A POINT-SCORE SYSTEM FOR THE DIFFERENTIAL DIAGNOSIS BETWEEN IDIOPATHIC CARDIOMYOPATHY AND ISCHEMIC HEART DISEASE

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FOR the past 20 years, idiopathic cardiomyopathy (ICM) has been a well-discussed topic in the field of cardiology. The first step in the diagnosis of ICM is to exclude other known cardiovascular diseases, particularly ischemic heart disease (IHD).¹ To confirm the diagnosis, many invasive examinations such as cardiac catheterization, angiocardiology, coronary angiography and histological examinations by biopsies have been carried out.² However, these invasive methods impose a physical and psychological burden on patients. Thus, a simple non-invasive screening test which can be performed at the bedside or in the out-patient clinic would be welcome, both by the patients and their physicians.

A multicenter cooperative study on ICM has been carried out in Japan since 1974. Based on epidemiological investigation, criteria which readily allow for a differentiation between ICM and IHD were designed. The object of the work presented herein was to establish new criteria which would distinguish hypertrophic cardiomyopathy from congestive cardiomyopathy or IHD by multivariate analysis which utilizes a point-score system and which refers to symptoms and findings on routine examinations available

anywhere, such as auscultation, chest X-ray and electrocardiogram (ECG).

METHODS

A research committee on ICM consisting of 15 institutes (Chairman: C. Kawai, Kyoto University) defined ICM as "a disorder of heart muscle of unknown cause or association" and adopted the classification of ICM from clinical features proposed by Goodwin and Oakley.¹ Namely, ICM has been divided into two groups: congestive cardiomyopathy (CCM) characterized by systolic pump failure, and hypertrophic cardiomyopathy (HCM) by diastolic compliance failure with or without obstruction of left ventricular outflow tract. Restrictive and obstructive cardiomyopathies, which are rare in Japan, were not included in this study.

The committee performed an investigation by questionnaires for many non-invasive and invasive findings regarding patients with ICM or IHD who were referred to the institutes of this committee. Out of a total of 540 cases of ICM collected, 340 cases, in which the diagnoses were confirmed by typical echocardiographic findings, invasive examinations or autopsies, were selected for further studies.

On the other hand, 166 cases of IHD in which the diagnoses were established by coronary angiography were surveyed.

Forty-one items, including 14 items of symptoms, 20 items of ECG findings, 5 items of aus-

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TABLE I FORTY-ONE ITEMS WHICH WERE REFERRED FOR ANALYSIS

Symptoms (14)

Palpitation, Dyspnea, Chest oppression, Chest pain, Bloody sputum, Dizziness, Syncope, Fatigue, Arrhythmia, Edema, Arthralgia, Thrombosis, Fever, Cyanosis

ECG findings (20)

Left ventricular hypertrophy (LVH), ST-T abnormality, Abnormal P wave, 1° atrioventricular (A-V) block, 2° A-V block, 3° A-V block, Left bundle branch block, Right bundle branch block, Left axis deviation, Right axis deviation, Abnormal Q wave, Loss of septal Q wave, Atrial premature contraction, Atrial fibrillation, Atrial flutter, Ventricular premature contraction, Ventricular tachycardia, WPW syndrome, Low voltage, Prolonged QRS duration

Auscultation (5)

Abnormal second sound, Third sound, Fourth sound, Systolic murmur, Diastolic murmur

New York Heart Association (NYHA) functional classification

Cardiothoracic ratio (CTR) on chest X-ray

TABLE II SUBJECTS FOR ANALYSIS IN THIS STUDY

	No.	M	F	Age	Mean
CCM	31	27	4	22 – 75	(40.7)
HCM	60	48	12	5 – 56	(32.9)
IHD myocardial infarction	38	37	1	16 – 75	(53.8)
intermediate syndrome	8	7	1	42 – 69	(58.0)
angina pectoris	20	18	2	24 – 70	(55.7)
others	31	28	3	36 – 65	(52.5)
total	97	90	7	16 – 75	(54.1)
Total	188	165	23	5 – 75	(45.1)

Abbreviations: CCM=congestive cardiomyopathy, HCM=hypertrophic cardiomyopathy, IHD=ischemic heart disease, M=male, F=female

cultation, New York Heart Association (NYHA) functional classification and cardiothoracic ratio (CTR) on chest X-ray, were referred for analysis (Table I). The cases without full answers for these items were excluded.

One hundred and eighty-eight cases remained for final analysis in this study (Table II).

Each item was answered by yes or no. The functional capacity of NYHA was classified into two groups: one in I & II and the other in III & IV, and CTR was also divided into two groups of "equal or above 0.55" and "below 0.55". The QRS duration was parted into "0.12 seconds or more" and "less than 0.12 seconds". The third sound and fourth sound were separated as audible and inaudible by auscultation. Left ventricular hypertrophy (LVH) was determined according to Sokolow and Lyon,³ and low

voltage was evaluated by the Minnesota code.⁴

All items, presented with nominal scale, were summarized as two canonical variates by the categorical discriminant analysis with reduction in dimensionality and were shown on the second dimension.^{5,6}

RESULTS

Among all 41 items in three groups, CCM, HCM and IHD, referred to the categorical discriminant analysis, the following twelve items showed statistical significance ($P < 0.05$) of the partial correlation coefficient: chest oppression, chest pain, syncope, edema, LVH, 1° atrioventricular (A-V) block, atrial premature contraction (APC), ventricular premature contraction (VPC), low voltage, third sound, systolic murmur and CTR.

TABLE III FREQUENCY OF THE 14 FINAL ITEMS IN CCM, HCM AND IHD WITH FIRST AND SECOND CANONICAL VARIATES BY CATEGORICAL DISCRIMINANT ANALYSIS

Item		CCM	HCM	IHD	I st Canonical Variate		II nd Canonical Variate	
		No (%)	No (%)	No (%)	A	B	A	B
Dyspnea	yes	25 (81)	23 (38)	27 (28)	0.0017	0.0293	-0.0106	0.0984
	no	6 (19)	37 (62)	70 (72)	-0.0012		0.0071	
Chest Oppression	yes	15 (48)	20 (33)	87 (90)	0.0094	0.2396**	-0.0075	0.1090
	no	16 (52)	40 (67)	10 (10)	-0.0173		0.0140	
Chest Pain	yes	11 (35)	14 (23)	86 (89)	0.0207	0.4188**	-0.0089	0.1087
	no	20 (65)	46 (77)	11 (11)	-0.0298		0.0128	
Syncope	yes	3 (10)	14 (23)	8 (8)	-0.0136	0.1257	0.0367	0.1854*
	no	28 (90)	46 (77)	89 (92)	0.0021		-0.0056	
Edema	yes	15 (48)	5 (8)	3 (3)	-0.0449	0.3094**	-0.0094	0.0373
	no	16 (52)	55 (92)	94 (97)	0.0063		0.0013	
LVH	yes	17 (55)	51 (85)	25 (26)	-0.0111	0.2203**	0.0219	0.2391**
	no	14 (45)	9 (15)	72 (74)	0.0108		-0.0215	
Atrial Fibrillation, or Atrial Flutter	yes	8 (26)	2 (3)	2 (2)	-0.0095	0.0539	-0.0483	0.1499*
	no	23 (74)	58 (97)	95 (98)	0.0006		0.0033	
Ventricular Arrhythmia	yes	19 (61)	6 (10)	19 (20)	-0.0073	0.0879	-0.0371	0.2410**
	no	12 (39)	54 (90)	78 (80)	0.0022		0.0113	
Low Voltage	yes	5 (16)	2 (3)	3 (3)	-0.0517	0.2698**	-0.0018	0.0052
	no	26 (84)	58 (97)	94 (97)	0.0029		0.0001	
QRS Duration	$\geq 0.12''$	9 (29)	1 (2)	5 (5)	-0.0179	0.1177	-0.0467	0.1679*
	$< 0.12''$	22 (71)	59 (98)	92 (95)	0.0016		0.0040	
Third Sound	yes	20 (65)	13 (22)	5 (5)	-0.0196	0.2007**	-0.0413	0.2321**
	no	11 (35)	47 (78)	92 (95)	0.0050		0.0105	
Systolic Murmur	yes	25 (81)	56 (93)	26 (27)	-0.0210	0.4344**	0.0172	0.2122**
	no	6 (19)	4 (7)	71 (73)	0.0278		-0.0227	
NYHA	III, IV	17 (55)	8 (13)	34 (35)	-0.0004	0.0064	-0.0178	0.1402
	I, II	14 (45)	52 (87)	63 (65)	0.0002		0.0081	
CTR	≥ 0.55	29 (94)	22 (37)	14 (14)	-0.0232	0.3171**	-0.0299	0.2308**
	< 0.55	2 (6)	38 (63)	83 (86)	0.0123		0.0158	
Correlation Ratio		31	60	97	0.8727 (60.7%)		0.7019 (39.3%)	

A=canonical discriminant coefficient, B=partial correlation coefficient, *= $p < 0.05$, **= $p < 0.01$

Abbreviations: LVH=left ventricular hypertrophy, NYHA=New York Heart Association functional class, CTR=cardiothoracic ratio.

Some of these items showing only statistical significance could be modified or exchanged with other findings which were frequently clinically experienced: APC was exchanged with "ventricular arrhythmia" including VPC and ventricular tachycardia; 1° A-V block was excluded; dyspnea, NYHA functional class and prolonged QRS duration (0.12 seconds or more) were added.

Thus, the final items for this point-score system were dyspnea, chest oppression, chest pain, syncope, edema, LVH, atrial fibrillation or atrial flutter, ventricular arrhythmia, low voltage, QRS duration, third sound, systolic murmur, NYHA functional class and CTR. For these 14 items, categorical discriminant analysis was done again (Table III). The correlation ratio was

TABLE IV POINT-SCORE SYSTEM FOR THE DIFFERENTIAL DIAGNOSIS AMONG CCM, HCM AND IHD

Item	X-Axis	Y-Axis
Dyspnea	1	-4
Chest Oppression	5	-4
Chest Pain	10	-4
Syncope	-3	8
Edema	-10	-2
LVH	-4	9
Atrial Fibrillation or Atrial Flutter	-2	-10
Ventricular Arrhythmia	-2	-10
Low Voltage	-10	0
QRS Duration ($\geq 0.12''$)	-4	-10
Third Sound	-5	-10
Systolic Murmur	-10	8
NYHA (III, IV)	0	-5
CTR (≥ 0.55)	-7	-9
Total		

Add the point-scores in each axis for only those items which are confirmed to have occurred.

0.8727 in the first canonical variate, 0.7019 in the second, and the contributive ratios for differentiation were 60.7% and 39.3%, respectively.

The point-score for each item was determined as follows: The sum of the absolute value of the canonical discriminant coefficient (A in Table III) both in "yes" and "no" of each item is multiplied by a constant value of 200 and is rounded off to the integral number. Depending upon the sign of "yes" in each item, this number turns out a positive or negative sign; so, the value of "no" in each item is zero.

According to this method, the "low voltage" in the first canonical variate was "-11", but in order to make calculation as easily as possible, this point was changed to "-10", because this change had no influence on the result. Each final point score is shown in Table IV. The value in the first or second canonical variate corresponds to the point in X-axis or Y-axis, respectively. The differential area for each group of disease is shown on the co-ordinates of X-axis and Y-axis in Figure 1. Three simple equators divide the graph into three areas on the two dimensional co-ordinates. These equators are given as follows:

Fig.1. This graph shows the differential areas of CCM, HCM and IHD. The value of the X-axis and Y-axis are calculated from Table IV. These values determine the point on this graph and the predicted diagnosis for each patient.

- 1) $Y = -0.6310X - 21.3189$
- 2) $Y = -4.3010X - 50.9537$
- 3) $Y = 3.1335X + 9.0292$

If positive items were present from a present state or a past history, the point-score for each of those items was individually added to form the co-ordinates for each of X and Y-axis. The disease of the case depends on the position of the point in the three areas.

The cases used for analysis were calculated with this point-score and were plotted on the co-ordinates (Figure 2). As a result, it was shown that most of these cases were classified in the area of the original diagnosis. The accuracy of diagnosis was 91.5% (172 cases in 188) (Table V).

Subsequently, this system was applied to other recent unanalysed cases in which the diagnoses were confirmed in the same institutes in order to estimate the reliability of this method. The subjects were 228 cases: 37 of CCM, 101 of HCM and 90 of IHD. The result was shown in Figure 3, and the accuracy of diagnosis for these cases was 82.0% (187 cases in 228) (Table VI).

TABLE V COMPARISON BETWEEN PREDICTED DIAGNOSIS BY THE POINT-SCORE SYSTEM (TABLE IV, FIGURE 1) AND ACTUAL DIAGNOSIS IN EACH OF THE THREE DISEASES

Predicted	Actual			Total
	CCM	HCM	IHD	
CCM	26 (83.9 %)	4	2	32
HCM	4	54 (90.0 %)	3	61
IHD	1	2	92 (94.8 %)	95
Total	31	60	97	188

Accuracy of diagnosis; 91.5%

Fig. 2. The differential diagnosis of the analysed subjects (Table II) by the point-score system. The closed circles represent the cases of HCM, the triangles those of IHD and the crosses CCM.

Fig. 3. The differential diagnosis of current cases by the point-score system. Symbols are as in Figure 2.

DISCUSSION

The criteria for the diagnosis of ICM have not been established. Usually, the diagnosis must first be made by excluding cardiac disease of a known cause, including a voluminous catalogue of secondary cardiomyopathies in which almost all other forms of known and poorly understood

diseases of the cardiovascular system are listed. Because there are many similar clinical findings between ICM and IHD, the differential diagnosis of ICM from IHD presents a most difficult problem both in the out-patient clinic and at the bedside. Acute myocardial infarction can easily be differentiated from ICM by clinical features and laboratory findings. The important diseases

TABLE VI COMPARISON BETWEEN PREDICTED DIAGNOSIS BY THE POINT-SCORE SYSTEM AND ACTUAL DIAGNOSIS OF CURRENT CASES

Predicted	Actual			Total
	CCM	HCM	IHD	
CCM	33 (89.2%)	11	3	47
HCM	2	76 (75.2%)	9	87
IHD	2	14	78 (86.7%)	94
Total	37	101	90	228

Accuracy of diagnosis; 82.0%

for differentiation are old myocardial infarction and angina pectoris. For example, the development of cardiac symptoms, such as chest oppression or chest pain, is often responsible for the clinical confusion of ICM with IHD in the older age group. When the ECG shows pathological Q waves and ST and/or T abnormalities,⁷⁻¹³ differentiation between ICM and IHD depends on findings in coronary angiography. Similarly, left ventricular pump failure secondary to coronary artery diseases is clinically impossible to distinguish from CCM, and the final arbiter is selective coronary angiography.¹² In many patients with HCM, a firm diagnosis can be established from clinical features and by non-invasive investigation, but in some cases in which the diagnoses cannot be confirmed only by these means, hemodynamic and angiographic studies combined with a biopsy examination are necessary.^{2,14}

On auscultation, the fourth sound is audible in most cases of both ICM¹⁵ and IHD, and a significant systolic murmur is frequently heard in patients with CCM and HCM¹⁶ and occasionally in those with IHD (Table III). In such cases, it is difficult to establish the differential diagnosis by auscultation alone.

Invasive methods such as cardiac catheterization, angiocardiology, coronary angiography and endomyocardial biopsy are necessary to confirm the diagnosis of ICM. But, to avoid physical and psychological burdens on the patient, we attempted to differentiate ICM from IHD using only non-invasive examinations.

As all data were constituted from categories, categorical discriminant analysis was adopted among many methods of statistical analysis. In

this study, it quantified their categories under a condition which maximizes the between variance/within variance ratio.

Twelve items, in which the partial correlation coefficient was large with the P value being statistically significant (less than 5%), were selected from among 41 items. These items were statistically significant for differential diagnosis, independent of their incidences.

In this study, A-V block did not occur in any patient with HCM. In contrast, 1° A-V block occurred in 23% (7 cases of 31) of the patients with CCM, and in 3% (3 of 97) of the patients with IHD. In both CCM and IHD, 2 cases of each 2° A-V block and 3° A-V block were included. Early reports showed that 1° A-V block was occasionally present in patients with ICM^{17,18} most of whom were probably cases of CCM as this finding was rarely evident in patients with hypertrophic obstructive cardiomyopathy.¹⁹ Although 1° A-V block was statistically significant for the differential diagnosis in this study, it was not included in this point-score system. This is because the A-V block is classified into three groups according to the severity: 1° A-V block is the mild form, 2° moderate and 3° severe, and the first discriminant coefficient was negative in 1° A-V block and positive in 2° and 3° A-V block. In addition, the partial correlation coefficient also failed to show such a progression. If the incidence of ICM does show an increase, these abnormal conductions may have a statistical significance which is compatible with the clinical features.

APC in this study appeared in CCM, HCM and IHD with an incidence of 6, 7 and 5%, respective-

ly. Although there was little difference between each group, this abnormal rhythm proved to be statistically significant for differentiation of the three groups. On the other hand, atrial fibrillation and atrial flutter had no significance, but did occur more frequently in patients with CCM than in those with HCM or IHD. Previous reports also indicated that these abnormal rhythms occurred with approximately the same incidence^{11,17-20}. Usually, atrial fibrillation is considered to occur only rarely in cases of hypertrophic obstructive cardiomyopathy.^{16,18} Thus, the item of APC was discarded and that of atrial fibrillation or atrial flutter was adopted from clinical experience. There was no significant difference in the accuracy of diagnosis between the above two items. This new item, "atrial fibrillation or atrial flutter", proved to be statistically significant on the second canonical variate in the final form (Table III).

VPC occurred in 61% of the patients with CCM much more than in HCM (8%) or IHD (18%). As previously reported, VPC was common in patients with ICM.²¹ But, it was also evident that in the patients with idiopathic hypertrophic subaortic stenosis (IHSS) this abnormal rhythm was uncommon.^{19,22} Ventricular tachycardia was a more common feature in CCM than in the others; however, the frequency of this abnormality was less than VPC and the partial correlation coefficient was small. Accordingly, VPC and ventricular tachycardia were included under one item of "ventricular arrhythmia", which has statistical significance on the second canonical variate in the final form (Table III).

Next, the three following items, prolonged QRS duration, dyspnea, and NYHA functional class were added to the point-score system.

The prolonged QRS duration was relatively infrequent and had no significance in the analysis of the 41 items. Previous publications on the subject included various types of intraventricular conduction defects, such as incomplete and complete left bundle branch block, right bundle branch block, non specific intraventricular conduction defects and anomalous atrioventricular conduction.^{11,16-19,23,24} Hollister and Goodwin¹⁸ reported that left bundle branch block was more frequently seen in patients with CCM than in those with hypertrophic obstructive cardiomyopathy or IHD. Patients with abnormal intraventricular conduction tended to be those who were more disabled.¹⁹ The prolonged QRS duration (0.12 seconds or more) was occasionally

demonstrated in patients with CCM (Table III). Therefore, the prolonged QRS duration which included the features of left bundle branch block, right bundle branch block and non specific intraventricular conduction defects was used and was statistically significant in the final form.

The most common manifestation of CCM is related to congestive heart failure.^{1,21} Symptoms of left-sided failure such as dyspnea, orthopnea, and paroxysmal nocturnal dyspnea occur earlier and more frequently than those of right-sided congestive heart failure, which include peripheral edema and hepatomegaly.²² Weakness and fatigue, presumably related to reduced cardiac output are also common. In systolic pump failure due to IHD, the clinical picture is that of low output congestive heart failure. Thus, it is most difficult to separate these two groups except by coronary angiography. In patients with HCM, however, symptoms of congestive heart failure such as dyspnea occur only rarely except at the advanced stage. In this study, dyspnea occurred most frequently in the patients with CCM (81%) the incidence being considerably higher than in those with HCM (38%) or IHD (28%) (Table III). Therefore, this symptom was added to the point-score system even though there was no statistical significance on the two canonical variates.

NYHA functional class proved to be superior for practical use at the bedside when attempting to estimate the functional ability or prognosis of patients with various cardiovascular diseases. Many of the hemodynamic parameters obtained by both invasive and non-invasive methods are compatible with this NYHA functional class. Thus, it was to be expected that the incidences of III or IV of NYHA functional class were more frequent in cases of CCM than IHD or HCM (Table III).

Recently, echocardiography has been increasingly employed in the diagnosis of all cardiovascular diseases²⁵ and is also a useful and popular tool in the diagnosis of ICM.²⁶⁻²⁸ Although some of the subjects in which the diagnoses were confirmed only by echocardiography were of course included, we excluded the findings of echocardiography from this point-score system for the following reasons. It is sometimes impossible for a physician to give an accurate diagnosis without an experienced technique, because standardization of echocardiographic measurements has not been established due to the various abnormal shapes of the left ventricle.^{29,30} At times, in some patients it is difficult even for

experienced physicians to get a good and clear tracing on echocardiograms. Henry and co-workers²⁷ proposed the concept of asymmetric septal hypertrophy (ASH) using echocardiography. But, in some cases it is not clear how to go about measuring the wall thickness of the interventricular septum because of the multi-layered characteristics of HCM. Furthermore, if systolic anterior motion of the mitral valve, a characteristic of hypertrophic obstructive cardiomyopathy (IHSS)²⁶ is incomplete, it cannot be used as a diagnostic clue. If even one of the above stated reasons is in question, the results obtained with echocardiography cannot be used in the point-score system. Therefore, echocardiographic findings were excluded in the present study.

Consequently, based upon 12 items with statistical significance, 3 items were added, 1 item was excluded and 2 items were exchanged with new items from the stand-point of the clinical features and experiences. The first canonical variate, X co-ordinate seems to separate ICM from IHD by chance. On the other hand, the second canonical variate, Y co-ordinate appears to distinguish between CCM and HCM (Table IV, Figure 1).

The accuracy of diagnosis of analysed cases using the final point-score system with 14 items (Table IV) was 91.5% (Table V). In addition, the result as this method was applied to the unanalysed cases in the same institutes was 82.0% (Table VI), which appears to be adequate for use as a screening test both at the bedside and in out-patient clinic.

Particularly, the accuracy of diagnosis in the cases of HCM was 75.2% being less than that in other groups (Table VI). Of 11 cases in which the diagnoses were mistaken for CCM, 10 had "above 0.55 of CTR" and 6 showed "ventricular arrhythmia". Six patients with both abnormal findings definitely positioned in the diagnostic area of CCM. But, 5 residual cases were plotted near the border line between HCM and CCM. Both cardiomegaly and ventricular arrhythmia frequently appear in the patients with congestive heart failure, especially CCM. And these items in this method have a large score, especially in Y-axis. Accordingly, it may be thought that the patients in the late stage of HCM, mimicking a feature of CCM, were included in HCM group. The diagnosis of these cases should be confirmed by echocardiography or myocardial perfusion imaging. All fourteen cases of HCM which were misdiagnosed for IHD had "chest pain" or "chest

oppression". Most of them were plotted near the border line between HCM and IHD. These items also have a large score, so have a considerably influence upon the diagnosis. Therefore, it is important that the physician obtain a thorough and accurate medical history as symptoms such as chest pain or edema with large point-score.

SUMMARY

A point-score system made from symptoms, electrocardiographic findings, auscultation, and chest X-ray has been presented for the differential diagnosis among congestive cardiomyopathy, hypertrophic cardiomyopathy and ischemic heart disease.

This system involved a multivariate analysis of 188 cases in which the diagnoses were established by typical echocardiographic findings, invasive examinations or autopsies. The accuracy of diagnosis by this point-score system was 91.5%. This point-score system appears to be useful as a screening test in differentiating idiopathic cardiomyopathy from ischemic heart disease.

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