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Abstract

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KEYWORDS: segmental STI, nitroglycerin

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**EFFECT OF MYOCARDIAL ISCHEMIA AND
NITROGLYCERIN ON SYSTOLIC TIME
INTERVALS IN THE SEGMENTAL
MYOCARDIUM**

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Abstract. Effects of ischemia and nitroglycerin on systolic time intervals in the segmental myocardial length were studied in anesthetized open-chest dogs. Two strain-gauges were sutured on the surface of the left ventricular wall; one was in the central area perfused by the left circumflex coronary artery (LCX) and the other was in the area perfused by the left anterior descending coronary artery. LCX was partially occluded with a screw type constrictor to the degree at which reactive hyperemia after the transient total coronary occlusion almost disappeared. After the hemodynamics stabilized nitroglycerin (20 $\mu\text{g}/\text{kg}$) was injected into the femoral vein. In the ischemic area, contraction time was shortened and precontraction time was prolonged in association with an elongation of end-systolic and early systolic segment-length, respectively. The systolic time intervals in the ischemic segment were improved as a result of the recovery in the segment-length toward the control.

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Key words: segmental STI, nitroglycerin

Since Tennant and Wiggers (1), the contractile characteristics of ischemic myocardium have been studied extensively. Experimental studies (2, 3) have indicated that coronary occlusion produces an immediate and substantial decrease in segmental length even in the mildly or moderately ischemic zone. The first mechanical event that occurs during coronary occlusion is a marked reduction in systolic shortening manifested by end-systolic bulging (4, 5). This is followed by early systolic elongation of ischemic segment with a development of end-systolic bulging. The difference in systolic shortening by the normal and ischemic myo-

cardium results in the lack of synchronous contraction of the ventricular wall and diminished left ventricular performance. Nitroglycerin considerably improves segmental myocardial functions as reflected in improvement of cardiac performance (6, 7). Clinically, in patients with left ventricular dysfunction due to chronic coronary disease, ventriculographic studies have shown that nitroglycerin is beneficial for ischemic regional myocardial function (8).

A recent study (9), using the Walton Brodie strain gauge, showed that during ischemia there was not only a reduction in force and rate of force development, but also a marked shortening of the time-to-peak force and the duration of contraction. In spite of the report, however, the systolic time intervals (STI) of the segmental myocardial length have not been sufficiently examined.

The present study was therefore designed to analyze the contraction pattern of the regional STI of the ischemic myocardium and the effects of nitroglycerin on the STI in comparison with left ventricular ejection time.

METHODS

The experiments were performed on 17 healthy dogs, ten were used for coronary constriction and seven for control, while anesthetized with sodium pentobarbital (25-30 mg/kg intravenously). The animals were ventilated with an endotracheal tube connected to an intermittent positive pressure pump. A polyethylene tube was introduced through the right femoral vein for intravenous injection. A stiff bore catheter was placed in the thoracic aorta through the right femoral artery for monitoring aortic pressure. This catheter was connected directly to a Nihonkoden MPU-0.5 strain-gauge. The heart was exposed through a thoracotomy in the left fifth intercostal space in the right lateral position and supported in a pericardial cradle. The circumflex coronary artery (LCX) was isolated and an electromagnetic blood flow transducer (Type MF-26, Nihonkoden, Tokyo) was positioned 1-2cm distal to its origin. A screw type constrictor and a loose ligature were placed just distal to the transducer. The ends of the ligature were threaded through a short plastic tube for occluding the vessel. Another electromagnetic flow probe was placed in aortic root for measuring aortic blood flow. A segment-length strain gauge (Type HDS-1T, Nihonkoden, Tokyo) was sutured onto the midlateral surface of the left ventricle, perpendicular to the interventricular septum. A segment of approximately 1.0cm of the myocardium was occupied between the struts of the strain gauge, and the suture bites penetrated to a depth of approximately 2-3mm.

In ten dogs (constricted group) the LCX was partially occluded with the constrictor to a degree that reactive hyperemic response following 15-second occlusion almost disappeared; peak reactive hyperemia was below 120% of control flow rate. The control group (seven dogs) were similarly instrumented except for coronary constriction.

After preparation was completed a bolus of 20 μ g/kg of nitroglycerin was

administered intravenously via the tube placed in the right femoral vein. Hemodynamic measurements and segmental length were recorded on a Saneisokki model RF-301 polygraph at paper speed of 100 mm/sec.

The unpaired Student's t-test was used for comparisons of the data between the groups, and paired Student's t-test was used for comparisons within the group.

The segmental length curve was named at the four points and analyzed as illustrated in Fig. 1. The point A and the point B were coincident with the end of diastole and the early phase of ejection, respectively.

The point C was the end of the segmental contraction. The precontraction time (PCT) was measured from the beginning of ejection (point A) to the point B and contraction time (CT) was from the point B to the point C. Left ventricular ejection time (LVET) was obtained from central aortic pressure curve.

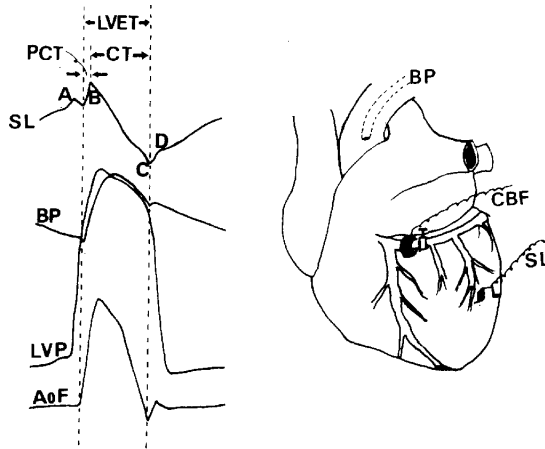


Fig. 1. Experimental preparation and analytical methods of segmental length tracing.

PCT=precontraction time

CT=contraction time

LVET=left ventricular ejection time

RESULTS

Effects of coronary constriction. The coronary constriction caused no significant changes in heart rate, aortic blood pressure or aortic blood flow, whereas LVET ($P < 0.01$) and CT ($P < 0.001$) were significantly shortened accompanied by a decrease in end systolic segment-length (Table 1). The extent of early systolic length (point B) was increased by 44.9% ($P < 0.01$) associated with a prolongation of PCT in the ischemic segment (Table 1, Figs. 2, 3). As PCT and CT changed in relation to a change of LVET (heart rate), the ratios of PCT and CT to LVET (PCT/LVET and CT/LVET) were used for representing the real

values of segmental systolic intervals independent of heart rate. The PCT/LVET was increased by 57.4% ($P < 0.001$) and CT/LVET was reduced by 20.2% ($P < 0.001$) as illustrated in Fig. 3.

TABLE 1. EFFECTS OF NITROGLYCERIN ON REGIONAL SYSTOLIC TIME INTERVALS IN THE GROUP WITH CORONARY CONSTRICTION.

		PCT (msec)	CT (msec)	LVET (msec)	B-C distance (g)	PCT/LVET	CT/LVET
Before constriction	Mean	32	146	166	20.3	0.192	0.874
	SD	14	20	30	4.3	0.066	0.168
After constriction	Mean	46	114	159	15.1	0.290	0.180
	SD	10	26	27	4.8	0.064	0.180
1 min after nitroglycerin	Mean	35**	124*	156	16.8#	0.228*	0.790**
	SD	10	33	25	4.1	0.073	0.191
3 min after nitroglycerin	Mean	40*	121**	158	17.4#	0.258#	0.766**
	SD	14	36	28	3.8	0.081	0.204
5 min after nitroglycerin	Mean	42#	123**	159	16.6	0.265#	0.772**
	SD	10	37	27	5.0	0.065	0.211
10 min after nitroglycerin	Mean	44	121	159	16.0	0.280	0.764#
	SD	14	36	27	4.6	0.093	0.207

PCT=precontraction time

CT=contraction time

LVET=left ventricular ejection time

Significant difference from the values before the injection of nitroglycerin (after constriction); ** $P < 0.001$, * $P < 0.01$, # $P < 0.05$

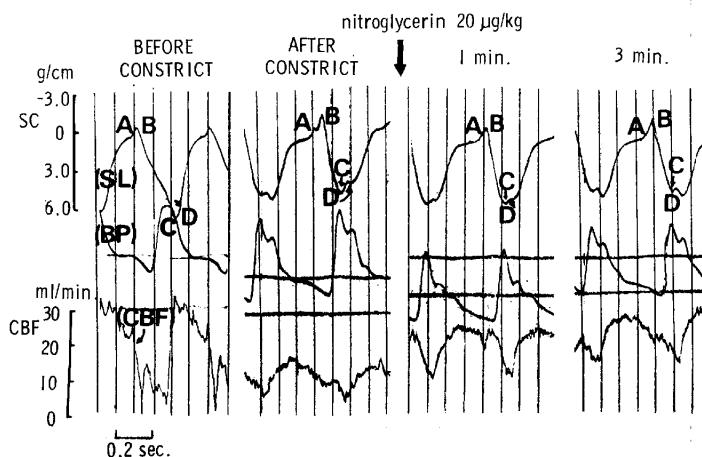


Fig. 2. An actual case where nitroglycerin was administered during partial coronary occlusion.

SL=segmental length

BP=aortic blood pressure

CBF=coronary blood flow

Effects of nitroglycerin. Effects of nitroglycerin are summarized in Tables 1 and 2.

Nitroglycerin decreased blood pressure and associated cardiac output by increasing heart rate within one minute after the injection. The percent changes in these variables in the group with partially occluded coronary artery were the same as those in the group with normal coronary artery.

The early systolic dimensions (point B) tended to fall ($34 \pm 37\%$, $P < 0.05$) in the ischemic group and fell ($16.7 \pm 12.4\%$) in the control group (NS) at one minute after nitroglycerin was injected. The distance between the point B and the point C (B-C distance) was slightly but significantly increased in the constricted group ($P < 0.05$) because of a decrease in the end-systolic dimension, while in the control group the B-C distance was not changed essentially. All variation in segmental systolic time intervals (segmental STI) tended to reduce in the control group; the maximum decrease was 10.7% in PCT (NS), 12.9% in CT ($P < 0.001$) and 3.3% in LVET ($P < 0.05$). In constricted group, however, nitroglycerin prolonged CT toward the pre-constriction value in spite of a greater decrease in PCT than that of control group (Fig. 4). These resulted in insignificant changes

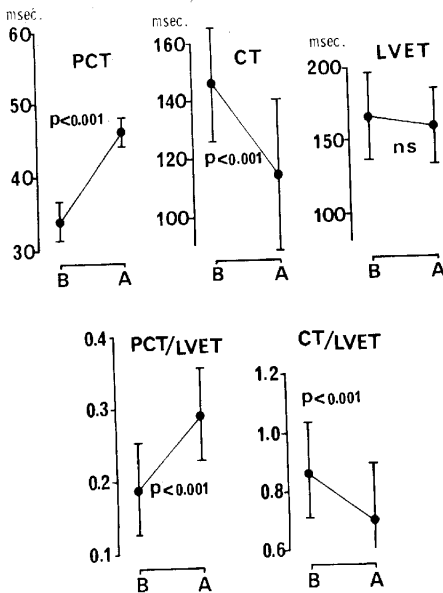


Fig. 3. Effects of the coronary constriction on systolic time intervals. PCT=precontraction time CT=contraction time LVET=left ventricular ejection time

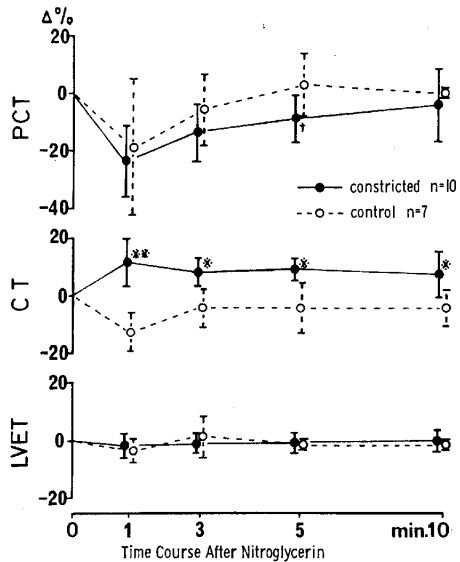


Fig. 4. Percent changes in precontraction time(PCT) and contraction time of segmental length, and left ventricular ejection time (LVET) following the injection of nitroglycerin. Significant difference in the changes between the coronary constriction group and the control group; ** $P < 0.001$, * $P < 0.01$, + $P < 0.05$,

in LVET. CT/LVET in the control group was rather lower with nitroglycerin. However, administration of nitroglycerin during the coronary constriction increased the ratio of CT to LVET significantly toward the pre-constriction level. The increase in CT/LVET lasted longer than 10 min after nitroglycerin. PCT/LVET was decreased marginally in the control group and significantly in constricted group until five min after the injection (Fig. 5).

TABLE 2. EFFECTS OF NITROGLYCERIN ON SEGMENTAL SYSTOLIC TIME INTERVALS IN THE CONTROL GROUP.

		PCT (msec)	CT (msec)	LVET (msec)	B-C distance (g)	PCT/LVET	CT/LVET
Before nitroglycerin	Mean	45	150	162	15.1	0.289	0.935
	SD	22	36	17	3.1	0.145	0.245
1 min after nitroglycerin	Mean	38	132**	157#	14.1	0.251	0.838**
	SD	17	40	20	2.4	0.105	0.219
3 min after nitroglycerin	Mean	42	144	165	16.1	0.261	0.875#
	SD	20	37	22	2.3	0.127	0.208
5 min after nitroglycerin	Mean	45	143	160	16.6	0.291	0.898
	SD	20	37	20	2.6	0.137	0.226
10 min after nitroglycerin	Mean	44	142	161	16.3	0.285	0.889
	SD	17	33	17	2.4	0.140	0.201

PCT=percontraction time, CT=contraction time,
LVET=left ventricular ejection time.

Significant difference from the values of the injection of nitroglycerin; ** $P < 0.001$,
$P < 0.05$

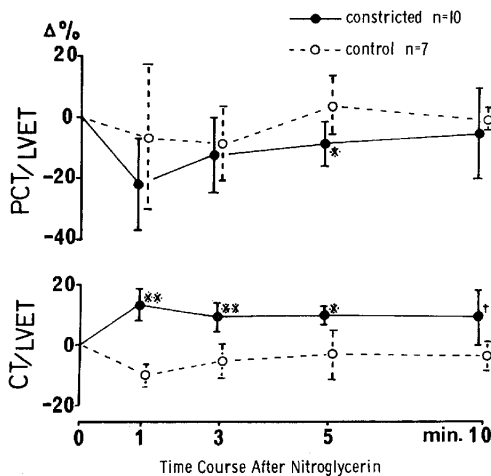


Fig. 5. The ratio of precontraction time (PCT) and contraction time (CT) to left ventricular ejection time (LVET).

Significant differences between the coronary constriction group and the control group; ** $P < 0.001$, * $P < 0.01$, † $P < 0.05$.

DISCUSSION

It is important to exercise caution in the use of data obtained from strain-gauge arches stitched to the epicardium (10, 11). Strict attention was paid to obtaining firm attachment of each limb of the gauge to muscle and an effort was made to apply the gauge in the same relative position on each heart.

The initial elongation (point B) at the epicardial surface of the base of the left ventricle was due to blood flow from the apex to the base, since the latter region was generally presumed to be the last portion of the ventricle to be excited (12). Sarnoff *et al.* (13) suggested that pressure in the heart was produced by the sequential and progressive development of tension in the myocardium while other portions remained uncontracted. When each of the several segments contracted independently of any programmed sequence, little work was accomplished (14, 15). Conversely, if the myocardial fibers contracted almost synchronously, external cardiac work is enhanced (16). Experimental (3-5) and clinical (17, 18, 20) observation revealed that ischemic myocardium displayed abnormal systolic wall motion expressed as hypokinesis, akinesis or dyskinesis. To our knowledge, though many works concerning regional function in the ischemic myocardium were reported, systolic time intervals in segmental myocardium have not previously been analyzed as indices of regional myocardial function. Theroux, *et al.* (19) and Tomoda, *et al.* (9) observed decreased duration and amplitude of shortening in the ischemic zone within ten beats following the total coronary occlusion, and the beneficial effects of nitroglycerin or reoxygenation on the segmental contraction. The pressure-length loop of ischemic zone demonstrated by Forrester, *et al.* (21, 22) suggested the progressive decrease in duration of shortening with stepwise coronary flow reduction. In these reports, however, no quantitative analysis was made of systolic time intervals of segmental contraction. In the present study, the moderately ischemic myocardium exhibited increased PCT and decreased duration of active shortening (CT) accompanied by a slight elongation of early systolic length and reduced amplitude of shortening in the ischemic segment. In addition, decreased systolic contraction induced by myocardial ischemia was ascribed to a shift of the endpoint of shortening (point C₀) not to the point C₂, but to the point C₁ as illustrated in Fig. 6. The reduction of CT and the prolongation of PCT resulted in a lack of synchrony in contraction between the ischemic and the normally perfused region. Accordingly, analyzing the segmental STIs might contribute favourably to verifying the asynchronous contraction of the ventricle.

The beneficial effects of nitroglycerin on the ischemic myocardium are well known. Klausner (23) observed in seven patients of angina pectoris that nitroglycerin, similarly postextrasystolic potentiation, normalized each segmental

ejection fraction. Improvement of systolic motion of some hypokinetic and akinetic segments with nitroglycerin was reported from many laboratories (23-25). In the present investigation, nitroglycerin during partial coronary occlusion improved both abnormally prolonged PCT and extraordinarily shortened CT, so that PCT/LVET and CT/LVET returned toward the control level. These results also suggest the favourable effect of nitroglycerin in reforming asynchronous movement of myocardium in the ischemic region.

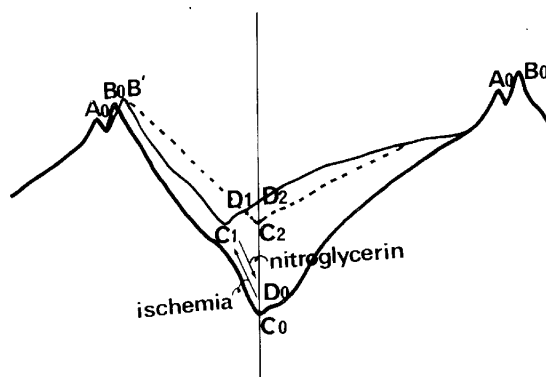


Fig. 6. The schematic illustration of the effects of myocardial ischemia and nitroglycerin on segmental myocardial length. Ischemia shifted the point C₀ to the point C₁, not to the point C₂. During coronary constriction nitroglycerin moved the point toward the control in the ischemic segment.

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