Accumulation of Technetium-99m Stannous Pyrophosphate in Contused Myocardium

James Downey, Robert Chagrasulis, David Fore, and Loren F. Parmley

University of South Alabama, Mobile, Alabama

The uptake of technetium-99m stannous pyrophosphate in contused myocardium was measured as a function of time from the insult. The free wall of the dog's left ventricle was surgically exposed and struck with a spring-loaded paddle. Pyrophosphate was injected intravenously from 1½ to 47½ hr after the injury. After ½ hr of incubation the hearts were removed and the Tc-99m content of contused and noncontused myocardium was measured. Pyrophosphate was concentrated in contused myocardium at all of the time periods tested. Contused-to-normal ratios for pyrophosphate uptake ranged from 8.1 (8 hr) to 41.9 (48 hr).

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Myocardial contusion is probably the commonest cardiac lesion resulting from non-penetrating trauma. Although it is a potentially fatal injury, the true clinical incidence of this lesion remains unknown. Autopsy studies (*1*) suggest that the frequency of myocardial contusion is relatively high in patients who have suffered a decelerative injury or blunt trauma to the thorax or abdomen. However, the diagnosis of cardiac contusion has been difficult to make for two reasons. First, the associated musculoskeletal injuries in these patients often mask the more subtle signs and symptoms of myocardial contusion. Second, even if the diagnosis is suspected, there are no reliable means to confirm the presence of myocardial contusion unless the more severe manifestations of cardiac injury appear—such as those due to valvular injury, or to disturbances of rhythm or conduction.

Because unanticipated cardiac death may occur in these patients, however, it is important that early identification of such lesions be made and appropriate precautionary measures taken. Electrocardiographic criteria are currently the primary means of diagnosing myocardial contusion (*2*). Unfortunately, the electrocardiographic changes are often nonspecific (*1,2*). Serum enzymes have been of little use in making the diagnosis, since enzymes of cardiac origin are usually masked by enzymes released from necrosing skeletal muscle (*2*). In addition, the most recent attempts to employ the cardiac-specific isozymes of CPK have met with only limited success in aiding the diagnosis (*5*).

Several recent studies (*6–8*) have indicated that radiolabeled pharmaceuticals may be of value in identifying cardiac contusions. At present, however, there are few quantitative data describing contused myocardium's ability to concentrate these tracers. The present study was undertaken, therefore, to measure this uptake and to see if it, like that in infarcted myocardium (*9,10*), varies with the age of the insult.

METHODS

Acute group (2–8 hr). Eleven mongrel dogs were used for the study. They were of either sex and weighed from 12 to 30 kg. Each was anesthetized with 4 mg/kg sodium pentobarbital intravenously. Under positive-pressure ventilation, the chest was opened in the fifth left interspace and the left-ventricular free wall was exposed by retracting the ribs and cutting the pericardium. Arterial pressure was monitored by a catheter inserted through a femoral artery and into the thoracic aorta. Ven-

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For reprints contact: James M. Downey, University of South Alabama, College of Medicine—MSB 3024, Dept. of Physiology, Mobile, AL 36688.

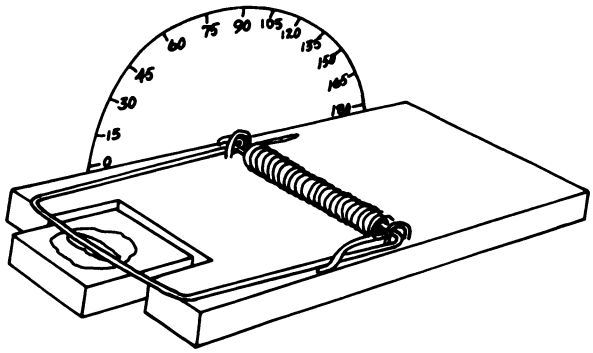

FIG. 1. Device used to produce open-chest myocardial contusion in dogs.

tricular pressure was monitored by another catheter inserted into the left carotid artery and past the aortic valve.

Contusions were induced by a spring-loaded paddle (Fig. 1). This was constructed from a rat trap with a 2-cm-square block attached to the bail. To induce a contusion the bail was pulled back with a force of 2.5 kg (an angle of 120°), and the base of the trap was pressed against the free wall of the left ventricle. The bail was then released, allowing the paddle to strike the epicardial surface.

From 1½ to 7½ hr after the contusion was created, Tc-99m stannous pyrophosphate (3 mCi and 8 mg of material) was injected intravenously as a bolus; after 30 min the hearts were removed, rinsed under tap water, and sectioned. Seven samples were removed from each heart: two epicardial and two endocardial samples from the contused region, an epicardial and an endocardial sample from a non-contused part of the left ventricle, and a sample of the full thickness of the right ventricle.

The tissue samples, approximately ¼ g apiece, were each placed in a counting vial containing 2½ ml of 10% formalin. The vials were counted in a well scintillation counter.

Chronic group (24 and 48 hr). In this group six dogs were prepared with cardiac contusions, allowed to recover, and then restudied at 24 or 48 hr after the initial insult. The dogs were anesthetized with 4 mg/kg of sodium pentobarbital intravenously and a small thoracotomy in the left fifth interspace was performed under sterile conditions. A contusion was made on the left free wall as in the acute group, and the chest wall was repaired using silk suture. The animals were returned to the kennels where all recovered from the operation uneventfully. At 23½ or 47½ hr after contusion the animals were reanesthetized and given the labeled pyrophosphate as an i.v. bolus. One-half hour later the heart was removed and prepared as described above. Hemodynamic measurements as described for the acute group were taken only during the restudy.

RESULTS

Following impact with the paddle, small epicardial hemorrhages often gave the region a variegated appearance. In all of the acute studies the region retained a bright red color in situ as if it were in a hyperemic state. Table 1 relates the uptake of the pyrophosphate in contused vs non-contused tissue. The counts per minute per gram of the three non-contused samples were consistently similar for each of the hearts. These were therefore pooled for each heart and used as a normalizing standard. The ability to concentrate the tracer is measured by the ratio of

TABLE 1. RATIO OF Tc-99m PP_i PER GRAM OF CONTUSED EPICARDIUM TO THAT IN UNINJURED MYOCARDIUM FROM SAME HEART*

	Hours				
Dog No.	2	4	8	24	48
1	17.1	8.6	10.9	8.8	102.7
	11.7	10.3	7.4	26.4	77.2
2	2.8	28.6	10.0	35.3	26.6
	1.2	2.5	7.2	29.3	9.9
3	23.0	16.6	9.0	52.2	23.4
	7.0	22.8	4.4	28.5	11.8
4		5.9			
		8.3			
5		11.6			
		12.9			
Mean	10.4	12.8	8.1	30.1	41.9
Range	1.2–23.0	2.5–28.6	4.4–10.9	8.8–52.2	9.9–102.7
No. of dogs	3	5	3	3	3

* Each dog yielded two samples; two ratios are listed for each.

cpm/g for contused myocardial tissue to the cpm/g for the noncontused, pooled average.

Figure 2 shows the average uptake ratio calculated for each time interval. The solid bars indicate epicardial samples while the open bars represent endocardial samples. The epicardial ratios were high, ranging around 10, even in the earliest samples, and they remained high, often increasing, even at 48 hr. The subendocardial samples consistently showed a lower uptake of pyrophosphate, probably because less damage was present at that depth.

At necropsy, the contused heart tissue in the 24- and 48-hr groups had the blanched appearance identical with that of an infarcted heart suffering from a coronary occlusion of comparable age.

Table 2 shows the hemodynamic data from these animals. The contusion had no effect on systolic or diastolic pressure, heart rate, or left ventricular end-diastolic pressure in the 2- to the 8-hr groups. Furthermore, the 24- and the 48-hr dogs were found to have hemodynamic findings within normal limits on restudy.

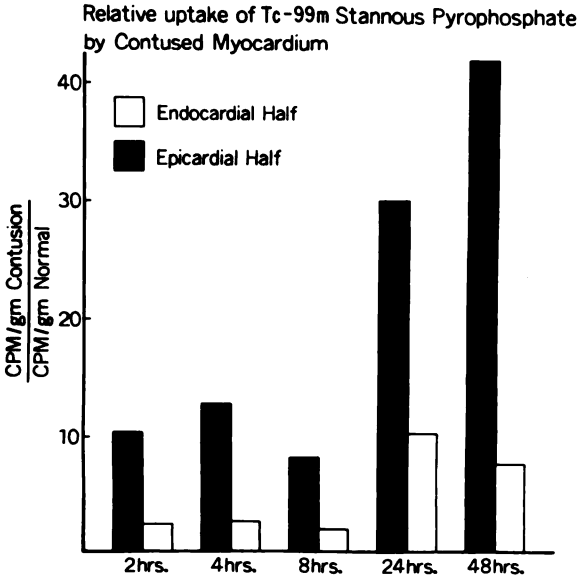

FIG. 2. Histogram showing uptake of Tc-99m stannous pyrophosphate by contused myocardium as a function of time after contusion and myocardial depth.

DISCUSSION

These experiments clearly indicate that contused myocardium does sequester pyrophosphate in quantity. Pyrophosphate has been shown to concentrate in burned myocardium (*11*) and probably has an affinity for dying muscle regardless of the cause of cell death. What is surprising is the speed with which the contused myocardium will take up pyrophosphate. Following occlusion of a coronary artery,

TABLE 2. HEMODYNAMIC DATA FROM CONTUSED ANIMALS

			Precontusion			Postcontusion*			
Dog No.	Kg	Heart weight (g)	AoP† mm Hg	LVEDP‡ mm Hg	Heart rate	AoP† mm Hg	LVEDP‡ mm Hg	Heart rate	Hr§
740	18	100	115/95	5	155	132/109	7	127	2
768	17	—	120/107	1	186	132/94	4	150	
770	15	77	118/104	10	126	127/105	5	144	
780	20	128	145/112	7	149	135/95	10	169	4
796	11	—	120/106	2	163	135/118	2	195	
811	24	121	160/115	4	144	125/95	15	184	
800	12	—	180/80	5	142	125/100	5	154	
819	24	91	137/107	2	166	115/90	2	197	
814	18	111	130/104	1	181	140/100	1	208	8
824	19	83	130/110	1	144	95/70	1	182	
29	30	195	125/100	5	178	115/88	5	178	
M ± s.d.			125 ± 13/103 ±10	4 ± 3	158 ± 18	125 ± 13/97 ± 12	5 ± 4	171 ± 25	
7	20	116	—	—	—	132/107	2	155	24
11	19	104	—	—	—	157/132	5	158	
27	26	117	—	—	—	139/116	6	143	
827	26	150	—	—	—	117/95	6	166	48
821	20	109	—	—	—	141/	2	217	
25	28	155	—	—	—	125/100	1	175	
M ± s.d.						143 ± 13/110 ± 13	3 ± 2	169 ± 25	

* Postcontusion measurements were taken just before removal of hearts for sectioning.
† Aortic pressure.
‡ Left-ventricular end-diastolic pressure.
§ Hours refer to time between contusion and administration of tracer. Dogs were killed ½-hr later.

pyrophosphate does not begin concentrating in the ischemic tissue until about 6 hr after occlusion, and does not reach peak specificity until after a day or two (*10,12*). In the present study, however, even the initial 2-hr study showed very high concentrations.

Figure 2 indicates that the uptake of pyrophosphate increased with increasing intervals between the time of contusion and administration of the tracer. This increase, however, may be only apparent. In the acute group the contused areas were difficult to visualize. Though the region struck by the paddle was hyperemic in situ, the hearts turned a uniformly dusky color upon removal from the chest. Other than occasional hemorrhages in the tissue, particularly where the edges of the paddle struck the heart, the affected myocardium often appeared the same as the non-involved muscle. Thus we had to rely on epicardial landmarks to remove the samples from the contused region. The early samples, therefore, probably contained a mixture of both dead and viable tissue, which would cause an underestimation of the true ratio. On the other hand, the 24- and 48-hr groups had clearly visible regions of necrosis, so it was easy to remove only the necrotic regions for counting. In any case, the uptake is of sufficient magnitude for scintigraphic imaging over the entire range of time periods studied.

Go et al. (*8*) produced large cardiac contusions in five closed-chest dogs using a captive-bolt handgun. Tc-99m-labeled polyphosphate produced positive scintigrams in all of these animals. Only two of these, however, were examined to determine the tissue distribution of the tracer. One of these, 3 hr after contusion, yielded an injured-to-normal ratio of 14, whereas the other, 48 hr after contusion, showed a ratio of only 4.5. In the present study pyrophosphate gave much higher ratios at all time intervals, and there certainly was no suggestion of diminished uptake at 48 hr.

Figure 2 also shows that little subendocardial uptake was realized. The insult was delivered to the epicardium and apparently did not induce transmural damage. Gross examination of the 24- and 48-hr hearts indicated that necrosis was limited to the outer half of the ventricular wall. When all of the epicardial samples from all time groups were pooled, a ratio of 19.7 resulted for the differential uptake of pyrophosphate. This is not far from the values of 22–28 reported for myocardial infarction in dogs (*11,12*).

The present model of cardiac contusion seems to produce reproducibly an injury that results in cell death, as evidenced by the 24- and 48-hr animals. Previous models of cardiac contusion have been described by others for both open chest (*13*) and the closed chest (*3,6,8*). Though the present model is the simplest, it seems to be quite adequate. In fact one of the advantages of this model is that it is not complicated by depressed pump function. Our hemodynamic data showed no significant changes. Previous animal (*3,6*) and clinical (*6,14*) reports indicate that impaired pump function may follow cardiac contusion. Such was clearly not our finding, since our contusions were small ($\approx$ 4 cm^3) and involved relatively little myocardium. Experimental occlusions of the left anterior descending coronary artery of the dog involve about the same volume of tissue, and in our experience these also cause little alteration of hemodynamic function (*15*).

In summary, contused myocardium over the period of 2 to 48 hr was found to concentrate Tc-99m stannous pyrophosphate in quantities comparable to those in ischemic injury.

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