Disappearance of Ventricular Arrhythmia Caused by Coronary Occlusion during Retrograde Bleeding through Collaterals

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It is well known fact that collateral circulation plays an important role in the physiological and pathological conditions of peripheral circulation. The magnitude of collateral circulation was reported to be sparse in the heart, compared with other organs, in normal animals. Gregg and Fisher, however, presented much evidence of considerable development of collateral circulation in chronically impaired hearts in experimental animals and human subjects. The physiologic significance of collateral circulation is an attractive subject for the study of coronary insufficiency.

The present authors made an attempt to study the relationship between the cardiac function and the hemodynamics of collateral circulation on acute coronary occlusion in normal dogs, especially the functional significances of collateral circulation for cardiac rhythmicity. Harris et al. have extensively studied electrophysiologically on the cardiac irregularities following occlusion of the main coronary branch. The magnitude, development and physiological significance of collateral circulation on acute and chronic myocardial ischemia were studied by Gregg and his collaborator. Different techniques have been devised by many research workers in order to estimate the magnitude and the distribution of collateral circulation. In the present study, the method of measuring the retrograde pressure and the retrograde blood flow was adopted. In the course of the study an interesting phenomenon was found by chance that the idioventricular ectopic beats, observed in the delayed stage after acute coronary occlusion, reverted to the regular sinus rhythm when retrograde blood flow was being measured by conducting blood externally in the graduated cylinder.

In this paper we report the relationship between the cardiac irregularity and the quantity of collateral circulation in acute coronary insufficiency and discussed some possible mechanisms for induction of ventricular arrhythmia after acute coronary occlusion.

Methods

Fifty-six mongrel dogs of either sex, 8 to 13 kg body weight, were anesthetized with intravenous sodium pentobarbital, 30 mg/kg. Under artificial respiration, by use of positive pressure respirator (Natsume, KN-50), the chest was opened through the left fourth or fifth intercostal space, and the heart was suspended in a pericardial cradle. The left auricle was retracted in order to look into the origin of the left coronary artery, and the left anterior descending coronary artery was dissected at close proximity to the origin with a special cut not to injure the nerve supply.

1. In the first series of experiments on forty-two dogs, acute coronary insufficiency was induced by an abrupt occlusion of the left anterior descending coronary artery, and the cardiac function and hemodynamic behaviour were observed for five or six hours. The septal artery was excluded from the occlusion. A polyethylene catheter was introduced through the left auricle into the left ventricular cavity to measure intra-

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ventricular pressure, and the rate of rise of the pressure pulses, i.e., dLVP/dt, was recorded through a differential electrical circuit with a time constant of 2.5 msec. In dogs, which escaped from ventricular fibrillation following the occlusion, the occluded artery was orthodromically cannulated with a polyethylene cannula in order to measure the retrograde pressure as shown in Fig. 1. The retrograde flow was intermittently measured by collecting the blood flowing back through the cannula for thirty seconds in a graduated cylinder. The retrograde pressure and blood flow, which were dependent on the systemic blood pressure, were expressed as mmHg/100 mmHg of mean blood pressure (MBP) and ml/min/100 mmHg of MBP, respectively. Data demonstrated in results are the mean values of rates successively determined three times every ten minutes. Retrograde pressure and blood flow were taken as indices of the magnitude of collateral circulation. Systemic blood pressure was measured at the left carotid artery.

2. In the second series of experiments on thirteen heparinized dogs, a polyethylene cannula was inserted into the left anterior descending coronary artery, which was perfused with the blood led from the left carotid artery. The coronary inflow was measured with an electromagnetic flowmeter (Nihon Kohden, MF-2) for about one hour. The retrograde flow for thirty seconds was determined during transient interruption of extracorporeal circulation two or three times every twenty minutes. Then the descending branch was persistently interrupted. The relative magnitude of collateral circulation was expressed as the ratio of the retrograde blood flow to the orthograde one in the occluded coronary artery. Systemic blood pressure was monitored at the right femoral artery.

![Diagram of experiment](image)

**Fig. 1.** Diagram of experiment. See the text for the details of the operation and procedures of experiment.

![ECG and blood pressure changes](image)

**Fig. 2.** Changes in ECG and blood pressure following acute coronary occlusion. Arrhythmia appeared in two stages, 3–13 minutes and 264 minutes after the occlusion. Blood pressure gradually decreased following the occlusion. ECG II: Electrocardiogram by standard limb lead II; BP: Systemic blood pressure.

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Retrograde and systemic blood pressure were measured by pressure transducers (Nihon Kohden, MP-24T). The lead II ECG was recorded by Fukuda Electro, RS-13. The heart rate was recorded by a cardiograph (Nihon Kohden, RT-2) which was triggered with the R wave of ECG. A polygraph recorder (Nihon Kohden, RM-150) was used for registration of these parameters except ECG. PO₂ and pCO₂ in the retrograde blood flow and in the femoral arterial blood were simultaneously sampled and analyzed by means of IL-meter (Instrumentation Laboratory Inc., Model-113) in some experiments.

Results

1. Cardiac rhythm following acute coronary occlusion

Twenty-one out of fifty-six dogs were killed by ventricular fibrillation within twenty minutes after the acute coronary occlusion. A majority died within ten minutes but one at about ninety minutes. The mortality rate in the early stage of occlusion was 39.5 per cent. Surviving animals showed usually varying degrees of ventricular arrhythmia which appeared within a few minutes and returned to a regular rhythm within next fifteen minutes. Some animals showed no irregular rhythm. Typical ECG patterns are shown in Fig. 2. Depression of ST segment was regularly observed, and systemic blood pressure decreased gradually after the occlusion.

Several hours later, the ECG again showed irregularities such as idioventricular ectopic rhythm and paroxysmal ventricular tachycardia. Arrhythmia in this stage can be referred to "delayed activity" by Harris² who reported that the delayed arrhythmia appeared in five to eight hours after the occlusion and lasted a few days. Various degrees of the delayed arrhythmia were observed in all surviving dogs in various times after the occlusion, and nine of the dogs showed very severe ventricular arrhythmia in a few hours.

The severity of arrhythmia in the early stage was graded arbitrarily in five classes by rating scales according to the frequency of ectopic beat per minute following occlusion. Ventricular fibrillation was considered as the most severe arrhythmia and rated as "5", and no ectopic beat as "0". Intermediate cases follow the rating scale shown in Fig. 3. When the number of ectop-
Table I  Relationship between the Severity of Arrhythmia and the Magnitude of Collateral Circulation

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>Rating Scale</th>
<th>BP: mmHg syst./diast. mean</th>
<th>INFL ml/min</th>
<th>RF ml/min</th>
<th>RF/INFL</th>
</tr>
</thead>
<tbody>
<tr>
<td>DH-880</td>
<td>1</td>
<td>160/100 (120)</td>
<td>9.0</td>
<td>2.0</td>
<td>0.22</td>
</tr>
<tr>
<td>DH-879</td>
<td>4</td>
<td>160/120 (133)</td>
<td>18.0</td>
<td>1.9</td>
<td>0.11</td>
</tr>
<tr>
<td>DH-878</td>
<td>1</td>
<td>120/ 80 ( 93)</td>
<td>5.0</td>
<td>2.2</td>
<td>0.45</td>
</tr>
<tr>
<td>DH-901</td>
<td>5</td>
<td>180/110 (133)</td>
<td>18.0</td>
<td>4.4</td>
<td>0.25</td>
</tr>
<tr>
<td>DH-902</td>
<td>5</td>
<td>85/ 60 ( 68)</td>
<td>9.0</td>
<td>1.7</td>
<td>0.15</td>
</tr>
<tr>
<td>DH-903</td>
<td>1</td>
<td>120/ 90 (100)</td>
<td>32.0</td>
<td>3.0</td>
<td>0.09</td>
</tr>
<tr>
<td>DH-904</td>
<td>0</td>
<td>135/ 90 (105)</td>
<td>16.0</td>
<td>2.9</td>
<td>0.18</td>
</tr>
<tr>
<td>DH-906</td>
<td>5</td>
<td>160/110 (127)</td>
<td>15.0</td>
<td>0.8</td>
<td>0.05</td>
</tr>
<tr>
<td>DH-907</td>
<td>5</td>
<td>105/ 80 ( 89)</td>
<td>37.0</td>
<td>0.6</td>
<td>0.02</td>
</tr>
<tr>
<td>DH-908</td>
<td>5</td>
<td>120/ 90 (100)</td>
<td>30.0</td>
<td>0.86</td>
<td>0.03</td>
</tr>
<tr>
<td>DH-909</td>
<td>1</td>
<td>100/ 60 ( 73)</td>
<td>12.0</td>
<td>1.08</td>
<td>0.09</td>
</tr>
<tr>
<td>DH-911</td>
<td>3</td>
<td>115/ 85 ( 95)</td>
<td>13.0</td>
<td>0.5</td>
<td>0.04</td>
</tr>
<tr>
<td>DH-912</td>
<td>5</td>
<td>135/110 (118)</td>
<td>8.0</td>
<td>0.9</td>
<td>0.12</td>
</tr>
</tbody>
</table>

The relative magnitude of collateral circulation was expressed by the ratio of RF to orthograde inflow. Ventricular fibrillation occurred without relation to RF, Inflow and RF/Inflow.

BP: Systolic/Diastolic blood pressure;  Infl.: Orthograde inflow.
Other abbreviations are the same as in Fig. 4.

**CORONARY OCCLUSION AT 11:03**
(DH-6587) 16:57

ECG

RF: 1.78 ml/min/100mmHg

BP

17:10

ECG-II

RF: 1.77 ml/min/100mmHg

RP

Fig. 5. Normalization of delayed ventricular arrhythmia during external bleeding from occluded artery. Abrupt drop and rise in RP tracings show the bleeding. The irregularity disappeared in around 10 seconds after bleeding, and reappeared after stopping the bleeding.

RP: Retrograde pressure. Other abbreviations are the same as in Fig. 2.

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ic beats was over seventy per minute, the systemic blood pressure fluctuated irregularly. While the ECGs of animals without ectopic beat showed little change in ST segment, in the dogs which suffered from a more severe arrhythmia, ST segment of lead II ECG was markedly depressed, and ECGs in intermediate rating scales showed a progressive deviation of ST segment from equipotential level. In two dogs, rsR' complexes with ST depression were observed, indicating a bundle branch block.

2. Relation between early arrhythmia and collateral circulation

The retrograde flow rate directly related to the retrograde pressure, and the flow rate was considered as an adequate index of collateral circulation in the present study. Values of retrograde blood flow were different from animal to animal: from 0.5 to 8 ml/min/100 mmHg of mean blood pressure (MBP) as shown in the abscissa of Fig. 4 and in Table I. The ordinate in the figure shows the severity of the early arrhythmia. The severity was inversely related to the magnitude of collateral circulation. Furthermore, the retrograde blood flow of 2 ml/min/100 mmHg of MBP seemed to be a critical value for determination of the severity of arrhythmia, because irregularities were less marked in the hearts in which the retrograde blood flow was over the critical value. As shown in the table, ventricular fibrillation took place without any relation to any of the retrograde blood flow, the inflow rate through the anterior descending artery and the ratio of retrograde blood flow to orthograde one.

3. Reversion of delayed arrhythmia to sinus rhythm by backward bleeding

In the course of measuring retrograde flow, we found by chance that the bleeding backward from the occluded artery was surprisingly effective to normalize the delayed arrhythmia. In five of nine dogs with severe delayed arrhythmia, the irregularity disappeared during the thirty second period of bleeding for measuring the retrograde blood flow. One heart required the period of bleeding over thirty seconds to get a regular rhythm. In the other three hearts the normalization could not be accomplished during a thirty second period of bleeding, but it was not tried to bleed for longer periods.

The reversion to the regular sinus rhythm was repeatedly obtained in every trial of backward bleeding in the same animal. Fig. 5 shows the repetition of such reversion to normal rhythm in successive trials performed every ten minutes. In this animal the cardiac rhythm showed a very severe irregularity at the fourth hour after coronary occlusion. The arrhythmia reverted to the regular rhythm in about ten seconds after bleeding, and it reappeared about twenty seconds after stopping bleeding. The systemic blood pressure was stabilized during this period.

Attempts were made to study how long the reversion of the arrhythmia to the regular sinus rhythm could be maintained; and how the cardio-dynamics were influenced by the backward bleeding. Fig. 6 shows the influence of a prolonged period of bleeding on cardiac function. Fig. 7 shows ECG before and during the backward bleeding. In this animal the severe irregularity appeared about two hours after the occlusion. The left ventricular pressure and its dLVP/dt were simultaneously registered as shown in Fig. 6. The systemic blood pressure, the left ventricular pressure and the maximum dLVP/dt remarkably decreased after coronary occlusion, and turned to increase during external bleeding. Therefore, the backward bleeding not only normalized the cardiac rhythm, but also improved the left ventricular function.

An additional point to be noticed in Fig. 6 is the delay of four minutes until reappearance of irregularity after cessation of retrograde bleeding for eleven minutes. Such delays were about 20, 90 seconds and 6 minutes after 30 seconds, 5 and 20 minutes of bleeding time, respectively. The longer the period of bleeding, the greater was the delay to the reappearance of the irregularity.

**DISCUSSION**

In 1928 Anrep and Häusler first measured the backward blood flow from the coronary artery after acute coronary occlusion and demonstrated the presence of collateral circulation of coronary artery. Later, Gregg et al. showed that the backward flowing blood was arterial in its origin, and they considered retrograde pressure and flow as a reasonable index of estimating the magnitude of collateral circulation. The present authors confirmed the results by Gregg et al. Harris et al. have extensively studied the arrhythmia following experimental coronary insufficiency in dogs. We observed in the present study two essentially different types of cardiac irregularities after coronary occlusion, which were referred to the "early" and "delayed" ven-
Fig. 6. Cardiac performance during long period of bleeding. Note not only the normalization of the arrhythmia, but also the increases in LVP, dLVP/dt and BP during the bleeding.

LVP: Left ventricular pressure; dLVP/dt: First time derivative of LVP.
Other abbreviations are the same as in Figs. 2 and 5.

<table>
<thead>
<tr>
<th>TIME</th>
<th>ELECTROCARDIOGRAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td><img src="image" alt="ECG tracing for C" /></td>
</tr>
<tr>
<td>30&quot;</td>
<td><img src="image" alt="ECG tracing for 30&quot;" /></td>
</tr>
<tr>
<td>1'30&quot;</td>
<td><img src="image" alt="ECG tracing for 1'30&quot;" /></td>
</tr>
<tr>
<td>3'</td>
<td><img src="image" alt="ECG tracing for 3'" /></td>
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<tr>
<td>5'</td>
<td><img src="image" alt="ECG tracing for 5'" /></td>
</tr>
<tr>
<td>11'</td>
<td><img src="image" alt="ECG tracing for 11'" /></td>
</tr>
</tbody>
</table>

Fig. 7. ECG tracings during long period of bleeding. Each time corresponds to the times signified in Fig. 6. Ectopic beats lessened significantly in one and a half minutes. Moreover, note no change in pattern of normally conducted ECG during bleeding.

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tricular arrhythmias by Harris. We found the ventricular arrhythmia in early stage was less severe in the hearts with more retrograde flows, when animals killed by ventricular fibrillation were excluded. It seemed that 2 ml/min/100 mmHg of mean blood pressure was the critical level of retrograde flow, below which the number of cases with severe arrhythmia increased. Then that value would be expected to correspond to the minimum requirement of blood supply to ensure the viability of ischemic myocardium. The occurrence of ventricular fibrillation in the early stage, however, did not relate, not only to the absolute value of retrograde flow, but also to the ratio of retrograde to orthograde blood flow before occlusion. Therefore, some additive mechanisms probably trigger the induction of ventricular fibrillation from premature ventricular arrhythmia.

The most interesting finding in the present study is a phenomenon of disappearance of the "delayed" arrhythmia during a period of measuring the retrograde blood flow. The retrograde bleeding not only restored the regular cardiac rhythm, but also improved the left ventricular performance. There was no relation between the latency of the reappearance of the arrhythmia and the rate of retrograde blood flow. The phenomenon can be interpreted by the extinction of abnormal excitability of myocardium in the boundary zone where ischemic condition partially exists. Then, the abnormal excitability might be depressed when the blood supply to the boundary zone, barely accomplished through collateral circulation, was externally by-passed. However, it is hardly understandable because such phenomenon can be repeated at each trial of backward bleeding.

On the other hand, some biogenic substances, such as catecholamines and other arrhythmogenic substances, may accumulate at the ischemic zone. The latency of several hours before appearance of the delayed ectopic activity was reported to approximate to the period of ischemia to be necessary for the development of histological evidence of necrosis, and it has been suggested that accumulation of some products from the necrotic tissue gives rise to the delayed ectopic activity. Arterioles and precapillary sphincters in the ischemic area must be maximally dilated as expressed by reactive hyperemia, and the excitants originated from necrotic myocardium will be moved out through the collateral artery during backward bleeding, resulting in the reduction of the excitants in the boundary zone. Harris et al. suggested potassium ion as the major excitant; while catecholamine was also suggested. Then it is of great importance to detect such substances in the backward flowing blood.

SUMMARY

Ventricular irregularities and their relations to collateral circulation were studied on acute occlusion of the left anterior descending coronary artery of dog heart. The size of the collateral circulation existing in normal hearts was estimated by measuring retrograde pressure and blood flow from the occluded artery. Two essentially different types of ventricular arrhythmias were observed in the early and later stages after acute occlusion. The mortality in the early stage resulting from ventricular fibrillation was 39.5%. The frequency of extrasystole in this stage was inversely related to the magnitude of collateral circulation. The arrhythmia in the later stage disappeared and reverted to regular sinus rhythm during a period of backward bleeding for measuring retrograde flow. The backward bleeding not only brought back a regular rhythm, but also improved left ventricular performance. Some arrhythmogenic substances originated from ischemic tissue probably take part in the genesis of the arrhythmia in the later stage.

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REFERENCES


