Spatial Ventricular Gradient in Patients with Wolff-Parkinson-White Syndrome in Comparison with Normal Subjects: Vectorcardiographic Evidence for Significant Repolarization Changes due to Preexcitation

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We investigated the use of the spatial ventricular gradient (VG) from vectorcardiogram (VCG) to determine whether significant repolarization differences were present in patients with WPW syndrome compared with normal subjects and also examined which VG parameter (i.e., elevation, azimuth, and magnitude) reflected the differences in repolarization properties during preexcitation. VG was calculated in 49 patients of Wolff-Parkinson-White (WPW) syndrome (group A: left-sided accessory pathway, $n=29$; group B: right-sided, $n=20$). Group N consisted of 607 normal subjects. In group A, the azimuth of VG was significantly ($p<0.01$) greater than in groups B and N. In group B, the elevation of VG was significantly ($p<0.01$) greater than in groups A and N. There were no significant differences in the magnitude of VG among groups. QRS duration was significantly ($p<0.01$) related with the elevation of VG in group B. These findings suggested that VG is useful for spatial evaluation of repolarization abnormalities during preexcitation, which are related to the site of the accessory pathway.

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Key words: accessory pathway, Wolff-Parkinson-White (WPW) syndrome, activation sequence, T-wave

Introduction

The ventricular gradient (VG) introduced by Wilson et al (1) has been reported to be largely independent of the activation sequence and dependent on repolarization properties. Although Abildskov and colleagues confirmed this concept using QRST isointegral map (2–4), they also reported small differences in the QRST isointegral map resulting from the altered activation sequence (5). Toyoshima and Burgess experimentally demonstrated that activation sequences modified refractoriness and suggested that this modification was attributable to electrotonic interaction (6). Costard-Jäckle et al measured monophasic action potentials during altered activation and found that the action potential duration slowly changed when the activation sequence was altered in rabbit hearts (7). Recently, marked T-wave changes have been reported after catheter ablation in patients with manifest Wolff-Parkinson-White (WPW) syn-

drome (8–10). These T-wave changes were speculated to be a continuation of repolarization abnormalities present before ablation (8–10). Thus, it has been shown experimentally and clinically that an altered activation sequence induces changes in repolarization properties (5, 6, 8–10). However, there have been few clinical reports concerning the repolarization changes during the abnormal activation sequence because of difficulties in studying repolarization properties in the presence of abnormal activation (11, 12). No report has shown which parameters (i.e., elevation, azimuth and magnitude) of spatial VG from vectorcardiograms (VCG) during preexcitation are associated with significant differences compared with normal subjects, and with a significant correlation between QRS durations. The purposes of this study were to determine whether any or all of the above-mentioned parameters are associated with repolarization abnormalities during preexcitation in patients with WPW syndrome compared with normal subjects, and to iden-

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tify any parameter significantly related to QRS duration during preexcitation in patients with WPW syndrome.

Methods

Study population

We selected 49 consecutive patients (32 men and 17 women; mean age, 43 years) whose digitized VCGs with Frank-lead system were recorded at the Nagoya University Hospital. Participants were required to satisfy the following criteria: manifest WPW syndrome confirmed by 12-lead ECGs; no antiarrhythmic drug administered, or discontinuation of the drug for at least five elimination half-lives at the time of mapping; absence of other cardiac disease, such as congenital heart disease, myocardial infarction, or valvular heart disease; no hypertension: heart rate between 50 to 100 beats/min, and no imbalance in serum electrolytes.

Patients were divided into two groups: Group A (29 patients with left-sided accessory pathway diagnosed by criteria proposed by Gallagher et al (13); 19 men and 10 women, mean age 46 years; age range 14 to 72 years), and Group B (20 patients with right-sided accessory pathway diagnosed by criteria proposed by Gallagher et al (13); 13 men and 7 women, mean age 39 years; age range 16 to 65 years).

Group N consisted of 607 normal individuals (376 men and 231 women; mean age, 42.3 years; age range, 17 to 81 years) registered in the Japanese Circulation Society Task Force Committee on Body Surface Mapping (14). They were free of cardiovascular disease as determined by routine clinical examinations including chest radiographs and ECGs.

Informed consent was obtained from all subjects before their participation in the study.

Digitized vectorcardiograms

Digitized Frank-lead VCGs were recorded with the VCM-3000 system (Chunichi Denshi Company, Nagoya, Japan). Because the details of data acquisition and the processing were reported previously (15, 16), we will describe them only briefly.

ECGs of leads X, Y and Z by Frank-lead system were recorded simultaneously. ECG data were scanned by multiplexers, digitized by analog/digital converters at a rate of 1,000 samples/sec and stored on floppy disks. A 2-point baseline adjustment was performed by choosing the flat portion of the TP segment before P and after T deflection of the selected PQRS complex. After baseline adjustment, a root-mean-square voltage versus time curve was plotted to help identify the beginning of P and QRS and the end of T deflection, which were manually selected from this curve. The orthogonal components of VG were calculated by integrating each lead over the appropriate interval (expressed in mV•msec). In rectilinear coordinate axes of the body, posterior (Z), downward (Y), and leftward (X) directions were designated as positive. The left end of the X axis and the anterior end of the Z axis were, respectively, designated as 0° and +90° for the azimuth. The inferior end of the Y axis was designated as 0° for the elevation. Data sampling was performed at the expiratory level with the subject

in the supine position. QRS duration was measured using a root-mean-square voltage of leads X, Y and Z by two observers in blind fashion.

Statistical analysis

Values are expressed as mean±SD. Statistical analysis was performed using one-way analysis of variance test (when a significant effect was observed, group comparison were made using Scheffé's test). A probability value of less than 0.05 was considered statistically significant.

Results

Ventricular gradient in representative patients with WPW syndrome

Twelve-lead ECG and VCG in a representative patient (37-year-old female) in group A are shown in Fig. 1. The left lateral atrioventricular accessory pathway was successfully ablated in this patient. ECG shows positive delta and R waves in lead V₁. In the horizontal plane, the figure-of-eight pattern QRS loop was displaced anteriorly with the anterior delta deflection and the maximum QRS vector located in the left anterior quadrant. In the frontal plane, the direction of the delta deflection was to the left, inferiorly, with the QRS loop inscribed clockwise. The azimuth, elevation, and magnitude in this patient were 34°, 38°, and 93 mV•msec, respectively.

Twelve-lead ECG and VCG in a representative patient (21-year-old male) in group B are shown in Fig. 2. The right posterior atrioventricular accessory pathway was confirmed by electrophysiological study in this patient. ECG shows a positive delta wave with S wave in lead V₁ and a negative delta wave in leads II, III and aV_F. In the horizontal plane, the QRS loop inscribed counterclockwise was located to the left with the leftward delta deflection and the maximum QRS vector in the left posterior quadrant. In the frontal plane, the delta deflection and the rest of the QRS loop were oriented to the left, superiorly, with counterclockwise inscription. The azimuth, elevation, and magnitude in this patient were 15°, 106°, and 109 mV•msec, respectively. The QRS duration was 148 msec.

Differences in ventricular gradient in patients with WPW syndrome compared with normal subjects

Table 1 shows the mean±SD of the azimuth, elevation and magnitude in groups A, B and N. The azimuth was significantly greater ($p<0.01$) in group A than in groups B and N. The elevation in group B was significantly greater ($p<0.01$) than in groups A and N. The elevation in group A was significantly greater ($p<0.01$) than in group N. There were no significant differences in magnitude among groups.

Correlation between parameters of VG and QRS duration

Figure 3 shows the correlation between elevation of VG and QRS durations in group B. The elevation was moderately but significantly ($p<0.01$) correlated with QRS durations in group B. There was no significant correlation between parameters of VG and QRS durations in group A and between other param-

Figure 1. Twelve-lead ECG (A), frontal and horizontal planes of VCG (B), and parameters from VG (C) in a patient (37-year-old female) of group A. In VCG, the delta deflection and QRS loop were oriented anteriorly with VG of 34° in azimuth, 38° in elevation and 93 mV·msec in magnitude.

eters of VG and QRS durations in group B.

Discussion

In the present study, we found significant differences in the azimuth of VG in group A and in the elevation of VG in group B as compared with group N. There were no significant differences in the magnitude of VG among groups during preexcitation even in the presence of differences in QRST configuration. The elevation of VG was significantly related to QRS durations in group B.

Repolarization in WPW syndrome

It has been generally accepted that T-wave changes in patients with WPW syndrome are secondary to QRS changes resulting from changes in activation sequences (17). However,

alteration in the activation sequence has been reported to induce changes in repolarization properties (5, 6). Toyoshima and Burgess demonstrated that collision of activation fronts shortens refractoriness at the site of collision compared with one-way propagation in dog hearts (6). They speculated these findings were explicable by electrotonic interaction (6). Costard-Jäckle et al reported that the action potential duration measured by monophasic action potential slowly changed to maintain correlation of the shorter activation time with the longer action potential duration when the activation sequence was altered in rabbit hearts (7). These findings have modified the classic concept of secondary T-wave changes. T-wave changes in patients with WPW syndrome may be caused by changes in repolarization properties resulting from preexcitation in addition to the classic secondary T-wave change. However, there have been few reports concerning repolarization properties

Ventricular Gradient in WPW Syndrome

Figure 2. Twelve-lead ECG (A), frontal and horizontal planes of VCG (B), and parameters from VG (C) in a patient (21-year-old-male) of group B. In VCG, the delta deflection and QRS loop were oriented to the left, superiorly, with VG of 15° in azimuth, 106° in elevation and 109 mV·msec in magnitude.

Table 1. Azimuth, Elevation and Magnitude in Groups A, B and N

Group	Azimuth (degree)	Elevation (degree)	Magnitude (mV·msec)
Group A (n=29)	41.9±14.6*	60.1±16.6†	115.6±49.3
Group B (n=20)	15.6±22.3	80.2±26.1**	109.8±37.7
Group N (n=607)	16.1±20.7	51.9±13.2	105.8±38.5

Values are mean±SD, *p<0.01 vs groups B and N, †p<0.01 vs group N, **p<0.01 vs groups A and N.

Figure 3. Scatterplots of the relation between QRS duration and elevation in patients of group B. The elevation was significantly correlated with QRS durations (p<0.01).

during preexcitation because of difficulties in investigating repolarization in the presence of abnormal activation (11, 12). Nicolai et al indicated T-wave abnormalities during normal conduction with antiarrhythmic agent administration in patients with WPW syndrome (11). We reported the presence of repolarization abnormalities during preexcitation using QRST isointegral map (12). The present study showed significant differences in VG between patients with preexcitation and normal subjects. VG was directed more anteriorly in group A and more superiorly in group B as compared with group N. These findings suggested the presence of significant differences in repolarization properties and the spatial direction of the differences in patients with WPW syndrome compared with normal subjects.

Ventricular gradient

Wilson et al demonstrated that QRST values in limb leads of ECG are independent of the activation sequence and introduced the concept of VG (1). Plonsey theoretically confirmed the concept if repolarization properties were not influenced by the activation sequence (18). Berkun et al showed no differences in spatial VG in patients with intermittent WPW syndrome and intermittent left bundle branch block (19). They reported that spatial VG is largely independent of the activation sequence. On the other hand, Okumura et al also compared spatial VG during normal conduction and preexcitation in patients with intermittent WPW syndrome and found significant differences in VG between the two activation sequences (20). However, because the difference was subtle, they concluded that it would be clinically acceptable to consider spatial VG to be independent of the activation sequence (20). Thus, there have been several reports concerning spatial VG in different activation sequences and its independence of the activation sequence. However, no report has compared spatial VG in normal subjects with that in patients with left-sided or right-sided accessory pathway by analysis of variance. Although we showed the significant differences in VG among patients with types A and B WPW syndrome and normal subjects in the present study, the concept of VG cannot necessarily be denied. We previously reported that QRST isointegral maps are largely independent of the activation sequence and dependent on repolarization properties (21). We think that VG is independent of the activation sequence as long as the altered activation sequence induces no changes in repolarization properties. But alteration of the activation sequence is reported to actually affect repolarization properties (6, 7). Accordingly, the differences in VG in the present study reflected the significant changes in repolarization properties due to preexcitation in patients with manifest WPW syndrome as compared with normal subjects. Furthermore, there has been no report discussing the normal mean value of the azimuth, elevation and the magnitude of VG calculated from data on more than 500 normal subjects.

Relationship between postablation T-wave changes and the present study

Kalbfleisch et al demonstrated T-wave abnormalities on

ECG following radiofrequency catheter ablation in patients with manifest WPW syndrome (8). They showed major T-wave abnormalities after ablation, such as peaked T-waves in precordial leads (V_2 to V_5) and negative T-waves in inferior leads in patients with the left lateral and posterior accessory pathways, respectively. They further showed the concordance of the direction of delta wave with the direction of postablation T-wave changes. Kalbfleisch et al suggested that these T-wave abnormalities resulted from myocardial memory of preablation repolarization properties, or the "cardiac memory" reported by Rosenbaum et al (22). Helguera et al (23) also showed postablation T-wave abnormalities in almost the same leads as in a previous report (8). However, there has been no report statistically comparing VG parameters between patients with WPW syndrome and normal subjects. In the present study, during preexcitation a significantly greater azimuth of VG in group A and a significantly greater elevation of VG in group B were found compared with those in normal subjects. These findings are in accordance with a previous study (8) that showed T-wave peaking in precordial leads in patients with left-sided accessory pathway and T-wave inversion in inferior leads in patients with right-sided accessory pathway in postablation 12-lead ECG. Our results thus provide supportive evidence for the continuity of the abnormalities before and after ablation. There were no significant differences in the magnitude of VG among groups despite differences in QRST configuration.

Kalbfleisch et al (8) reported more frequent postablation T-wave abnormalities in patients with a QRS duration of greater than 0.1 second compared to those with less than or equal to 0.1 second. Because electrotonic interaction has been thought to be one mechanisms of repolarization modulation resulting from changes in activation sequences (8), greater electrotonic interaction induced by greater QRS duration may result in greater postablation repolarization abnormalities. In the present study, there was no significant relationship between parameters of VG and QRS duration in group A. On the other hand, there was a significant relationship between the elevation of VG and QRS durations in group B. The reason for this is not clear from this study. However the significant correlation in group B might be partly explained by the greater repolarization abnormalities resulting from greater preexcitation in patients with right-sided accessory pathways as compared with those with left-sided accessory pathways (9, 12). These findings suggest that greater T-wave abnormalities after ablation in patients with less preexcitation may need further clinical investigation to determine whether they complicate repolarization abnormalities resulting from other causes such as injury due to ablation in addition to cardiac memory.

Limitations

In consideration of the limitations, first, since our study population was small, further study with a greater number of patients with the identified accessory pathway connection site is needed. Second, although we showed the presence of significant differences in repolarization during preexcitation, we did not directly measure the differences in the action potential.

However, it would be clinically difficult to record monophasic action potentials from both the endocardium and epicardium to investigate the cause of the repolarization abnormalities.

Conclusions

The present study showed that patients with WPW syndrome were associated with significant differences in direction of VG during preexcitation compared with normal subjects, and that the parameters with the differences were related to the accessory pathway site. QRS duration was significantly related to the VG elevation in group B. VG indeed may be useful in evaluating the spatial differences in repolarization properties in the presence of preexcitation, which is difficult using the conventional analysis of ECG.

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