Isointegral Analysis of Body Surface Electrocardiographic Mapping for Assessing Exercise-Induced Changes in Repolarization Properties in Patients with Coronary Artery Disease

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To assess the exercise-induced changes in repolarization properties in patients with coronary artery disease, we analyzed body surface ECG mapping. The patients studied had a normal resting 12-lead ECG and were divided into 2 groups: group A ($n = 15$; coronary artery narrowing [–], exercise thallium defect [–], ST depression ≥ 0.1 mV [–]) and group B ($n = 17$; [+], [+], [+]). All patients in group B showed significant area (< -10 μV·s) in the postexercise ST-T isointegral map. Of the patients in group B, 10 (59%) showed significant area in the postexercise QRST isointegral map and 15 (88%) showed "–2SD area (less than mean –2SD values in group A)" in the difference map between resting and postexercise QRST isointegrals. The correlation coefficient between resting and postexercise QRST isointegrals in 87 lead points was significantly lower in group B (0.28 ± 0.56) than in group A (0.91 ± 0.06, $P < 0.001$). Our results indicate that patients with ischemic ST depression have a greater decrease in the QRST isointegral values in the precordial region than patients without ischemia and ST depression. There are also low similarities between resting and postexercise QRST isointegral maps. We conclude that ischemic ST depression is related to the dispersion of the exercise-induced changes in repolarization properties.

Key words: body surface ECG mapping; coronary artery disease; exercise test; QRST isointegral mapping

ST depression is used as a marker of myocadial ischemia in the exercise-stress ECG test for the detection of coronary artery disease. ST depression is commonly accompanied by a decrease in the height or inversion of the T wave. These ST-T changes are attributed to local repolarization abnormalities due to ischemia. Body surface QRST isointegral mapping has been used to assess repolarization properties in a variety of diseases (Montague et al., 1981; Kubota et al., 1984; Gardner et al., 1986; De Ambroggi et al., 1986; Hayashi et al., 1988, 1989; Tsunakawa et al., 1989; Hirai et al., 1991, 1993; Dambrink et al., 1995). However, there are few reports on the exercise-induced changes in the QRST isointegral in body surface ECG mapping in patients with coronary artery disease. In order to determine whether ischemic

ST depression reflects the dispersion of the exercise-induced changes in repolarization properties or not, we quantitatively analyzed body surface QRST isointegral maps recorded at the same time when exercise-stress thallium-201 myocardial imaging test was performed for the detection of coronary artery disease.

Subjects and Methods

Subjects

We retrospectively studied 32 patients who underwent exercise-stress thallium-201 myocardial imaging and body surface ECG mapping for the detection of coronary artery disease. The patients we studied had a normal resting 12-lead ECG and were divided into 2 groups. Group A consisted of 15 patients (9 men and 6 women,

Abbreviations: bpm, beats per minute; ECG, electrocardiography or electrocardiogram

mean age 60 years, range 44 to 75) who had atypical chest pain and had neither significant coronary artery narrowing nor exercise thallium defect nor significant exercise-induced ST change. Group B consisted of 17 patients (13 men and 4 women, mean age 68 years, range 57 to 80) who had significant exercise-induced ST depression, significant narrowing in at least one of major coronary arteries and reversible thallium defect. Excluded were patients with exercise-induced ST elevation, bundle branch block or atrial fibrillation, or any physical disability for undergoing an exercise tolerance test. No patients had congenital or valvular heart disease, hypertrophic or dilated cardiomyopathy, hypertensive heart disease or chronic obstructive lung disease. Vasodilators were not discontinued. No patients received antiarrhythmic drugs. Excluded were also those who showed no separation of T and P waves during body surface ECG mapping. Patient characteristics are shown in Table 1.

Table 1. Patient characteristics

	Coronary narrowing	Thallium imaging	12-Lead ECG
Group A [15]	< 50%	No defect	No ST depression
Group B [17]	≥ 75%	Reversible defect	Down-sloping, ST depression ≥ 0.1 mV

[ ], number of patients.

Informed consent was given by all patients for undergoing this exercise test.

Coronary arteriography and left ventriculography

All patients underwent coronary arteriography and left ventriculography within 1 month of this exercise test. Patients in group A had no coronary artery narrowing ≥ 50% and had normal left ventricular wall motion. Patients in group B had narrowing ≥ 75% in at least one of major coronary arteries. Those with akinesis, dyskinesis or aneurysm in any segment of the left ventricular wall were not included in group B.

Exercise-stress thallium-201 myocardial imaging

Supine bicycle exercise was begun at 25 W, and the work rate was increased by 25 W every 3 min. A dose of 111 MBq of thallium-201 was injected intravenously at peak exercise, and patients continued to exercise for an additional minute. A modified 12-lead ECG according to the Mason and Likar method (1966) was recorded at rest, every minute during exercise, and after 1, 2 and 3 min of recovery. Blood pressure was measured with an automatic sphygmomanometer (Nippon Colin, STBP-680, Tokyo, Japan) on the left arm. The end point of exercise was determined by the development of moderate anginal chest pain, severe shortness of breath or severe leg fatigue, new ST depression ≥ 0.2 mV at 80 ms from the J point in at least one lead except leads aVR, aVL and V1, or the achievement of 85% of age-adjusted predicted maximum heart rate. Significant ST depression was defined as new
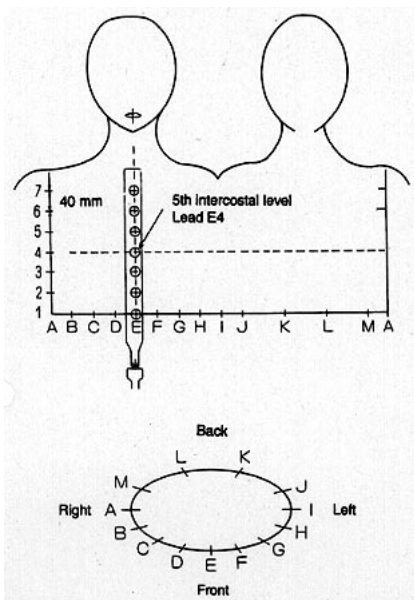

Fig. 1. Electrode placement for 87 lead points. The vertical distance between two lead points is 40 mm. E4 is located on the level of the fifth intercostal space. Leads G4, H4 and I4 correspond to V4, V5 and V6 of 12-lead ECG.

down-sloping depression ≥ 0.1 mV at 1 min of recovery. Tomographic thallium-201 imaging was performed using a gamma camera (Hitachi, GAMMA-VIEW, Tokyo) equipped with a high-resolution, low-energy parallel-hole collimator and interfaced to a dedicated computer system (Hitachi, HARP). Initial imaging was begun 10 min after the termination of exercise and delayed imaging was repeated 4 h later. Thirty-two projections over a 180-degree arc

Fig. 2. Resting (**R**) (upper panel) and postexercise (**P**) (lower panel) ST-T isointegral maps of a patient in group A. Isointegral contours are separated by 10 µV·s. Shading indicates negative areas. Maximum and minimum are indicated by plus and minus signs.

were obtained with a 64×64 matrix. Short-axis, vertical long-axis and horizontal long-axis tomograms were reconstructed. The left ventricle was divided into the anterior wall (anterior and apical segments) and the posterior wall (inferoposterior and posterolateral segments). Images were interpreted by three observers. A defect was classified as reversible (partial or complete redistribution) or irreversible (no redistribution or equivocal). A consensus of the opinions of the three observers was taken. A reversible defect was used as a positive criterion for myocardial ischemia.

Body surface ECG mapping

Body surface ECG maps were recorded using a VCM-3000 system (Chunichi Denshi, Nagoya, Japan) at the resting expiratory level before and 1.5 min after exercise. Unipolar ECGs were recorded simultaneously from 87 lead points on the chest and back (59 and 28 leads, respectively) with reference to Wilson's central terminal (Fig. 1). The Frank X, Y, Z ECGs were also recorded simultaneously. The PR-segment was used as a baseline. The onset of QRS, the J point and the offset of the T-wave were determined from the spatial magnitude. The ST-T
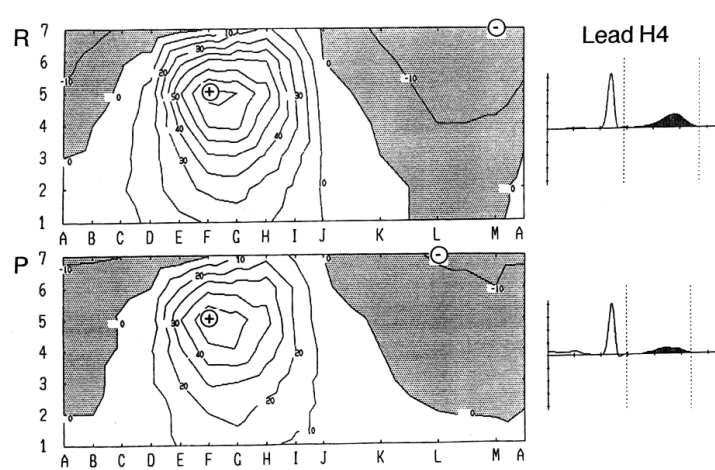
and QRST isointegrals were calculated for each lead as the algebraic sum of potentials from the J point or QRS onset to the T-wave offset and expressed in µV·s. Resting and postexercise ST-T isointegral maps, resting and postexercise QRST isointegral maps and the difference map between resting and postexercise QRST isointegrals were constructed. The ST-T and QRST isointegral contours were separated by 10 µV·s. A previous study of normal adults showed that the normal QRST isointegral map pattern has a dipolar character with two extremes: one positive (maximum) and one negative (minimum) (Montague et al., 1981). A QRST isointegral extreme was defined as a circumscribed peak in the smooth and graduated potential distribution. The map pattern was defined as nondipolar if three or more extremes were present. An additional extreme was considered present if an area of equal polarity included at least 2 lead points (Dambrink et al., 1995). Body surface was divided vertically into right (columns A to D, L and M) and left (columns E to K) regions, and divided horizontally into inferior (lines 1 and 2), mid (lines 3 and 4) and superior (lines 5 to 7) regions. Significant area in the postexercise ST-T or QRST isointegral map was defined as a new negative area including at least 3 lead
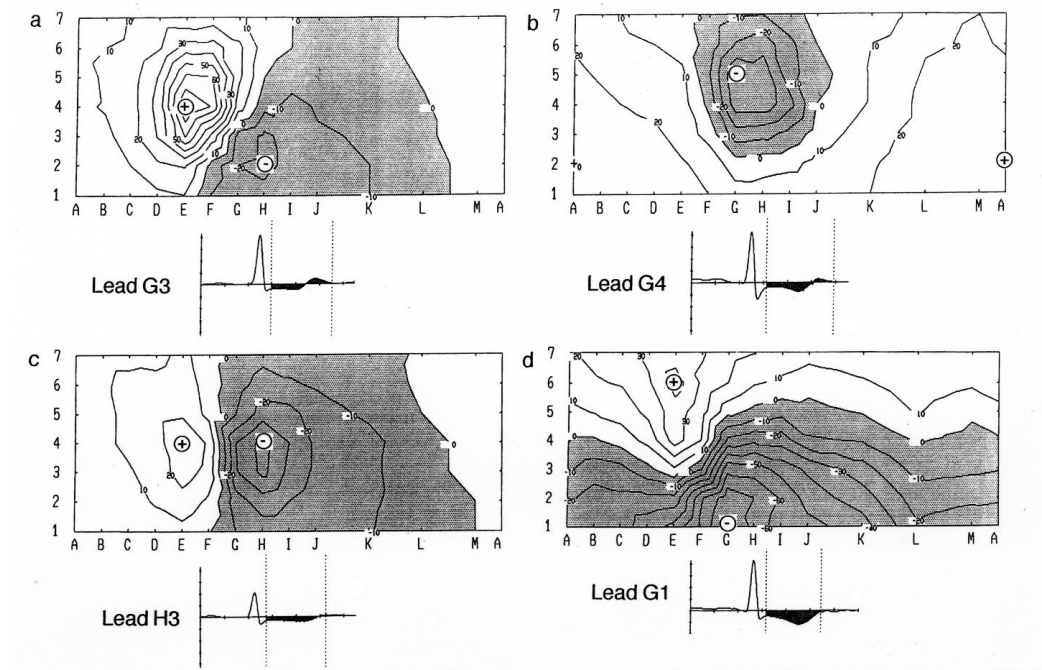
Fig. 3. Four types of abnormal negative areas in the postexercise ST-T isointegral maps in patients in group B. Isointegral contours are separated by 10 µV·s. Shading indicates negative areas. Significant area (< -10 µV·s) is located in the left-inferior and left-mid regions (**a**: 57-year-old man), in the left-mid and left-superior regions (**b**: 77-year-old woman), in all of the three left regions (**c**: 78-year-old man) or in both right and left regions (**d**: 73-year-old man).

points in which each isointegral value was less than -10 µV·s. The mean and mean $-2SD$ difference maps between resting and postexercise QRST isointegrals in group A were constructed. When the QRST isointegral difference value was less than the mean $-2SD$ in group A in at least 3 lead points, the decrease was considered significant ("$-2SD$ area"). The correlation coefficient between resting and postexercise QRST isointegrals in 87 leads was used as a marker of similarities in the potential distributions.

Statistical analysis

Data are shown as the mean ± SD or as a percentage. For the comparison of statistical significance between 2 groups, the unpaired *t*-test was used. A value of $P < 0.05$ was considered significant.

Table 2. Relationship between significant area in the postexercise ST-T isointegral map and ischemic area in the thallium-201 myocardial imaging

Ischemic area	Significant area in the ST-T isointegral map			
	Left-inferior and left-mid [7]	Left-mid and left-superior [2]	All of the 3 left regions [4]	Right and left [4]
Anterior	2	0	0	2
Posterior	4	1	2	0
Anterior and posterior	1	1	2	2

[ ], number of patients.

110

Results

Exercise variables

Group A

The end point of exercise was leg fatigue in 11 and shortness of breath in 4 patients. Work load was 77 ± 29 W. Heart rate at peak exercise was 120 ± 12 bpm. Systolic blood pressure at peak execise was 186 ± 24 mmHg.

Group B

The end point of exercise was anginal chest pain in 9, ST depression in 5 and leg fatigue in 3 patients. Work load was 51 ± 19 W ($P < 0.01$ versus group A). Heart rate at peak exercise was 108 ± 17 bpm ($P < 0.01$ versus group A). Systolic blood pressure at peak exercise was 171 ± 19 mmHg.

Thallium-201 myocardial imaging and postexercise 12-lead ECG

Group A

No patients had thallium defect and significant ST change.

Group B

All patients showed reversible thallium defect. Four patients showed reversible thallium defect in the anterior wall, 7 patients in the posterior wall and 6 patients in both anterior and posterior walls. All patients had significant down-sloping ST depression. Maximal ST depression was -0.21 ± 0.08 mV.

ST-T isointegral maps

Group A

Figure 2 shows resting and postexercise ST-T isointegral maps of a representative patient (60-year-old man). All patients had smooth dipolar pattern maps both at rest and after exercise with the positive area located over the precordium and the negative area over the right chest and back. This was considered a normal response.
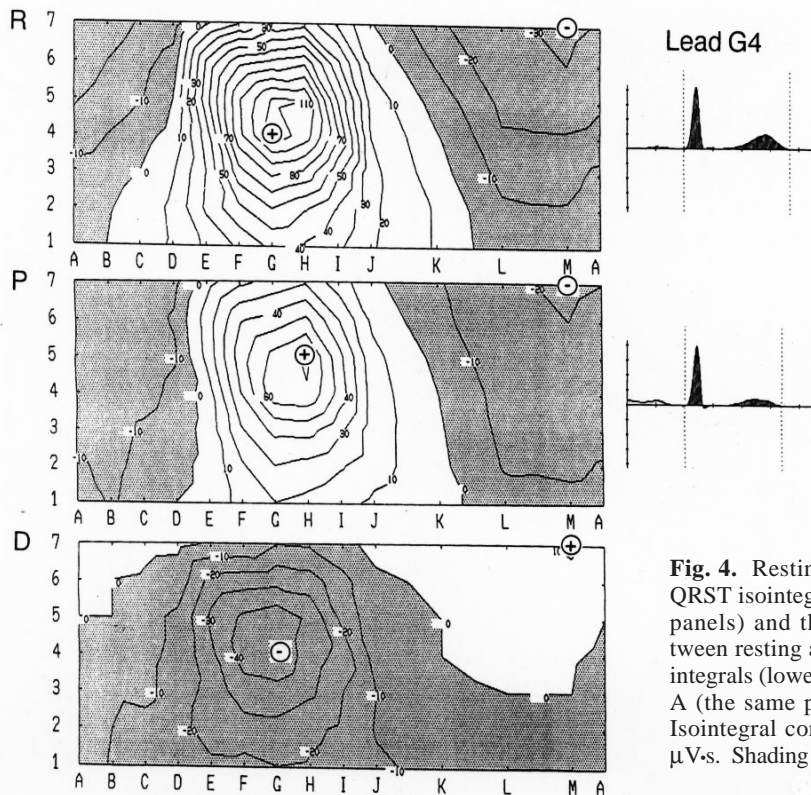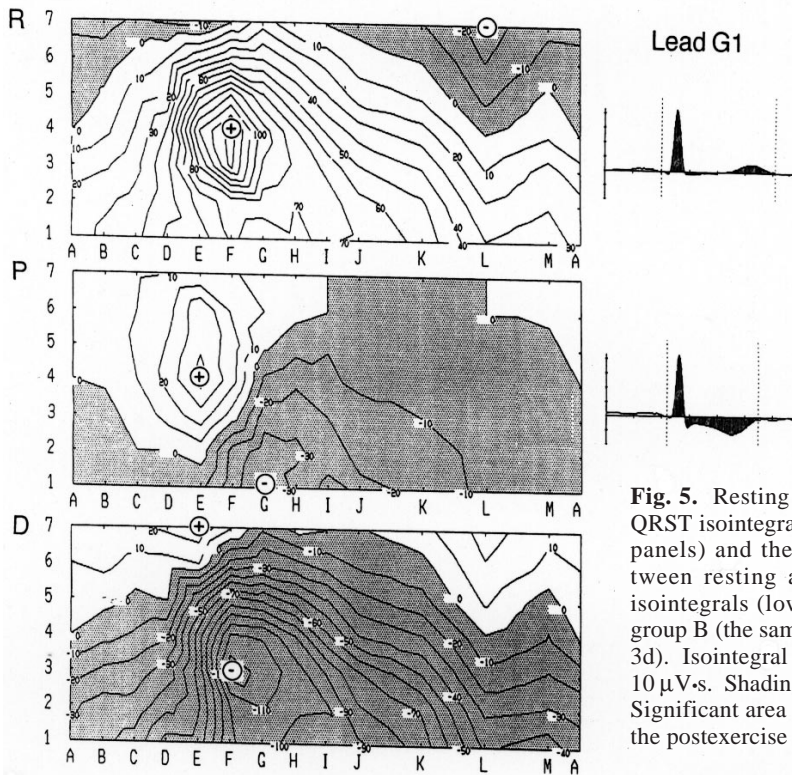

Fig. 4. Resting (**R**) and postexercise (**P**) QRST isointegral maps (upper and middle panels) and the difference (**D**) map between resting and postexercise QRST isointegrals (lower panel) in a patient in group A (the same patient as shown in Fig. 2). Isointegral contours are separated by 10 μV·s. Shading indicates negative areas.

Fig. 5. Resting (**R**) and postexercise (**P**) QRST isointegral maps (upper and middle panels) and the difference (**D**) map between resting and postexercise QRST isointegrals (lower panel) in a patient in group B (the same patient as shown in Fig. 3d). Isointegral contours are separated by $10\,\mu V\cdot s$. Shading indicates negative areas. Significant area ($< -10\,\mu V\cdot s$) is present in the postexercise map.

Group B

All patients had significant area in the postexercise map. Seven patients (41%) had significant area in the left-inferior and left-mid regions in the postexercise map, 2 patients (11%) in the left-mid and left-superior regions, 4 patients (24%) in all three of the left regions and 4 patients (24%) in the right-inferior, (right-mid,) left-inferior and left-mid regions. Four types of significant area in the postexercise map are shown in Fig. 3. Significant area in the post-exercise map was not correlated with the is-chemic area determined by thallium imaging (Table 2).

QRST isointegral maps

Figure 4 shows resting and postexercise QRST isointegral maps and the difference map be-tween resting and postexercise QRST isointe-grals in a patient in group A (the same patient as Fig. 2). All three maps show smooth dipolar patterns. Figure 5 shows resting and postexer-cise QRST isointegral maps and the QRST iso-integral difference map of a representative pa-tient in group B (the same patient as Fig. 3d). Sig-nificant area is observed in the postexercise map. Figures 6a and b show mean and mean –2SD dif-ference maps between resting and postexercise QRST isointegrals in group A. Figure 6c shows the QRST isointegral difference map of a pa-tient in group B (the same patient as Figs. 3d and 5), in which an extensive "–2SD area" is observed. Figure 7 shows the relationship between resting and postexercise QRST iso-integral maps in a patient (group A) with a high correlation coefficient and in a patient (group B) with a low correlation coefficient.

Group A

All patients showed smooth dipolar pattern maps both at rest and after exercise. The posi-tive area covered the precordium with the maxi-mum located in the middle of the left chest and the minimum at the upper region of the right chest or right back. All patients showed a smooth dipolar difference map between resting and postexercise QRST isointegrals. The nega-
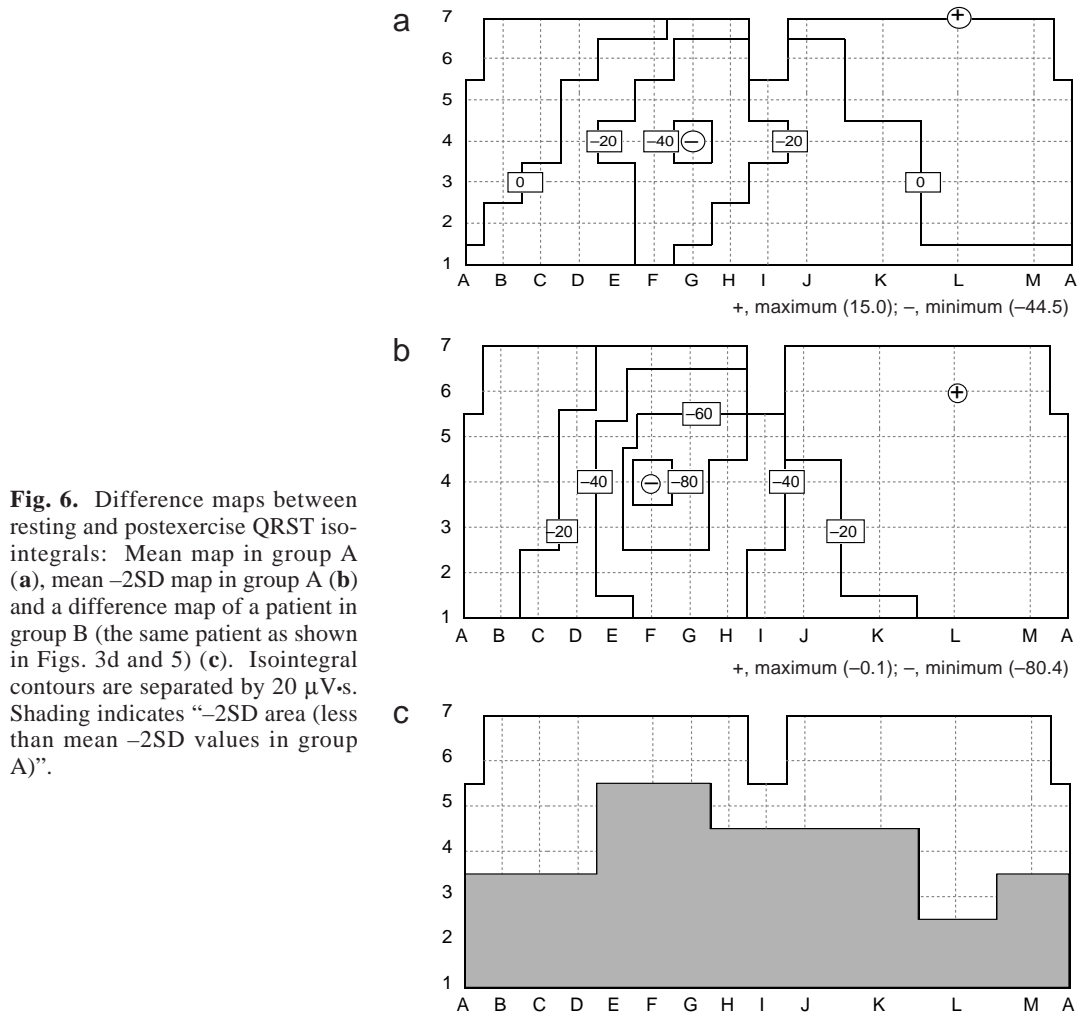
Fig. 6. Difference maps between resting and postexercise QRST iso-integrals: Mean map in group A (**a**), mean –2SD map in group A (**b**) and a difference map of a patient in group B (the same patient as shown in Figs. 3d and 5) (**c**). Isointegral contours are separated by 20 µV·s. Shading indicates "–2SD area (less than mean –2SD values in group A)".
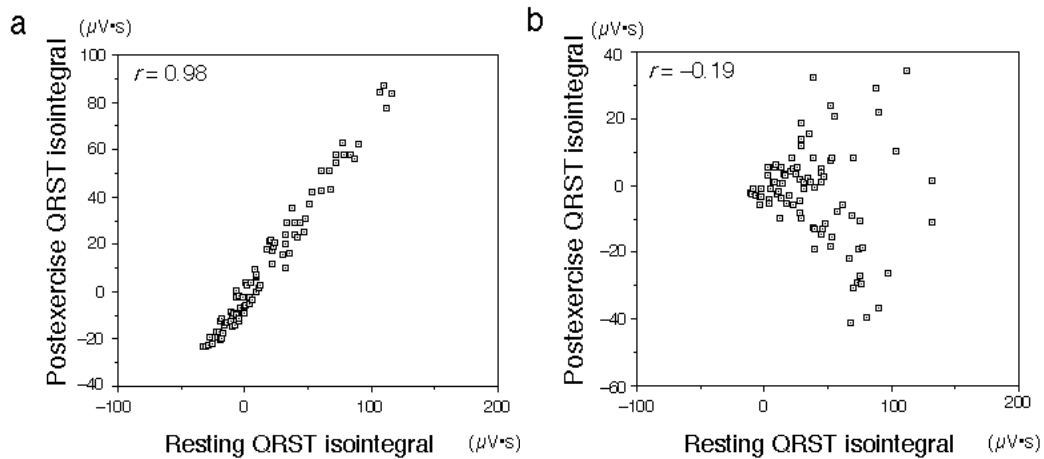

Fig. 7. Relationship between resting and postexercise QRST isointegrals: a patient (group A, the same patient as in Figs. 2 and 4) with a high correlation coefficient (**a**) and a patient (group B, the same patient as shown in Figs. 3d and 5) with a low correlation coefficient (**b**).

113

tive area covered most of the chest with the minimum located in the middle of the left chest and the maximum at the upper region of the right chest or right back. The minimum in mean and mean –2SD difference maps between resting and postexercise QRST isointegrals was located in lead F4 (mean = –44.5 µV·s; mean –2SD = –80.4 µV·s). The correlation coefficient between resting and postexercise QRST isointegrals in 87 lead points was 0.91 ± 0.06.

Group B

Ten patients (59%) had significant area in the postexercise map. No patients had a non-dipolar pattern map. Fifteen patients (88%) had "–2SD area" in the difference map between resting and postexercise QRST isointegrals. The correlation coefficient between resting and postexercise QRST isointegrals in 87 lead points in group B (0.28 ± 0.56) was significantly lower than that in group A ($P < 0.001$) (Fig. 8).

Discussion

The present study demonstrates that patients with ischemic ST depression had a greater decrease in the QRST isointegral values in the precordial region than patients without ischemia and ST depression and had low similarities between the resting and postexercise QRST isointegral maps. These findings indicate that ischemic ST depression is related to the dispersion of the exercise-induced changes in repolarization properties.

Body surface ECG mapping offers information about potential distributions around the entire thorax. In patients with coronary artery narrowing, exercise-induced ST depression most often occurs in the left anterior chest leads. According to the data from exercise-stress ST isopotential mapping, predicting the location of ischemic areas is thought to be difficult from the body surface distributions of ST depression (Kubota et al., 1989). Montague and colleagues (1990) studied exercise-stress ST isointegral maps in coronary artery disease and observed that, with exercise-induced angina,
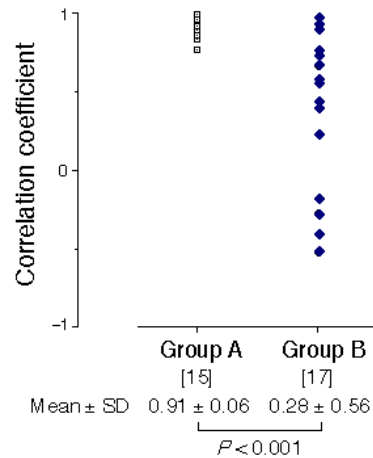

Fig. 8. The correlation coefficient between resting and postexercise QRST isointegral maps for each group, A and B. [ ], number of patients.

patients with two or three vessel disease had a significantly greater decrease in the ST isointegral values than patients with single vessel disease. There was, however, considerable overlap among individuals. The reason for a lack of correlation between body surface distribution of ST depression and anatomic site of coronary artery disease is unclear. Exercise-induced ST depression is commonly accompanied by a decrease in the height or inversion of the T wave. Nakajima and coworkers (1988) studied exercise-stress ST-T isointegral maps in patients with angina pectoris in the absence of previous myocardial infarction. They observed that postexercise ST-T isointegral maps were divided into 4 types (anterior chest, infero-posterior chest, lateral chest and global) according to the distributions of negative area, which were well correlated with the extent of ischemic area determined by thallium imaging. However, our results demonstrated that significant area in the postexercise ST-T isointegral map was not correlated with the ischemic area. The reason for the discrepancy is not clear. Studies in a large number of patients are needed.

Exercise-induced ST depression is attributed to a current of injury with ischemia in sub-endocardial layers. T wave inversion is thought to be related to the presence of delayed recovery. Exercise-induced ischemia causes not only

114

ST-T but also QRS changes. R wave amplitude on the surface ECG is decreased in normal subjects while the increase is seen in patients with coronary artery disease (Bonoris et al., 1978a, 1978b). Ikeda and colleagues (1988) reported that intraventricular conduction delay secondary to ischemia plays an important role in the increase in R wave amplitude. ST-T isointegral map reflects ventricular recovery sequence. The recovery sequence is affected by activation sequence and regional recovery properties. The QRST isointegral map has been reported to be useful in investigating recovery properties. Wilson and researchers (1934) reported that the QRST isointegral is independent of the activation sequence and dependent on repolarization properties. They proposed the concept of a ventricular gradient. Based on this concept of the ventricular gradient, Abildskov and workers (1980) introduced the QRST isointegral map. They demonstrated that the QRST isointegral map was independent of the activation sequence and useful in detecting abnormalities in repolarization properties, even in the presence of QRS deflection abnormalities. Although body surface QRST isointegral mapping has been used to assess repolarization abnormalities in a variety of diseases, few reports on exercise-stress QRST isointegral mapping are available. Ohyama and others (1984) studied exercise-induced changes in QRST isointegral map patterns in patients with effort angina in the absence of akinesis or dyskinesis in the left ventricular wall motion. These investigators observed that after exercise the maximum of the map moves far from the resting position and splits into multiple extremes in patients with multivessel coronary artery disease.

In this study, to assess exercise-induced changes in repolarization properties, we performed quantitative analysis of QRST isointegral mapping. Normal responses of QRST isointegral values to exercise have not been determined. We constructed a mean –2SD difference map between resting and postexercise QRST isointegrals in control subjects (group A). When the QRST isointegral value in at least 3 lead points was less than the mean –2SD, the decrease was considered significant ("–2SD area"). The correlation coefficient between QRST isointegral maps is independent of the difference in potential magnitudes and indicates the similarities in potential distributions (Hayashi et al., 1989). However, the relationship between resting and postexercise maps has not been analyzed.

Control subjects (group A) showed a decrease in the maximum QRST isointegral value, which may result from shortening of QT interval and a decrease in the R wave and T wave amplitudes in the left precordial leads. These patients showed smooth dipolar ST-T isointegral maps both at rest and after exercise. They also showed smooth dipolar QRST isointegral maps both at rest and after exercise and a high correlation coefficient between the two maps. These findings indicate that control subjects have higher similarities between resting and postexercise repolarization properties.

Patients with ischemic ST depression in the absence of previous myocardial infarction (group B) showed a high incidence of the occurrence of a significant area in the postexercise QRST isointegral map and "–2SD area" in the QRST isointegral difference map. In addition, these patients showed a low correlation coefficient between resting and postexercise QRST isointegral maps. These findings indicate that ischemic ST depression is associated with remarkable changes in ST-T and QRST isointegrals and may be related to the regional abnormalities in repolarization properties.

We conclude that isointegral analysis of body surface ECG mapping has advantages in assessing repolarization properties in the exercise test for the detection of coronary artery disease. Further studies in patients with previous myocardial infarction, intraventricular conduction disturbance or left ventricular hypertrophy are needed.

References

1 Abildskov JA, Evans AK, Lux RL, Burgess MJ. Ventricular recovery properties and QRST deflection area in cardiac electrograms. Am J Physiol 1980;239:H227–H231.

2 Bonoris PE, Greenberg PS, Castellanet MJ, Ellestad MH. Significance of changes in R wave amplitude during treadmill stress testing: angiographic correlation. Am J Cardiol 1978a;41:846–851.

3 Bonoris PE, Greenberg PS, Christison GW, Castellanet MJ, Ellestad MH. Evaluation of R wave amplitude changes versus ST-segment depression in stress testing. Circulation 1978b; 57:904–910.

4 Dambrink J-HE, SippensGroenewegen A, van Gilst WH, Peels KH, Grimbergen CA, Kingma JH. Association of left ventricular remodeling and nonuniform electrical recovery expressed by nondipolar QRST integral map patterns in survivors of a first anterior myocardial infarction. Captopril and Thrombolysis Study Investigators. Circulation 1995;92:300–310.

5 De Ambroggi L, Bertoni T, Locati E, Stramba-Badiale M, Schwartz PJ. Mapping of body surface potentials in patients with the idiopathic long QT syndrome. Circulation 1986;74:1334–1345.

6 Gardner MJ, Montague TJ, Armstrong CS, Horacek BM, Smith ER. Vulnerability to ventricular arrhythmia: assessment by mapping of body surface potential. Circulation 1986;73: 684–692.

7 Hayashi H, Watabe S, Ohsugi S, Takami K, Kojima H, Yabe S, et al. Sites of origin of ventricular premature beats in patients with and without cardiovascular disease evaluated by body surface mapping. J Electrocardiol 1988;21:137–146.

8 Hayashi H, Watanabe S, Yabe S, Takami K, Ohsugi S, Hirai M, et al. Diagnostic value of QRST isointegral maps in detecting myocardial infarction complicated by bundle branch block. Circulation 1989;80:542–550.

9 Hirai M, Hayashi H, Ichihara Y, Adachi M, Kondo K, Suzuki A, et al. Body surface distribution of abnormally low QRST area in patients with left ventricular hypertrophy: an index of repolarization abnormalities. Circulation 1991;84: 1505–1515.

10 Hirai M, Tsuboi N, Hayashi H, Ito M, Inden Y, Hirayama H, et al. Body surface distribution of abnormally low QRST areas in patients with Wolff-Parkinson-White syndrome: evidence for continuation of repolarization abnormalities before and after catheter ablation. Circulation 1993;88:2674–2684.

11 Ikeda K, Kubota I, Yamaki M, Igarashi H, Nakamura K, Tsuiki K, Yasui S. Local conduction delay causes R-wave amplitude increase in patients with effort angina. J Electrocardiol 1988;21:39–44.

12 Kubota I, Ikeda K, Yamaki M, Watanabe Y, Tsuiki K, Yasui S. Determination of the left ventricular asynergic site by QRST isointegral mapping in patients with myocardial infarction. Jpn Heart J 1984;25:311–324.

13 Kubota I, Hanashima K, Ikeda K, Tsuiki K, Yasui S. Detection of diseased coronary artery by exercise ST-T maps in patients with effort angina pectoris, single-vessel disease, and normal ST-T wave on electrocardiogram at rest. Circulation 1989;80:120–127.

14 Mason RE, Likar I. A new system of multiple-lead exercise electrocardiography. Am Heart J 1966;71:196–205.

15 Montague TJ, Smith ER, Cameron DA, Rautaharu PM, Klassen GA, Felmington CS, et al. Isointegral analysis of body surface maps: surface distribution and temporal variability in normal subjects. Circulation 1981;63:1166–1172.

16 Montague TJ, Witkowski FX, Miller RM, Johnstone DE, MacKenzie RB, Spencer CA, et al. Exercise body surface potential mapping in single and multiple coronary artery disease. Chest 1990;97:1333–1342.

17 Nakajima T, Kawakubo K, Toda I, Mashima S, Ohtake T, Iio M, et al. ST-T isointegral analysis of exercise stress body surface mapping for identifying ischemic areas in patients with angina pectoris. Am Heart J 1988;115:1013–1021.

18 Ohyama T, Kubota I, Watanabe Y, Tsuiki K, Yasui S. Treadmill stress test in patients with coronary artery disease: isointegral analysis of body surface map. Jpn J Electrocardiol 1984;4: 11–17.

19 Tsunakawa H, Nishiyama G, Kusahana Y, Harumi K. Identification of susceptability to ventricular tachycardia after myocardial infarction by nondipolarity of QRST area maps. J Am Coll Cardiol 1989;14:1530–1536.

20 Wilson FN, MacLeod AG, Barker PS, Johnston FD. The determination and the significance of the areas of the ventricular deflections of the electrocardiogram. Am Heart J 1934;10:46–61.