Signal-Averaging Electrocardiogram in Patients with Diabetes Mellitus

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SUMMARY

In order to detect silent impairment of the heart due to diabetes mellitus, the signal-averaging electrocardiograms (ECG) of 21 healthy subjects and 22 diabetic patients without ventricular tachycardia were compared. The QRS duration in the signal-averaging ECG was longer in diabetic patients than in the normal subjects (87.3 ms vs. 114.5 ms, $p < 0.01$). Moreover, late potentials in the terminal portion of the QRS complex were observed in 7 diabetic patients (32%), but in only one normal subject (5%, $p < 0.01$). These findings suggested that patients with diabetes mellitus frequently have intraventricular conduction disturbances, presumably due to diabetic microangiopathy.

Additional Indexing Words:

Signal-averaging Late potentials Interventricular conduction defect Diabetic cardiomyopathy

THERE has long been thought to be a relationship between diabetes mellitus and impairment of the cardiovascular system. Increasing clinical and experimental evidence indicates that the prevalence of atherosclerosis, arrhythmias and heart failure in diabetics is higher than in normal subjects.¹⁾⁻⁴⁾ Furthermore, cardiovascular disease continues to be the main cause of morbidity and mortality of diabetics. The reasons for cardiovascular lesions in these patients are still controversial, but microangiopathy is thought to be important in their etiology.^{5),6)}

Recently there have been improvements in techniques for the evaluation of electro-instability and intraventricular conduction disturbance in

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diabetics. In this study we used the signal-averaging ECG to examine the late potential, QRS voltage and QRS duration in diabetics to determine whether they suffered from silent intraventricular conduction impairment and ventricular electro-instability, which cannot be detected with the standard ECG.

SUBJECTS AND METHODS

The control group consisted of 21 normal subjects, 10 males and 11 females, 25–68 years old (mean age: 53.1 ± 12.4 years). They had no history of hypertension, heart disease or diabetes mellitus, and had no detectable abnormality on physical examination, roentgenogram, or standard ECG. Their fasting blood levels of glucose, and levels of cholesterol and triglyceride were within normal limits.

The diabetic group consisted of 22 patients with non-insulin-dependent diabetes mellitus (type II), 12 males and 10 females, 31–73 years old (mean age: 59.6 ± 10.3 years). The clinical diagnosis of diabetes mellitus was based on the criteria of the WHO Expert Committee on diabetes mellitus.³⁾ Their fasting blood glucose (venous plasma) level was more than 140 mg and/or the results of an oral glucose tolerance test (75 g glucose) were abnormal. All 22 patients had a blood pressure of less than 150/90 mmHg, and showed a normal sinus rhythm, and no bundle branch block, atrial ventricular conduction block or atrial fibrillation. They had no history of ventricular tachycardia (VT) and showed no VT on a 24-hour ambulatory ECG. No patient had cardiomegaly. Moreover, no patient had evidence of other systemic disease or was taking any medicine that might affect mechanical and conduction functions of the heart. There was no significant difference between the mean age of the control group and that of the diabetic group.

The signal-averaging ECG was obtained with a multipurpose electrocardiograph (Fukuda Denshi, VCM-3000). The instrument was equipped with a signal-averaging computer system.^{7),8)} After averaging, the records were filtered with a high-pass filter at 40 Hz to eliminate low frequencies. The signal-averaging bipolar X, Y and Z ECGs were recorded by a routine method.^{7)–9)} The end of the QRS complex and the onset of the late potential were identified visually on a low-gain QRS recording, and the end of the late potentials was defined as the point at which the signal amplitude exceeded the average baseline noise by a factor of two or three. The vector magnitude (the root-mean-square of the magnitude, RMS) of the voltage was calculated for each point of the average wave as: $\text{RMS} = \sqrt{X^2 + Y^2 + Z^2}$. The standard ECG (lead II) was recorded simultaneously at a paper speed

of 200 mm/sec.

The method of measurement is shown in Figs. 1 and 2. The indices of the signal-averaging ECG recorded were (1) the RMS voltage of the QRS complex in the last 40, 30 and 20 ms, (2) the late potentials identified as signals of under $25 \mu\text{V}$ during the last 40 ms of the QRS complex, (3) the total duration of the QRS complex, (4) the duration of the QRS while its amplitude remained under $40 \mu\text{V}$, and (5) the voltage in the first 40 ms of the QRS complex. The indices in the standard ECG recorded at the same time were (6) the voltage of the QRS complex in lead II, and (7) the duration of the QRS complex.

Results are presented as means $\pm$ standard deviations. Student's t-test was used to evaluate the significance of differences between values for the control and diabetic groups. Differences were considered significant at $p < 0.05$.

RESULTS

Figure 1 shows the signal-averaging ECG of a normal subject (48 years old, male). Note the rapid decline in the vector-magnitude record toward

Fig. 1. Recording of the signal-averaging ECG and standard ECG (lead II) from a normal subject (48 years old, male). Note the rapid decrease in the vector magnitude toward the end of the QRS complex. The RMS voltage values in the last 40, 30 and 20 ms of the QRS complex are 82, 79 and $72 \mu\text{V}$, respectively. No late potentials are seen during the last 40 ms of the QRS complex. In the standard ECG, the duration (86 ms) and the magnitude (1.5 mV) of the QRS complex are within normal limits. S=the start of the QRS complex; E=the end of the QRS complex.

the end of the QRS complex. The last 40, 30 and 20 ms of the QRS complex have RMS voltage values of 82, 79 and 72 μV , respectively. There are no late potentials and both the duration and the voltage are within normal limits.

Table I shows the RMS of the voltage of the QRS complex in the signal-averaging ECG. In the diabetics, the voltages in the last 40, 30 and 20 ms of the QRS complex were 32.4, 25.3 and 7.3 μV , respectively. These values were significantly lower ($p < 0.01$) than those in normal subjects (76.8, 69.3 and 66.4 μV , respectively). Late potentials were observed in seven diabetics (32%) and in only one normal subject (5%, $p < 0.01$).

Figure 2 shows a recording of the signal-averaging ECG of a patient with diabetes mellitus (57 years old, female). The duration of the QRS

Table I. Voltage of QRS Complex in the Signal-Averaging ECG in Control and Diabetic Groups

group	first 40 ms (μV)	last 40 ms (μV)	last 30 ms (μV)	last 20 ms (μV)
control (21)	80.2 ± 11.2	76.8 ± 12.9	69.3 ± 10.4	66.4 ± 9.5
diabetic (22)	76.5 ± 5.4	$32.4 \pm 8.2^{**}$	$25.3 \pm 4.7^{**}$	$7.3 \pm 2.4^{**}$

Results shown are means $\pm$ SD.

** Significant difference between groups by Student's t-test ($p < 0.01$).

Fig. 2. Recording of the signal-averaging ECG and standard ECG (lead II) from a patient with diabetes mellitus (57 years old, female). In the signal-averaging ECG, the duration of the QRS complex is prolonged to 125 ms and late potentials are seen. The standard ECG shows no abnormality. LS = late potentials. Other abbreviations are as for Fig. 1.

complex is prolonged to 125 ms. (The normal value is less than 110 ms, according to Simson et al.⁷⁾) Late potentials are clearly seen in the last 40 ms of the QRS complex. In the standard lead II ECG, however, the duration of the QRS complex is within normal limits (86 ms).

An example of a single-averaging ECG with a prolonged QRS duration from a patient with diabetes mellitus is shown in Fig. 3. The duration of the QRS complex is prolonged to 128 ms, but no late potentials are seen in the last 40 ms of the QRS complex. Twelve patients (54.5%) showed prolongation of the QRS complex in the signal-averaging ECG, and among these, 7 showed late potentials in the terminal portion of the QRS complex.

There was no significant difference between the control and the diabetic groups in the duration (87.2 ms vs. 91.2 ms) or voltage (1.3 mV vs. 1.2 mV) of the QRS complex in the standard ECG (lead II), as shown in Table II.

Fig. 3. Recording of the signal-averaging ECG and standard ECG (lead II) from a patient with diabetes mellitus (63 years old, male). In the signal-averaging ECG, the duration of the QRS complex is prolonged to 128 ms, but no late potentials are seen. Abbreviations are as for Fig. 1.

Table II. Duration and Voltage of QRS in the Standard Lead II ECG

group	duration (ms)	voltage (mV)
control (21)	87.2 ± 21.4	1.3 ± 0.4
diabetic (22)	91.2 ± 22.4	1.2 ± 0.3
	NS	NS

NS=not significant.

Fig. 4. QRS durations in the signal-averaging ECGs of the control and diabetic groups. The duration is significantly longer in the diabetic group (114.5 ms vs. 84.6 ms, $p < 0.01$).

Fig. 5. Periods in which the terminal portion of the QRS complex remained under $40 \mu V$ in the signal-averaging ECGs of the control and diabetic groups. The duration is significantly longer in the diabetic group (28.4 ms vs. 19.1 ms, $p < 0.01$).

Figure 4 shows mean values for the QRS duration in the signal-averaging ECG in the 2 groups. The duration was significantly longer in the diabetic group than in the control group (114.5 ms vs. 84.6 ms, $p < 0.01$).

Figure 5 indicates that the period in which the terminal portion of the filtered QRS complex in the signal-averaging ECG remained under $40 \mu V$ was significantly longer in the diabetic group than in the control group (28.4 ms vs. 19.1 ms, $p < 0.01$).

DISCUSSION

An increased incidence of death from cardiovascular disease in diabetics has been recognized for many years. As early as 1966, it was reported that cardiovascular diseases (including all types) were responsible for the deaths of 54% of all diabetics.¹⁰ Clinical evidence of heart disease is seldom apparent in diabetics during the first 20 years of life, and so these patients rarely receive special examination of the heart until its deterioration becomes marked.^{11,12} An important task for doctors is to detect subclinical abnormalities in patients with diabetes mellitus as early as possible. Therefore, in this study we attempted to detect silent impairment and conduction disturbances of the heart in diabetics by a noninvasive method.

The main findings in this study were as follows: (1) The incidence of late potentials was high (7/22, 32%) in the diabetic group, even though none of the patients had VT. (2) The intraventricular conduction time was

significantly longer in the diabetic group than in the control group. (3) The terminal voltage of the QRS complex tended to be decreased in the diabetic group. These results indicated that the patients with diabetes mellitus have intraventricular conduction disturbances.

Recently, late potentials have been thought to indicate delayed electrical activity in ischemic zones or regions of old myocardial infarction.⁷⁾⁻¹⁰⁾ Late potentials have been shown to be closely related to reentrant ventricular arrhythmias both in experimental animals and in humans.¹³⁾⁻¹⁶⁾ In normal subjects the incidence of late potentials in the signal-averaging ECG is reported to be zero (Zimmermann et al¹⁵⁾), 3/50 (6%, Coto et al¹⁶⁾) and 3/42 (7%, Denes et al¹⁴⁾). We observed a similar low incidence of 1/21 (5%) in this work. On the other hand, the incidence of late potentials in patients with ventricular tachycardia (VT) was reported to be as high as 32/92 (35%, Zimmermann et al¹⁵⁾), 5/11 (46%, Coto et al¹⁶⁾) and 30/41 (73%, Vassallo et al¹⁷⁾). Moreover, disappearance of late potentials after successful surgical therapy of VT has been reported.¹⁸⁾ Thus there seems to be an intrinsic connection between late potentials and VT, although late potentials do not always predict the occurrence of VT. In this study, the signal-averaging ECGs of 7 patients showed late potentials, but none of these patients had had cardiomegaly or cardiovascular symptoms, or episodes of VT before. Even so, it is our opinion that these patients should be followed up for many years to detect and manage arrhythmias, if they develop. Silent impairment of the heart in patients with diabetes mellitus is a serious problem, as has been emphasized by others.^{2),19)}

In patients with diabetes mellitus cardiac impairment is attributed to microangiopathy of the heart, including arteriosclerosis, dilation of venules, thickening of capillary walls and endothelial proliferation with the formation of mounds or microaneurysms,⁶⁾ which induce narrowing or complete blockage of the lumen of small arteries and impair the cardiac microcirculation.^{5),12)} In severe cases, small, multifocal areas of fibrosis of the myocardium are observed.¹⁹⁾ These lesions induce not only myocardial ischemia, but also abnormal depolarization and repolarization of the ventricular myocardium, which are thought to cause intraventricular conduction disturbances.

Selvester et al¹⁹⁾ investigated 64 patients with maturity-onset diabetes mellitus, who had no apparent heart disease. They proposed quantitative vectorcardiographic criteria for diagnosis of myocardial infarction and found that by their criteria 55 (86%) of the patients had small myocardial infarctions and 5 patients were suspected of having small infarctions. Atagi et al²⁰⁾ reported the results of body surface isopotential mapping in diabetic

patients, which showed that the maximum and minimum potentials of the QRS complex were significantly lower in diabetic patients than in normal subjects. They found that the patients with diabetes mellitus had myocardial injury. Riff and Riff²¹⁾ found that patients with subclinical diabetes mellitus had abnormalities of myocardial depolarization. These reports are consistent with our results by the signal-averaging ECG.

In the early stage of involvement of the heart, patients with diabetes mellitus are often asymptomatic and sometimes their cardiac abnormalities are not detectable by routine examinations. The present study indicates that patients with diabetes mellitus are likely to have intraventricular conduction disturbances. Consequently, special examinations are necessary to detect early or silent impairment of the heart in diabetic patients.

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