Sequence of Occurrence of Abnormal Regional Cardiac Function, Global Pump Function and Electrocardiogram after Brief Ligation and Reperfusion of a Coronary Artery

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SUMMARY
The following results were obtained.
A) During brief ligation of the coronary artery, a change in the cardiac wall motion appeared as the first abnormality of the CMG. Succedingly, epicardial ECG changes were recognized, and lastly, changes of dP/dt appeared.
B) After reperfusion of the coronary artery, dP/dt was quickly normalized, followed by restoration of ST elevation. Cardiac motion, measured by CMG, was the last abnormality to improve.

Additional Indexing Words:
Regional cardiac function   Global cardiac function   Electrocardiogram   Myocardial ischemia

Myocardial ischemia can be recognized by evaluating many parameters such as excitation, contraction and metabolism within the negative cybernetic loop of cardiac muscle function. For the clinician, it is imperative to diagnose the early recognition of myocardial ischemia. Therefore, the question is whether it is necessary to evaluate these parameters simultaneously. If one of these parameters is more sensitive and adequate than the others, the clinical workup can be simplified.

These parameters may vary in order of time of occurrence of changes. Furthermore, the methodology for the detection of each parameter may create differences in sensitivity for the recognition of ischemia.

It has been implicated that regional cardiac function is the best parameter for the early recognition of myocardial ischemia. However, studies to compare these parameters during occlusion and reperfusion of the coronary

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artery are still limited and fragmentary. Therefore, the purpose of this experiment was to examine the temporal differences in the appearance of changes in the regional cardiac wall motion, pump function and electrocardiogram after brief ligation and reperfusion of the coronary artery of dogs.

**Materials and Methods**

A. Experimental model (Fig. 1)

Adult mongrel dogs between 7.5 to 14.0 Kg were anesthetized with morphine (5 mg/Kg, iv) and urethane (500 mg/Kg, iv). After thoracotomy, the pericardium was opened and the heart elevated. A tube of large bore was inserted directly from outside into the left ventricle to monitor the left ventricular pressure and its first derivative (dP/dt). The aortic pressure was also monitored and the end of systole was identified by the dichrotic notch, as shown in Fig. 2. The left anterior coronary artery (LAC) was carefully dissected to apply the occluder. The probe of the electromagnetic flow meter (Nihonkohden) was applied at the root of LAC in order to monitor the coronary flow.

B. Regional cardiac motion

The cardiac wall motion of the ischemic area was assessed using a cardiomoveogram (CMG) which was developed in our laboratory based on a principle similar to cardiokymogram developed by Vas. The coil of the LC oscillator was mounted near the regional cardiac wall without contacting it. The size of the probe was 2.5 cm in diameter. The basic principles and instrumentation of CMG and its device are described elsewhere. The principle of this device can be briefly described as follows. The frequency of the LC oscillator was changed by capacitance between the coil and the cardiac

![Fig. 1. Schematic illustration of this experiment for the evaluation of the myocardial ischemia in an open chest dog preparation.](image-url)
Fig. 2. Analysis of systolic changes in a cardiomoveogram (CMG). The whole systole was defined between the onset of q wave until the dichrotic notch (DN) in the aortic pressure curve. The whole systole in the CMG was divided into the 5 segments.

In order to evaluate the regional cardiac function by CMG, the sensitivity of deflection of CMG was analysed during systole (Fig. 2), i.e., the whole systole was taken from the beginning of the q wave until the dichrotic notch of the aortic pressure curve. This systole was divided into 5 segments. The first vertical lines were drawn at the initial one third, middle and initial two third points of whole systole. The deflection of CMG was examined at these three points on the vertical lines and at the point of the dichrotic notch. The deflection was measured from the base line, which was a line connecting the lowest negative deflections at the beginning of the q wave. Since the absolute magnitude of the deflection could not be measured in this study, all numbers are expressed as percentile change from the control levels.

C. Epicardial electrocardiogram

A small electrode of platinum was mounted on the regional epicardium. Special attention was paid to avoid injury changes in the ST segment due to the experimental manipulation. The region was selected where discolora-
tion occurred after ligation of the coronary artery. The electrocardiogram of lead II was also recorded.

D. Global pump function

The left ventricular pressure curve was measured through a solid tube with a large bore that was inserted directly in the left ventricle. This was connected directly to a pressure transducer. The first derivative of left ventricular pressure (dP/dt) was calculated.

E. Experimental protocol

During the control period, the pressure curves of the aorta and the left ventricle, CMG and electrocardiogram were recorded. The coronary artery was then completely occluded at its root. The occlusion was maintained for 10 min. After this, the occlusion was released and reperfusion of the ligated artery was started. After reperfusion, observations were continued for more than 20 min until complete recovery of all parameters to the control level was noted (Figs. 3 and 4).
RESULTS

Typical experimental records are shown in Figs. 3 and 4. After ligation of the coronary artery (Fig. 3), CMG deflection at end-systole became significantly abnormal. This was followed by appearance of an abnormal ST segment of the epicardial electrocardiogram at 1 min. The dP/dt value then changed at 5 min. On the other hand, after release of the ligation (Fig. 4), the dP/dt abnormalities returned to the control level in 30 sec, ST of the electrocardiogram recovered in 3 min and CMG deflection recovered to the control level in 10 min.

A. Regional myocardial function

In 37 dogs, the change in CMG deflection after ligation and the reperfusion of the coronary artery were examined as shown in Fig. 5 and Table I. In order to detect the differences in sensitivity for recognition of the changes in CMG at early, mid- and late systolic periods, four points were selected as already shown in Fig. 2. After ligation of a coronary artery, each of these deflections started to change immediately. The earliest change was recognized at 15 sec after ligation. However, the sensitivity of the change in magnitude was different between these. At point C4, namely at the end of systole, the change was most significant throughout systole compared with
the rest of the points. The order of this sensitivity was determined successively from $C_4$, $C_3$, $C_2$ to $C_1$. Furthermore, after reperfusion of this coronary artery, the sensitivity of the recovery of these changes to the control level was examined in a similar manner. As shown in Table I and Fig. 5, $C_4$ was also the most sensitive for recognition of the occurrence of changes in magnitude compared with the rest of the points. Therefore, the late systolic point was the most sensitive timing for this recognition. This $C_4$ point was selected

![Fig. 5. The changes in the magnitude of CMG deflections after occlusion or reperfusion of a coronary artery at 4 points during systole.](image)

Table I. The Changes in the Magnitude of CMG Deflections during Systole after the

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>15″</th>
<th>30″</th>
<th>45″</th>
<th>1'</th>
<th>1'30″</th>
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<td>$C_1$</td>
<td>Mean</td>
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<td>6.86</td>
<td>8.67</td>
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<td>3.53</td>
<td>30.36</td>
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<td>$C_2$</td>
<td>Mean</td>
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<td>15.95</td>
<td>26.28</td>
<td>38.41</td>
<td>35.67</td>
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<tr>
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<td>54.50</td>
<td>55.85</td>
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<td>33.51</td>
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<td>0.02</td>
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as the most sensitive and the most representative point for comparison with the rest of the parameters which will be described in the following discussion.

B. Epicardial electrocardiogram (Fig. 6)

After occlusion of the coronary artery, the ST segment was abnormally elevated at 30 sec compared with the control period as shown in Figs. 3 and 6. This significantly abnormal change was noted until the end of the ligation period. After reperfusion of the coronary artery, the ST segment started to return to the control levels. At 13 min, namely 3 min after the start of reperfusion, this abnormality in the ST segment had returned to normal.

The T wave was also analysed (Fig. 7). The initially inverted T wave during the control period was restored to the base line. The start of this change was significant at 1.5 min. The abnormality was maintained until release of the occlusion. Therefore, the changes in the electrocardiogram were not significantly different between the T wave and the ST segment in this experiment.

C. Correlation of regional cardiac motion, ST segment and dP/dt of the left ventricle (Fig. 8)

After occlusion of the coronary artery, the C₄ deflection of CMG changed within 15 sec. This was the most sensitive and the quickest change compared to the rest of the parameters. Later, at 30 sec, the ST segment of the epicardial electrocardiogram started to change. This was the second to change. Lastly, the dP/dt of the left ventricle became significantly negative. This temporal sequence change was clearly noted. These changes remained abnormal during the rest of the time of the occlusion.

| Occlusion and Reperfusion of a Coronary Artery in Comparison with the Control Period |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | 2'              | 10'             | 10'15''         | 10'30''         | 11'             | 11'30''         | 13'             | 20'             |
|                 | 47.37           | 85.31           | 76.27           | 62.37           | 46.01           | 36.49           | 32.98           | 26.23           |
|                 | 62.96           | 106.25          | 111.23          | 91.63           | 74.49           | 65.09           | 73.09           | 65.11           |
|                 | 0.001           | 0.001           | 0.001           | 0.001           | 0.001           | 0.01            | 0.05            | 0.05            |
|                 | 186.15          | 106.00          | 94.30           | 70.22           | 53.71           | 44.24           | 36.13           | 29.78           |
|                 | 642.45          | 116.33          | 115.56          | 100.70          | 84.24           | 78.00           | 80.22           | 77.35           |
|                 | n.s.            | n.s.            | n.s.            | n.s.            | n.s.            | n.s.            | n.s.            | n.s.            |
|                 | −118.93         | 127.54          | 108.82          | 82.87           | 59.92           | 45.46           | 36.95           | 32.44           |
|                 | 1010.19         | 179.66          | 175.45          | 125.79          | 96.21           | 84.67           | 84.18           | 87.95           |
|                 | n.s.            | n.s.            | n.s.            | n.s.            | n.s.            | 0.01            | 0.05            | n.s.            |
|                 | 122.17          | 144.13          | −7.01           | 87.72           | 55.44           | 48.11           | 27.03           | 26.32           |
|                 | 242.12          | 270.19          | 668.85          | 181.53          | 111.90          | 111.55          | 83.13           | 126.48          |
|                 | 0.02            | 0.01            | n.s.            | 0.02            | 0.02            | 0.05            | n.s.            | n.s.            |
After reperfusion, the negative dP/dt returned to the control value at 45 sec. In 3 min, the epicardial electrocardiogram reached control levels. Finally, after 5 min the $C_4$ in CMG recovered to the control level. These changes, in terms of sequence, were the opposite of those during the occlusion period.

Therefore, recognition of the occurrence of changes after occlusion and also after reperfusion of the coronary artery was the easiest in the $C_4$ of the CMG. The global pump function, represented as dP/dt of the left ventricle, and the ST segment in the surface electrocardiogram were less sensitive compared with the regional cardiac function by CMG.
DISCUSSION

In this experiment, we attempted to characterize the different times of onset for abnormalities in regional myocardial contraction, the epicardial electrocardiogram and dP/dt changes during coronary arterial occlusion and reperfusion.

Regional consequences in myocardial ischemia: Tennant and Wiggers in 1935\textsuperscript{1}) already demonstrated that the immediate loss of the muscular contraction occurred after ligation of the coronary artery. These data also indicated that the regional cardiac muscular contraction changed earlier than the electrocardiographic changes. This implication has now been firmly proven.\textsuperscript{2)-6),16),17})

The cardiomoveogram was developed to detect these cardiac motion abnormalities of cardiac contraction.\textsuperscript{9},10) The CMG was devised to provide a more sensitive and stable tracing than the cardiokymogram.\textsuperscript{8}) The validity of this device to detect abnormal cardiac motion was examined during ergometer induced myocardial ischemia.\textsuperscript{11)}) In this experiment, 9 smaller probes of 2.5 cm in diameter were used. The CMG detected the cardiac movement perpendicular to the probe. The movement towards the probe was shown as a positive deflection and the movement away from the probe was drawn as a negative deflection. However, calibration of CMG was not performed in this experiment, even though this can be done and was already solved with a specially developed calibrator.\textsuperscript{12}) Therefore, in this experiment the magnitude of the deflection itself was not reproducible and it was calculated as per-
centile change from the control level. Abnormalities of this regional cardiac function were examined to identify the most sensitive timing regarding cardiac systole. We decided in this experiment that the most sensitive timing for recognition of the occurrence of myocardial ischemia was the endsystolic period. These findings are supported by data in the literature,11,14 Since the affected area showed more prolonged contraction compared to the unaffected area, systole was determined from the q wave of the electrocardiogram to the dichrotic notch in aortic pressure.

Global left ventricular consequences: Waters et al.7) reported that the peak negative dP/dt of the left ventricle was a more sensitive parameter for the recognition of mild myocardial ischemia than ST changes. They implied that this might be more sensitive than ST displacement in myocardial ischemia. Under different experimental conditions, many reports13–16) demonstrated
that peak dP/dt was the most sensitive indicator of global dysfunction of the left ventricle in myocardial ischemia. In our experiment, however, negative peak dP/dt was less sensitive than ST displacement. By contrast, during reperfusion this peak negative dP/dt was more sensitive than ST elevation.

Electrocardiographic consequences: The electrocardiogram has been developed and utilized as the most convenient method to detect myocardial ischemia. The electrocardiographic abnormalities due to myocardial ischemia are changes in the ST segment and T wave. The mechanism of ST segment displacement has not been completely clarified. Furthermore, this may be caused by either cardiac conditions or non-cardiac conditions. Therefore, the problem for the clinician is that those electrocardiographic signs are not necessarily specific changes of myocardial ischemia. In true myocardial ischemia, such as in this experiment, the displacement of ST occurs 30 to 60 sec later. However, classical experiments have clearly shown that these electrocardiographic changes occur later than the changes in regional myocardial contraction. In this experiment, we employed the epicardial electrocardiogram because it is more sensitive to regional ischemia than the precordial electrocardiogram. Since the ST elevation and the inversion of the T wave were almost simultaneous, only the ST segment was chosen for analysis in this study.

Correlation between regional muscular disorders, global pump dysfunction and electrocardiographic abnormalities in myocardial ischemia.

Ample evidence can be found by collecting each fragment of the experiment that the time sequential changes of these parameters were as follows; namely firstly regional dysfunction, secondarily global dysfunction and electrocardiographic changes both by ligation and reperfusion of the coronary artery. Sayen et al found that regional mechanical abnormalities preceded epicardial electrocardiographic changes. A comparison between electrocardiographic changes and dP/dt over time has not been clearly reported.

Clinical implication: Our experimental data may be extrapolated to a clinical context with two caveats. First, abrupt occlusion of this kind would not occur in clinical medicine and second, anesthesia and thoracotomy altered the physiological conditions. Nevertheless, the epicardial electrocardiogram should be more sensitive than the precordial electrocardiogram. For the detection of regional changes, the diagnostic sensitivity of the cardiomoveogram would not be so strongly affected by the thoracic cage. Peak negative dP/dt with short and large bore catheters is enough for the evaluation of this type of experiment.

The increase in the deflection of the cardiomoveogram at endsystole may
be a useful indicator for the detection of myocardial ischemia.\textsuperscript{11}) Its measurement and recognition were easier than the electrocardiographic changes. Furthermore, the CMG is easier to perform than recognition of peak negative dP/dt because the cardiomoveogram is a non-invasive method. Comparative studies with other non-invasive methods such as radioisotopes and the echocardiogram are now in progress in our new laboratory.

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