

Mechanisms of Ventricular Arrhythmias Induced by Myocardial Contusion

A High-resolution Mapping Study in Left Ventricular Rabbit Heart

Emmanuelle Robert, Ph.D.,* Jean E. de La Coussaye, M.D., Ph.D.,† Antoine G. M. Aya, M.D., M.Sc.,‡
 Jean-Pierre Bertinchant, M.D., Ph.D.,§ Anne Polge, M.D.,|| Pascale Fabbro-Pèray, M.D., Ph.D.,#
 Christine Pignodel, M.D.,** Jean-Jacques Eledjam, M.D.††

Background: The aims of the Langendorff-perfused rabbit heart study were to evaluate the arrhythmogenic consequences of myocardial contusion and to determine the mechanism of arrhythmia.

Methods: Six hearts were in the control group, and 24 hearts (intact heart protocol) were submitted to one of four different contusion kinetic energies (75, 100, 150, or 200 millijoules [mJ]; n = 6). Occurrence of arrhythmia, of an electrically silent area (*i.e.*, area with no electrical activity), and of line of fixed conduction block were reported before and for 1 h after contusion. In 16 hearts (frozen hearts) submitted to cryoprocurement and

contusion impact of 100 or 200 mJ, ventricular conduction velocities, anisotropic ratio, wavelengths, ventricular effective refractory period, and its dispersion were measured before and for 1 h after contusion. Using high-resolution mapping, arrhythmias were recorded and analyzed.

Results: The intact heart study showed that the number and seriousness of contusion-induced arrhythmias increased with increasing contusion kinetic energy, as did the number of electrically silent areas (five of six ventricular fibrillations and five of six electrically silent areas at 200 mJ). In the frozen heart study, immediately after contusion ventricular effective refractory periods were shortened and dispersed, and wavelengths were also shortened. The arrhythmia analysis showed that all ventricular tachycardias but one were based on reentry developed around an electrically silent area or a line of fixed conduction block.

Conclusions: Myocardial contusion has direct arrhythmogenic effects, and the seriousness of arrhythmia increases with the level of contusion kinetic energy. The mechanism of arrhythmia was mainly based on reentrant circuit around a fixed obstacle. (Key words: Heart trauma; reentry; isolated heart.)

* Scientist, Laboratory of Anesthesiology and Cardiovascular Physiology.

† Professor of Anesthesiology and Chairman, Department of Emergency and Critical Care, University Hospital of Nîmes.

‡ Staff Anesthesiologist, Department of Anesthesiology, University Hospital of Nîmes.

§ Cardiologist, Department of Cardiology, University Hospital of Nîmes.

|| Biochemist, Department of Biochemistry, University Hospital of Nîmes.

Biostatistician, Department of Epidemiology-Biostatistics, University Hospital of Nîmes.

** Pathologist, Department of Pathology, University Hospital of Nîmes.

†† Professor and Chair of Anesthesiology, University Hospital of Nîmes.

Received from the Laboratory of Anesthesiology and Cardiovascular Physiology, Medical School of Montpellier-Nîmes, Nîmes, France. Submitted for publication April 19, 1999. Accepted for publication November 17, 1999. Supported by the Conseil Régional du Languedoc-Roussillon, Montpellier, France; the Conseil Général du Gard, Nîmes, France; and the Fondation pour la Recherche Médicale, Paris, France. Presented in part at the 40th National Congress of the French Society of Anesthesiology and Critical Care Medicine, Paris, France, September 24-27, 1998, and at the 11th Annual Meeting of the American Society of Critical Care Anesthesiologists, Orlando, Florida, October 16, 1998.

Address reprint requests to Dr. de La Coussaye: Département de l'Urgence-Réanimation, CHU Gaston Doumergue, 5 rue Hoche, 30029 Nîmes Cédex, France. Address electronic mail to: jean.emmanuel.delacoussaye@chu-nimes.fr

BLUNT chest trauma can be responsible for cardiac injury,¹ arrhythmia, and sudden death. The arrhythmias may be facilitated by metabolic or hemodynamic alterations caused by associated injuries or consequent to acute heart failure.¹⁻³ Myocardial contusion with structural myocardial damage may induce serious arrhythmias or conduction defects.⁴⁻⁶ However, sudden death and arrhythmia also occur in blunt chest trauma patients who have no clinical evidence of cardiac injury or no cardiac structural damage.^{1-3,7} Maron *et al.* reported 25 sudden deaths in young sport players after blunt impact, but no cardiac structural abnormalities were detected during autopsy.⁷ In a model of commotio cordis in anesthetized pigs, Link *et al.* showed that low-energy chest wall impact induces ventricular fibrillation (VF) only when the impact happens within a window of 15-30 ms before the peak of the T-wave of the electrocardiogram.⁸ This impact occurring at this precise period could only

CONTUSION-INDUCED ARRHYTHMIAS

cause immediate arrhythmia. In contrast, myocardial contusion could cause immediate but also delayed arrhythmia.^{3,9-11} The aims of the present study were to evaluate the arrhythmogenic effects of impact with graded kinetic energy on the left ventricle of isolated rabbit heart and to analyze the initiation mechanisms of arrhythmia induced by myocardial contusion using high-resolution ventricular mapping.

Materials and Methods

Heart Preparation

Surgical Preparation. The principles for the care and treatment of experimental animals complied with the national guidelines of the French Ministry of Agriculture. Forty-six New Zealand rabbits weighing a mean of 3.6 ± 0.6 kg (\pm SD) were anesthetized with ketamine (50 mg/kg intramuscular), the trachea was intubated, and the lungs were mechanically ventilated with 100% O₂ (Logic 07, ATM, Maurepas, France). The surgical excision of the heart was performed as previously described.^{12,13} The heart was connected to a Langendorff perfusion system using Tyrode's solution at 37°C. The coronary arteries were perfused with a constant flow of 40–50 ml/min (Watson-Marlow 101U pump, Falmouth Cornwall, UK), resulting in a perfusion pressure of 70 ± 10 mmHg (Gould P23 Transducer, Oxnard, CA; CGR monitor, St-Cloud, France). The composition of Tyrode's solution was NaCl 130 mM, NaHCO₃ 20.1 mM, KCl 4.0 mM, CaCl₂ 2.2 mM, MgCl₂ 0.6 mM, NaH₂PO₄ 1.2 mM, and glucose 12 mM. The solution was saturated with a mixture of 95% O₂ and 5% CO₂, and pH was adjusted to 7.40 ± 0.02 .

Mechanism of Injury. Forty hearts were submitted to a localized injury. The heart was placed horizontally, and a metal stem was introduced into the left ventricle through the left atrium to hold the heart during contusion. Myocardial impact was produced by a ball decreasing from a predefined height within a hollowed cylinder that was placed just above the left ventricle and inflicted a precise blow nearly on the center of the left ventricle. The height was determined to deliver four different contusion kinetic energies: 75, 100, 150, and 200 millijoules (mJ). The ball weight was 12 g for contusions of 75, 100, and 150 mJ and 21.7 g for a contusion of 200 mJ.

Epicardial Mapping Study. High-resolution mapping of epicardial excitation was performed by applying to the epicardial surface a spoon-shaped electrode containing 256 unipolar electrodes at a regular distance of 2.25

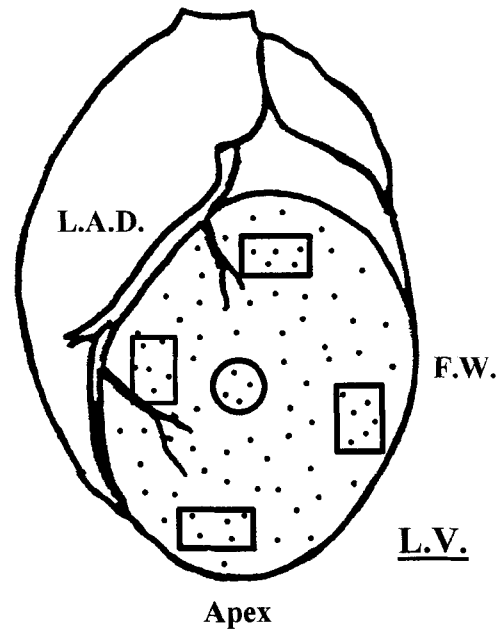


Fig. 1. The location of the spoon-shaped electrode on the left ventricle (LV). Unipolar electrograms were recorded from the mapping array (dotted area). The central circle indicates the main pacing site for the measurement of conduction velocities and ventricular effective refractory periods (VERP). Boxed areas on the left ventricle show the four other sites at which VERP was measured. FW = ventricular free wall; LAD = left anterior descending coronary artery.

mm (fig. 1). A computerized mapping system allowed simultaneous recording, storage, and automatic analysis of all 256 electrograms and on-line presentation of color-coded activation maps (Maptech System; Maastricht, The Netherlands).¹⁴

Protocols

Thirty hearts were used to study arrhythmogenic effects of myocardial contusion (intact hearts), and 16 hearts were submitted to an endocardial cryoprotocol to analyze the initiation mechanisms of arrhythmia (frozen hearts).

Intact Heart Protocol. The 30 hearts in the intact heart protocol were divided in five groups of six hearts each. In one group, no contusion energy was applied, but these six hearts were placed on the contusion apparatus to serve as a control group. In the other four groups, a contusion with kinetic energy of 75, 100, 150 or 200 mJ was produced. Variables were recorded before contusion (T-1), immediately after contusion (T0), and 5 min (T5), 15 min (T15), 30 min (T30), 45 min (T45), and 60 min (T60) after contusion. At the end of each experiment, the heart was removed from the per-

fusion system and fixed in formaldehyde 10% for histopathologic study.

Electrophysiologic Study. The number, nature, and time of occurrence of arrhythmias were studied. Moreover, we noticed in preliminary experiments that the impact might induce an electrically silent area or a line of fixed block. The electrically silent area was defined as an area with no significant electrical activity and where no pacing with twice the threshold intensity was possible. The occurrence of electrically silent area, the time for its disappearance, and line of fixed block occurrence were also reported.

Creatine Kinase Release. During the experiment, effluent samples of about 3 ml were collected in tubes for creatine kinase (CK) measurement and stored at -20°C until biochemical assays were performed. The concentration of CK was measured using the immunoinhibition method at 25°C by means of the *N*-acetylcysteine activated test on a Cobas Bio (Roche, Diagnostic GmbH, Mannheim, Germany).¹⁵ CK concentrations were expressed in International Units per liter (IU/l). The comparison of CK release between control and contusion groups was performed using the difference value between the concentrations just after the contusion (T0) and before the contusion (T-1) for each group.

Histopathologic Study. Hearts were dehydrated using graded ethanol, embedded in paraffin (Histocentre, Shandon, Runcorn, England), and cut into $5\text{-}\mu\text{m}$ -thick rings using a microtome (Reichert-Yung, Nussloch, Germany). Horizontal sections were mounted on glass slides with albumin (0.1% m/vol, BioLyon, Lyon, France). Three pieces of each heart were stained with hematein-eosin-safran for optical microscopic examination. These three pieces were removed from the bottom, center and tip of the impact area, as perceived macroscopically. The depth and extent of tissue disruption and tissue disorganization were noted for each specimen. The pathologist was blinded according to the control group and the different kinetic energy levels used.

Frozen Heart Protocol.

Cryoprocurement and Pacing Protocol. In 16 hearts, a previously described endocardial cryoprocurement^{12,16,17} was used to avoid epicardial breakthrough of longitudinal wavefronts from deeper layers and to allow complete mapping of electrical activation in two dimensions.^{12,13} As a result of this procedure, only a thin ($\approx 1\text{-mm}$ -thick) epicardial layer of the left ventricle free wall survived; the rest of myocardium was completely destroyed.¹⁶ It was previously demonstrated that in this thin surviving layer, refractoriness and conduction veloc-

ities were not affected by the procedure and remained stable for many hours, suggesting that the circulatory condition was adequate.^{12,16,17} At the end of the experiment, hearts were dissected to verify the efficacy of the cryoprocurement. When the freezing was not adequate, the heart was excluded from the study.

Programmed electrical stimulation was performed using a programmable constant current stimulator, which delivered square pulses of 2 ms duration at twice the diastolic threshold for both regular stimulation and induction of premature beats (Maptech System). Induction of ventricular arrhythmia was performed using a bipolar stimulation protocol in all frozen hearts and consisted of application of one, two, and three premature stimuli (S2, S3, and S4, respectively) delivered with decreasing coupling intervals after 10 basic stimuli (S1-S1) at 300-ms intervals, and application of a train of 10 stimuli at a regular cycle length that was progressively decreased in increments of 10-ms until one-to-one capture of the ventricle failed (Fmax).

Protocol and Electrophysiologic Measurements.

Forty-five min after freezing, two groups of hearts were administered a contusion with kinetic energy of 100 mJ ($n = 8$) or 200 mJ ($n = 8$). The contusion procedure was similar to that in the intact heart protocol. Parameters were determined before contusion (T-1), immediately after contusion (T0), and 20 min (T20), 40 min (T40), and 60 min (T60) after contusion. The following electrophysiologic parameters were studied: Ventricular effective refractory period (VERP, in milliseconds) at five sites, longitudinal ventricular conduction velocity (θ_L , in meters/second), transverse ventricular conduction velocity (θ_T , in meters/second), anisotropic ratio (θ_L/θ_T), longitudinal and transverse wavelength (λ_L and λ_T , respectively, in millimeters), index of VERP dispersion (DI) and maximum VERP dispersion (Dmax, in milliseconds).

Conduction velocity was defined as the distance traveled by the wavefront per time unit. In each experiment, both longitudinal and transverse conduction velocities and anisotropic ratio were measured after 10 basic stimuli (S1-S1) at 300-ms intervals. VERP was defined as the shortest S1-S2 interval still resulting in a propagated premature impulse during regular pacing with a S1-S1 interval of 300 ms. VERP was determined by decreasing the coupling interval of premature stimulus in 1-ms increments. Measurement of VERP was performed at the same five sites throughout the experiment (fig. 1). Wavelength was defined as the product of longitudinal (λ_L) or transverse (λ_T) ventricular conduction velocity, and the

CONTUSION-INDUCED ARRHYTHMIAS

Table 1. Arrhythmia and Electrical Disturbances Induced by Contusion in Intact Hearts

Contusion Energy	Arrhythmia		Electrically Silent Area		Line of Fixed Block	
	Nature	Time of Occurrence	Number	Time of Disappearance	Number	Time of Occurrence
Control	0	—	0	—	0	—
75 mJ	1 VF 1 NSVT	T5 T0	1	T60	2	1 T0, 1 T60
100 mJ	5 PVC	1 T5, 2 T15, 1 T30, 1 T40	4	1 T5, 1 T15, 1 T30, 1 T60	4	2 T0, 1 T30, 1 T60
150 mJ	1 NSVT 2 VF	1 T0 1 T0, 1 T30	3	2 T15, 1 lasting after T60	1	1 T15
200 mJ	5 VF	5 T0	5	2 T30, 3 lasting after T60	1	1 T30

n = 6 for each group.

VF = ventricular fibrillation; NSVT = nonsustained ventricular tachycardia; PVC = premature ventricular contraction.

VERP was measured at the center site. VERP dispersion was quantified by DI, defined as the quotient of SD and mean of VERPs for each heart, and Dmax, calculated by the difference between the maximum and the minimum values of VERP for each heart.

Definition of Ventricular Arrhythmia

We defined ventricular arrhythmia as VF with sustained or nonsustained ventricular tachycardia (SVT and NSVT, respectively). NSVT was defined as a ventricular tachycardia (VT) lasting more than three successive beats but less than 30 s before spontaneous termination. SVT was defined as a VT that lasted more than 30 s. Finally, a separation into monomorphic and polymorphic ventricular tachycardia (MVT and PVT, respectively) was made. The term MVT implies a uniform beat-to-beat QRS morphology. The term PVT was defined as the occurrence of continuous change in QRS configuration. When several types of arrhythmia occurred during a given experimental step, the worst arrhythmia was used.

Statistical Analysis

Except for the difference value between CK at T0 and CK at T-1, which was expressed in median and percentiles (5% and 95%), all parameters were expressed as mean \pm SD. The Kruskal-Wallis test and Bonferroni correction were used for the comparison of the CK release difference between intact heart groups. To show an arrhythmogenic and gradual effect of different contusion kinetic energies, Fisher exact test followed by a test of linear trend were performed. Two-way analysis of variance for repeated measures, followed by a contrast method, Neumann-Keuls test, and Bonferroni correction were used to list time or group effect on other parameters. $P < 0.05$ was considered to be statistically significant.

Results

Intact Heart

Arrhythmogenic Effect of Contusion. In the control group, no arrhythmias, no electrically silent areas, and no lines of fixed block were observed. All contusion groups showed arrhythmias (VF, VT, premature ventricular contraction), electrically silent areas, lines of fixed block, or a combination of these (table 1). In 13 of 24 hearts, electrically silent areas occurred after contusion: Four lasted more than 60 min, four others completely disappeared, and five were replaced by a line of fixed block. Lines of fixed block occurred in 8 of 24 hearts, either immediately (n = 3) or after occurrence of an electrically silent area (n = 5). All lines of fixed block lasted after 60 min. Numbers of arrhythmias ($P = 0.03$) and electrically silent areas ($P = 0.02$) increased with increasing kinetic energy of contusion.

Effect on the release of Creatine Kinase. The release of CK for each group is reported in figure 2. No change occurred in the control group. In contusion groups, concentration of CK increased transiently, with a maximum at T0. The median value (T0-T-1; 5% and 95%) was 14 IU/l (1, 80), 10 IU/l (5, 129), 87 IU/l (7.4, 129), and 103.75 IU/l (21.4, 245) for 75, 100, 150, and 200 mJ, respectively. All differences (T0-T-1) between control and contusion groups were statistically significant ($P = 0.02$); however, the differences between different contusion groups were not significant.

Histopathologic Study. The optical microscopic study of pieces of heart showed that all hearts that underwent contusion had cellular damage. In the impact area, myocardial fibers were disrupted on the surface. Vacuoles and nucleus pyknosis were observed in fiber cytoplasm. In the impact area, the fiber diameter was reduced, fibers were made round, and the extracellular

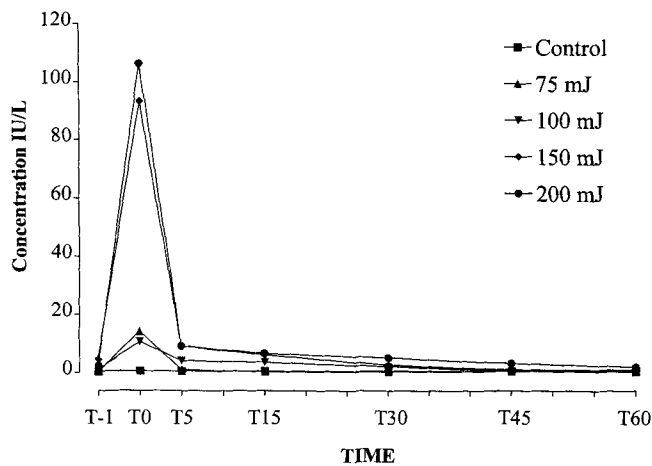


Fig. 2. Effect of four different contusion energies on creatine kinase release. Data are expressed as the median. ■ = control group; ▲ = 75-mJ group; ▼ = 100-mJ group; ◆ = 150-mJ group; ● = 200-mJ group.

medium was enlarged. The damage depth was significantly increased according to the kinetic energy impact: 45 ± 81 , 325 ± 157 , 517 ± 147 , 600 ± 77 , and $767 \pm 225 \mu\text{m}$ for control, 75, 100, 150, and 200 mJ, respectively ($P = 0.009$).

Frozen Heart

Two of eight hearts were excluded for inadequate freezing in the 100-mJ group. Data are therefore given for six hearts in this group.

Electrophysiologic Effects of Contusion. Ventricular conduction velocities were not significantly modified by contusion whatever the kinetic energy (fig. 3A). However, longitudinal conduction velocity was slightly slowed just after contusion ($P = 0.09$). Anisotropic ratio was not significantly modified; it changed from 2.01 ± 0.20 at T-1 to 1.87 ± 0.16 at T0 in the 100-mJ group and from 2.09 ± 0.24 at T-1 to 1.98 ± 0.43 at T0 for the 200-mJ group ($P = 0.368$). In contrast, VERPs were immediately shortened after contusion ($P = 0.0004$) and progressively lengthened in time ($P = 0.004$) over the two groups (fig. 3B). Longitudinal and transverse wavelengths for each group were shortened immediately after contusion ($P = 0.026$ for λ_L , and $P = 0.012$ for λ_T ; fig. 3C). Both λ_L and λ_T recovered their baseline values at T20. Parameters evaluating the dispersion of VERPs were modified in the same manner in the two groups of hearts. DI and Dmax were increased at T0 ($P = 0.0008$ and $P = 0.0052$, respectively) and returned progressively to their baseline values at T60 (figs. 4A and 4B).

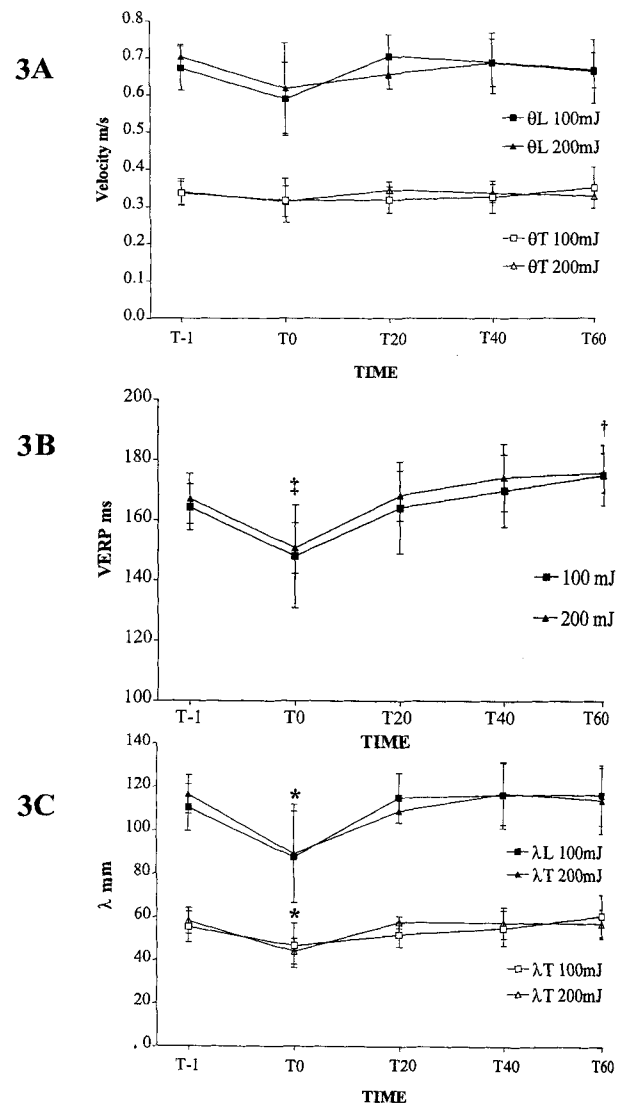


Fig. 3. Effect of contusion (100 mJ and 200 mJ) on (A) longitudinal and transverse conduction velocities (θ_L and θ_T , respectively), (B) ventricular effective refractory period, and (C) longitudinal and transverse wavelengths (λ_L and λ_T , respectively). Data are expressed as the mean \pm SD. Closed symbols correspond to longitudinal parameters (velocities and wavelength), and open symbols correspond to transverse parameters. Squares are used for 100-mJ group, and triangles are used for 200-mJ group. * $P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$; P depicted a significant time effect; no group effect was significant.

Arrhythmogenic Effects. Contusion-induced arrhythmias are reported in table 2. Both contusions with kinetic energy of 100 mJ and 200 mJ caused arrhythmias, electrically silent areas, or lines of fixed block. These arrhythmias were mainly monomorphic, and they were induced for the majority within the first 15 min after

CONTUSION-INDUCED ARRHYTHMIAS

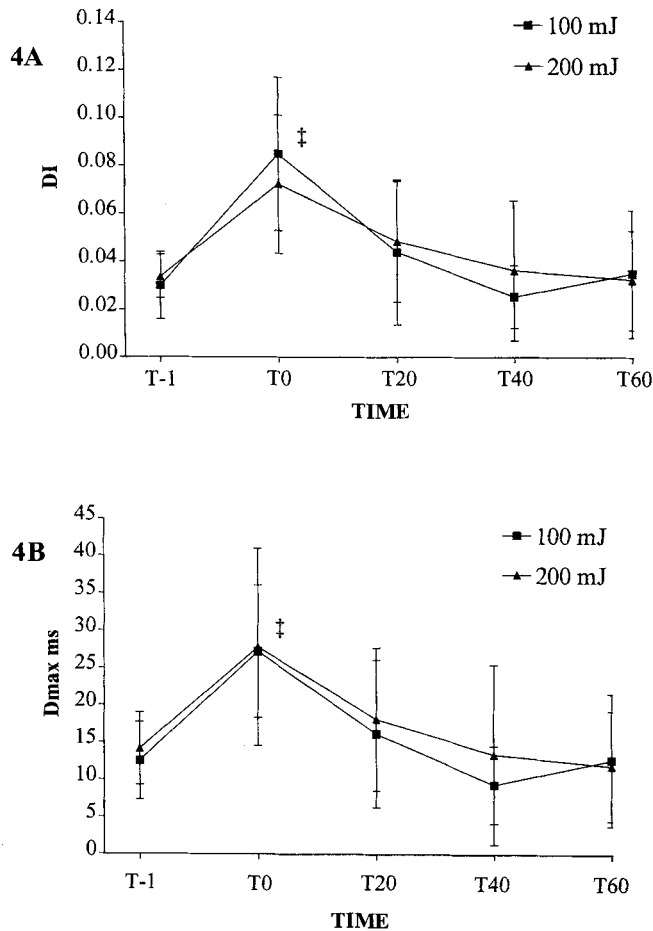


Fig. 4. Contusion effect on ventricular effective refractory period dispersion parameters: (A) dispersion index (DI), (B) maximal difference (Dmax). Data are expressed as mean \pm SD. \blacksquare = 100-mJ group; \blacktriangle = 200-mJ group. $\ddagger P < 0.001$; P depicted a significant time effect; no group effect was significant.

contusion. Analysis of the arrhythmias showed that all but one were based on a reentrant mechanism. Only one nonsustained arrhythmia in the 200-mJ group was the result of ectopic activity. This initiation mechanism was illustrated in four maps (fig. 5). Map 5A represents the epicardial activation before contusion. The pacing site was at the center, and the impulse propagated in two directions (longitudinal and transverse; $\theta_L = 0.75$ m/s, $\theta_T = 0.38$ m/s, $\theta_L/\theta_T = 1.97$) in an ellipsoidal manner. The next map (5B) was the epicardial depolarization after contusion and during the regular pacing cycle at 300 ms. An electrically silent area was observed at the center of the map. Thus, the impulse had to travel around it to depolarize epicardium behind the electrically silent area. Map 5C was obtained with an extrastimulus pacing ($S_2 = 153$ ms); the propagation of elec-

trical impulse occurred as in the previous mapping. The wavefront moved around the unexcitable area using two directions on each border of electrically silent area. The collision point of the two waves was 115 ms. On map 5D, spontaneous activity was illustrated. The ectopic site was located at the border of contusion impact area, and the propagation occurred surrounding the electrically silent area in the two directions.

All other VTs were based on a reentrant mechanism, but two different fixed obstacles were observed. In the two groups, two reentrant tachycardias were developed around the electrically silent area induced by the ball impact. One other VT in each group was due to a reentrant circuit around a line of fixed block that replaced the electrically silent area. An example of each reentrant mechanism is shown in figures 6 and 7. Figure 6 illustrates a sustained monomorphic ventricular tachycardia around an electrically silent area that was induced by a contusion of 100 mJ with a programmed pacing of three extrastimuli 13 min after contusion. However, analysis showed that this tachycardia was initiated after the second extrastimulus (S_3). Map 6A shows an epicardial depolarization after contusion with regular pacing ($S_1-S_1 = 300$ ms). At the map center is the electrically silent area that was produced by the impact. The impulse had to move around this region to depolarize other epicardial areas. Slowed conduction was observed close to the left anterior descending coronary artery; thus, the collision point of clockwise and counterclockwise waves was 54 ms, and this point was located above the electrically silent area. The activation of the epicardium after the second extrastimulus (S_3) is represented on map 6B. The propagation occurred only in the counterclockwise direction around the electrically silent area because of the appearance of a functional conduction block in the left anterior descending coronary artery corridor close to the pacing site. Thus, the epicardium previously activated by pacing (34 ms) could be depolarized again at 127 ms. Therefore, the reentrant circuit was initiated and propagated in an counterclockwise movement around the electrically silent area (6C). Panel 6D shows electrograms at some sites around the contusion area, and these allow observation of the advancement of the tachycardia.

The second reentrant mechanism is illustrated in figure 7. Rapid pacing induced a sustained monomorphic ventricular tachycardia (F_{max} , $S_1-S_1 = 145$ ms, but the tachycardia was induced before the last pacing [S_1] 16 min after a contusion impact with a kinetic energy of 100 mJ. Map 7A was the impulse propagation during the

Table 2. Arrhythmia and Electrical Disturbances Induced by Programmed Electrical Stimulation after Contusion in Frozen Hearts

Contusion Energy	Arrhythmia	Electrically Silent Area	
		Number	Recovery
100 mJ	2 SMVT, 1 NSMVT	3/6	T20
200 mJ	2 SMVT, 2 NSVT*	8/8	2 T20, 1 T40, 5 lasting after T60

* One monomorphic, one polymorphic.

SMVT = sustained monomorphic ventricular tachycardia; NSMVT = nonsustained monomorphic ventricular tachycardia; NSVT = nonsustained ventricular tachycardia.

regular pacing cycle (S1-S1 = 300 ms) immediately after contusion. On this mapping, an electrically silent area was observed; therefore, the impulse had to encircle this area to depolarize the epicardium. Thereafter (16 min after contusion), the electrically silent area disappeared and was replaced by a wide line of block (*i.e.*, line of

fixed block + functional conduction block that is located at the low part of block; 7B). The response of the epicardium to the last pacing is shown on map 7B. The wide line of conduction block delimited a zone near the left anterior descending coronary artery that was activated later. Thus, the area in front of the block, which

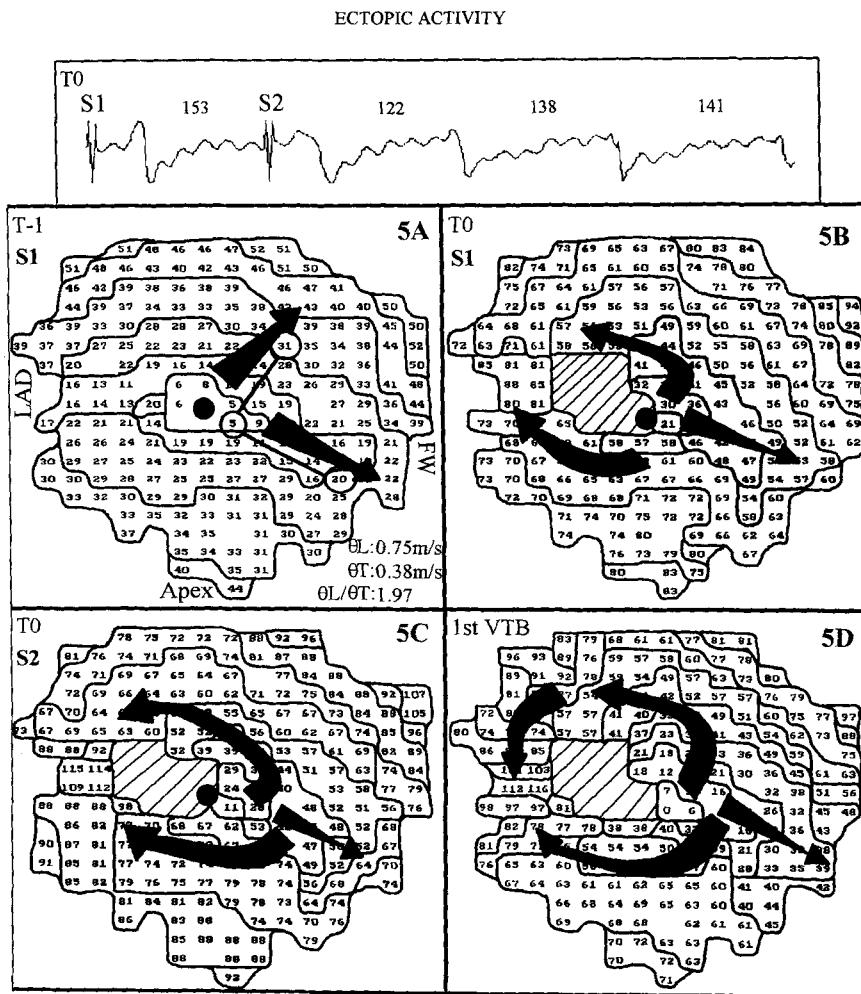


Fig. 5. Initiation of a nonsustained ventricular tachycardia induced after a 200-mJ contusion in left frozen ventricular epicardium. Electrogram recorded during induction of ventricular tachycardia using one extrastimulus (S2). Numbers above the recorded electrogram indicate time interval (in milliseconds) between two ventricular activations. Four consecutive activation maps are given and show the spread of depolarization. Numbers indicate local activation times in milliseconds. Isochrones are drawn at 10-ms intervals. Arrows indicate the direction of activation. The closed circle represents the pacing site. Surrounded activations time indicate the sites between which longitudinal (θ_L) and transverse (θ_T) conduction velocities were measured. The hatched area corresponds to the impact contusion zone with no electrical activity. (A) Shows activation of epicardium after the last stimulus (S1) before contusion (T - 1). (B) Depicts the activation of the epicardium after the last stimulus (S1) just after contusion (T0). (C) The depolarization of the epicardium after the extrastimulus (S2). The first beat of the nonsustained ventricular tachycardia (first VTB) is shown in D. All maps present the same frontal view of the heart. FW = ventricular free wall; LAD = left anterior descending coronary artery. (See text for further descriptions.)

REENTRY AROUND A LINE OF CONDUCTION BLOCK

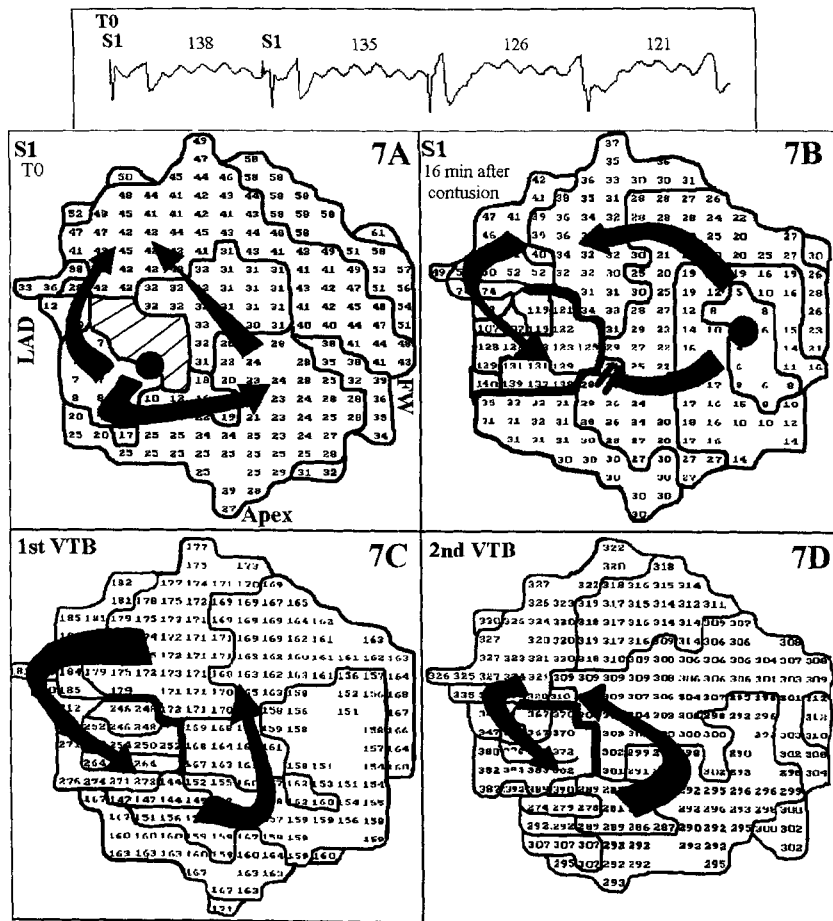


Fig. 7. Initiation of a reentrant ventricular tachycardia after a 100-mJ contusion in the left ventricular epicardium. (Top) Electrogram recorded during induction of ventricular tachycardia using rapid pacing (S1). Numbers above the recorded electrogram indicate time interval (in milliseconds) between two ventricular activations. Four consecutive activation maps are given and show the spread of depolarization. Numbers indicate local activation times in milliseconds. Isochrones are drawn at 10-ms intervals. The thick isochrones indicate local conduction blocks. Arrows indicate direction of activation. Double bars indicate the stop of influx propagation in the direction considered. The closed circle represents the pacing site. The hatched area corresponds to the impact contusion zone with no electrical activity. (A, B) Correspond to the epicardial depolarization after the regular pacing cycle (S1-S1 = 145 ms). A was recorded immediately after contusion (T0), B was recorded 16 min after contusion impact. The first beat of the sustained ventricular tachycardia (first VTB) is shown in C. The pattern of the depolarization during sustained monomorphic ventricular tachycardia (second VTB) is shown in D. All maps present the same frontal view of the heart. FW = ventricular free wall; LAD = left anterior descending coronary artery. (See text for further descriptions.)

whereas an impact with a velocity of 24 m/s, which corresponds to a kinetic energy of 108 J, results in VF.²⁰ In a model of isolated rat heart, Baxter *et al.*⁵ applied a direct contusion on the heart with impacts of 78 mJ/g and 87 mJ/g. These kinetic energies were chosen to generate a 25% and 50% decrease in ventricular function, respectively. In rabbit heart, other direct kinetic energies (from 358.2 to 432 mJ) were used to induce a 40% decrease in the maximum rate of left ventricular pressure change (dp/dtmax).²¹ In these studies, the chosen contusion kinetic energy criterion was hemodynamic depression. The current study used kinetic energy levels 4 to 10 times less than those used by Baxter *et al.*⁵; (delivered energies in our study were 9.4 mJ/g, 12.5 mJ/g, 18.8 mJ/g, and 25 mJ/g in the 75-mJ, 100-mJ, 150-mJ, and 200-mJ group, respectively, if we consider that a rabbit heart weighs about 8 g). However, the aim of the study was to evaluate the ability of an impact to impair elec-

trophysiologic parameters and to analyze the occurrence of arrhythmias. All contusion kinetic energies produced a release of CK and cell damage. The histopathologic study confirmed that hearts were injured and that impact kinetic energy was sufficient to produce gradual cell damage and myocardial contusion. The current study shows that the number and the seriousness of the arrhythmias were greater with increasing power of the injury.

Electrophysiologic Effects of Myocardial Contusion

In the frozen heart study, VERPs were significantly and transiently shortened by contusion. Additionally, a slight transient slowing of longitudinal ventricular conduction velocity was observed just after contusion. Consequent to the shortening of VERP and the slight slowing of conduction velocities, wavelengths were significantly shortened. Therefore, as it is well-established, the shorter the wavelength, the easier the reentry initiation.²²

The second electrophysiologic consequence of contusion was an accentuated dispersion of VERPs. Both of the two parameters used to evaluate epicardial heterogeneity were significantly raised after contusion. The increase in refractoriness dispersion and in the maximal difference between the longest and the shortest refractory periods were reported to be associated with the creation of epicardial functional block and the occurrence of reentrant arrhythmias (dispersion-based reentry).²³⁻²⁶ Therefore, all of these electrophysiologic alterations could enhance contusion-induced reentrant arrhythmia.

Arrhythmogenic Effect

The intact heart study confirms that myocardial contusion can induce lethal arrhythmias. Whatever the kinetic energy level used, rhythmic disturbances were observed; however, the occurrence and seriousness of arrhythmias increased with increasing kinetic energy. The impact area usually showed a transient electrically silent area, and the recovery time of electrical activity was longer when higher contusion kinetic energies were used. In some cases, the electrically silent area was replaced by a line of fixed block. One VF occurred with a contusion energy of 75 mJ, whereas none was observed at 100 mJ; however, five of six hearts presented premature ventricular contractions at 100 mJ, and none did so in the 75-mJ group. Moreover, the electrically silent area and the line of fixed block numbers are greater in the 100-mJ group than in the 75-mJ group, and we showed that these fixed blocks and areas could be responsible for arrhythmia initiation.

In the frozen heart study, two different mechanisms of arrhythmia initiation were analyzed. The first was an ectopic activity that initiated one NSVT after extrastimuli (fig. 5). The real mechanism of this spontaneous activity cannot be determined because our technique did not allow us to distinguish abnormal automatism from triggered activity. Therefore, we can only speculate that, as in acute myocardial infarction, the border area of the contusion could facilitate the occurrence of abnormal automatism.²⁷

The frozen heart study clearly shows that the main mechanism of arrhythmia due to myocardial contusion is based on reentry developed around a fixed obstacle. Two kinds of fixed obstacles were observed: An electrically silent area and a line of fixed block. Although the partial (*i.e.*, area becomes line) or complete excitability recovery of the electrically silent area remains unclear, the initiation of reentrant arrhythmias does not seem to differ from the model used by Brugada *et al.*²⁸ Using

high-resolution epicardial mapping in rabbit left ventricular epicardium, these authors studied reentrant tachycardia initiated around a fixed obstacle.^{28,29} In their model, the impulse used a circuit around a fixed obstacle leading to travel parallel, oblique, and transverse to the fiber direction; therefore, conduction velocities varied in the circuit according to the direction considered. Brugada *et al.*²⁸ observed that unidirectional block typically occurred in the longitudinal direction because of the lower safety factor in the longitudinal direction than in the transverse.³⁰ In our study, the unidirectional conduction block could therefore be due to the anisotropy of conduction around the fixed obstacle; however, the dispersion of refractoriness and shortened wavelengths were also observed. Spach *et al.*³¹ showed, in dog atria, that functional conduction block could result from a combination of repolarization heterogeneity and anisotropic propagation. We can therefore postulate that all these factors are simultaneously involved in the facilitation of reentrant arrhythmias induced by myocardial contusion.

In a recent study using a similar cryotechnique, Haberl and Alessie³² showed that a high concentration of potassium could terminate VT, whereas heptanol, which induced a similar depressed conduction, could reset arrhythmia. These different effects are explained by the fact that during potassium concentration increase the number of available sodium channels is reduced; thus, conduction block occurred and stopped VT. In our study, cellular lysis leads to a release of potassium in the extracellular medium. This increase in potassium level could explain the occurrence of functional conduction block, the slight slowing of longitudinal conduction velocity, or the transient electrically silent area and fixed block. However, in our Langendorff model, adequate perfusion of heart was maintained during the contusion experiment, inducing a quick wash-out of potassium and other substances released during cellular lysis. Further studies are necessary to determine the mechanism of block initiation and influx slowing.

Clinical Implications and Study Limitations

The current experimental study confirms that myocardial contusion *per se* induces lethal arrhythmias. However, a distinction must be made between ventricular arrhythmias induced by commotio cordis and that induced by myocardial contusion. Maron *et al.*⁷ reported 25 sudden deaths in young athletes after blunt impact. There were no cardiac structural abnormalities; only small contusions on the left side of the chest were

observed in 12 of 22 autopsies. These authors hypothesized that sudden death might be the result of apnea, vasovagal reflex, or ventricular arrhythmia. More recently, Link *et al.*⁸ demonstrated in a model of commotio cordis in anesthetized pigs that low-energy chest wall impact induces VF. VF occurs only when the impact happens within a window of 15–30 ms before the peak of the T-wave of the electrocardiogram. Because no significant cardiac injury was observed during autopsy, these authors concluded that commotio cordis induced by low-energy chest trauma (e.g., a baseball) could be responsible for immediate sudden death due to VF depending on the precise timing of impact on the chest. Clinical reports of these catastrophic events also described immediate sudden death after impact.⁷ Although an impact sufficient to cause a myocardial contusion could also induce immediate VF, probably due to the same mechanism, the fact remains that experimental clinical studies and the current study also reported delayed arrhythmias. In an open-chest dog model, Stein *et al.*³³ observed that fatal arrhythmia did not occur immediately, but appeared within 2 or 3 min after the impact. Fabian *et al.*¹⁰ reported that the major portion of patients with myocardial contusion developed significant arrhythmias within 24 h of admission. Baxter *et al.*³ observed that patients had arrhythmias and conduction defects more than 12 h after myocardial injury. In our study, the main cause of reentry initiation was the impact-induced occurrence of fixed conduction block (electrically silent area or line) and functional conduction block. These alterations could last for more than 60 min. Additionally, the current study and another experimental study of myocardial contusion showed that the occurrence and the seriousness of arrhythmias depend on the kinetic energy power.³⁴ All of these facts seem to justify early and postoperative cardiac monitoring, even in patients suffering from only moderate blunt chest trauma. Finally, Link *et al.*⁸ did not study various kinetic energies because they specifically studied commotio cordis. Our model was a myocardial contusion model, and the impact was not timed according to the cardiac cycle. Nevertheless, because the incidence of VF increases with increasing contusion power, and because the incidence of arrhythmia seems to depend especially on the appearance of a fixed obstacle, we can speculate that the more powerful the chest trauma, the more likely the occurrence of arrhythmia, whatever the cardiac cycle phase at impact.

Care must be taken before extrapolating our results to

the clinical setting. This study shows that contusion was responsible for arrhythmia, independent of hemodynamic or metabolic conditions. It is well-established that blunt chest trauma can cause hypoxia and a decrease in cardiac contractility and in output.^{21,33,35} These hemodynamic conditions could facilitate dysrhythmia. Furthermore, in the current study, hearts were denervated, and sympathetic nervous system stimulation induced by trauma is known to enhance the occurrence of cardiac arrhythmia.³⁶ One could argue that in the intact heart study, ventricular arrhythmia spontaneously occurred, whereas in the frozen heart study, VTs were induced by pacing. We can therefore only speculate that reentry facilitated by block, wavelength shortening, and repolarization dispersion as the main mechanism of contusion-induced arrhythmia. One could also argue that in the intact heart study, VFs were observed, whereas in the frozen heart study, there were especially MVTs. This difference may be related to the fact that elimination of four fifths of the left ventricular wall by the cryoprocure diminished the ventricular mass to such an extent that multiple reentering wavelets could no longer persist.³⁷ Because the impact was directly applied on the left ventricle, we cannot directly extrapolate our findings to blunt chest trauma. Finally, we studied only the left ventricle, yet the right ventricle is also widely involved in myocardial contusion.^{9,35} Nevertheless, the fact remains that impact on left ventricle can induce lethal arrhythmias that have been described in blunt chest trauma patients.

This study, performed in rabbit left ventricular epicardium, shows that myocardial contusion has direct arrhythmogenic effects that are independent from hemodynamic and metabolic conditions. The incidence and the seriousness of arrhythmias increase with increasing power of impact kinetic energy. Using a high-resolution mapping system, the analysis of arrhythmias in frozen heart shows that VTs are based mainly on reentry. Reentry is based on two mechanisms induced by the impact: A fixed block (electrically silent area or line of block) and a unidirectional conduction block facilitated by the shortening of the wavelength and an increase in the dispersion of refractoriness.

The authors thank the entire Pharmacy Staff of the University Hospital of Nîmes; Patrick Chartreux, Christian Francou, and the entire personnel of the Medical School Laboratory, especially Robert Sempère, for their skillful technical assistance; and Margaret Manson for her English assistance.

CONTUSION-INDUCED ARRHYTHMIAS

References

1. Prêtre R, Chilcott M: Blunt trauma to the heart and great vessels. *N Engl J Med* 1997; 336:626-32
2. Doty DB, Anderson AE, Rose EF, Go RT, Chiu CL, Ehrenhaft JL: Cardiac trauma: Clinical and experimental correlations of myocardial contusion. *Ann Surg* 1974; 180:452-60
3. Baxter BT, Moore EE, Moore FA, McCroskey BL, Ammons LA: A plea for sensible management of myocardial contusion. *Am J Surg* 1989; 158:557-61
4. Dodd KT, Mundie TG, Lagutchick MS, Morris JR: Cardiopulmonary effects of high-impulse noise exposure. *J Trauma* 1997; 43:656-66
5. Baxter BT, Moore EE, Synhorst DP, Reiter MJ, Harken AH: Graded experimental myocardial contusion: Impact on cardiac rhythm, coronary artery flow, ventricular function, and myocardial oxygen consumption. *J Trauma* 1988; 28:1411-7
6. Liedtke JA, Allen RP, Nellis SH: Effects of blunt trauma on coronary vasomotion, perfusion, myocardial mechanics, and metabolism. *J Trauma* 1980; 20:777-85
7. Maron BJ, Polliac LC, Kaplan JA, Mueller FO: Blunt impact to the chest leading to sudden death from cardiac arrest during sports activities. *N Engl J Med* 1995; 333:337-42
8. Link MS, Wang PJ, Pandian NG, Bharati S, Udelson JE, Lee MY, Vecchiotti MA, VanderBrink BA, Mirra G, Maron BJ, Estes NAM: An experimental model of sudden death due to low-energy chest-wall impact (commotio cordis). *N Engl J Med* 1998; 338:1805-11
9. Orliaguet G, Bodin L, Riou B: Contusion myocardique. *J Eur Urgences* 1993; 6:3-15
10. Fabian TC, Cicala RS, Croce MA, Westbrook LL, Coleman PA, Minard G, Kudsk KA: A prospective evaluation of myocardial contusion: Correlation of significant arrhythmias and cardiac output with CPK-MB measurements. *J Trauma* 1991; 31:653-9
11. Frazee RC, Mucha P, Farnell M, Miller FA Jr: Objective evaluation of blunt cardiac trauma. *J Trauma* 1986; 26:510-20
12. Robert E, Bruelle P, de La Coussaye JE, Juan JM, Brugada J, Peray P, Dautat M, Eledjam JJ: Electrophysiologic and proarrhythmic effects of therapeutic and toxic doses of imipramine: A study with high resolution ventricular epicardial mapping in rabbit hearts. *J Pharmacol Exp Ther* 1996; 278:170-8
13. Aya AGM, Robert E, Bruelle P, Lefrant JY, Juan JM, Pèray P, Eledjam JJ, de La Coussaye JE: Effects of ketamine on ventricular conduction, refractoriness, and wavelength. Potential antiarrhythmic effects: A high-resolution epicardial mapping in rabbit hearts. *ANESTHESIOLOGY* 1997; 87:1417-27
14. Alessie MA, Hoeks APG, Schmitz GML, Reneman RS: On-line mapping system for the visualisation of the electrical activation of the heart. *Int J Cardiac Imaging* 1987; 2:59-63
15. Bergmeyer HU, Breur H, Büttner H, Delbrück A, Laue D, Pilz W, Schmidt E, Schmidt FW, Stamm D, Szasz G: Empfehlungen der Deutschen Gesellschaft für Klinische Chemie. Standard-methode zur bestimmung der aktivität der creatine-kinase. *J Clin Chem Clin Biochem* 1977; 15:249-54
16. Alessie MA, Schalij MJ, Kirchhof C, Boersma L, Huybers M, Hollen J: Experimental electrophysiology and arrhythmogenicity: Anisotropy and ventricular tachycardia. *Eur Heart J* 1989; 10:8-14
17. de La Coussaye JE, Brugada J, Alessie MA: Electrophysiologic and antiarrhythmic effects of bupivacaine: A study with high resolution ventricular epicardial mapping in rabbit hearts. *ANESTHESIOLOGY* 1992; 77:132-41
18. Baosong L, Zhengguo W, Zhihuan Y, Huaguang L, Xiaoyan L: Experimental studies on the hemodynamic changes after thoracic impact injury. *J Trauma* 1996; 40:S68-70
19. Shears LL, Hill RC, Timberlake GA, Bearmer KC, Gustafson RA, Graeber GM, Murray GF: Myocardial performance after contusion with concurrent hypovolemia. *Ann Thorac Surg* 1993; 55:834-7
20. Lau VG, Viano DC, Doty DB: Experimental cardiac trauma: Ballistics of a captive bolt pistol. *J Trauma* 1981; 21:39-41
21. Pu Q, Mazoit JX, Cao LS, Mao W, Samii K: Effect of lignocaine in myocardial contusion: An experiment on rabbit isolated heart. *Br J Pharmacol* 1996; 118:1072-8
22. Rensma PL, Alessie MA, Lammers WJEP, Bonke FIM, Schalij MJ: Length of excitation wave and susceptibility to reentrant atrial arrhythmias in normal conscious dogs. *Circ Res* 1988; 62:395-410
23. Ogawa S, Furuno I, Satoh Y, Yoh S, Saeki K, Sadanaga T, Katoh H, Nakamura Y: Quantitative indices of dispersion of refractoriness for identification of propensity to re-entrant ventricular tachycardia in a canine model of myocardial infarction. *Cardiovasc Res* 1991; 25:378-83
24. Han J, Moe GK: Nonuniform recovery of excitability in ventricular muscle. *Circ Res* 1964; 14:44-60
25. Alessie MA, Bonke FIM, Schopman FJG: Circus movement in rabbit atrial muscle as a mechanism of tachycardia. II. The role of non-uniform recovery of excitability in the occurrence of unidirectional blocks, as studied with multiple microelectrodes. *Circ Res* 1976; 39:168-77
26. Robert E, Aya AGM, de La Coussaye JE, Pèray P, Juan JM, Brugada J, Davy JM, Eledjam JJ: Dispersion-based reentry: Mechanism of initiation of ventricular tachycardia in isolated rabbit hearts. *Am J Physiol* 1999; 276:H413-23
27. Wit A: Cellular electrophysiologic mechanisms of cardiac arrhythmias. *Cardiol Clin* 1990; 8:393-409
28. Brugada J, Boersma L, Kirchhof CHJ, Heynen VVTh, Alessie M: Reentrant excitation around a fixed obstacle in uniform anisotropic ventricular myocardium. *Circulation* 1991; 84:1296-306
29. Schalij MJ, Lammers WJ, Rensma PL, Alessie MA: Anisotropic conduction and reentry in perfused epicardium of rabbit left ventricle. *Am J Physiol* 1992; 263:H1466-78
30. Spach MS, Miller WT Jr, Geselowitz DB, Barr RC, Kootsey JM, Johnson EA: The discontinuous nature of propagation in normal canine cardiac muscle: Evidence for recurrent discontinuities of intracellular resistance that affect the membrane currents. *Circ Res* 1981; 48:39-54
31. Spach MS, Dolber PC, Heidlage JF: Interaction of inhomogeneities of repolarization with anisotropic propagation in dog atria: A mechanism for both preventing and initiating reentry. *Circ Res* 1989; 65:1612-31
32. Haberl K, Alessie M: Differential effects of a segment of slow conduction on reentrant ventricular tachycardia in the rabbit heart. *Circulation* 1999; 99:949-62
33. Stein PD, Sabbah HN, Viano DC, Vostal JJ: Response of the heart to nonpenetrating cardiac trauma. *J Trauma* 1982; 22:364-73
34. Anderson AE, Doty DB: Cardiac trauma: An experimental model of isolated myocardial contusion. *J Trauma* 1975; 15:237-44
35. Diebel LN, Tagett MG, Wilson RF: Right ventricular response after myocardial contusion and hemorrhagic shock. *Surgery* 1993; 114:788-93
36. Podrid PJ, Fuchs T, Caudinas R: Role of the sympathetic nervous system in the genesis of ventricular arrhythmia. *Circulation* 1990; 80:1103-13
37. Garrey WE: The nature of fibrillary contraction of the heart: Its relation to tissue mass and form. *Am J Physiol* 1914; 33:397-414