the amplifier was displayed on a 50-ohm input oscilloscope and recorded for later analysis. Using this system, pulses of variable current strengths and duration can be programmed and changed rapidly and reproducibly. We have found a precise correlation between the dial-indicator of the CCU and the oscilloscopic visualization of the amplifier signal.

Male mongrel dogs were anesthetized with pentobarbital sodium, 30 mg/kg intravenously. Arterial blood pressure was measured using a femoral artery cannula attached to a Statham pressure transducer. Several standard electrocardiographic leads, the stimulus artifacts, and the arterial blood pressure were recorded on a Hewlett-Packard multichannel direct-writing recorder. The animals were ventilated through endotracheal tubes with a Harvard respiration pump adjusted to maintain arterial pH, $P_{AO_2}$, and $P_{ACO_2}$ within normal physiological limits during the study.

[1] Supported by a grant-in-aid from the Tennessee Heart Association.

[2] S-88 Stimulator, Grass Instrument Co., Quincy, Mass.

[3] SIU-5 Isolation transformer, Grass Instrument Co., Quincy, Mass.

[4] CCU-1, Grass Instrument Co., Quincy, Mass.

[5] P6042 probe and amplifier, Tektronix, Inc., Beaverton, Ore.

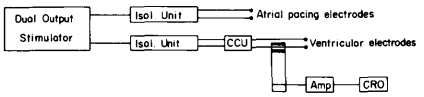


FIG. 1. Schematic of instrumentation for measuring MVR and VF thresholds. Isolation units (isol unit) are used in both pacing and threshold circuits. CCU identifies the constant current unit. Amp refers to the dc current probe and amplifier; CRO is the cathode ray oscilloscope.

Through a midline sternotomy, a pericardial cradle was fashioned and the left anterior descending coronary artery was prepared for single stage occlusion approximately midway from the apex to the base of the heart. The stellate ganglia and upper thoracic sympathetic trunks were excised bilaterally in order to decrease intrinsic heart rate and permit atrial pacing at regular rates up to 140/min, assuring constant R–R intervals.

Bipolar stainless steel stimulating electrodes (interelectrodal distance 10 mm) were inserted into the ventricular myocardium which was clearly within the area supplied by the artery to be occluded. Following 10–12 atrial paced cycles (7), single test pulses of 10 msec duration were introduced throughout the vulnerable period of the following cardiac cycle with progressive 10 msec delay intervals beginning in the absolute refractory period. We increased the stimulus strength in 2–2.5 mA steps for each successive exploration of the VP. The MVRT threshold was the initial test pulse strength which resulted in three or more repetitive beats and we continued to increase stimulus strength until VF resulted (8). In four animals, we repeated the control VFT measurements on three occasions and found them to be within 2.5 mA in every test and, in order to minimize the number of episodes of VF, performed only one control measurement in the remaining seven dogs. Whenever VF occurred, we defibrillated the dog with dc shocks of 20–30 W-secs using internal surface electrodes placed directly on the heart. After about a 1-hr delay, the artery was occluded in a single stage and repeat measurements of both thresholds were performed during the next 60–90 min. In five animals, atrial pacing at rates of 2.8–4.0/sec were performed before threshold measurements in order to compare this experimental model of myocardial infarction with that published by Scherlag *et al.* (9).

Differences in thresholds were tested for significance using Student's $t$ test for paired analysis.

*Results.* The control MVRT was 18.9 ± 1.7 (mean ± SEM) and the VFT was 23.6 ± 1.5 mA. Although the means do not differ significantly ($P > 0.05$), the VFT exceeded the MVRT by at least 2.5 mA in every animal and averaged 4.3 ± 1.52 mA. The initial MVR never degenerated into VF in the preocclusion period. As shown in Fig. 2 and Table I, within 10 min of coronary occlusion, both thresholds decreased by about 64% and remained depressed for the entire ensuing period of study. The study was terminated electively after 60 min in three animals and one 30-min threshold determination was omitted. Two dogs developed recurrent VF during the postocclusion period and could not be successfully defibrillated. It was elected not to employ any anti-arrhythmic agents during the course of this study. Ventricular extrasystoles were frequent in the first 3–8 min in eight animals and spontaneous single episodes of VF occurred in three of the eight prior to the 10-min threshold determination. As shown in Table I, the initial MVR degenerated into VF in 22 of 36 threshold determinations during the postocclusion period (61%), in striking contrast to its absence in the control period.

The atrial pacing rate was gradually increased to a mean of 3.4/sec (range 2.8–3.8/sec) in five dogs before each threshold determination. Prior to the appearance of incomplete atrioventricular block, no ventricular extrasystoles were noted in any experiment.

*Discussion.* Measurement of MVRT and VFT using the classic technique of the exploration of the vulnerable period of the cardiac cycle requires single constant current pulses of variable duration and intensity which can be easily and precisely quantitated. A constant current source is required during measurement of threshold electrophysiologic events because of the nonlinear relationship between imposed voltage change and current density using metal electrodes in a biological tissue such as mammalian myo-

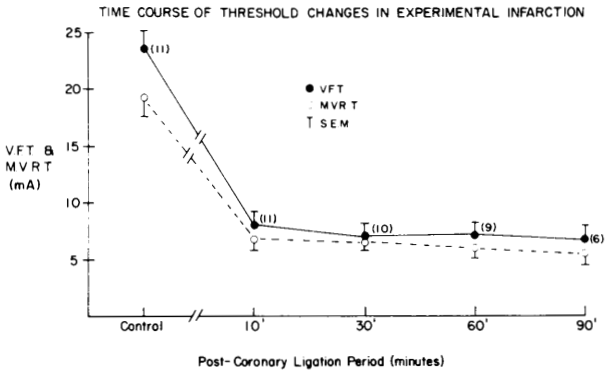


FIG. 2. Time course of MVRT and VFT following coronary occlusion. The slashed lines in the abscissa represent a 1-hr period between the time the control data were obtained and the time of occlusion. The numbers in parentheses represent the number of observations (see text for details).

TABLE I. MVRT AND VFT PRIOR TO AND DURING POSTCORONARY LIGATION PERIOD

| | MVRT (mA) | VFT (mA) | Frequency of identical thresholds |
|---|---|---|---|
| Control | 18.9 ± 1.7 | 23.6 ± 1.5 | 0/11 |
| 10 min postligation | 6.4 ± 0.9 | 8.0 ± 0.9 | 6/11 |
| 30 min postligation | 6.5 ± 0.8 | 7.0 ± 1.2 | 9/10 |
| 60 min postligation | 5.8 ± 0.8 | 7.2 ± 0.9 | 4/9 |
| 90 min postligation | 5.9 ± 1.0 | 6.7 ± 1.2 | 3/6 |

cardium (10). Since other techniques of current measurement using the voltage drop technique require pre- and post stimulation assessment of current-voltage relationships, the availability of the dc current probe and CCU represents a significant improvement in experimental design.

The 64% decrease in VFT observed as early as 10 min postocclusion and its maintenance for the 60–90 min of observation substantiate similar observations of Burgess *et al.* (2), as well as the studies of Shinohara (11). However, there was no tendency for the VFT to drift toward preocclusion levels in either our study or that of Shinohara (11), as occurred in the Burgess report using a different technique (2). Interest in the early time course of altered vulnerability to VF seems relevant to the observation that 40–60% of the 30-day mortality from myocardial infarction occurs within 1 hr of the onset of clinical symptoms and is most probably due to ventricular fibrillation (11). Occlusion of the anterior descending coronary artery as described in this study clearly produced a different type of lesion than that described by Scherlag *et al.* (9), where spontaneous VF occurred within 4 min of ligation in eight of ten animals and where rapid atrial pacing led to frequent ventricular extrasystoles, presumably as a result of reentry. The lesion produced in this study demonstrated a rapid onset of and persistent decrease in both MVRT and VFT demonstrated over a 60–90 min period, during which the magnitude of the injury currents, measured epicardially, tended to become less prominent (unpublished observations). It may well be that the geometric distribution of the injury currents, as well as their magnitudes, determine the enhancement of vulnerability to VF in early infarction, as suggested in a previous experimental model of regional hyperkalemia (8). It was also of interest to note the frequency with which the first multiple response degenerated into VF following coronary occlusion, since a similar observation was made during simulation of myocardial ischemia utilizing regional hyperkalemia (8). This model should permit the evaluation of the efficacy of anti-fibrillatory drug regimens in experimental infarction.

*Summary.* Sophisticated instrumentation is described which allows the rapid estima-

tion of vulnerability of the ventricle to multiple responses and fibrillation with the classical technique described by Wiggers and Wegria. It seems particularly pertinent to the assessment of the significance of "R on T" type of ventricular extrasystoles in myocardial infarction. The thresholds to tachyarrhythmia were decreased by about 64% within 10 min of coronary occlusion and persisted at that level for 60–90 min, suggesting the usefulness of this model in assessing anti-fibrillatory drug regimes during the early evolutionary stage of myocardial infarction.

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