Diagnostic and Prognostic Significance of Serum Transaminase Levels in Coronary Occlusive Disease

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With technical assistance of Joe Yamashita

Clinical and experimental studies of acute myocardial infarction suggest that serum glutamic oxalacetic transaminase (SGO-T) levels may have both diagnostic and prognostic significance. The authors report their experience in 255 patients hospitalized because of chest pain strongly suggestive of acute myocardial infarction. The results of serial determinations are compared with the clinical data and the electrocardiographic findings. The data indicate that abnormally high levels have both diagnostic and prognostic significance.

CLINICAL and experimental studies of acute myocardial infarction1-7 have suggested that the serum glutamic oxalacetic transaminase (SGO-T) test devised by LaDue and his associates may have both diagnostic and prognostic significance. The present report contains data on 255 patients all of whom were hospitalized with chest pain strongly suggesting myocardial infarction in the differential diagnosis.

These data indicate that the test is of diagnostic value, particularly in patients in whom the diagnosis cannot be made with certainty from the electrocardiographic findings and other clinical features. A study of the fatal cases suggests that the test also has prognostic significance.

Methods

The patients were all hospitalized either at the Wadsworth General Veterans Administration Hospital or at the UCLA Medical Center. All but 3 of the patients were men ranging in age from 37 to 85 years. Efforts were made to obtain serial SGO-T determinations, particularly during the first few days following the onset of pain, since the time-concentration curve of the SGO-T levels has been shown to be far more informative than single random samples.8 Cases with only 1 determination were excluded from the study unless that sample was markedly elevated and appeared to be significantly related in time to the onset of pain or to the death of the patient.

The SGO-T levels were determined by the method of Karmen8 with slight modifications as described earlier. Some batches of malic dehydrogenase required dilution of 1 to 10 in phosphate buffer rather than 1 to 25 as previously done.

In order to assess the diagnostic value of the test the cases were divided into those with proved myocardial infarction and those in whom the diagnosis of myocardial infarction could not be made with certainty.

The cases were considered to have proved infarction if the history was compatible with the diagnosis and the electrocardiograms showed pathologic Q waves and typical evolutionary ST and T-wave patterns of acute myocardial infarction; 111 cases fell into this group.

There were 144 cases in whom the diagnosis of myocardial infarction remained in question, either because the clinical manifestations were not clear or the electrocardiograms failed to show the typical pattern of acute myocardial infarction. In many instances the electrocardiographic patterns were obscured by pre-existing abnormalities. It is true that a number of the cases in this group did have clinical manifestations that merited strong suspicion of acute myocardial infarction, but in none of them could the diagnosis be made with certainty. Seven patients classified initially as probable myocardial infarctions were later shown to have infarcts at autopsy.

The idea of the study was to examine the reliability of the test in patients with known myocardial infarction and then to ascertain whether the test would enable us to pick the instances of infarction from the cases in which the diagnosis was uncertain. To determine the prognostic value of the SGO-T test the peak of the time-concentration curve was examined in the fatal cases.

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Results

Evidence of Diagnostic Significance

Patients with Proved Myocardial Infarction. All but 1 of 111 cases of proved myocardial infarction had elevated SGO-T. The distribution of SGO-T levels during the acute phase of the attacks is illustrated in figure 1. Normal values of SGO-T may be found during the first few hours after the onset of pain. The values rise rapidly to a peak that is usually reached between 24 and 48 hours after the onset. There is then a gradual fall over the succeeding 3 or 4 days to normal levels. The patient with no rise in SGO-T died only 31/2 hours after the onset of pain. Thus, all cases of proved myocardial infarction showed an elevation of SGO-T, provided serial blood samples were taken during the first 4 days of the disease. The elevation may be missed if blood samples are taken too early or after the third or fourth day.

It is of interest that 7 of the 111 cases of proved myocardial infarction showed elevation of SGO-T before the electrocardiographic patterns became clearly diagnostic, which thus provided early evidence of myocardial necrosis.

Patients with Uncertain Diagnosis. Among 144 cases in which the diagnosis of myocardial infarction could not be established with certainty, 63 had SGO-T elevations with peak levels of 44 to 800 units. These 63 cases have been classified as "probable myocardial infarction," since they all had elevations of SGO-T with time-concentration curves similar to those of cases with proved infarction. Eight of the probable cases died and 7 of them came to autopsy; all 7 showed recent myocardial infarction. Examples from the group of probable infarctions are presented in the section on illustrative cases.

The electrocardiographic features that obscured diagnosis in this group are listed in the first column of table 1 and the peak levels of SGO-T are illustrated in figure 2.

Among the uncertain cases were 10 patients who had slight elevations of SGO-T ranging from 40 to 43 units, hardly out of the normal range. Each of these, however, had a well-defined curve with a rise to the peak value and a subsequent fall to much lower levels. Because of our conviction that the sequence of SGO-T levels is more important than any single value, we have thought it likely that these patients did have small infarctions. We have listed them as "possible infarctions" in table 1 and plotted them as such in figure 2.

Fig. 1. Frequency distribution of SGO-T levels on each of 6 successive days following the clinical onset of the disease in 118 patients with proved myocardial infarction. The ordinate is logarithmic. All cases showed elevations above 40 units at some time during these 6 days.
SIGNIFICANCE OF SERUM TRANSAMINASE LEVELS

**Fig. 2.** Distribution of peak SGO-T levels in various clinical categories with subdivisions indicating electrocardiographic patterns. The category marked “other” includes cases of ventricular “strain,” arrhythmias, flat T waves, cor pulmonale, dissecting aneurysm, and normal electrocardiogram. Seven of 8 fatal cases with uncertain diagnosis during life became proved cases at autopsy. (• Indicates survivals and † indicates deaths.)

**Table 1.—Cases with Chest Pain of Uncertain Diagnosis**

<table>
<thead>
<tr>
<th>Electrocardiographic and clinical diagnosis</th>
<th>Number of cases with SGO-T elevations: “probable infarct”</th>
<th>Number of cases with slight SGO-T elevations: “possible infarct”</th>
<th>Number of cases with no SGO-T elevations: “angina without infarct”</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injury or ischemia</td>
<td>37</td>
<td>5</td>
<td>34</td>
<td>76</td>
</tr>
<tr>
<td>Previous MI</td>
<td>15</td>
<td>3</td>
<td>21</td>
<td>39</td>
</tr>
<tr>
<td>LBBB*</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Ventricular “strain”</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Normal electrocardiogram</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flat T waves</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cor pulmonale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissecting aneurysm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No electrocardiogram taken</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
<td>10</td>
<td>71</td>
<td>144</td>
</tr>
</tbody>
</table>

* Left bundle-branch block
† Myocardial infarction

There were 71 patients who showed no rise of SGO-T in serial determinations. Several of these had levels as high as 40 units but on serial determinations these showed very little or no variation. It was concluded that these patients in all likelihood had anginal pain without infarction. These cases are listed in the third column of table 1 and plotted in the top section of figure 2.

In the groups listed as “possible infarction” and “angina without infarction” there were no deaths, so that autopsy confirmation was not possible in any of these cases.

**Extension of Known Myocardial Infarction.** Among the patients with proved myocardial infarction, 14 had recurrences of chest pains accompanied by secondary rises of the SGO-T levels. In a number of these, additional electrocardiographic changes could not be discerned. In such cases SGO-T elevations provided the strongest evidence of extension of previously known acute myocardial infarction. Three of these cases are illustrated in the next section.

**Illustrative Cases.** Figure 3 depicts the course of a 60-year-old white man who had severe substernal crushing pain with sweating and dyspnea. The electrocardiograms showed only the slightest abnormalities consisting of some loss of voltage and flattening of the T waves. The leukocyte counts and the sedimentation rates did not help in the diagnosis, but the SGO-T curve gave strong evidence of the presence of infarction.
Figure 4 shows the course of a 60-year-old white diabetic man, who was admitted with severe chest pain and dyspnea. The electrocardiogram showed only slight ST sagging in V4. SGO-T levels remained normal and it was concluded that the patient had anginal pain without infarction. He continued to have intermittent substernal pains during the next several weeks. Subsequently there was a recurrence of severe chest pain accompanied by marked ST depressions in the electrocardiogram without Q waves. SGO-T rose sharply and the patient expired. At autopsy, there was extensive subendocardial myocardial infarction. In this

![Figure 3](http://circ.ahajournals.org/)

**Fig. 3.** Almost normal electrocardiogram. Probable infarction suggested by history and high SGO-T levels.

![Figure 4](http://circ.ahajournals.org/)

**Fig. 4.** Coronary insufficiency with normal SGO-T levels followed by subendocardial injury and high SGO-T. Infarction established at autopsy.
case the SGO-T test first aided in excluding the presence of myocardial infarction and later helped to confirm its presence.

Figure 5 illustrates the case of a 67-year-old white man who was admitted with substernal pain and fever. The electrocardiogram showed only slight ST depressions but the elevation and subsequent fall of SGO-T gave evidence of myocardial infarction. Two months later a recurrence of pain was accompanied by electrocardiographic changes indicative of posterior myocardial infarction. SGO-T elevations present at this time fell to normal. A subsequent attack of pain was not accompanied by definitive electrocardiographic changes, but the rise in SGO-T indicated extension of the infarction.

Figure 6 depicts the course of a 55-year-old white man with a history of an old myocardial infarction. The patient suffered 4 different episodes of chest pains during which the electrocardiogram continued to show a slightly varying pattern of myocardial injury and ischemia. Three of these episodes appeared to be true infarctions, since each was accompanied by elevations of SGO-T. The last episode was associated with no rise and presumably was a bout of coronary insufficiency.

Figure 7 shows the value of the low-level curve. This patient was a 58-year-old white man with chest pain and electrocardiographic evidence of posterior myocardial infarction. Although the peak SGO-T level of 44 units was only slightly higher than the normal range, the rise and fall of the level was strongly suggestive of myocardial infarction.

Figure 8 depicts the course of a 64-year-old white man who had clear-cut electrocardiographic evidence of acute posterior infarction accompanied by SGO-T elevation. Two further episodes of chest pains were not accompanied by further electrocardiographic changes but marked secondary and tertiary elevations of SGO-T gave strong evidence of the presence of extensions of the area of infarction. There was infarction of the entire posterior wall of the heart including septum and left and right ventricles at autopsy. Areas of fresh red hemorrhagic necrosis were clearly delineated from older areas of grey and yellow necrosis.

Evidence of Prognostic Significance

Experimental work in animals\textsuperscript{5-7} has indicated that the height of the peak level of SGO-T is roughly proportional to the size of myocardial infarcts. If this is also true in man, then
the SGO-T test should have important prognostic implications: the larger the infarct, the poorer should be the prognosis and the higher the mortality. One might expect, therefore, that the patients who died would have higher peak levels of SGO-T than the survivors of myocardial infarction, and furthermore, that the larger infarctions would be associated with higher levels of SGO-T than the smaller infarcts.

**Fig. 6.** Four episodes of chest pain with electrocardiograms showing only ischemia. During 3 of the episodes SGO-T is elevated, suggesting infarction. In the fourth SGO-T is normal, suggesting anginal pain without infarction.

**Fig. 7.** Shows that low-level SGO-T elevations are significant. Electrocardiogram shows typical posterior myocardial infarction. SGO-T rises only to 44 units.
To find evidence bearing on this problem a study was made of the 37 fatal cases. All but 3 of these were autopsied. It was apparent that many of the fatal cases had peak SGO-T levels no higher than the survivors. Many were associated with complicating factors such as previous myocardial infarction, other diseases, or a failure to obtain blood samples at a time when peak values of SGO-T were to be expected.

For a valid evaluation of the significance of SGO-T in fatal cases it is necessary that death be clearly due to the acute infarction and that it occur after the peak of the SGO-T. It is also necessary that other complicating factors be absent that might make the patient succumb to myocardial damage which, in itself, might not be lethal. In our series only 11 of the 37 fatal cases fulfilled these conditions reasonably well.

Table 2 summarizes the data on the fatal cases. The 11 cases that fulfilled our conditions are listed separately. The 26 cases with complicating factors are summarized in 4 groups. One group of 7 cases contains patients who died of recent infarctions superimposed on well-established previous infarction. In this situation it might be presumed that a relatively small infarct would be sufficient to destroy the previously damaged heart. Another group contains the 6 patients who died of infarctions complicating other disease processes: 2 occurred following major surgery, 3 were associated with lobar pneumonia, and 1 complicated cirrhosis of the liver. In the third group are 7 fatal cases with insufficient SGO-T tests to define the peak level. The last group is composed of 6 patients who died a week or more following the primary SGO-T curve without further determinations.

The 11 separately listed cases, with one exception, did indeed have higher peak SGO-T levels than any of the survivors. The highest level found among survivors of proved or probable myocardial infarction was 336 units. There were only 5 survivors with peak levels over 300. The very high levels above 1000 units were all associated with profound shock in the preterminal state. The highest level of all, 5567 units, occurred in a patient in whom hypothermia at 85 F. had been induced in an effort to prolong his life. That shock does not always produce extremely high levels is indicated from the observation that patient F.S.
had severe shock with a peak level of 675, while patient G.A. had no shock when his level was 800. One survivor went through a period of 11 hours of severe shock with a level of SGO-T that did not rise above 298.

These data give convincing evidence that high levels of SGO-T do indeed carry a poor prognosis. The nature of the pathologic examination has not permitted study of a quantitative relationship between the peak levels of SGO-T and the amount of infarcted muscle. All patients who died with levels of 357 to 5567 had large and extensive infarction. Patient P.W., who died with a peak level of 156, had a smaller area of infarction measuring 3 by 4 cm. We are currently attempting more quantitative estimates of the amount of infarcted myocardium in the hope of obtaining data on the relationship between the SGO-T curve and the extent of the infarct.

**Discussion**

To date we have not observed a case of proved myocardial infarction in which the SGO-T failed to rise, provided serial blood samples were drawn during the first 4 days of the disease. In other words, we have not found false negative tests in our series of 118 cases of proved myocardial infarction. These findings are in agreement with those of Chinsky and his associates. Others have reported false negatives with an incidence ranging from 1 to 8 per cent.

False positive SGO-T tests may occur if there is associated damage to liver, kidney, skeletal muscle, pancreas, or lung. Such cases will be described in the second paper of this series. We cannot be certain that some of these factors were not present in all of the cases of probable and possible myocardial infarction, but in each case every effort was made to exclude them. Thus we believe that all patients with known myocardial infarction have elevation of SGO-T during the acute phase of the attack, with a decline to normal levels after 4 or 5 days. In patients suspected of myocardial infarction, elevations of SGO-T with a decline to normal levels at the expected time give indication that myocardial necrosis is indeed

<table>
<thead>
<tr>
<th>Patient</th>
<th>Peak SGO-T</th>
<th>Clinical</th>
<th>Autopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.M. 60 yr. W. M.</td>
<td>5567</td>
<td>Profound coronary shock-induced hypothermia to 84 F.</td>
<td>Extensive infarction of left ventricle</td>
</tr>
<tr>
<td>W.B. 61 yr. W. M.</td>
<td>2900</td>
<td>Entered moribund, single sample before death</td>
<td>Massive infarction left ventricle and septum, small infarcts left kidneys and adrenals</td>
</tr>
<tr>
<td>D.S. 63 yr. W. M.</td>
<td>1940</td>
<td>Profound shock, poor response to Levophed</td>
<td>Extensive posterior infarction</td>
</tr>
<tr>
<td>I.W. 57 yr. W. M.</td>
<td>820</td>
<td>Profound shock, recurrent infarction</td>
<td>Extensive posterolateral infarction</td>
</tr>
<tr>
<td>G.A. 54 yr. W. M.</td>
<td>800</td>
<td>No shock, two extensions</td>
<td>Massive infarction of posterior right and left ventricle and septum</td>
</tr>
<tr>
<td>F.S. 64 yr. W. M.</td>
<td>675</td>
<td>Shock and ventricular tachycardia</td>
<td>Extensive infarction of septum and posterolateral left ventricle</td>
</tr>
<tr>
<td>S.H. 46 yr. N. M.</td>
<td>580</td>
<td>No shock</td>
<td>Massive posterior and old anterior infarct</td>
</tr>
<tr>
<td>A.W. 33 yr. W. M.</td>
<td>560</td>
<td>Congestive failure, no shock</td>
<td>Extensive posterior infarction</td>
</tr>
<tr>
<td>C.G. 60 yr. W. M.</td>
<td>523</td>
<td>Congestive failure, no shock</td>
<td>Extensive infarction of posterolateral left ventricle and posterior right ventricle</td>
</tr>
<tr>
<td>R.M. 64 yr. W. M.</td>
<td>357</td>
<td>No shock</td>
<td>Extensive infarction left ventricle and septum</td>
</tr>
<tr>
<td>P.W. 56 yr. W. M.</td>
<td>156</td>
<td>No shock, sudden death on 4th day</td>
<td>3 x 4 cm. infarction of posterior left ventricle and septum</td>
</tr>
</tbody>
</table>

| | 7 cases | 50 to 210 | Died of recent infarct complicating old one |
| | 6 cases | 50 to 218 | Died with infarct complicating other diseases |
| | 7 cases | 25 to 293 | Died with peak value not known |
| | 6 cases | 146 to 242 | Died a week or more after primary curve |
SIGNIFICANCE OF SERUM TRANSAMINASE LEVELS

present. In 7 of our 63 uncertain cases these assumptions were verified at autopsy.

The same considerations may be applied conversely to those patients who failed to show a rise of SGO-T. Those cases without a rise of SGO-T following an episode of chest pain may be considered not to have myocardial necrosis. While supporting evidence for this view is derived from animal experiments, the point cannot be easily proved in man. Such proof would require a number of autopsies on patients dying of intercurrent causes shortly after attacks of anginal pain during which period the patients had been followed with serial SGO-T tests. At the present time such proof is lacking. Whether or not such patients might have small or microscopic infarcts as suggested by Sampson must also await pathologic examination.

The data on the fatal cases strongly suggest that SGO-T levels above 350 units carry very grave prognoses and probably indicate extensive myocardial infarction.

Whether or not peak levels of SGO-T will prove to be proportional to the extent of the myocardial infarction must await more detailed study of autopsied hearts. That the problem will be difficult to solve in the human is suggested by the case illustrated in figure 8. Here there was continuous elevation of SGO-T for 10 days with peaks of SGO-T varying between 390 and 800 units. It is suggested that the volume of infarcted muscle may correlate better with the area of the time-concentration curve than with peak values of SGO-T.

SUMMARY AND CONCLUSIONS

Determinations of serum glutamic oxalacetic transaminase were made in 255 patients suspected of having acute myocardial infarction. In 111 patients the diagnosis of myocardial infarction could be established on clinical evidence and the electrocardiograms. All these patients had elevations of SGO-T, provided serial levels were obtained during the first 3 to 6 days following onset of pain. Sixty-three patients in whom the diagnosis could not be established with certainty had elevations of SGO-T similar to those seen in the proved infarctions. These were classified as probable myocardial infarcts. Seven were proved at autopsy to have infarcts. Ten patients showed small elevations hardly out of the normal range. These were classified as possible infarcts. Seventy-one patients had no elevations of SGO-T. These were classified as angina without infarction. Of 37 fatal cases of myocardial infarction, 11 were uncomplicated by other factors. All but 1 of these 11 had peak levels of SGO-T higher than 350 units. The highest level among survivors was 336 units. Levels of SGO-T over 350 units carry a grave prognosis. The SGO-T test appears to be useful in the diagnosis of uncertain cases of myocardial infarction.

SUMARIO IN INTERLINGUA

Determinaciones de seral transaminase glu-tamic-oxalacetic (SGO-T) esseva executate in 255 patientes suspecte de acute infarimento myocardial. In 111 patientes le diagnose de infarimento myocardial poteva esser establite super le base de datos clinic e electrocardiographic. Omne iste patientes habeva elevate nivello de SGO-T, providite que illos esseva determinate durante le prime 3 a 6 dies post le declaration del dolores. Sexanta-sex patientes in qui le diagnose non poteva esser establite con certitude habeva nivello de SGO-T simile a lo que esseva constatare in le gruppo a infarimentos demonstrate. Iste 66 patientes esseva classificate como casos de probabile infarimento myocardial. Dece patientes mons-trava leve elevationes que a pena exceedeva le limites normal. Iste cases esseva classificate como infarimentos possibile. Septanta-un patientes habeva nulle elevation de SGO-T. Lor cases esseva classificate como angina sin infarimento.

In un serie de 37 casos mortal de infarimento myocardial, 11 non esseva complicate per al-tere factores. Con un exception, omne le 11 habeva nivello maximal de SGO-T que exceedeva 350 unitates. Inter le superviventes, le plus alte nivello esseva 336 unitates.

Nivello de SGO-T de supra 350 unitates rende le prognose multo grave. Il pare que le determination de SGO-T es utile in le diagnose de indecise casos de infarimento myocardial.
I have no great quickness of apprehension or wit which is so remarkable in some clever men, for instance, Huxley. I am therefore a poor critic: a paper or book, when first read, generally excites my admiration, and it is only after considerable reflection that I perceive the weak points. My power to follow a long and purely abstract train of thought is very limited; and therefore I could never have succeeded with metaphysics or mathematics. My memory is extensive, yet hazy: it suffices to make me cautious by vaguely telling me that I have observed or read something opposed to the conclusion which I am drawing, or on the other hand in favour of it; and after a time I can generally recollect where to search for my authority. So poor in one sense is my memory that I have never been able to remember for more than a few days a single date or a line of poetry.

Some of my critics have said, 'Oh, he is a good observer, but he has no power of reasoning!' I do not think that this can be true, for the Origin of Species is one long argument from the beginning to the end, and it has convinced not a few able men. No one could have written it without having some power of reasoning. I have a fair share of invention, and of common sense or judgment, such as every fairly successful lawyer or doctor must have, but not, I believe, in any higher degree.

On the favourable side of the balance, I think that I am superior to the common run of men in noticing things which easily escape attention, and in observing them carefully. My industry has been nearly as great as it could have been in the observation and collection of facts. What is far more important, my love of natural science has been steady and ardent.—CHARLES DARWIN (1809–1882).
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