AN ELECTROGRAPHIC STUDY ON THE FUNCTIONAL CAPACITY OF THE CORONARY COLLATERAL CIRCULATION IN DOGS WITH CHRONIC CORONARY OCCLUSION

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The functional capacity of coronary collaterals was investigated under resting and stress conditions in 15 dogs with chronic occlusion of the anterior descending coronary artery. ST-elevation in epicardial and intramyocardial electrograms was used for assessing the degree of regional myocardial ischemia. In resting condition, epicardial and intramyocardial electrograms from collateral, intermediate and circumflex areas revealed no significant ischemic changes. In 6 of 15 dogs in which atrial pacing was performed, ST-elevation appeared in electrograms from collateral and intermediate areas. In another 9 dogs, pacing tachycardia produced no significant changes in all electrograms. In these dogs more than 50% constriction of the donor coronary artery was necessary to induce ST-elevation in electrogram from collateral area. These findings indicate that the coronary collateral vessels in dog play beneficial role to prevent the myocardium from ischemic injury under stress condition, although their functional capacity is not comparable to that of normal coronary artery.

ALTHOUGH recent studies using coronary angiography demonstrated the presence of coronary collateral vessels in the ischemic heart, there are diverse opinions about the role of the coronary collateral circulation in the preservation of regional myocardial function and in the prognosis of the ischemic heart disease. Many experimental studies, on the other hand, reported the beneficial effects of the collaterals on regional myocardial flow, electrical ischemic injury, ventricular fibrillation threshold, survival rate after coronary ligation and regional myocardial contraction.

Flameng et al. reported that blood supply to the myocardium by collateral vessels is equal to normally perfused area in resting condition, but a marked difference in myocardial perfusion between two areas appears following administration of coronary vasodilating agents plus tachycardia. The degree to which these collateral vessels serve to supply blood to the ischemic myocardium still remains to be solved. It is, therefore, necessary to define the functional capacity of collateral vessels not only in resting condition, but also in stress condition. Thus, observation was made under the atrial pacing and in addition, under the constriction of the

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donor coronary artery. In order to estimate the degree and extent of myocardial ischemia, epicardial and intramyocardial electrograms were used in this study. Especially, ST-elevation in each electrogram was adopted as an index of regional myocardial ischemia.¹⁴,¹⁵

METHODS

Nineteen adult mongrel dogs weighing 10–19 Kg were used in this study. All dogs were subjected to chronic coronary artery occlusion before the observation. After anesthesia with sodium pentobarbital, 25 mg/Kg, i.v. and ventilation by a mechanical respirator, the chest was opened in the fifth left interspace and the heart was exposed. The proximal portion of the left anterior descending coronary artery was dissected free and an Ameroid constrictor was placed around the vessel.¹⁶ Subsequently, dogs were allowed to recover. To estimate the functional capacity of different degrees of collateral development, studies were performed in the surviving dogs 3 to 12 weeks after the placement of an Ameroid constrictor. All surviving dogs were anesthetized and ventilated and a left lateral thoracotomy was performed. An electrographic study was done before the second surgery and dogs with abnormal Q wave in epicardial electrogram were discarded from the following study. The circumflex branch of the left coronary artery was isolated from the adjacent tissue at the bifurcation for applying an electromagnetic flow probe and a metal constrictor device. After the sinus node was crushed, right atrium was stimulated with pace-maker. Usually, heart-rate was kept constant at 120/min during the resting condition. A polyethylene catheter was inserted into the aortic arch through a femoral artery for monitoring aortic blood pressure. A distal branch of the circumflex coronary artery was cannulated with another polyethylene tube for coronary perfusion pressure recording. Coronary blood flow in the circumflex artery and aortic blood flow were measured with electromagnetic flowmeter (Nihonkoden, MF-26). Peripheral coronary pressure and retrograde coronary flow were measured from the distal part of the anterior descending artery which had been chronically occluded with an Ameroid constrictor. These parameters were used as indices of the development of the coronary collateral vessels.¹⁷,¹⁸ All hemodynamic parameters were recorded using a direct writing recorder.

Three pairs of epicardial and intramyocardial

![Fig.1. Schematic diagram of the experimental preparation.](image)

EPT: electric pressure transducer, EMF: electromagnetic flowmeter, ECG: electrogram, LAD: left anterior descending coronary artery, Cx: circumflex coronary artery.

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electrodes with five recording sites were used as reported previously. Epicardial and intramyocardial electrodes were placed at following three sites on the anterior surface of the left ventricle, i.e. (1) the area perfused by the coronary collateral vessels, which had been nourished by the anterior descending artery before its occlusion (Collateral area), (2) the area which was perfused by the circumflex artery (Circumflex area), (3) the area located between aforementioned two areas (Intermediate area) (Fig.-1). Electrograms were obtained at paper speed of 50 mm/sec and sensitivity of 1 mm/mV. ST-segment voltage was measured at 0.06 sec after the end of S-wave. One hour after the insertion of intramyocardial electrodes into the left ventricular wall, the following observations were done. 1) In the resting condition, ST-segment voltage in electrograms from three areas was measured and analysed. 2) After the measurement of systemic, coronary and coronary collateral hemodynamic parameters in resting condition, the heart rate was increased by atrial pacing in increments of 30 beats/min, each period of pacing maintained for 5 minutes, until elevation of ST-segment voltage appeared in any electrograms or atioventricular block developed. In dogs showing no ST-elevation with atrial-pacing alone, the following procedure was applied. 3) Metal constrictor devices were prepared to produce a known degree of fixed constriction of the donor coronary artery. They are 5 mm long and constructed with different internal diameters ranging by 0.1 mm increments from 1.0 to 4.0 mm in diameter. After measurement of the external diameter of the circumflex coronary artery by a caliper, the appropriate constrictor device to constrict the artery to 50%, 75% and 85% of the external diameter, was selected and applied respectively to the circumflex artery just distal to the flow probe. After applying the constrictor device, the heart-rate was increased by atrial pacing in the same manner as described previously and the changes in ST-segment voltage were observed. In dogs which showed no significant ST-elevation with a 50% coronary constriction, further increases in coronary constriction were applied and atrial pacing was repeated until ST-elevation appeared in any electrograms. All values are expressed as mean ± standard error and statistical analysis was performed using Student's t-test.
RESULTS

Epicardial and intramyocardial ST-segment voltage in resting condition.

In 4 of 19 dogs, abnormal Q wave was detected in epicardial electrogram from collateral area. Data from these 4 dogs were discarded and the further observations were not done in these dogs. The magnitude of ST-segment voltage from three areas was shown in Fig. 2. No significant difference of ST-segment voltage was observed among three intramyocardial electrograms in each area, while ST-segment voltage of each epicardial electrogram was significantly lower compared to that of corresponding intramyocardial electrograms in each area. In addition, epicardial ST-segment voltage in electrogram from circumflex area was lower than those from collateral and intermediate areas. ST-segment voltage in electrograms from each intramyocardial layer revealed no difference in its voltage among three different areas. Electrographic response to the atrial pacing

Dogs were divided into two groups according to the electrographic response to the atrial pacing. In 6 of 15 dogs in which atrial pacing was performed ST-elevation appeared during pacing without any constriction of the donor coronary artery (Group-A), while more than 50% constriction in the donor artery was necessary to induce the electrographic changes in another 9 dogs (Group-B).

1. ST-segment elevation during atrial pacing in dogs of Group-A.

In dogs of Group-A, ST-segment elevation was observed in electrograms from collateral and intermediate areas, but not from circumflex area during the pacing period. The pacing-rate to induce ST-elevations was different in each dog, but ST-elevation always appeared in the electrogram from the inner layer of collateral area (Fig. 3-B). Further increases in pacing-rate produced not only ST-elevation of advanced degree in this lead, but also new ST-elevation in the other intramyocardial electrograms of collateral area (Fig. 3-C). ST-elevation was also observed in electrograms from intermediate area at the higher rate of atrial pacing in several dogs, but no ST-elevation was detected in epicardial electrograms from any areas.
2. ST-segment elevation during atrial pacing in dogs of Group B.

In another 9 dogs, in which atrial pacing induced no significant ST-elevation in electrograms, atrial pacing was performed with different degrees of the donor coronary artery constriction. Pacing induced tachycardia produced a significant ST-elevation in electrograms from collateral and intermediate areas in 3 of 9 dogs with a 50% coronary constriction and in 5 dogs.
TABLE I  SYSTEMIC, CORONARY AND CORONARY COLLATERAL HEMODYNAMIC PARAMETERS IN RESTING CONDITION

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<th>Expt. No.</th>
<th>BW kg</th>
<th>Duration days</th>
<th>sAP mmHg</th>
<th>dAP mmHg</th>
<th>A F L/min</th>
<th>CBF ml/min</th>
<th>R F ml/min</th>
<th>sPCP mmHg</th>
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**BW**: body-weight, **Duration**: duration of an Ameroid constrictor placement, **sAP**: systolic aortic pressure, **dAP**: diastolic aortic pressure, **A F**: aortic blood flow, **CBF**: coronary blood flow, **R F**: retrograde coronary blood flow, **sPCP**: systolic peripheral coronary blood pressure, **dPCP**: diastolic peripheral coronary blood pressure.

with a 75% constriction. Electrograms of one dog in which the pacing tachycardia produced ST-elevation with a 75% coronary constriction was shown in Fig. 4. In this dog, no significant ST-elevation was observed at the pacing rate of 120/min, but a marked elevation of ST-segment was found in one intramyocardial electrogram from collateral area when pacing rate was increased to 180/min. Further increase to 210/min resulted in the advanced degree of ST-elevation in the same area and in the evolution of ST-elevation in intermediate area. In all dogs in which atrial pacing was performed with a 75% donor artery constriction, any ST-elevation was not detected in electrograms from circumflex area. In one dog, the donor coronary artery constriction up to 85% was necessary to induce ST-elevation. ST-elevation appeared simultaneously in electrograms from the inner layer of all three areas and the middle layer of circumflex area at the pacing rate of 210/min (Fig. 5).

**Systemic, coronary and coronary collateral hemodynamic parameters.**

All hemodynamic parameters are presented in Table I. Aortic blood pressure and flow were not different between Group-A and B. Coronary blood flow in the circumflex artery under the resting condition was also identical between two groups, but coronary collateral hemodynamic parameters revealed a statistically significant difference between them (Fig. 6). Retrograde flow of Group-B was greater in comparison to that of Group-A (p < 0.02). Diastolic peripheral coronary pressure and diastolic peripheral coronary pressure/diastolic aortic pressure ratio also revealed a significant difference between two groups (p < 0.05 and < 0.02, respectively), while systolic peripheral coronary pressure of Group-A was comparable to that of Group-B. Furthermore, the duration of placement of an Ameroid constrictor was significantly longer in Group-B than in Group-A.
DISCUSSION

It was reported that regional intramyocardial electrogram reflected more exactly the changes in regional myocardial blood flow than epicardial electrogram. Furthermore, it was also observed that a relationship existed between the degree of ST-elevation in intramyocardial electrogram and the changes in intramyocardial gas tensions during coronary insufficiency. Our previous studies confirmed that the intramyocardial electrogram reflected sensitively and exactly the local ischemia. Accordingly, ST-elevation in regional electrogram was regarded as a good index of regional ischemia in this study.

In the resting condition, there was no marked difference of ST-segment voltage among intramyocardial electrograms from three different areas. This implies that the collateral area is well nourished through the collateral vessels or the oxygen demand in this area is lowered to meet the limited oxygen supply through the collateral vessels. ST-segment voltage in epicardial electrograms, however, was considerably different among three areas. As previously reported, ST-segment depression was observed in the circumflex area of normal dog. The genesis of this ST-depression remains obscure, but the depression might be produced by the operative procedure to isolate coronary artery. Isolation of the anterior descending artery usually results in the damage of pericoronary nerve, while the pericoronary nerve around the circumflex artery is kept intact despite wide isolation of it.

Pacing induced tachycardia without constriction resulted in the evolution of ST-elevation in electrograms from collateral area in 6 dogs of Group-A. This is partly due to the augmentation of the oxygen demand by tachycardia and also due to the limitation of blood supply through the collateral vessels during the tachycardia, because the blood supply to the collateral area is inhibited during cardiac contraction and increase in systolic period during tachycardia will be act to reduce the flow.

In collateral area, ST-elevation appeared first in the inner layer and proceeded to the outer direction with an increase in the pacing rate. These findings are consistent with the results reported by Flameng et al. They revealed that the

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endocardial layer of the collateral areas has the lowest coronary reserve, while the epicardial layer is significantly better perfused even in the stress condition. In dogs of Group-B, on the other hand, evolution of ST-segment elevation during the pacing period appeared with more than 50% donor coronary artery constriction. This finding suggests that the development of functioning collateral vessels of Group-B is greater than that of Group-A. All dogs of Group-B, except one, however, showed ST-elevation in collateral area with less than 75% coronary constriction of the donor artery. In this situation, no significant ST-elevation was found in electrograms from circumflex area. This means that blood supply to collateral area was restricted with constriction of the donor artery under the tachycardial period, but the supply to collateral area was still kept well to prevent the myocardium from ischemic injury. In this study, coronary blood flow in the circumflex artery was measured only at the resting condition, but Gould et al. reported that the vasodilatory response was diminished, but observed with a constriction up to 90% decrease in luminal diameter. In one dog with a 85% donor arterial constriction, ST-elevation appeared simultaneously in the inner layer of three different areas and in the middle layer of circumflex area during the tachycardial period. It is reasonable to presume from this finding that blood supply to three different areas was simultaneously disturbed in this dog and that the well developed collaterals in this dog have a function comparable to that of the normal coronary artery. Both indices of the development of the collaterals indicated the maximal development of the collaterals in this dog (Table I, Exp. No.-145).

Systemic and coronary hemodynamic parameters revealed no difference between two groups. Collateral parameters, however, showed statistically significant difference between them. These results indicate that blood supply to the ischemic myocardium depend on the degree of the development of collaterals. Schaper et al. reported that a marked improvement of the dilatory reserve of collaterals appears as a function of time after coronary occlusion. Lambert et al. demonstrated that the mature coronary collaterals supply adequate flow to the ischemic myocardium not only at rest, but also during the stress of exercise. There is a possibility that the well developed collaterals in dogs have a function comparable to the normal coronary artery. The measurement of the collateral indices in man, however, revealed the poor development of collaterals in comparison with those in dog. Accordingly, it might be difficult to expect a good blood supply to the ischemic myocardium through the collateral vessels in human like as those observed in dog.

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