Silent Myocardial Ischemia is not a Benign Sign

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1. Objectively, provoked angina is different from non-provoked angina.
   a) During pacing stress testing, provoked angina showed lesser increase in coronary sinus blood flow.
   b) During Ergotamine testing, variant angina showed a more marked decrease in flow.
   c) The myocardial lactate extraction ratio was lower during the pacing induced angina.
2. During the asymptomatic period, the polyparametric changes which would become manifest appeared following differing intervals. The early recognition of the myocardial ischemia was achieved by detection of the abnormality of the regional cardiac wall motion using a newly developed device, the cardiowavegram.
3. Therefore, we can at least conclude that silent myocardial ischemia is not a good prognostic sign.

Since the introduction of Holter monitoring, transient abnormal ST-T changes without concomitant cardiac symptoms have frequently been observed.\(^{1-3}\) The significance of these phenomena is the matter of controversy.\(^{2}\) One reason for controversy lies in the low specificity for the diagnosis of myocardial ischemia by Holter monitoring, even though the sensitivity is high. This problem is mainly due to the dynamic response of the system.\(^{3}\) Another difficulty is posed by the basic limitations of electrocardiography for the detection of the myocardial ischemic events.\(^{5}\)

The clinical problem concerning silent myocardial ischemia is that nobody can be certain whether this ischemia is a malignant or benign prognostic sign when using non-invasive diagnostic procedures such as the electrocardiogram.\(^{2,4,6,7}\) Moreover, this ischemia is asymptomatic and it would be impractical to perform invasive procedures in everyone at risk.

The object of this study was to address the following questions; 1) Is there the objective difference between angina pectoris and silent myocardial ischemia? 2) Is there a difference in the time at which each of the polyparametric abnormalities caused by myocardial ischemia can be recognized? and 3) How can we achieve early recognition of myocardial ischemia?

1. Is there an objective difference between angina pectoris and silent myocardial ischemia?

A) Polyparametric evaluation of the myocardial ischemia\(^{24}\)

A representative case of variant angina in which the polyparametric diagnostic evaluations were performed is shown in Fig. 1. In this case, the electrocardiogram in the control period, i.e. resting, and in the asymptomatic state was normal. However, in the resting state, either Holter electrocardiogram asymptomatic or symptomatic, similar ST elevation was found regardless of the patient's complaints. That is in this case ST change was not presumed from the

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1. Electrocardiogram

No.17, C.K., 50y.o., male

<table>
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<tr>
<th>No.</th>
<th>Status</th>
<th>Chest pain</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>aVR</th>
<th>aVL</th>
<th>aVF</th>
<th>V1</th>
<th>V2</th>
<th>V3</th>
<th>V4</th>
<th>V5</th>
<th>V6</th>
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<td></td>
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</tr>
<tr>
<td>1</td>
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<td>2</td>
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<tr>
<td>3</td>
<td>Exercise</td>
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2. Cardiac catheterization studies
A) Coronary arteriogram

B) Coronary sinus catheterization

<table>
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<tr>
<th>Items</th>
<th>Pacing stress</th>
<th>before</th>
<th>during</th>
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<tr>
<td>Coronary sinus blood flow</td>
<td></td>
<td>0</td>
<td>36.7</td>
</tr>
<tr>
<td>(increment, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial lactate extraction ratio (%)</td>
<td></td>
<td>44.0</td>
<td>7</td>
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Fig.1. The polyparametric evaluation of a case of variant angina.

Fig.2. Changes in coronary sinus blood flow during the pacing stress.
Fig. 3. Changes in coronary sinus blood flow were examined by Ergotamine tartrate
provocation test to variant angina. The provocation induced the pain and ST
elevation in these cases. Nitroglycerine was given at the time indicated by the
arrow.

Presence or absence of symptoms. Likewise, the presence or absence of symptoms was not
judged from ST abnormalities. The limitations of electrocardiographic diagnosis are impotent
here.

Anginal pain was provoked by pacing stress
testing and the increment of coronary sinus
blood flow was low compared to normal. The
myocardial lactate extraction ratio was also
decreased. Coronary arteriographic findings
showed significant morphological stenosis of the
right coronary artery. Therefore, the myocardial
ischemic events in this case would be summarized
as follows: The pacing stress increased the
coronary sinus blood flow. However, the mor-
phological stenosis of the coronary artery defi-
nitely limited this increase. Thus, the decreased
flow caused the anaerobic myocardial metabolism
in this lesion. The electrocardiogram showed the
ST elevation and the anginal pain was recognized.

Using this polyparametric diagnostic approach
to each patient, the objective difference between
angina pectoris and silent myocardial ischemia
was examined.

B) Changes in coronary sinus blood flow in
myocardial ischemia

a) Changes in coronary sinus blood flow
during effort angina as determined by pacing
stress testing are shown in Fig. 2. The upper
panel shows the percentile change of this incre-
ment and the lower panel indicates this flow
change corrected by heart rate. The left column
shows the results from the control group which
showed no sign of myocardial ischemia. This
group was compared with the myocardial is-
chemic group which was proved to have signifi-
cant coronary arterial stenosis by the coronary
angiography. Compared with the control group,
the myocardial ischemic group showed dearly a
lower increment of coronary sinus blood flow at
maximal pacing rate. Therefore, the increase in
coronary blood flow was significantly less in
the myocardial ischemic group under stress.
Fig. 4. Changes in myocardial lactate extraction ratio caused by pacing stress.

Fig. 5. A schematic illustration of the evaluation of myocardial ischemia.

testing compared to the control. However, in the myocardial ischemic group there were no significant differences in this coronary flow between the provoked angina group and the non-provoked angina group.

b) Changes of the coronary sinus blood flow during a provocation test with Ergotamine tartrate to variant angina are shown in Fig. 3.21

During the provoked anginal period a significant decrease in coronary blood flow was noted with marked ST elevation and chest pain. Thereafter, these changes were improved by the administration of nitroglycerine. Therefore, the primary decrease of the coronary sinus blood flow was the cause of this induced angina.

c) Changes in myocardial metabolism caused by myocardial ischemia.

The change of myocardial lactate extraction ratio caused by pacing stress testing is shown in Fig. 4. The control group showed no change in this ratio. In the myocardial ischemic group, the non-provoked anginal patients in the middle of the figure showed a similar change of ratio at the maximal pacing rate compared to that in the control period.

On the other hand, in the angina provoked group the myocardial lactate extraction ratio clearly decreased at the point of the appearance of the anginal pain in all cases. That is the anaerobic myocardial metabolism caused by stress testing produced the anginal state. Therefore, at the time of the appearance of the anginal pain under the pacing stress the coronary blood flow increment decreased and the myocardial lactate extraction ratio was decreased, which is clearly different from the non-anginal state.

From these date, we conclude that the polyparametric evaluation for the diagnosis of the angina pectoris was useful for the definite diagnosis of myocardial ischemia.

2. Is there the difference in the time at which each of the polyparametric abnormalities following myocardial ischemia can be recognised

From the above mentioned results, the following questions were raised. A) Are these polyparametric factors equally important in the diagnosis of myocardial ischemia? B) If there are differences in diagnostic weight between these factors, how is it significant?

Since the early and precise diagnosis of

myocardial ischemia is advantageous, the following experiment was performed to clarify the differences in the times at which these poly-parametric abnormalities of the myocardial ischemia can be recognised (Fig. 5)³

TABLE 1  THE SPECIFICITY AND SENSITIVITY OF ECG AND CMG (%)  

<table>
<thead>
<tr>
<th>N = 66</th>
<th>ECG</th>
<th>CMG</th>
<th>ECG+CMG</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>75.7</td>
<td>75.7</td>
<td>89.2</td>
</tr>
<tr>
<td>Specificity</td>
<td>58.6</td>
<td>55.2</td>
<td>79.3</td>
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ECG = exercise electrocardiographic stress testing; CMG = exercise cardiomyographic stress testing

The cardiac motion abnormalities in late-systole detected by CMG were noted 15 seconds after the occlusion of a coronary artery (Fig. 6). This was the first objective abnormality in this experiment. After a delay, ST segment elevation of the involved epicardial region was recognized. Lastly, \(-\text{dp}/\text{dt}\) of the left ventricle changed. After reperfusion of the coronary artery \(-\text{dp}/\text{dt}\) was normalized followed by the ST segment change of the epicardial electrocardiogram returning to normal. A noteworthy change is that the regional cardiac wall motion change at late-systole was restored last. The implications of this animal experiment are as follows. The above mentioned polyparametric events did not change simultaneously after the induction of

Fig. 7. A schematic showing sequential changes of the polyparameters after myocardial ischemia based on our data. The clinical recognition of this event is shown in the lower panel compared with the animal experimental data.

myocardial ischemia. Regional wall motion change was the most sensitive parameter for the recognition of myocardial ischemia. Other investigators have found similar results\textsuperscript{9,10,11,14}. Therefore the question to be solved clinically is how to detect and monitor wall motion abnormality non-invasively.

3. How should we achieve the early diagnosis of myocardial ischemia?

A) The clinical detection and the estimation of the significance of cardiac motion abnormalities by Cardiomoveogram

There are many clinical methods to detect wall motion abnormalities, such as echocardiography and nuclear methods. However, any method can be clinically satisfactory yet fail to answer the above question\textsuperscript{12}. We have developed a new device for this purpose, the cardiomoveogram (CMG)\textsuperscript{19–22}. This apparatus measures the cardiac motion in the given electromagnetic field as the signal change of the resistance and the capacitance under the magnetic coil. The device is based on cardiokymography which was developed by Vas, R.\textsuperscript{18}

The detection of myocardial ischemia was performed by treadmill exercise electrocardiographic testing and also by ergometer exercise cardiomoveographic testing in the same patients who were angiographically proven to be abnormal. The sensitivity and the specificity of these 2 methods were as shown in Table I\textsuperscript{5}. Neither the sensitivity nor the specificity of these 2 method differed. However, a combination of the 2 methods remarkably improved not only the sensitivity but also the specificity. We concluded that a combination of these 2 quantitatively different methods should be applied for the detection of myocardial ischemia.

B) The diagnostic significance of the polyparametric diagnostic evaluation of myocardial ischemia

Lastly, the differences in time of appearance of the polyparametric changes induced by myocardial ischemia are schematically shown based on our data so far obtained (Fig. 7). The lower panel shows the clinical detection of myocardial ischemia in our hands at present. After myocardial ischemia the coronary sinus blood flow decreased, then the cardiac regional motion at the late systole became abnormal and then there were ST-T changes in the electrocardiogram. Later, changes in $-\text{dp/dt}$ of the left ventricle and lactate production from the involved myocardium took place. At that time, chest pain began to be recognized by the patient. Therefore, the key for the early recognition of myocardial ischemia clinically lies here. For the clinician, the recognition of chest pain in the patient is very important in patient care\textsuperscript{23}. However, awareness of the polyparametric changes which follow myocardial ischemia is far more important\textsuperscript{13,15,16}. The most sensitive parameter, regional cardiac wall motion, should be detected non-invasively. This approach is the most practical approach to the early recognition of myocardial ischemia.

The sequential changes shown in animal experiments are clearly different from the above clinical evaluations. The main reasons for this are technical limitations. However these limitations should be reduced in the near future.

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