patients with diseases of the liver such as hepatitis, cirrhosis and hepatic cancer. As the most common abnormalities, lowering of T wave, depression of ST segment, low voltage and prolongation of QT duration were observed. These electrocardiographic changes were correlated with aging of the patients and severity of the clinical symptoms. It was noticed that the grade of the electrocardiographic changes had marked correlation with the lowering of serum protein level, especially that of serum albumin level in cirrhosis. The abnormal electrocardiogram was found in all patients with less than 5.5 g/dl of serum protein level or with less than 2.0 g/dl of serum albumin level. The electrocardiographic findings were also correlated with some abnormalities of serum electrolyte level such as hyper- or hypopotassiumemia, changes of serum Na/K ratio and hypocalcemia. In addition, the relationship between “Verfließen” of ST-T junction(Wuhrmann) or Hegglin’s syndrome and dysproteinemia or dyselectrolytemia was investigated. From the above results, it was suggested that dysproteinemia, dyselectrolytemia or combinations of these metabolic disorders were responsible for the electrocardiographic findings. As to the prognostic significance of the electrocardiographic findings, it seemed more valuable to follow up the change of T/P ratio in comparison with that of QT/TQ ratio. Finally, the relationship between the electrocardiographic changes and pathological findings of the heart was discussed to some extent.

ACKNOWLEDGMENT

The author wishes to express his appreciation to Professor G. Wakisaka, Department of Internal Medicine, Kyoto University, for his kind advice and his helpful criticism.

REFERENCES

3. Hepatogenic Myocardosis, Especially on the Electrocardiographic Changes During Induced Anoxemia

Takeshi Nangu

[The Department of Medicine (Director: Prof. K. Hara), Osaka Medical Colledge, Takatsuki]

Since F. Wuhrman's presentation of the concept of “Myocardose” in 1950, myocardial damage in various hepatic disturbances have been reported, although the investigation about its origin and clinical significance is yet incomplete.

During the past ten years, the author studied quantitative relationships between electrocardiographic changes and serum protein patterns in various hepatic diseases. On the other hand, it is important to study the meaning of serum electrolytes to the ECG findings especially in liver diseases. Besides, a study with the induced anoxia test was designed to study a part of the myocardial metabolism in hepatic disease.

Material and Method

Three hundred and one cases of various hepatic diseases without former organic circulatory diseases, who were admitted to the medical clinic (Director: Prof. K. Hara) of Osaka Medical College or Hiraoka City Hospital (Director: Prof. K. Hara), were examined.

As a rule, serum sampling was done on the same day as the electrocardiographic examination.

As the anoxia test, the Levy's original method of 10% oxygen inhalation for 20 minutes was used.

† (Received for Publication August 31, 1963)
RESULT AND DISCUSSION

I) Electrocardiographic findings in hepatic diseases

Seven important findings are presented in Fig. 1. One or more of these were found in 72% of the patients. Among the seven, changes related to myocardial damage such as low T (46%), QT prolongation (42%), ST depression (23%) and low voltage (14%) are common and more often seen in hepatic cirrhosis and severe hepatitis than in acute and chronic hepatitis.

Multiplicity of electrocardiographic abnormalities in each patient was examined, (Fig. 2) and when only one of the seven findings was present, the patient was designated (+), and when 2 or more were present, they were considered (++) or (+++), respectively.

Cases with two abnormal findings are found in about 25% of acute and chronic hepatitis, while in hepatic cirrhosis they are seen in 60%, and higher multiplicities of abnormalities (++, +++), are not uncommon.

II) Causes of death and prognosis of hepatic cirrhosis

Influence of such electrocardiographic abnormalities upon the fate of hepatic cirrhosis and the multiplicity of abnormal electrocardiographic findings was investigated. The relation between the fate of hepatic cirrhosis and the multiplicity of abnormal electrocardiographic findings is presented in Fig. 3; in the electrocardiographically negative groups the lethality is 5.6% (only one in 18 cases), whereas in the two positive group (+) it is 32%, in the group (++) or (+++) about 50% and in the (++++) group 80% i.e. the higher multiplicity, the higher lethality.

The survival rate of 111 cases of hepatic cirrhosis was investigated by long term observation (Fig. 4); about one half of the cases in the ECG negative group are still living after 5 years, whereas in (++) and (+++) positive groups only one third remain alive after 2 years and this survival rate in the (++++) group is seen after 6
months. These results are in good accordance with the hospitalized cases.

The two observations mentioned above show that myocardial damage expressed by ECG findings is related to the fate and prognosis of hepatic cirrhosis.

It may be considered that the more multiple the electrocardiographic abnormalities are, the more various and complicated the myocardial changes are.

Hitherto, hemorrhage from venous plexes, hepatic coma and primary liver cancer are known as the three main causes of death in hepatic cirrhosis. Cardiac death, however, has not been mentioned except in one report with 4 cases from the Kure medical clinic, Tokyo University.

Furthermore, in some papers there are a number of cases without definite descriptions of the direct causes of death.

The author examined the direct causes of death in hepatic cirrhosis, with special consideration on cardiac insufficiency based on myocardial damage with the following results; in 63 cases that died, hepatic coma was the most frequent with 18 cases (29%), hemorrhage from venous plexes was 7 (11%) and liver cancer 16 (25%). Cases with multiple ECG findings and without any of these three causes were 16 (25%). In most of the latter cases the direct cause of death can be considered to be cardiac debility.

Thus in hepatic cirrhosis, ECG findings should be studied not only for prognostic evaluation but also for the consideration of the direct cause of death.

III) Correlations between electrocardiographic abnormality and serum protein or electrolyte pattern in hepatic diseases

Concerning the factors which cause electrocardiographic abnormalities in hepatic cirrhosis, disturbances of protein metabolism were pointed out by Wuhrmann. However, the correlation between the ECG findings and the types of dysproteinemia was not made clear.

The author studied this relation and reported that unbalance with decrease of albumin and increase of \( \gamma \)-globulin has more correlation with the electrocardiographic changes than the decrease of total serum protein.

On the other hand, it is well known that electrolytes have important effects on the ECG and especially on the T wave. But this relation had not been carefully investigated in liver diseases.

The author investigated this point statistically and compared the results with those of dysproteinemia (Tab. 1):

i) Height of R: Concerning the quantitative relations between the highest value of R in limb leads (mV) and serum A/G or K and Na values, showed a positive correlation of \( r = 0.35 \) was seen only with A/G.

ii) Height of T: The highest value of T in limb leads showed correlations of \( r = 0.67 \) and \( r = 0.40 \) with A/G and with K respectively. With Na/K, negative relationship of \( r = -0.38 \) were found.

iii) QTc: A negative relationship of \( r = -0.52 \) was noted with A/G, but no relation with electrolytes existed.

iv) ST depression: Concerning the presence or absence of ST depression, no correlation was found with dysproteinemia and dyselectrolytemia.

Low voltage, low T and QT prolongation are related with the decrease in serum A/G, while with serum electrolytes, only decreased K and increased Na/K have correlation with low T, and alteration of Na has no relation with electrocardiographic findings, so it can be considered that the relations between increased Na/K and low T is simply due to decreased K.

Depressed ST has no correlations with proteins and electrolytes. Perhaps a problem of myocardial oxygen demand and supply is concerned.

Table I Correlation of Maximum R, T Voltages and QTc in Limb Leads and ST Depression to Serum Protein and Electrolyte

<table>
<thead>
<tr>
<th></th>
<th>A/G</th>
<th>Na</th>
<th>K</th>
<th>Na/K</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-Voltage</td>
<td>(+)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>T-Voltage</td>
<td>(+)</td>
<td>(-)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>QTc</td>
<td>(+)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>S-T Depres.</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
</tbody>
</table>

\[ pr(\chi^2 > 2.647) = 0.01 \]
When the average $A/G$, $K$ and $Na$ values are compared simultaneously with the multiplicity of abnormal ECG findings (Fig. 5), most $K$ and $Na$ values are in the normal range, although the $A/G$ decreases gradually as the multiplicity increases and it tends to parallel the grade of myocardial damage.

It can be said that the electrocardiographic change in hepatic disease has more important correlations to dysproteinemia (especially with low voltage, QT prolongation and low T) than dyselectrolytemia (only with low T).

IV) Induced anoxia test in hepatic diseases

As mentioned above, ST depression was found in 23% of the ECG in hepatic diseases during rest. But, it was not related to dysproteinemia and dyselectrolytemia. The Levy's anoxia test was performed to examine the myocardial balance of oxygen demand and supply in hepatic diseases.

Evaluations were made by the Levy-Patterson's criteria\(^\text{10}\); when any one of the fol-

![Fig. 5. Relation Between Myocardial Damage and Serum Protein and Electrolyte.](image)

lowing was present, the test was considered positive; 1) STI, II, III, V\(_4\) or V\(_5\), depression over 0.3 mV. 2) T\(_r\) inversion with STI depression over 0.1 mV. 3) TV\(_4\) or V\(_5\) complete inversion.

i) Rate of positive Levy's test (Fig. 6):

All 17 cases of normal healthy subjects were Levy negative\(^7\). In 32 cases with hepatic diseases, 10 cases were positive (31%). It is second in number to the coronary disease group in the list and appears at the same rate as heart disease and hypertension groups.

ii) Electrocardiogram at rest and positive rate of Levy's test:

Relation between abnormality of ECG before the anoxia test and positive Levy's test was studied. Even in the negative myocardial damage group (before anoxia) 5 out of 18 cases were Levy positive (28%).

This is probably due to the presence of potential coronary or myocardial metabolic dysfunction in hepatic disease. Therefore, even if there is no abnormality in the ECG at rest, the anoxia test is useful for the clinical diagnosis of myocardiosis.

iii) Rate of increase in coronary blood flow and oxygen uptake by the myocardium during induced anoxia

It is known that the coronary blood flow increases as a compensatory mechanism to maintain myocardial oxygen consumption during induced anoxia.

Ogawa\(^8\) of the Hara clinic investigated the relation between coronary blood flow and the rate of myocardial oxygen uptake in his experimental study of coronary circulation. This is shown in Fig. 7 with the dotted line surrounding Levy positive and negative groups respectively. Levy's negative group is enclosed obliquely and almost vertically and the positive group low obliquely in the left space; two factors are seen in the Levy positive group, one is decreased coronary blood flow and another is decreased myocardial oxygen uptake. A tendency of the latter was noted in a case of cirrhosis of the liver.

From these findings, it is suggested that the deficiency of myocardial oxygen uptake is stronger than the inability of the coronary ar-

---

*Japanese Circulation Journal Vol. 28, March 1964*
Fig. 7. Correlation Between Changes in Coronary Blood Flow and Changes in Myocardial Oxygen Extraction Coefficient.

tory to react and this may be responsible for the positive Levy's test in hepatic disease.

CONCLUSION

Various electrocardiographic findings of myocardial damage were seen in 72% of 301 cases with hepatic diseases, it was especially remarkable in cirrhosis of the liver.

It is suggested that the myocardial damage in hepatic cirrhosis is important not only for the evaluation of prognosis but also as a direct cause of death due to cardiac insufficiency.

Abnormal electrocardiographic findings in hepatic diseases are more closely related to dysproteinemia than to dyselectrolytemia.

The occurrence of a positive anoxia test is high in hepatic disease and it is second only to coronary disease. Moreover, the anoxia positive rate was as high as 28% in the group with normal electrocardiograms at rest.

It can be considered that the origin of a positive Levy's test in hepatic disease is due more to dysfunction of myocardial oxygen uptake than to a dysability of coronary vascular reaction.

Acknowledgement

The author wishes to express sincere gratitude to Prof. K. Hara for his guidance.

REFERENCES


4. Some Problems upon the Interrelationship between Wuhrmann's Myocardosis and Hegglin's Syndrome with the Special Reference to their Clinical and Pathological Diagnosis

YOSHIKAI INAGAKI
[The 2nd Clinical Department of Internal Medicine (Director: Prof. Dr. Soroku Saihki), School of Medicine, Chiba University]

KIYOSHI TERAO
[Department of Pathology (Director: Prof. Dr. Nobujiro Takizawa), School of Medicine, Chiba University]

Based upon the clinical cases which were fully examined in our laboratories since these ten years, the problem of overlapping of Wuhrmann's myocardosis and Hegglin's energetic-dynamic heart insufficiency was studied not only on the clinical date intra vitam, but also on the pathologic findings.

A. CLINICAL OBSERVATIONS

I. About the diagnosis of Wuhrmann's myocardosis

196 observations were performed in 150 cases without primary cardio-vascular diseases (Wuhrmann), 55 observations on 31 cases of hepatic diseases, 38 observations on 35 cases of malignant neoplasms, 36 observations on 28 cases of metabolic and endocrine diseases, 28 observations on 26 cases of renal diseases and 39 observations on 30 cases of other diseases. The