Myocardial injury and induction of arrhythmia by direct current shock delivered via endocardial catheters in dogs

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ABSTRACT Although electrical ablation of ventricular tachycardia via percutaneous catheters has been recently accomplished in human beings, little is known of its pathologic or arrhythmogenic effects. We studied 21 open-chest anesthetized dogs in which an endocardial electrode catheter was percutaneously introduced into the left ventricle. Direct current (DC) shock was delivered by a standard defibrillator through the distal electrode to a back paddle. Cross-sectional two-dimensional echocardiographic studies were performed in the plane of the catheter (confirmed by epicardial metal beads), and blood flow was determined by the microsphere technique before DC shock and when the animals were killed 2 to 8 days later. Of 11 dogs receiving a total of 100 to 400 J, only three survived 48 hr compared with nine of 10 receiving 50 J and all three control dogs. Holter monitoring demonstrated sustained ventricular tachycardia (VT) (≥30 sec) in all 11 dogs monitored (six received ≥100 J), beginning within 5 hr of the DC shock; three control dogs had no VT. Two dogs that died suddenly while being monitored showed ventricular fibrillation. Histologic examination revealed hemorrhagic contraction band necrosis in the shock zone, a type of injury similar to that observed in reperfusion necrosis. Necrosis of the left ventricle was 0.5% to 5%. There was no significant difference in necrosis between dogs receiving 100 J or more and those receiving 50 J (2.5 vs 1.7; p > .1). Percent systolic thickening determined in eight equally divided regions around the left ventricle showed no difference between the shock zone, perishock zone, or remote normal zone in dogs receiving 50 J. Blood flow was diminished in the shock zone by 21 ± 6% (p < .005) but was unchanged elsewhere. Thus DC shock with as little as 50 J through an endocardial catheter results in localized nontransmural hemorrhagic necrosis. Despite its involvement of a relatively small portion of the left ventricle, this lesion is markedly arrhythmogenic, resulting in sustained VT/sudden death during the first week after DC shock. Circulation 69, No. 5, 1006–1012, 1984.

THERAPEUTIC interventions to treat medically refractory ventricular tachyarrhythmias include experimental antiarrhythmic drugs, antitachycardiac pacemakers, endocardial resection, and the automatic implantable defibrillator.1–4 Recently, closed-chest ablation in the His bundle was successfully performed in patients with medically refractory supraventricular tachyarrhythmias by delivery of a direct current (DC) shock through a standard electrode catheter.5,6 Reasoning that high-energy discharge would also interrupt reentrant pathways responsible for ventricular tachycardia (VT), Hartzler7 has also used this procedure in the ventricle for ablation of VT in human beings. However, the hemodynamic and electrophysiologic consequences of DC shock on endocardium are unknown. Previous studies limited to either transthoracic or epicardial DC shock have reported impaired ventricular function,8–13 myocardial necrosis,14,15 and ventricular arrhythmias.16,17

This study was therefore designed to assess the long-term effects of DC shock delivered through an endocardial catheter on regional structure, function, and cardiac rhythm of the canine left ventricle.

Methods

Experimental preparations. Twenty-one mongrel dogs weighing 18 to 26 kg were anesthetized with 30 mg/kg sodium pentobarbital and ventilated with a Harvard respirator. A left lateral thoracotomy was performed in the fifth intercostal space,
and the heart was suspended in a pericardial cradle. Polyethyl-ene catheters were placed in the internal mammary artery and left atrium and were externalized at the back of the neck through a subcutaneous tunnel. A 1 million U dose of penicillin and a 1 g dose of streptomycin were given intramuscularly after surgery.

Experimental protocol. The surface lead II electrocardiogram and arterial pressure were continuously monitored (Statham P23Db) on a direct-writing recorder (Gould, Inc.). Under sterile technique, a standard No. 6F quadripolar catheter (United States Catheter and Instrument Corp., Billerica, MA) with 1 cm interelectrode distance was inserted through the common carotid artery and advanced retrogradely under fluoroscopic control to lie squarely in the perpendicular plane against the left ventricular endocardium. With bilaplane fluoroscopy and an epicardial metal probe, the epicardial site directly above the endocardial tip of the catheter was determined. A metal bead (3/16 inch stainless steel shot) was sewn to the epicardium at this site (figure 1). A second bead was sewn to the left ventricular epicardium approximately 90 degrees from the first bead and at the same distance from the cardiac apex as the first bead. A third bead was sewn to the epicardium at a site approximately 180 degrees from the second bead, again at the same distance from the apex. These three beads therefore defined the cross-sectional plane containing the tip of the endocardial catheter for reproducible echocardiographic evaluation of regional systolic wall thickening.

Regional myocardial blood flow was assessed by injecting into the left atrium approximately $2.0 \times 10^7$ microspheres, 7 to 10 $\mu$m in diameter and labeled with $^{125}$I, $^{14}$Ce, $^{85}$Sr, $^{90}$Nb, or $^{48}$Sc (3M Co.), with polysorbate 80 added. Microsphere vials were agitated for 5 min before use. An arterial reference blood sample was withdrawn by a Harvard pump at a rate of 2.16 ml/min starting just before injection and continuing for 2 min. Before DC shock, radioactive microspheres were injected and two-dimensional echocardiographic studies were performed. The distal electrode of the endocardial catheter was connected to the cathodal output of a defibrillator (Physio-Control Life Pak 6) by a custom-made attachment. The back pad was placed between the spine and left scapula and connected to the anodal sink of the defibrillator. The position of the catheter was confirmed by fluoroscopic examination. If the position or plane of the catheter had moved from its original site it was repositioned. Stored energy between 50 to 200 J was delivered directly through the catheter. In all but four animals only a single shock was administered. Phasic and mean arterial pressures were recorded before and for 2 hr after each DC shock. The chest was then closed and the pneumothorax was evacuated. A Holter monitor (445-Avionics, Irvine, CA) was securely fastened around the thorax of the dog, and recording tapes were replaced after each 24 hr period.

Between 2 and 8 days later each dog was again sedated with adequate doses of sodium pentobarbital and the chest was re-opened. Microsphere injection and two-dimensional echocardiographic studies were repeated. The dogs were killed with a lethal dose of anesthetic and the hearts were removed, washed free of blood, and weighed. The ventricular cavities were packed with gauze and the hearts were fixed in 10% formalin. Three control dogs underwent the full protocol except that DC shock was not delivered.

Echocardiographic studies. Two-dimensional echocardiographic examination was performed with a mechanical ultrasonograph (Model MK 300 IC; Advanced Technology Laboratories) and a 5 MHz transducer on anesthetized, open-chest dogs. To separate the transducer from the epicardial surface and minimize mechanical interference, a stand-off device with a polyethylene membrane filled with mineral oil served as the interface between epicardium and transducer head. The transducer and stand-off device were angulated so that a cross-sectional view was obtained that encompassed all three beads (the cross-sectional plane containing the catheter tip). Data were stored on 0.5 inch videotape (60 fields/sec, Sony Beta I).

Echocardiograms were analyzed by a two-dimensional echocardiographic contouring system (Model EVII; Microsonics), and the echocardiographic image was displayed on a video screen. A transparency tracing the cross-sectional slice of the ventricle containing the three beads and catheter tip (see below) was placed over the screen. The echo image of the beads was aligned and marked with respect to the landmarks on the transparency. In this manner we verified that the cross-sectional myocardial ring that was analyzed for myocardial blood flow, histologic appearance, and function was the same. The computer divided the image into eight equally spaced myocardial segments and contouring the endocardial and epicardial circumferences. Regional percentage of thickening ($% \text{Th}$) was calculated for each of the eight myocardial segments as follows

$$\frac{\text{Th}_{\text{ES}} - \text{Th}_{\text{ED}}}{\text{Th}_{\text{ED}}} \times 100$$

where $\text{Th}_{\text{ES}}$ is the thickness of the myocardial segment at end-systole (cm) and $\text{Th}_{\text{ED}}$ is the thickness at end-diastole. Negative values denote systolic wall thinning. End-diastolic thickness was measured at the onset of the QRS complex. One representative sinus cycle preceded by at least 10 sinus beats was analyzed for each dog. For purposes of analysis, the segments were divided into the shock segment, the remote segment (directly opposite the shock zone), and six additional segments between these two (figure 1).

Morphologic studies. Each heart was sectioned transversely in 1 to 1.5 cm slices from apex to base, and each slice was photographed. One section included the three metal beads that corresponded to the echocardiographic plane of the catheter tip. The left ventricular rings were separated from the right ventricle, atria, and fatty tissue and were weighed. A transparency covering a plexiglass overlay was placed over each ring and the

![Diagram](https://via.placeholder.com/150)

**Figure 1.** Diagrammatic representation of left ventricular cross section containing the catheter tip. All three epicardial beads are aligned in the plane of the catheter. The ventricle has been divided into eight regions for purposes of functional and anatomic analysis. $S$ = shock zone; $A_1$ = adjacent clockwise zone; $A_2$ = adjacent counterclockwise zone; $A_3$ = adjacent to $A_1$; $A_4$ = adjacent to $A_2$; $A_5$ = adjacent to $A_3$; $A_6$ = adjacent to $A_4$; $R$ = remote zone directly opposite shock zone.

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endocardial and epicardial borders, visibly injured areas, location of metal beads, and catheter tip were traced. The slices were aligned according to the papillary muscles, septal wall, and metal beads. Samples for histologic studies were taken from the visibly injured area (shock zone), adjacent areas (no visible damage), and remote areas. An average of 20 sections of left ventricle stained with hematoxylin and eosin were prepared from each animal.

To determine whether epicardial vessels were managed by endocardial DC shock, the hearts of two dogs (receiving 50 J) were studied angiographically after death. A barium sulfate–gelatin mass at a controlled pressure of 160 mm Hg was injected simultaneously through cannuulas inserted into the origins of the right, left anterior descending, and circumflex arteries. Radiographs of the intact and serially sectioned heart were then obtained.

**Regional myocardial blood flow.** Tissue samples for measurement of blood flow were obtained as described above. The samples were weighed, placed in formalin-filled vials, and evaluated for radioactivity levels (Model 5986 multichannel gamma scintillation counter; Packard). Energy windows were adjusted to include the main photon peak of each isotope. Flows were corrected for true and apparent microsphere loss as previously described. Flows in the shock zone and perishock zone were expressed as a percent of the control zone.

**Holter monitoring.** Continuous 24 hr Holter recordings were obtained with a two-channel recorder. Tapes were read by a trained analyst using a computerized scanner (Avionics Trendsetter). Episodes of VT were printed out in real time for verification. Mean predictive positive accuracy and sensitivity rates for detecting ventricular extrasystoles in our laboratory are approximately 90%, and the false-positive rate is 10% (Model 686; Dynamic Electrocardioevaluator). For this study, sustained VT was defined as that lasting 30 sec or longer. Since in some cases the signal recorded was less than 0.5 mV, the minimum detected by the computerized scanner, quantitative analysis of the number of ventricular extrasystoles was not performed.

**Statistics.** Percent systolic wall thickening was analyzed by repeated-measures analysis of variance to test for differences among the shock, perishock, and control zones. To test the null hypothesis that there was no difference in regional blood flow among these regions, one-way analysis of variance was performed. Data are expressed as mean ± SD.

**Results**

Two groups of dogs were delineated for analysis. The first group comprised 11 dogs that received total DC shock between 100 and 400 J. One dog received 100 J, six dogs 200 J and four dogs 200 J, twice consecutively. Only three dogs from this group survived 48 to 96 hr, all of which received 200 J. The other eight dogs died suddenly within 18 to 36 hr of DC shock. Therefore statistical determination for significance of blood flow and wall motion data was not performed in this group.

The second group comprised 10 dogs that each received a single DC shock of 50 J; nine survived 48 to 192 hr and were then killed.

**Holter monitoring.** A total of 720 hr of monitoring was performed on 14 dogs. Six received 50 J shocks, five received shocks of 100 J or more, and three were control animals. Holter tapes were started approximately 1 hr after DC shock. The onset of VT was between 10 min and 4 hr after initiation of recording; the majority began within 1.5 to 3 hr. Rates of VT ranged from 150 to 300 beats/min (figure 2). All 11 experimental dogs monitored had at least one episode of sustained VT and all but one had multiple episodes (>20) lasting at least 1 min (table 1). No qualitative difference was evident between 24 hr periods in the seven dogs in which 48 hr consecutive monitoring was performed.

Two dogs died suddenly while being monitored. Antecedent rhythm was VT for 1 hr or more before degenerating into ventricular fibrillation. Postmortem examination showed no gross evidence of pulmonary edema, ruptured papillary muscle, or myocardial rupture.

No control dog manifested sustained VT during 192 hr of monitoring. Ectopy was rare and manifested as either uniform ventricular extrasystoles or ventricular couplets.

**Regional myocardial blood flow.** Blood flow to the shock zone (visible injury) was reduced by 21 ± 6% compared with that to the control zone in dogs receiving 50 J shocks (p < .005). There was no significant difference in blood flow between the perishock zone

![FIGURE 2. Spontaneous initiation of an episode of VT 24 hr after endocardial DC shock. The rate of VT is 220 beats/min.](image-url)
and the control zone (figure 3). In the three dogs receiving 200 J shocks, the shock zone and perishock zone were reduced compared with the control zone by 14 ± 6% and 11 ± 7%, respectively.

**Gross anatomic and histologic findings.** Gross examination revealed no evidence of myocardial rupture or formation of thrombus. Serial transverse sections revealed discrete, circumscribed hemorrhagic lesions that spread from endocardium and extended to the mid-myocardium (figure 4). Transmural injury was not demonstrated in any case regardless of energy administered. In all dogs receiving 50 J shocks, visible lesions were confined to only one transverse section (1 to 1.5 cm thickness). In dogs receiving 100 to 400 J, injury was more varied, extending across one or two transverse slices. The total of gross injured tissue for all dogs was 0.5 to 5.0 g. This represented between 0.5% to 4% of left ventricular mass. Dogs receiving shocks of 100 J or more had more gross damage than those receiving 50 J (2.5 vs 1.7 g, respectively), but this was not statistically significant (p > .10). In the former group, the four dogs that received 200 J twice consecutively had a mean of 2.9 g of necrotic tissue, compared with 2 g in dogs receiving 200 J and 1.4 g in the dog receiving 100 J. The three dogs in this group that survived at least 48 hr had a mean of 0.7 g of necrotic tissue (all received 200 J).

Postmortem coronary angiographic studies performed in two dogs showed continuity of epicardial vessels without evidence of obstructive lesions. No coronary injury was evident by gross inspection in any of the study animals.

Histologic examination showed contraction band necrosis, with extensive disruption of fibers and hemorrhage in the region of the grossly evident lesions (figure 5).

**Echocardiographic results.** The change in percent systolic thickening, as determined by the difference between the control value and that obtained at least 48 hr after a 50 J shock, was not statistically different among any of the eight cross-sectional regions (figure 6).

**Discussion**

The most significant finding in our study was the prevalence of VT and incidence of sudden death resulting from endocardial DC shock. All dogs monitored had sustained VT and 38% died suddenly. Recordings of spontaneous arrhythmias were performed for up to 8 days after DC shock, with the majority of dogs observed for the initial 48 to 72 hr. There was a trend toward diminished frequency of ventricular extrasystoles beginning the third day after DC shock, suggesting an early period of vulnerability, perhaps as noxious substances redistribute or continue to wash out of necrotic cells that were well perfused by intact vasculature.

Recently, successful closed-chest ventricular ablation of VT by DC shock via endocardial catheters has been reported, but little information is available regarding the type, extent, or consequence of this type of controlled but “blinded” injury. This is of concern since ventricular dysfunction may result from high-energy transthoracic or epicardial DC shock. Clinical observations of pulmonary edema after cardioversion are well documented. Recently, assessment of regional myocardial dysfunction by sonomicrometers
has demonstrated impaired systolic function subepicardially when DC shock was delivered directly to canine epicardium.\textsuperscript{12} Diastolic properties are also altered. There is a modest increase in the time constant for isovolumic fall in left ventricular pressure,\textsuperscript{13} suggesting impairment of left ventricular relaxation.\textsuperscript{22}

We evaluated ventricular function by quantifying regional systolic wall thickening, which has been shown to be an accurate index of fiber shortening,\textsuperscript{23} by means of two-dimensional echocardiography. We found no difference in systolic thickening between the shock, adjacent, and remote zones. This may be explained in part by the minimal degree of gross injury produced, 0.5\% to 4\% of left ventricular mass. If abnormal systolic function did occur, it was beyond the sensitivity of our technique to measure it and was therefore likely to be of little clinical consequence.

Existing data concerning the influence of direct epicardial DC shock on regional myocardial blood flow are conflicting. Investigators using thallium-201 found reduction in regional myocardial blood flow when shocks of greater than 30 J were discharged.\textsuperscript{15} Howev-
er, Kerber et al.,12 using radioactive microspheres, found no alteration in blood flow 2 hr after direct epicardial DC shock. DiCola et al.24 also found no change at 24 hr in regional microsphere flow after transthoracic DC shock.

Our findings indicate that high energy endocardial DC shock leads to minimal reduction in blood flow (21%) in the shock zone 2 to 8 days after the procedure. Myocardial blood flow was unaltered in the adjacent and remote areas. Radiographs of the epicardial vessels indicated no vascular disruption or occlusion in two animals. Focal microvascular damage was the most probable cause for reduced flow in the injured zone.

Ideally, the optimal lesion resulting from ablation of a tachycardia circuit should be discrete, circumscribed, and confined to the subendocardium. Consequently, only tissue participating in the circuit would be damaged and normal myocardium would be spared. Histologically, the lesion should eventually result in a homogeneous fibrous scar, since interspersed viable cells could result in new arrhythmogenic foci and potential reentry circuits.25, 26 For these reasons, high-density current was delivered through the distal catheter electrode. The resulting lesions were visible, circumscribed zones of necrosis beneath the catheter tip, which did not extend full thickness into the ventricle at any point. The injury was characterized histologically by contraction band necrosis, i.e., the necrotic pattern seen when lethally injured cells undergo reperfusion (which in part reflects the massive influx of calcium into injured cells, resulting in their hypercontraction and disruption). Whether this pattern of injury observed in our study resulted from microvascular thrombosis and reperfusion is not clear.

Other investigators have reported myocyte contraction bands, nuclear pyknosis, and cytoplasmic granulation after epicardial DC shock.15 Electron microscopy has demonstrated dehiscence of intercalated discs and extensive necrosis with contraction bands and mitochondrial swelling.15, 27

The amount of energy delivered had no direct correlation with the extent of myocardial injury. Several factors may have accounted for this. Although the electrode contact was always oriented perpendicular to the endocardial plane (electrode-endocardial contact surface area was approximately 3 mm²), the catheter electrode position varied between anterior, septal, lateral, and posterior endocardial sites. The back paddle, however, always remained in a fixed position between the spine and left scapula. Therefore, unless the catheter was directed at a posterior site (dog lying in the right lateral decubitus position) the paddle was not directly opposite the electrode-endocardial interface. The path of current and presumably the depth and location of the resulting myocardial injury in our preparation therefore may have depended on the geometrical relationship between the catheter electrode and back paddle. Other factors determining the degree of injury include the amount of energy discharged, contact pressure of the electrode with endocardium, and the relative conductance of blood and myocardium. Finally, although statistical significance was not achieved between extent of injury and energy delivered, the statistical trend suggested that, had a larger number of dogs been examined, an energy-injury relationship may have been demonstrated.

The incidence of sudden death was higher in dogs receiving large shocks (>100 J). The three surviving dogs in this group had 0.7 g of necrotic tissue compared with 3 g in the eight dogs that died suddenly. This suggests that although the degree of necrosis was quite variable for a given discharged energy, the occurrence of malignant VT may have been related to the amount of myocardial necrosis.

Of greatest concern in this study were the malignant
ventricular arrhythmias that resulted from endocardial DC shock. Our results are limited to arrhythmias occurring during the first week of observation and suggest that the type of injury and not just its extent could be a factor in causing such rhythm disturbances during the early phases of myocardial necrosis. Whether the magnitude and malignancy of arrhythmias found are clinically relevant remains to be seen. The dogs in our study were free of coronary artery disease, scarred left ventricles, wall motion abnormalities, or sustained VT before DC shock. It appears, however, that although myocardial blood flow and systolic function are minimally impaired, the marked prevalence of VT and incidence of sudden death in our study should encourage further investigation to determine the long-term sequelae of this procedure before it becomes accepted as a standard therapeutic method in human beings.

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