A FACTOR ANALYTIC ASSESSMENT OF PROGNOSIS IN ISCHEMIC HEART DISEASE USING THALLIUM-201 MYOCARDIAL SCINTIGRAPHY, RADIOCARDIOGRAPHY AND ORTHOGONAL ELECTROCARDIOGRAPHY

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One hundred and three subjects with ischemic heart disease (IHD) were followed-up in an attempt to assess the most important factors affecting morbidity and mortality. At the time of initial examination 23 patients had congestive heart failure. During the one year follow-up after the examination 11 patients died. Various parameters including perfusion defects (SCORE) on ^{201}Tl -myocardial scintigrams, radiocardiographic hemodynamic data and orthogonal electrocardiographic parameters were analysed at the onset of the study, according to the method of "factor analysis". The factor analytic technique enabled a summary of the data obtained from these non-invasive approaches into five major interpretable components termed factors 1 to 5; factor 1 as "the extent of myocardial ischemia", factor 2 "heart size", factor 3 "cardiac pump function", factor 4 "peripheral blood volume" and factor 5 "QRS forces". The relationship between these five factors with a one-year mortality rate was then investigated. Of these factors, factor 1 which included SCORE, spatial G/QRS, T/QRS and QRS-T angle proved to be the most important as related to morbidity and mortality in IHD. Factors 2 and 3 were also shown to be useful prognostic indicators of subsequent mortality. Thus, a combination of these non-invasive parameters is useful not only to diagnose IHD but also serves as one form of evaluation of the prognosis in patients with IHD.

ELECTROPHYSIOLOGICAL derangements and impaired cardiac pump function due to decreased myocardial perfusion are characteris-

Key Words:

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tics in ischemic heart disease. Radionuclide imaging of the myocardium and non-invasive assessment of ventricular function should contribute to elucidation of the pathophysiology of ischemic heart disease. Thallium-201 (^{201}Tl) myocardial scintigraphy is a valuable tool used to assess regional myocardial perfusion and myocardial imaging defects are compatible with the extent of ischemia and/or damage.¹⁻³

Radiocardiography (RCG) has been used to

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calculate cardiac output since the first analysis of a time-activity curve termed "Radiocardiogram" by Prinzmetal⁴ Kuwahara et al. proposed a compartment analysis of RCG with analog simulation⁵ and this approach enabled quantification of cardiac output and mean blood volume in the right heart, the lung, the left heart and the body according to mean transit time of each compartment. In our institute more than ten thousand patients with various heart disease have been examined on a routine basis and the validity of this method has been confirmed in clinical studies⁶⁻⁹

The concept of the ventricular gradient (G) stands on a sound theoretical basis and provides an important means of analysis in electrocardiography^{10,11} The clinical validity and usefulness of G, however, has not been established. On the other hand, it has been suggested that changes of the QRS complex can be used as an index of left ventricular function.¹²⁻¹⁴

Factor analysis is a method of reducing a set of variables to a smaller set of factors that may be taken as source variables which can account for interrelations in the data¹⁵

The purpose of our study was (1) to see if there was an underlying pattern of relationships

TABLE I DEATHS DURING A ONE-YEAR FOLLOW-UP

Cause	Number
Congestive heart failure	7/11
Recurrent myocardial infarction	2/11
Sudden death without chest pain	1/11
Noncardiac	1/11

among a set of non-invasive variables obtained from ²⁰¹Tl-myocardial scintigraphy, RCG and orthogonal scalar electrocardiography by factor analytic techniques and to extract factors which may be taken as source variables to account for the interrelations in the data, (2) to investigate the relation of these extracted factors to the incidence of congestive heart failure and to one-year mortality, and (3) to identify important factors affecting the severity and prognosis in patients with IHD.

MATERIALS AND METHODS

One hundred and three Japanese patients, 90 men and 13 women with a mean age of 57 years and a clinical diagnosis of ischemic heart disease (IHD) seen between 1977 and 1978 were in-

Fig.1. Scoring of perfusion defects on ²⁰¹Tl-myocardial scintigrams. Perfusion defects were scored from 1 to 4 according to the degree of open angles of the defects measured from a center of the heart. Score 0 was defined as no evident perfusion defect. Representative scintigrams were demonstrated.

Cardiac output : $F = \text{Blood volume} / \text{MTT}_{\text{one-circulation}}$

$$\begin{aligned} \text{Right heart volume} &= \text{MTT}_r \times F \\ \text{Pulmonary blood volume} &= \text{MTT}_p \times F \\ \text{Left heart volume} &= \text{MTT}_l \times F \\ \text{Body blood volume} &= \text{MTT}_b \times F \end{aligned}$$

Fig.2. Radiocardiogram. Original curve of radiocardiogram (upper left) and simulation curves composed by analog computer (upper right) were shown. Calculated mean blood volumes (ml) of four compartments were listed at the bottom.

MTT = mean transit time (sec); subscript r,p,l and b = right heart, lung, left heart and body, respectively.

involved in the study. The criteria for this diagnosis were based on (1) typical angina pectoris induced by exertional or emotional stress and relieved by rest or nitroglycerin; (2) prior myocardial infarction with appropriate clinical symptoms and electrocardiographic evidence of myocardial infarction or significant enzyme changes, or both. Patients with atrial fibrillation or bundle branch block were excluded. There were 50 patients with confirmed angina pectoris and 53 with old myocardial infarction (at least 3 months since the last acute event). The severity of IHD depended on whether there was a congestive heart failure (CHF). Of 103 patients, 23 had CHF, defined as dyspnea on effort plus either orthopnea or paroxysmal nocturnal dyspnea.

In July, 1979 these patients themselves or their relatives were asked to provide information on their health or the date, cause and place of death. The prognosis was evaluated by a one-year mortality rate. Eleven patients died within one year after the initial examination. Table I shows the cause of death in 11 cases. One patient died following cerebral thrombosis.

Thallium-201 myocardial scintigraphy:

Thallium-201 was given intravenously in a dose of 2 mCi. Imaging was performed with standard scintillation cameras: Searle Pho Gamma HP and Hitachi Gamma View with a high

resolution, parallel-hole collimator. A energy window of 25% was centered at the 80 KeV mercury X rays in the former system and 20% window at both 80 KeV and 140 KeV in the latter. Polaroid images were obtained from five different views (anterior, left anterior oblique 30°, 45° and 60°, and left lateral).

The scoring system to grade myocardial perfusion defects used in our institute was based on the original polaroid scintiphotographs and the largest imaging defect among five views was assessed for grading according to the degree of open angles of the defects measured from a center of the heart (Fig. 1). SCORE 0 was defined as no perfusion defect, SCORE 1 equivocal (an imaging defect less than 15° in open angle from a center of the heart), SCORE 2 small (15° – 45°), SCORE 3 a medium (45° – 90°), and SCORE 4 a large (over 90°) perfusion defect. All scorings were made independently by three investigators who had none of the clinical information. In instances where the point score differed, the three reviewers examined the photos together and agreed upon a final score.

Radiocardiography:

Radiocardiography (RCG) was carried out with patients in the supine position 2 weeks before or after ²⁰¹Tl-scintigraphy. As previously reported in detail⁵⁻⁷ three scintillation counters

Fig.3. A. A method of calculation of the spatial ventricular gradient and spatial mean QRS-T angle from orthogonal scalar ECGs (paper speed = 100 mm/sec). QRS_X , QRS_Y and QRS_Z were X, Y and Z components of the spatial mean QRS area vector, respectively. T_X , T_Y and T_Z were X, Y and Z components of the spatial mean T area vector, respectively. Also G_i ($i = X, Y$ and Z) were X, Y and Z components of the spatial ventricular gradient vector.

B. A method of calculation of the spatial maximal QRS magnitude. A, B and C were X, Y and Z components of the spatial maximal QRS vector. C. ΣR was calculated as arithmetic summation of $R_X + R_Y + R_Z$. R_X , R_Y and R_Z were the X, Y and Z amplitude of R wave.

were placed over the subclavian vein, the heart and the left sternal border of the second intercostal space (2LIS). Approximately $50\mu\text{Ci}$ of ^{131}I -labelled human serum albumin (RISA) was injected as a bolus into the antecubital vein by the abrupt cuff-releasing method, and three time-activity curves (the input curve, RCG and 2LIS-RCG) were recorded on a strip chart for one minute. Seven minutes after the tracer injection, the equilibrium state was again recorded at the same geometry and the blood was sampled to calculate circulating blood volume (CBV). Heart rate and systemic blood pressure were also obtained at this time. The RCG thus obtained was placed on the half-mirror apparatus attached to high-speed analogue computer. The simulated RCG, displayed on the CRT, was fitted to the original RCG tracing by adjusting the potentiometers of the computer. When the best fitted curve was obtained (Fig. 2-upper), mean transit time of each right heart (MTTr), lung (MTTp),

left heart (MTTl) and body (MTTb) was measured from the values of the potentiometer. Cardiac output was calculated from the 2LIS-RCG in order to exclude background activity from tissues other than the heart. The mean blood volume (ml) of the right heart, lung, left heart and the body were calculated as shown in Fig. 2-lower.

Orthogonal electrocardiography:

Three orthogonal scalar leads using the Frank lead system were recorded simultaneously at a paper speed of 100 mm/sec. From scalar tracings of X, Y and Z leads, a magnitude of spatial mean QRS, T and G vectors was measured, as well as a spatial G/QRS ratio (G/QRS), a spatial T/QRS ratio (T/QRS) and a spatial QRS-T angle (QRS-T angle) as shown in Fig. 3-A. A magnitude of spatial maximal QRS (max QRS-Mag) was measured (Fig. 3-B), and ΣR (arithmetic summation of $R_X + R_Y + R_Z$) was calculated as demon-

strated on Fig. 3-C.

Cardio-thoracic ratio (CTR) was measured as the ratio of the maximal cardiac diameter to the maximal intrathoracic diameter on the chest X-ray.

Data analysis and statistical methods:

Seventeen variables thus obtained: 1. SCORE, 2. heart rate, 3. mean blood pressure, 4. circulating blood volume, 5. cardiac index, 6. stroke index, 7. right heart volume, 8. left heart volume, 9. pulmonary blood volume, 10. body blood volume, 11. mean QRS-Mag, 12. G/QRS, 13. T/QRS, 14. QRS-T angle, 15. ΣR , 16. max QRS-Mag and 17. CTR, were analysed by factor analysis.

In the statistical package for the social sciences (SPSS),¹⁵ factor analysis involves a fairly large variety of procedures. We made a factor analysis in the following steps using HP system 45: (1) starting from correlation matrix R, (2) determining the initial factors by performing principal component analysis and then, (3) performing varimax rotation to obtain the final solution.

Statistical significance between the means of each group was determined by a t-test. Comparison of a one-year mortality rate or an incidence of congestive heart failure between each group was evaluated with a chi-square test with Yates' correction. A p value < 0.05 was considered significant. Results were expressed as the mean $\pm$ standard deviation (SD).

RESULTS

Seventeen variables in 103 patients with IHD were computed with R-type factor analysis. Table II shows the correlation matrix between 17 variables, which were used for calculating principal components. Table III shows eigen values of 17 principal components in a descending order of magnitude. Varimax rotation was employed at more than 1.1 of eigen value (at 73.7% of cumulative percentage) in order to look for the interpretable components. Five major components in terms of eigen values were extracted. Table IV shows five principal components termed factors 1 to 5 after the varimax rotation. The numbers printed under factors 1 to 5 are factor loadings which indicate weights of the variables to the factors. Fig. 4 shows these five factors with variables more than 0.5 of factor loading schematically. In view of the factor loadings, factor 1 is regarded to represent "the extent of myo-

cardial ischemia", since the weights of SCORE, G/QRS, T/QRS and QRS-T angle are relatively large. Factor 2 is regarded to represent "heart size", since it is related to left heart volume, right heart volume and CTR. Factor 3 with weights on stroke index and cardiac index is interpreted to represent "cardiac pump function". Factor 4 is assumed to be "peripheral blood volume", since it is related to body blood volume and circulating blood volume. Factor 5 is regarded as representing "QRS forces", since it is related to max QRS-Mag, ΣR and mean QRS-Mag.

These results by factor analysis strongly suggest that G/QRS, T/QRS and QRS-T angle appear to be related with myocardial perfusion. Fig. 5 shows a relationship between scintigraphic score of myocardial deficits and G/QRS (A), T/QRS (B) and QRS-T angle (C), respectively. The circles show patients with angina pectoris and triangles with myocardial infarction. Both closed circles and triangles indicate patients with abnormal deflection of G, which shifts away from the normal left, anterior and downward direction. All patients without myocardial perfusion defects (SCORE 0) had normal direction of G. In contrast, all those with moderate or large perfusion defects (SCORE 3 or 4) showed abnormal deflection of G. As the score became larger, a progressive decrease in G/QRS and T/QRS and a progressive increase in QRS-T angle were demonstrated.

Factor scores, one for each factor in the final solution, were calculated for each patient with a mean of 0 and variance of 1. For factors 1 to 5, all the patients were classified in two subgroups in terms of factor scores; one group had a positive factor score and another group a negative factor score. Between these two groups, a one-year mortality rate after the initial examination and an incidence of congestive heart failure (CHF) were compared.

Factor 1 as a prognostic guide:

Of 103 patients, 44 patients had positive factor scores (group F-1-A) and 59 negative factor scores (group F-1-B). As shown in Fig. 6, the patients in group F-1-B had larger SCORES and QRS-T angles, and smaller G/QRS and T/QRS than those in group F-1-A ($p < 0.001$). Thus, the group F-1-B with a negative factor score seems to represent more severe myocardial ischemia and/or injury than the group F-1-A. Of the 44 patients in group F-1-A, no patient had CHF in contrast to group F-1-B, in which 23 out of 59

TABLE II CORRELATION MATRIX

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. SCORE	1.00	0.01	-0.42	0.38	-0.55	-0.39	0.59	0.14	-0.19	-0.22	-0.17	0.28	0.35	0.56	0.30	0.03	0.33
2. Max QRS-Mag	0.01	1.00	0.65	0.72	-0.32	-0.28	0.24	-0.11	0.28	-0.14	-0.29	-0.01	-0.10	0.13	-0.03	-0.02	0.19
3. ΣR	-0.42	0.65	1.00	0.24	0.14	0.05	-0.24	-0.18	0.32	0.13	0.03	-0.22	-0.26	-0.20	-0.14	-0.10	-0.14
4. mean QRS-Mag	0.38	0.72	0.24	1.00	-0.52	-0.45	0.42	-0.15	0.06	-0.13	-0.29	0.22	0.16	0.37	0.18	0.09	0.23
5. G/QRS	-0.55	-0.32	0.14	-0.52	1.00	0.85	-0.75	-0.09	-0.09	0.36	0.39	-0.25	-0.18	-0.44	-0.20	-0.11	-0.29
6. T/QRS	-0.39	-0.28	0.05	-0.45	0.85	1.00	-0.35	-0.04	-0.10	0.21	0.26	-0.16	-0.15	-0.30	-0.14	-0.04	-0.14
7. QRS-T angle	0.59	0.24	-0.24	0.42	-0.75	-0.35	1.00	0.20	0.04	-0.42	-0.36	0.31	0.25	0.52	0.22	0.15	0.42
8. Heart rate	0.14	-0.11	-0.18	-0.15	-0.09	-0.04	0.20	1.00	0.02	-0.58	-0.07	0.15	0.09	0.27	0.03	0.05	0.21
9. mean BP	-0.19	0.28	0.32	0.06	-0.09	-0.10	0.04	0.02	1.00	-0.11	-0.08	-0.21	-0.26	-0.16	-0.21	-0.06	-0.12
10. Stroke index	-0.22	-0.14	0.13	-0.13	0.36	0.21	-0.42	-0.58	-0.11	1.00	0.82	-0.08	-0.02	-0.19	0.17	-0.11	-0.34
11. Cardiac index	-0.17	-0.29	0.03	-0.29	0.39	0.26	-0.36	-0.07	-0.08	0.82	1.00	-0.02	-0.02	-0.11	0.15	-0.07	-0.28
12. CBV	0.28	-0.01	-0.22	0.22	-0.25	-0.16	0.31	0.15	-0.21	-0.08	-0.02	1.00	0.50	0.52	0.64	0.79	0.42
13. RHV	0.35	-0.10	-0.26	0.16	-0.18	-0.15	0.25	0.09	-0.26	-0.02	-0.02	0.50	1.00	0.63	0.45	0.06	0.34
14. LHV	0.56	0.13	-0.20	0.37	-0.44	-0.30	0.52	0.27	-0.16	-0.19	-0.11	0.52	0.63	1.00	0.39	0.08	0.53
15. PBV	0.30	-0.03	-0.14	0.18	-0.20	-0.14	0.22	0.03	-0.21	0.17	0.15	0.64	0.45	0.39	1.00	0.34	0.24
16. BBV	0.03	-0.02	-0.10	0.09	-0.11	-0.04	0.15	0.05	-0.06	-0.11	-0.07	0.79	0.06	0.08	0.34	1.00	0.25
17. CTR	0.33	0.19	-0.14	0.23	-0.29	-0.14	0.42	0.21	-0.12	-0.34	-0.28	0.42	0.34	0.53	0.24	0.25	1.00

Abbreviations: CTR = cardio-thoracic ratio, Max QRS-Mag = spatial maximal QRS magnitude, BP = blood pressure, CBV = circulating blood volume,
 RHV = right heart volume, LHV = left heart volume, PBV = pulmonary blood volume, BBV = body blood volume

TABLE III EIGEN VALUES OF 17 FACTORS (COMPONENTS)

	1	2	3	4	5	6	7	8	9
<i>Eigen values</i>	5.005	2.812	2.023	1.552	1.114	0.969	0.706	0.663	0.555
<i>Cumulative contribution</i>	0.294	0.460	0.579	0.670	0.737	0.794	0.836	0.875	0.908
	10	11	12	13	14	15	16	17	
<i>Eigen values</i>	0.460	0.386	0.278	0.233	0.118	0.049	0.023	0.022	
<i>Cumulative contribution</i>	0.935	0.957	0.974	0.987	0.994	0.997	0.999	1.000	

TABLE IV FACTOR LOADINGS AFTER VARIMAX ROTATION

		Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
1.	SCORE	-0.65	0.48	-0.10	0.03	0.20
2.	Max QRS-Mag	-0.24	0.01	-0.08	0.02	-0.92
3.	ΣR	0.26	-0.20	0.12	0.07	-0.83
4.	mean QRS-Mag	-0.55	0.24	0.03	-0.08	-0.64
5.	G/QRS	0.93	-0.09	0.18	0.10	0.10
6.	T/QRS	0.84	0.02	0.01	0.05	0.11
7.	QRS-T angle	-0.66	0.30	-0.36	-0.12	-0.04
8.	Heart rate	0.09	0.20	-0.67	-0.01	0.21
9.	mean BP	-0.09	-0.44	-0.13	0.04	-0.36
10.	Stroke index	0.02	0.05	0.94	0.01	0.02
11.	Cardiac index	0.33	0.12	0.71	0.01	0.20
12.	CBV	-0.13	0.45	-0.06	-0.85	0.04
13.	RHV	-0.10	0.80	0.01	-0.11	0.09
14.	LHV	-0.33	0.80	-0.19	-0.09	-0.07
15.	PBV	-0.15	0.52	0.25	-0.53	0.04
16.	BBV	-0.02	-0.05	-0.11	-0.96	0.03
17.	CTR	-0.11	0.54	-0.44	-0.24	-0.15

Abbreviations: CTR = Cardio-thoracic ratio, Max = Maximal, Mag = Magnitude, BP = Blood pressure, CBV = Circulating blood volume, RHV = Right heart volume, LHV = Left heart volume, PBV = Pulmonary blood volume, BBV = Body blood volume

(39%) had CHF, $p < 0.001$ ($\chi^2 = 19.9$). Ten of 59 patients (17%) in group F-1-B died within one year after the examination, while only one of 44 patients (2%) died in group F-1-A ($\chi^2 = 4.3$, $p < 0.05$). Therefore, factor 1 seems to have an important influence both on the severity and on the prognosis in IHD.

Factor 2 as a prognostic guide:

As shown in Fig. 7, 41 patients with positive factor scores (group F-2-A) had larger LHV,

RHV and CTR than 62 patients with negative factor scores (group F-2-B) at the $p < 0.001$ level. Therefore, those in group F-2-A had a larger heart than those in group F-2-B. Twenty patients (49%) in group F-2-A and 3 patients (5%) in group F-2-B had CHF ($\chi^2 = 25$, $p < 0.001$). Eight of 41 patients (20%) in group F-2-A and 3 of 62 (5%) in group F-2-B died ($\chi^2 = 4.1$, $p < 0.05$). Therefore, factor 2 also influences the morbidity and the mortality in IHD.

Fig.4. Schematic representation of the variables with more than 0.5 of factor loading in each of five factors.

Fig.5. A relationship between scintigram SCORE and the value of spatial G/QRS ratio (A), T/QRS ratio (B) and spatial QRS-T angle (C), respectively.

Factor 3 as a prognostic guide:

Fifty-seven patients with positive factor scores (group F-3-A) had a higher CI and SI than 46 patients with negative factor scores (group F-3-B) ($p < 0.001$) (Fig. 8). This seems to indicate that group F-3-B had a greater depressed cardiac pump function than did group F-3-A. The difference in the incidence of CHF and of a one-year mortality rate in these two groups is significant at the $p < 0.01$ ($\chi^2 = 7.4$ and $\chi^2 = 8.7$, respectively). Thus, depressed cardiac pump function is an important predictor of the morbidity

and the mortality in IHD.

Factor 4 as a prognostic guide:

Fifty-six patients and positive factor scores (group F-4-A) and 47 negative factor scores (group F-4-B) (Fig. 9). Group F-4-B had a larger BBV and CBV than group F-4-A. Those in group F-4-B appear to have an increased peripheral blood volume as compared to group F-4-A. The incidence of CHF in group F-4-A and in group F-4-B is 14% (8/56) and 32% (15/47), respectively ($\chi^2 = 4.6$, $p < 0.05$). The one-year mortality

Fig.6. The average value of G/QRS, T/QRS, QRS-T angle and SCORE (mean $\pm$ SD) in two groups classified with factor score (F.S.) of factor 1; Group F-1-A has positive F.S. and Group F-1-B has negative one. The incidence of congestive heart failure (CHF) and a one year mortality rate (MR) between the two groups.

rate in group F-4-B (16%) was higher than in group F-4-A (7%), but not statistically significant.

Factor 5 as a prognostic guide:

Those in group F-5-A seem to have a higher QRS force than those in group F-5-B because the former has a larger max QRS-Mag, ΣR and mean QRS-Mag than the latter ($p < 0.001$) (Fig. 10). The incidence of CHF and a one-year mortality rate in the two groups are not significantly different, and the QRS-forces do not influence the severity or the prognosis in IHD.

Thus, factors 1, 2 and 3 appear to be important predictors of mortality. Fig. 11 shows distribution of patients' factor scores (F.S.). All of the 23 patients with CHF had negative F.S. of factor 1, and among them 20 patients (78%) had positive F.S. of factor 2. Sixteen (80%) of those 20 patients had negative F.S. of factor 3. Of 11 expired patients, 8 (73%) had both negative F.S. of factor 1 and positive F.S. of factor 2, and all had negative F.S. of factor 3. One patient with a positive F.S. of factor 1 died of cerebral thrombosis. Therefore, all of those who died with cardiac events had a negative F.S. of factor 1.

These results indicate that the patients with altered repolarization, increased heart volume and depressed cardiac performance are clinically serious and that the prognosis is poor. Thus, a

combination of factors 1 to 3 may provide more precise information about mortality and morbidity in patients with ischemic heart disease.

DISCUSSION

The first purpose of this paper is to study the interrelationships of scintigraphic, electrocardiographic and hemodynamic data at rest. Factor analysis is a technique which has been widely used to obtain principal factors and the factor with the largest eigen value (factor 1) accounts for the largest portion of the total variance and carries the most information. Of particular interest in our study was the finding that factor 1 including SCORE, G/QRS, T/QRS and QRS-T angle appears to characterize IHD, because both regional myocardial perfusion defects and electrocardiographic abnormalities in the repolarization phase reflect myocardial ischemia and/or damage. Theoretically, the main cause of G is the non-homogeneous duration of recovery which is due to difference in duration of action potential in different parts of the ventricles, and the G vector points from the slowest repolarizing areas to the rapid repolarizing areas. Autenrieth et al¹⁸ have shown by experimental data that the T wave is a sensitive indicator of small changes in the duration of action potential, even if these changes are confined to a mass comprising less than 10% of

Fig.7. The average value of cardiothoracic ratio (CTR), right heart volume (RHV) and left heart volume (LHV) in two groups: Group F-2-A has positive F.S. and Group F-2-B a negative F.S. The incidence of CHF and MR between the two groups is shown.

Fig.8. The average value of stroke index (SI), cardiac index (CI) and heart rate (HR), and the incidence of CHF and MR between two groups; Group F-3-A has positive F.S. and Group F-3-B has negative one.

the ventricular myocardium and that certain abnormalities of repolarization at the cellular level may change the amplitude of the T wave. This means that G is very sensitive to local differences in duration of repolarization and that the T wave

may be considered as "some kinds of special detector for differences in repolarization of the various parts of the ventricle". It may be possible that the size and location of the region with altered repolarization by myocardial ischemia

Fig.9. The average value of body blood volume (BBV) and circulating blood volume (CBV), and the incidence of CHF and MR between two groups; Group F-4-A has positive F.S. of factor 4 and Group F-4-B has negative one. NS = not significant.

Fig.10. Max QRS-Mag, ΣR and mean QRS-Mag (mean $\pm$ SD), and the incidence of CHF and MR between two groups: Group F-5-A has positive F.S. of factor 5 and Group F-5-B has negative one.

and/or damage influence the magnitude of “the primary T wave change”. Clinically it has been suggested that the ratio of G to the QRS area (G/QRS) is less variable and therefore a more discriminating measurement than the absolute value

of G¹⁹ and widening of spatial QRS-T angle is also assumed to represent an early sign of altered repolarization²⁵. Therefore, these values may be utilized as a quantitative tool when attempting to detect the extent of repolarization abnormal-

Fig.11. Factor score distribution. Circles represents positive factor score (F.S.) of factor 3 and triangles negative ones. The horizontal axis shows F.S. of factor 1 and the vertical axis one of factor 2. Closed circles and triangles indicate the patients with CHF. The expired patients are indicated by a cross sign.

ities.

On the other hand, ventricular hypertrophy, electrolyte imbalance, quinidine and digitalis therapy, and nonpathologic factors such as exercise, food intake, smoking and changes in heart rate also commonly produce T wave and ST changes. Thus, interpretation of the spatial G/QRS, T/QRS and QRS-T angle should not be based solely on the index of myocardial ischemia, and the effects of these factors should be considered. Ashman³⁸ has shown that the variety of nonpathologic condition, such as increased heart rate, digitalis, etc., may diminish the magnitude of G without greatly altering its direction. As shown in Fig. 5, some cases with no perfusion defects or with equivocal defects (SCORE 0 or 1) have small G/QRS and T/QRS, and wide QRS-T angles. Therefore, the value of these might not always reflect myocardial perfusion, but most of their deflections of G are normal. By contrast, all patients with moderate or large perfusion defects (SCORE 3 or 4) have both the diminution of the magnitude and the abnormal deflections of G. This indicates that the value of G/QRS, T/QRS and QRS-T angle

could reflect myocardial perfusion to some extents but the deflection of G is also clinically important to detect the ischemic changes.

Another interesting result is that spatial G/QRS, T/QRS, and QRS-T angle all representing factor 1 were separated from spatial mean QRS-Mag, ΣR and QRS-Mag representing factor 5. The former reflects the ventricular repolarization phase and the latter the depolarization phase. These two phases are independent each other and alteration in the former is more evident than that in the latter for a reflection of ischemia in IHD.

The 103 patients with clinical evidence of IHD manifested by angina pectoris, myocardial infarction (MI), congestive heart failure (CHF), or a combination of these were studied for evaluation of several factors which influence to the functional severity and the prognosis in IHD as a whole. Clearly, a patient with prior MI and CHF has increased risk.^{21,32} The results of this study points towards a similar conclusion: 3 of 50 patients without prior MI (5%) were died, in contrast to 8 of 53 patients with prior MI (15%). Seven of 23 patients with prior CHF (30%) were died of CHF.

Factor 1 as a prognostic guide:

The extent of myocardial damage is one of the important factors determining mortality in patients with acute myocardial infarction.^{20,21} Ritchie et al. showed that the noninvasive technique using radionuclide scanning defines a broad spectrum of ischemia in survivors of sudden cardiac death due to ventricular fibrillation.²²

Several investigators have revealed that ST-T wave abnormalities on the resting ECG are associated with an increased risk of dying in patients with IHD.²³⁻²⁵ These evaluations of ECG, however, are not quantitative. As the significance of G is of a quantitative nature, it can be used to evaluate the extent of repolarization abnormalities due to ischemic changes. However, little information is available concerning significance of G with regard to the prognosis. Our study revealed that the extent of myocardial perfusion defects by ²⁰¹Tl-scintigraphy is an important predictor of the prognosis in IHD, and that patients with decreased G/QRS and T/QRS and with widening of QRS-T angle, which presumably reflect myocardial perfusion defects, have a poor prognosis.

Factor 2 as a prognostic guide:

We found that a correlation between the heart size and the incidence of CHF ($p < 0.001$), and the mortality rate for patients with an enlarged heart was significantly higher than those with a smaller heart size, 20 versus 5 per cent ($p < 0.05$). Our present data supports the observations of others.²⁷⁻²⁹ Oberman et al. reported that the mortality rate for patients with a large heart was 23 per cent compared to only 3 per cent in those with a smaller heart.²⁹ It has been made clear in experimental, clinical and pathological studies that an increased heart size is associated with increased muscle damage and extensive coronary disease.^{30,31} Therefore, it seems logical that the heart size should prove to be a relatively sensitive indicator of the magnitude of myocardial damage and thereby help to predict morbidity and mortality.

Factor 3 as a prognostic guide:

Undoubtedly, left ventricular function is a major determinant of short-term prognosis in patients with IHD.^{21,32} for the severity of pump failure is clearly related to the extent of the necrotic area.^{33,34} Cardiac output has been the most commonly used for assessment of left ventricular function. In our study, the patients with

decreased cardiac index and stroke index had a poor prognosis, which indicates that impairment of left ventricular performance seems to determine the prognosis.

Factor 4 as a prognostic guide:

The fact that the circulating blood volume (CBV) increases in patients with CHF has long been known.^{35,36} Evans reported no significant decrease in heart volume which would account for the decrease in the CBV during recovery from CHF,³⁷ and Saito also suggested that the increase of the CBV in CHF is mainly caused by increase in body blood volume (BBV).⁶ In this factor analysis, both CBV and BBV are in the same component termed factor 4, which indicates that BBV seems to determine CBV. The patients with increased BBV and CBV had a significantly higher incidence of CHF. Although little information is available on the significance of BBV to prognosis, our data suggests that increased BBV and CBV do influence the morbidity but do not determine the mortality.

Factor 5 as a prognostic guide:

Gottwik et al. reported that the orthogonal ΣR value ($R_X + R_Y + R_Z$) was an adequate and practical index that had a linear correlation with ejection fraction¹² and previous studies have also suggested that QRS forces may be used as an index of left ventricular function.^{13,14} In our patient population, however, none of ΣR , mean QRS-Mag and max QRS-Mag correlated with stroke index or cardiac index (Table II). Moreover, ΣR , mean QRS-Mag and max QRS-Mag as factor 5, which means QRS forces, were not significant predictors of morbidity or mortality in IHD as were the parameters which indicated repolarization abnormalities.

Clinical implications:

Myocardial scintigraphy was used in order to detect the extent of myocardial ischemic injury. Radiocardiography is a non-invasive method to measure cardiac output and blood distribution accurately. The use of an orthogonal vectorcardiographic lead system allowed for evaluation of the electrophysiological derangements. Factor analytic techniques made feasible a summarization of these non-invasive data into five major factors. Of these factors "the extent of myocardial damage", "the enlarged heart" and "the depressed cardiac performance" were good predictors of the prognosis. Thus, the combined use of

these three non-invasive methods may allow for an even more precise characterization of ischemic heart disease and provide information on mortality and morbidity in patients with ischemic heart disease. It may be more helpful, however, to utilize some form of stress test to analyse the latent preclinical state and to detect coronary reserve in IHD.

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