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Prevalence and Mortality of the Brugada-Type Electrocardiogram in One City in Japan

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OBJECTIVES We sought to study the prevalence and mortality of subjects exhibiting the Brugada-type electrocardiogram (ECG) in a community-based population in Japan.

BACKGROUND The Brugada syndrome has been associated with sudden death in subjects without structural heart disease. Hospital-based studies showed 11% to 38% annual fatal arrhythmic events in patients with the Brugada syndrome.

METHODS Prevalence and mortality of the Brugada-type ECG were studied in subjects who had ECGs during a health examination in Moriguchi, Osaka, Japan. Information about death and relocation from Moriguchi city was obtained prospectively.

RESULTS The Brugada-type ECG was found in 98 of 13,929 study subjects (0.70%, 95% confidence interval [CI]: 0.57% to 0.86%). The typical coved-type with an rsR′ pattern in V_1 lead ("typical" Brugada-type) was found in 0.12% of subjects (95% CI: 0.07% to 0.20%). The prevalence for male subjects with the Brugada-type ECG (81%) was significantly higher than it was for those without (26%, $p < 0.0001$). In male subjects, the Brugada-type ECG was found in 2.14% (95% CI: 1.70% to 2.66%), and the "typical" Brugada-type was found in 0.38% (95% CI: 0.21% to 0.64%). After 2.6 ± 0.3 years of follow-up, there was 1 death (1.0%, 95% CI: 0.03% to 5.6%) of a subject with the Brugada-type ECG, whereas there were 139 deaths (1.0%, 95% CI: 0.85% to 1.2%) of those without the Brugada-type ECG ($p = 0.9943$, log-rank test).

CONCLUSIONS A substantial number of the Brugada-type ECG were observed in subjects in a community-based population in Japan, especially in men. The total mortality of subjects with the Brugada-type ECG did not differ from the mortality of those without the Brugada-type ECG in a community-based population. (J Am Coll Cardiol 2001;38:771–4) © 2001 by the American College of Cardiology

In 1992, Brugada et al. (1) first reported a specific electrocardiogram (ECG) pattern of right bundle-branch block and ST-segment elevation in leads V_1, V_2 to V_3 associated with sudden death in patients without demonstrable structural heart disease. Several reports have been published about this syndrome in various populations (2–8). Previous observations demonstrated that patients with the Brugada-type ECG were at high risk for fatal arrhythmic events of 11% to 38% annually in a hospital-based population (3–5).

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However, there are few data available on the mortality of subjects with the Brugada-type ECG in a community-based population.

We studied the prevalence of the Brugada-type ECG in a community-based population in Japan and prospectively examined whether this sign was associated with an increased mortality.

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METHODS

Study subjects. Our study population consisted of subjects who had ECGs during a health examination for adult citizens in Moriguchi, Osaka, Japan, in 1997.

The city of Moriguchi is representative of a mid-sized urban city in Japan. At the time of our study, the population in the city of Moriguchi was about 156,300, 49% of the population were men, and approximately 77,100 of the total population were ≥40 years old. The city of Moriguchi offered annual health examinations for adult citizens who had not received a health examination from their company or organization. Most of the subjects in our study population were ≥40 years old. Although all subjects ≥40 years old who received the health examination in Moriguchi had an ECG recording, ECG recording was limited to subjects who were suspected to have a cardiac abnormality during their physical examination, if the subject was <40 years old. There were 85 of 13,929 total study subjects who were <40 years old. Of those, 1 subject had the Brugada-type ECG and no one died during follow-up period.

Definition and diagnosis of the Brugada-type ECG. All ECGs were recorded at standard gain (1 mV/10 mm) and paper speed (25 mm/s). An ECG was considered to be a Brugada-type ECG when the 12-lead ECG with right bundle-branch block (rsR′ or Rsr′ pattern in V_1 lead) and ST-segment elevation in the right precordial leads looked

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Abbreviations and Acronyms
CI = confidence interval
ECG = electrocardiogram

like the ECGs shown in the figures of the original publication by Brugada et al. (1). We also used ECG characteristics of our own to diagnose patients with definite Brugada syndrome. ST-segment elevation was defined as an elevation of the J point of ≥0.1 mV in leads V_1 to V_2 to V_3. According to the configuration, ST-segment elevations were designated as either coved or saddleback (Fig. 1).

To diagnose Brugada-type ECG, we (Y.M. and H.T.) examined ECGs without any information about the subject including age, gender, or medical history. Diagnosis of the Brugada-type ECG was made when both investigators considered an ECG to be the Brugada-type ECG.

To compare the prevalence of the Brugada-type ECG with recent reports of healthy populations, we defined the "typical" Brugada-type ECG, which only included an rsR′ pattern in the V_1 lead with the ST-segment elevation of a coved-type ECG.

Outcome event and follow-up. The outcome event was all-cause mortality. Information about death and relocation from Moriguchi city was obtained prospectively from the city residents' record.

Statistical analysis. Interobserver agreement was determined by overall proportion of agreement and the Kappa statistic. Confidence intervals (CI) of the binomial distribution for the prevalence rates were calculated. Fisher's exact test was used to test the difference in prevalence rate. The log-rank test was used for comparison of the difference in mortality between the subjects with and without the Brugada-type ECG. All calculations were performed by the Statistical Analysis System version 6.12. Values were expressed as the mean ± SD. A p value of <0.05 was considered statistically significant.

RESULTS

Our study population consisted of 13,929 subjects with a mean age of 58 ± 10 years, 26.5% of the population were men (n = 3,691). One investigator (Y.M.) found 104 ECGs to be the Brugada-type, and another investigator (H.T.) found 133 ECGs to be the Brugada-type. Of those, there were 98 ECGs (0.70%, 95% CI: 0.57% to 0.86%) that both investigators considered to be the Brugada-type ECG. The overall proportion of agreement was 99.7% with the Kappa score of 0.824.

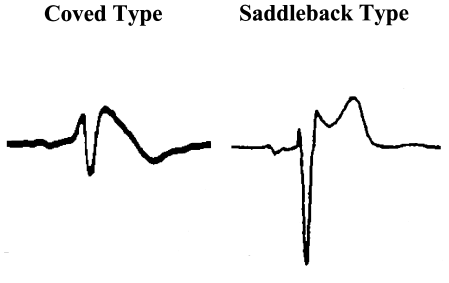

Figure 1. Examples of the ST-segment elevations of coved and saddleback type. **Left panel** shows the ST-segment elevation of coved type. **Right panel** shows the ST-segment elevation of saddleback type.

Table 1. The Brugada-type ECG and the "Typical" Brugada-Type ECG

	ST-Segment Elevation		
Lead V_1	Coved	Saddleback	Total
rsR′	17*	23	40 (41%)
Rsr′	20	38	58 (59%)
Total	37 (38%)	61 (62%)	98 (100%)

*"Typical" Brugada-type ECG.

Subjects with the Brugada-type ECG had a similar mean age (58 ± 9 years) to that of those without (58 ± 10 years). The prevalence of male subjects with the Brugada-type ECG (81%) was significantly higher than that of those without (26%, $p < 0.0001$). In the Brugada-type ECG, the coved-type ST-segment elevation was found in 38% of the subjects, and the rsR′ pattern in the V_1 lead was found in 41% of the subjects. The "typical" Brugada-type ECGs with the coved-type ST-segment elevation and rsR′ pattern in the V_1 lead were found in 17 subjects (0.12%, 95% CI: 0.07% to 0.20%) (Table 1). In male subjects, the Brugada-type ECG was found in 2.14% (95% CI: 1.7% to 2.66%), and the "typical" Brugada-type ECG was found in 0.38% (95% CI: 0.21% to 0.64%).

During 2.6 ± 0.3 years of follow-up, 2.7% of subjects without the Brugada-type ECG and 2.0% of subjects with the Brugada-type ECG relocated from Moriguchi city ($p = 1.000$). There was 1 death among the 98 subjects (1.0%, 95% CI: 0.03% to 5.6%) with the Brugada-type ECG, whereas there were 139 deaths of 13,831 subjects (1.0%, 95% CI: 0.85% to 1.2%) without the Brugada-type ECG (Fig. 2). The log-rank test showed no significant difference in all-cause mortality between subjects with and without the Brugada-type ECG ($p = 0.9943$). The subject who died with the Brugada-type ECG was a 56-year-old man. He had a saddleback ST-segment elevation and died suddenly. There was no information about his history of syncope or family history of sudden death.

DISCUSSION

Prevalence of the Brugada-type ECG. Tohyou et al. (6) reported a 0.07% prevalence of the Brugada-type ECG in 4,092 healthy Japanese adult subjects. In their criteria of the Brugada-type ECG, the saddleback-type ST-segment elevation and Rsr′ pattern in the V_1 lead were excluded. Hermida et al. (8) reported one subject with the Brugada-type ECG with the typical coved-type ST-segment elevation and rsR′ pattern in V_1 of 1,000 apparently healthy subjects (0.1%) (8). Viskin et al. (7) reported there were no patients with the "definite" Brugada-type ECG based on

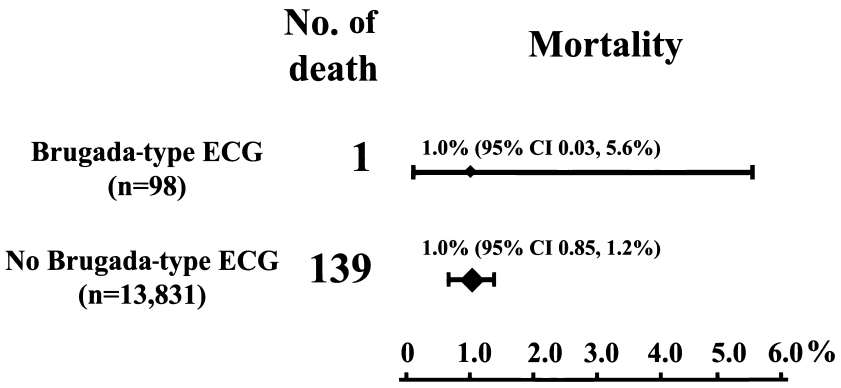

Figure 2. Comparison of all-cause mortality between subjects with and without the Brugada-type electrocardiogram (ECG) during 2.6 ± 0.3 years of follow-up period. CI = confidence interval.

their definition in 592 healthy control patients (0%) referred to their hospital. Monroe et al. (9) reported 52 subjects with the Brugada-type ECG including saddleback-type and the coved-type ST-segment elevation out of approximately 12,000 noncardiac patients. However, in their report, demographic data of their study subjects such as age or gender were not available (9). In this study, the "typical" Brugada-type with the coved-type ST-segment elevation and rsR′ pattern in the V_1 lead was found in 0.12% of the subjects. These results were fairly similar suggesting that the prevalence of the "typical" Brugada-type ECG in a healthy population would be 0.11% (Table 2). Since our study population predominantly consisted of women, sex specific prevalence of the "typical" Brugada-type ECG is also presented in Table 2. An estimated prevalence of the "typical" Brugada-type ECG was 0.23% in men. In this analysis, the prevalence of the "typical" Brugada-type ECG was observed about eight times more frequently in men than it was in women.

We originally included the saddleback-type ST-segment elevation or Rsr′ pattern in V_1 because the original publication of the Brugada syndrome (1) and other publications (7) considered the saddleback-type ST-segment elevation as the Brugada-type ECG, and it is well known that ST-segment elevation of the Brugada-type ECG changes into a saddleback from a coved-type (3). As a result, the Brugada-type ECG, as originally defined, was found in 0.70% with a 95% CI of 0.57% to 0.86% in a community-based population in Japan.

Mortality of the Brugada-type ECG. The previous observations demonstrated that patients with the Brugada-type ECG were at high risk for sudden death (11% to 38% per year), and sudden death was associated with syncope or family history of sudden death (3–5,10). However, these observations were studied in a hospital-based population. We studied a community-based population in Japan.

Brugada et al. (5) reported 22 individuals who were asymptomatic when their Brugada sign was recognized incidentally or after diagnosis of a symptomatic relative. Six of them eventually had arrhythmic events (27%, 95% CI: 11% to 50%) during a mean follow-up of 34 months (5). However, 9 of 22 asymptomatic individuals were detected because they had a family history of sudden death. Although one subject, a 56-year-old man with the saddleback-type ST-segment elevation, died suddenly in our study, total mortality of subjects with the Brugada-type ECG did not differ from those without. An estimated upper limit during a mean follow-up of 2.6 years was 5.6%. This result was consistent with the observations of a few previous reports about asymptomatic subjects with the Brugada-type ECG (3,10–12).

Conclusions. We conclude that a Brugada-type ECG may be found in a substantial number of people, especially men. The mortality of subjects with the Brugada-type ECG did not differ from that of subjects without the Brugada-type ECG in a community-based population. We suggest that mortality of the Brugada-type ECG in a community-based

Table 2. Comparison of the Prevalance of the "Typical" Brugada-Type ECG in Healthy Populations

Reference	Total Subjects	Mean Age (yr)	Men	Prevalence (95% CI)		
				Total	Men	Women
Present study	13,929	58 ± 10	27%	0.12% (0.07, 0.20)	0.38% (0.21, 0.64)	0.03% (0.01, 0.09)
Tohyou et al. (6)	4,092	46*	78%	0.07% (0.02, 0.21)	0.09% (0.02, 0.27)	0.00% (0.00, 0.41)
Viskin et al. (7)	592	36 ± 10	58%	0.00% (0.00, 0.62)	0.00% (0.00, 1.06)	0.00% (0.00, 1.50)
Hermida et al. (8)	1,000	39 ± 10	63%	0.10% (0.00, 0.56)	0.16% (0.00, 0.88)	0.00% (0.00, 1.00)
Overall	19,613			0.11% (0.07, 0.16)	0.23% (0.14, 0.36)	0.03% (0.01, 0.08)

*No data of standard deviation.
CI = confidence interval.

population is much lower than the mortality seen in a hospital-based population, as previously reported.

Study limitations. The contour of the ST segment has been reported to change. Although we included subjects with saddleback ST-segment elevation, it is still likely to underestimate the prevalence of the Brugada-type ECG. Our mean follow-up period of 2.6 years was not long enough. However, there have been no studies to evaluate mortality of Brugada-type ECG in a community-based sample in this number of subjects. Moreover, no study has compared the mortality between subjects with and without the Brugada-type ECG. In our study, only 27% of the population were men. However, our study subjects still included 3,691 men. Our study subjects were mainly older than 40 years. Mean ages of patients with reported Brugada syndrome were 40 to 50 years (3–5). The prognosis of the Brugada-type ECG in a patient less than 40 years old was not included in this study. Repetitive ECG recordings with younger subjects and long-term follow-up should be considered in future studies.

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