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# Incidence and Prognostic Value of Early Repolarization Pattern in the 12-Lead Electrocardiogram

Daisuke Haruta, MD, PhD; Kiyotaka Matsuo, MD, PhD; Akira Tsuneto, MD, PhD; Shinichiro Ichimaru, MS; Ayumi Hida, MD, PhD; Nobuko Sera, MD, PhD; Misa Imaizumi, MD, PhD; Eiji Nakashima, PhD; Koji Maemura, MD, PhD; Masazumi Akahoshi, MD, PhD

**Background**—Early repolarization pattern is a common ECG finding characterized by J-point elevation and QRS notching or slurring in the inferior and/or lateral leads, yet little is known about its incidence and long-term prognosis in Asian populations.

**Methods and Results**—We reviewed all the ECG records of the 5976 atomic-bomb survivors who were examined at least once during our biennial health examination in Nagasaki, Japan, between July 1958 and December 2004. We defined early repolarization pattern as  $\geq 0.1$ -mV elevation of the J point or ST segment, with notching or slurring in at least 2 inferior and/or lateral leads. We assessed unexpected, cardiac, and all-cause death risk by Cox analysis. We identified 1429 early repolarization pattern cases (779 incident cases) during follow-up, yielding a positive rate of 23.9% and an incidence rate of 715 per 100 000 person-years. Early repolarization pattern had an elevated risk of unexpected death (hazard ratio, 1.83; 95% confidence interval, 1.12 to 2.97;  $P=0.02$ ) and a decreased risk of cardiac (hazard ratio, 0.75; 95% confidence interval, 0.60 to 0.93;  $P<0.01$ ) and all-cause (hazard ratio, 0.85; 95% confidence interval, 0.78 to 0.93;  $P<0.01$ ) death. In addition, both slurring and notching were related to higher risk of unexpected death (hazard ratio, 2.09; 95% confidence interval, 1.06 to 4.12;  $P=0.03$ ), as was early repolarization pattern manifestation in both inferior and lateral leads (hazard ratio, 2.50; 95% confidence interval, 1.29 to 4.83;  $P<0.01$ ).

**Conclusions**—Early repolarization pattern is associated with an elevated risk of unexpected death and a decreased risk of cardiac and all-cause death. Specific early repolarization pattern morphologies and location are associated with an adverse prognosis. (*Circulation*. 2011;123:2931-2937.)

**Key Words:** death, sudden ■ epidemiology ■ electrocardiography ■ mortality

Sudden cardiac death is a major health issue, and accounts for 300 000 to 400 000 deaths per year in the United States.<sup>1,2</sup> Coronary artery disease, cardiomyopathy, left ventricular hypertrophy, valvular disease, congenital heart disease, and primary electrophysiological abnormalities are the major causes of sudden cardiac death.<sup>1,2</sup> Approximately 5% of sudden cardiac deaths caused by ventricular tachyarrhythmias occur in the absence of structural heart or coronary artery disease and are attributable to primary electrophysiological abnormalities. Some cases with ventricular tachyarrhythmia show a characteristic 12-lead ECG pattern such as a long-QT interval (long-QT syndrome) and a coved-type ST-segment elevation in the right precordial leads ( $V_1$ ,  $V_2$ , and  $V_3$ ; Brugada syndrome).<sup>3,4</sup>

## Clinical Perspective on p 2937

Early repolarization pattern (ERP) is characterized by an elevation of the QRS-ST junction (J point) and QRS notching or slurring (J wave) in multiple leads, especially in the inferior and/or left precordial leads, and is found in a relatively large

proportion (1% to 13%) in previous reports.<sup>5-8</sup> Although conventionally considered benign,<sup>5</sup> it is potentially arrhythmogenic,<sup>9</sup> and in 2 clinical case-control studies, patients with a history of idiopathic ventricular fibrillation (VF) showed an increased prevalence of ERP.<sup>7,8</sup> It has recently been reported that ERP in the inferior leads is associated with increased risk of cardiac death in Western populations.<sup>10</sup> Not much is known, however, about the incidence and long-term prognosis of ERP in Asian populations. Thus, we prospectively examined the incidence and prognostic value of ERP in terms of unexpected death, cardiac death, and all-cause death in Nagasaki Adult Health Study (AHS) subjects.

## Methods

### General Procedures

Since July 1, 1958, 7564 atomic-bomb survivors (3374 men) in Nagasaki, Japan, have been invited to participate in biennial health examinations as part of a follow-up program conducted by the Radiation Effects Research Foundation (RERF). Detailed descriptions of the program have been published elsewhere.<sup>11,12</sup> Each

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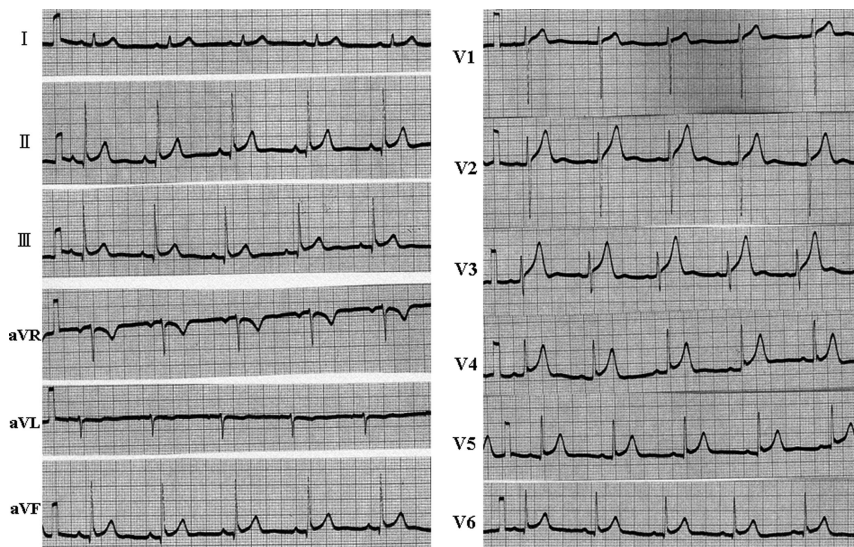
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**Figure 1.** Twelve-lead ECG of a typical pattern of the early repolarization pattern. A slurring morphology is seen in the inferior leads (II, III, aVF), and a notching morphology is seen in leads V<sub>4</sub> through V<sub>6</sub> with  $\geq 0.1$ -mV elevation from baseline. In our grouping method, this case is classified as both notching and slurring in morphology and as both inferior and lateral leads in lead location, respectively.

examination includes a standard 12-lead ECG obtained by the regular procedure. We extracted 5976 subjects (2612 men) who had been examined at least once between July 1, 1958, and December 31, 2004, and did not have intraventricular conduction disturbances and pacemaker implantation at the first examination and reviewed all the ECG records ( $12.2 \pm 7.5$  ECG records per subject) obtained during the follow-up period. The mean length of follow-up for ECG recordings was  $23.6 \pm 14.7$  years. The date of the first examination is different for each individual. During the first 2 years from July 1, 1958, to June 30, 1960, 2912 subjects underwent examination; the remaining 3064 subjects underwent their first examination after that period. We treated subjects who already had ERP at their first examination regardless of the date of examination as prevalent cases and subjects who first showed ERP after their second examination as incident cases. We used the current dosimetry System DS02 to estimate the bone marrow atomic-bomb radiation doses of individual subjects.<sup>13</sup> The Research Protocol Review and Human Investigation Committees of RERF approved the protocol (RP A 14–08).

### Definition and Confirmation of Early Repolarization Pattern and Brugada-Type Electrocardiogram

Using criteria similar to those of Haïssaguerre and colleagues,<sup>7</sup> we defined ERP cases as having (1) an elevation of the QRS-ST junction (J point) in notching formation (positive J deflection inscribed on the S wave) or of the ST segment in slurring formation (smooth transition from QRS complex to the ST segment) in at least 2 leads and (2) an amplitude of QRS-ST junction (J point) or ST-segment elevation  $\geq 0.1$  mV above the baseline as QRS notching or slurring in the inferior leads (II, III, aVF), lateral leads (I, aVL, V<sub>4</sub> through V<sub>6</sub>), or both<sup>7</sup> (Figure 1) at least once during follow-up. In slurring formation, because the transition from QRS complex to ST segment is smooth or the J point may be hidden in the QRS complex, we used  $\geq 0.1$  mV of the ST-segment elevation to indicate high-takeoff QRS-ST junction as the criterion. We classified the time course of the J-point abnormality into 1 of 2 categories: a persistent course showing permanent abnormalities or an intermittent course showing transient disappearance of the J wave itself or normalization of the magnitude of the J point during follow-up (Figure 2). During follow-up, we classified cases by positive-ERP lead location (inferior, lateral, or both) and by J-wave morphology (notching, slurring, or both). We defined the onset of ERP as the date of its first appearance during follow-up and used the age at the onset of ERP in calculating the incidence. One cardiologist (D.H.) reviewed the 12-lead ECGs of all subjects without knowledge of the clinical diagnosis or death certificate information. A second cardiologist (K. Matsuo) blindly reviewed all the ECG records of 200 subjects

(50 with ERP and 150 without ERP) who were randomly selected from the 5976 subjects. The concordance rate was 86.0% for ERP diagnosis. Next, he blindly reviewed all the ECG records obtained during follow-up for 194 subjects (94 subjects with only slurring in either inferior or lateral lead and 100 subjects with only notching in either inferior or lateral lead) among the 1429 subjects diagnosed as having ERP by the first cardiologist. The concordance rate was 83.8% for lead location and 81.3% for morphology.

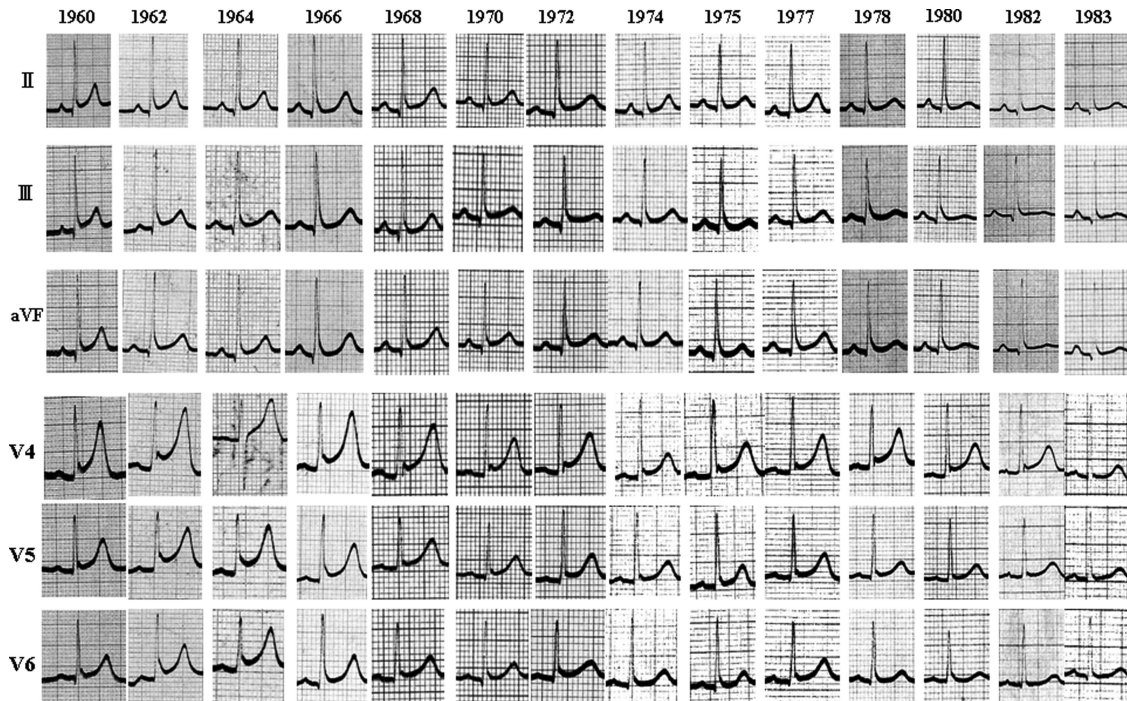
In the diagnostic criteria of Brugada syndrome by consensus reports,<sup>14,15</sup> type 1 characterized by  $\geq 0.2$ -mV coved-type ST segment elevation is essential, whereas types 2 and 3 characterized by saddleback-type ST elevation are not.<sup>14,15</sup> Therefore, in this study, we defined subjects with type 1 characterized by  $\geq 0.2$ -mV coved-type ST-segment elevation in  $\geq 1$  right precordial leads (V<sub>1</sub> through V<sub>3</sub>) at least once during follow-up as Brugada-type ECG cases.

### Definition and Confirmation of Sudden Death, Unexplained Accidental Death, and Cardiac Death

The RERF followed the vital status of all participants using Japan's family registration system. We collected all of the death certificates from July 1958 to December 2004 to check the cause and circumstance of death for deceased subjects and defined 3 types of death as we did in our Brugada-type ECG study: sudden death, an out-of-hospital death occurring within 1 hour of the onset of acute symptoms; unexplained accidental death, an accidental death in which VF might have been the cause of the accident; and unexpected death, a sudden death or an unexplained accidental death.<sup>16</sup> We treated death resulting from congestive heart failure and ischemic heart disease as cardiac death.

### Statistical Analysis

We calculated the 46.5-year (July 1, 1958, to December 31, 2004) incidence on the basis of the age of incident cases at ERP appearance by a person-year method, stratified according to age. We used Cox regression analysis to assess the long-term prognosis of ERP and Brugada-type ECG cases after controlling for age and sex. We compared ERP and Brugada-type ECG cases with control subjects who had neither ERP nor Brugada-type ECG with respect to unexpected death, cardiac death, and death resulting from all causes. We also assessed unexpected death risk according to lead location and J-wave morphology in ERP cases. Survival time is the time from the date of the first examination for controls and prevalent ERP and Brugada-type ECG cases and the date of the first appearance for incident ERP and Brugada-type ECG cases to the date of death or December 31, 2004, whichever came first. All analyses were conducted with SAS for UNIX (SAS Institute, Cary, NC).<sup>17</sup> We expressed the data as mean  $\pm$  SD and considered  $P < 0.05$  to be statistically significant.



**Figure 2.** Time course of the ECG (inferior and left precordial leads) in a case of unexpected death in a man. We observed early repolarization pattern with slurring in inferior leads (II, III, aVF) and notching in left precordial leads V<sub>4</sub> through V<sub>6</sub> with ≥0.1-mV elevation from baseline at the first visit in 1960. At the follow-up, the J-wave morphology was consistent in the inferior leads, but the magnitude of ST elevation fluctuated, whereas in the left precordial leads, both the morphology (slurring and notching) and J-point magnitude fluctuated during follow-up. In 1984, the patient died of sudden death at home at 71 years of age.

**Results**

**Incidence of Early Repolarization Pattern**

We identified 1429 ERP cases (815 men) among 5976 AHS subjects during the whole study period (July 1, 1958, to December 31, 2004); 650 cases (413 men) were classified as prevalent cases and 779 cases (402 men) were classified as incident cases (mean±SD age at first appearance of ERP, 47.2±15.4 years), yielding a follow-up positive rate of 23.9% (1429 of 5976) and an incidence of 715 per 100 000 person-years (Table 1). Incidence was highest in the second decade of life for men and women and was almost identical between

the sexes, whereas the male preponderance became obvious thereafter, leading to twice as high an overall incidence for men (Table 1). Radiation dose was not associated with ERP in both prevalent and incident cases (*P*=0.89, data not shown).

We identified 30 Brugada-type ECG cases (see Table 2). Brugada-type ECGs showed a J-point elevation in the anterior precordial leads. Among them, 6 cases had both ERP and Brugada-type ECG (Figure 3).

**Lead Location and Morphology of the J Wave**

Table 3 shows the morphology and lead location of the J wave observed during the follow-up period. Almost all of the

**Table 1. Number of Subjects at the First Examination for Each Individual and Incidence From July 1958 to December 2004**

Age, y	Subjects, n		Person-Years*		Incident ERP Cases, n		Incidence, n/100 000 Person-y	
	Men	Women	Men	Women	Men	Women	Men	Women
≤19	160	155	287	358	9	12	3136	3352
20–29	432	551	1798	2532	38	41	2113	1619
30–39	609	1250	5434	10 024	96	103	1767	1028
40–49	492	598	7009	14 811	71	77	1013	520
50–59	533	478	9199	16 573	75	59	815	356
60–69	296	236	8718	14 724	79	59	906	401
70–79	80	78	4810	8858	29	24	603	271
≥80	10	18	1292	2587	5	2	387	77
Total	2612	3364	38 547	70 467	402	377	1043	535
	5976		109 014		779		715	

ERP indicates early repolarization pattern.

\*Aggregate numbers of years contributed to each age category from 1958 to 2004 by all subjects remaining at risk for ERP.

**Table 2. Cause of Mortality in Subjects With Early Repolarization Pattern, Brugada-Type ECG, and Neither Early Repolarization Pattern nor Brugada-Type ECG**

	Subjects, n	Cause of Death		
		All	Unexpected	Cardiac
ERP (with Brugada-type ECG)	1429 (6)	628 (4)	27 (0)	100 (0)
Brugada-type ECG without ERP	24	14	4	1
Neither ERP nor Brugada-type ECG	4523	2262	45	434
Total	5976	2904	76	535

ERP indicates early repolarization pattern.

ERP cases (98.3%) showed intermittent manifestations, and both characteristics changed over time (Figure 2).

### Mortality From Unexpected Death, Cardiac Death, and All-Cause Death

Table 2 shows the breakdown of the 5976 subjects into ECG category and their cause of death. The 27 ERP cases with or without Brugada-type ECG (19 men; age at death,  $68.6 \pm 19.1$  years; age range, 20.7 to 96.1 years), 4 Brugada-type ECG cases without ERP (3 men; age at death,  $59.5 \pm 12.4$  years; age range, 42.3 to 71.7 years), and 45 controls (23 men; age at death,  $65.6 \pm 16.3$  years; age range, 24.2 to 95.8 years) had unexpected death. Age at unexpected death was not different among the 3 groups. The time interval between the first ECG appearance of ERP and unexpected death based on 16 incident ERP cases was  $21.7 \pm 13.8$  years (range, 2.5 to 42.3 years). In Cox proportional hazards analysis, ERP predicted unexpected death (hazard ratio [HR], 1.83; 95% confidence interval [CI], 1.12 to 2.97;  $P=0.02$ ) and had a favorable effect on cardiac (HR, 0.75; 95% CI, 0.60 to 0.93;  $P<0.01$ ) and all-cause (HR, 0.85; 95% CI, 0.78 to 0.93;  $P<0.01$ ) death (Table 4).

With respect to lead location and J-wave morphology, ERP cases with a broad range of J-wave-positive leads (both inferior and lateral) had a significantly higher HR for unexpected death (HR, 2.50; 95% CI, 1.29 to 4.83;  $P<0.01$ ) and

**Table 3. Lead Location and Morphology of the J Wave During Follow-Up Among Subjects With Early Repolarization Pattern**

Lead location	Morphology, n patients			
	Notching	Slurring	Notching and Slurring	Total
Inferior	337	44	41	422
Lateral	335	54	172	561
Inferior and lateral	141	50	255	446
Total	813	148	468	1429

both slurring and notching predicted unexpected death (HR, 2.09; 95% CI, 1.06 to 4.12;  $P=0.03$ ) when we used controls as the reference group (Table 4). We saw no unexpected deaths for patients with ERP with Brugada-type ECG and so could not calculate that HR for unexpected death.

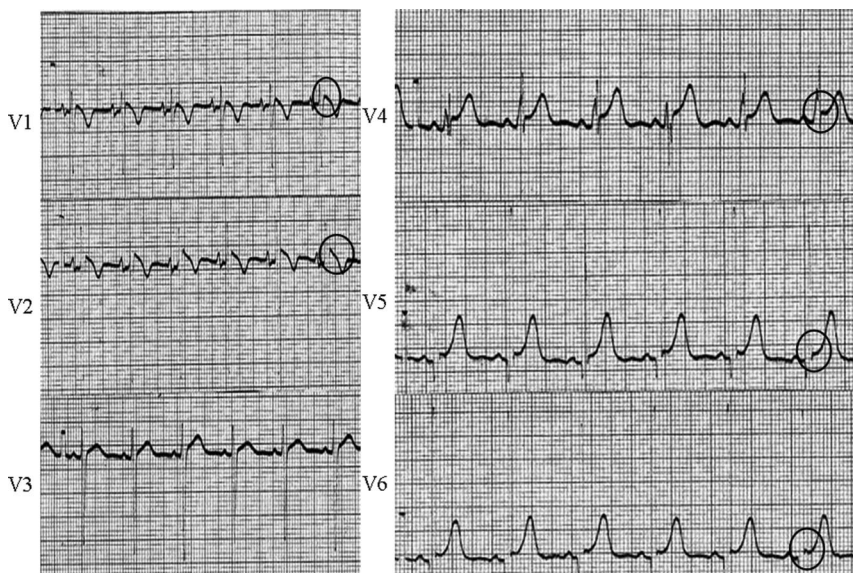
Brugada-type ECG cases had the highest HR for unexpected death (HR, 27.15; 95% CI, 9.35 to 78.85;  $P<0.01$ ), whereas in contrast to ERP cases, it had no favorable effects on cardiac and all-cause death (Table 4). Radiation dose was not associated with unexpected death ( $P=0.45$ ; data not shown).

### Discussion

As far as we know, this 5-decade study is the first Asian population-based study of the incidence and prognosis of ERP. We learned that ERP was a common ECG finding, with a follow-up positive rate of 23.9% and an incidence of 715 in 100 000 person-years, and was associated with a higher risk of unexpected death and a lower risk of cardiac and all-cause death. Although the subjects were atomic-bomb survivors, radiation dose was not associated with ERP or unexpected death, so the results should be generalizable.

### Incidence of Early Repolarization Pattern

The prevalence of ERP has been reported to be 1% to 13%.<sup>5-8</sup> However, because ERP (defined by the modified criteria of Haïssaguerre and colleagues<sup>7</sup>) appeared intermittently, we based



**Figure 3.** A case with both early repolarization pattern and Brugada-type ECG in chest leads  $V_1$  through  $V_6$ . Covered-type ST elevation with 0.2 mV at the J point was seen in  $V_1$  and  $V_2$ , and early repolarization pattern with notching morphology 0.1 mV at the J point was seen in  $V_4$  through  $V_6$ . Covered-type ST elevation of Brugada-type ECG ( $V_1$  and  $V_2$ ) and notching morphology of early repolarization pattern ( $V_4$  through  $V_6$ ) at the last recorded beat are highlighted by circles.

**Table 4. Age- and Sex-Adjusted Hazard Ratio for Each Group (Cox Analysis)**

	Subjects, n	Unexpected Deaths, n	HR (95% CI)		
			Unexpected Death	Cardiac Death	All-Cause Death
Control*	4523	45	1.00	1.00	1.00
ERP	1429	27	1.83 (1.12–2.97)	0.75 (0.60–0.93)	0.85 (0.78–0.93)
<i>P</i>			0.02	<0.01	<0.01
Lead location					
Inferior	422	8	1.91 (0.88–4.14)		
<i>P</i>			0.10		
Lateral	561	7	1.37 (0.61–3.04)		
<i>P</i>			0.45		
Both	446	12	2.50 (1.29–4.83)		
<i>P</i>			<0.01		
Morphology					
Notching	813	11	1.36 (0.70–2.65)		
<i>P</i>			0.37		
Slurring	148	5	1.60 (0.61–4.24)		
<i>P</i>			0.34		
Both	468	11	2.09 (1.06–4.12)		
<i>P</i>			0.03		
Brugada-type ECG	24	4	27.15 (9.35–78.85)	0.47 (0.07–3.35)	1.09 (0.65–1.85)
<i>P</i>			<0.01		
Total	5976	76		0.45	0.74

HR indicates hazard ratio; CI, confidence interval; and ERP, early repolarization pattern.

\*Subjects with neither ERP nor Brugada-type ECG.

our calculation on both prevalent and incident cases and found that 23.9% manifested ERP at least once during follow-up, indicating that ERP was not a rare ECG finding. In past studies, only the prevalence, not incidence, of ERP has been reported because longitudinal studies covering the period before the diagnosis of ERP were lacking. We report the incidence of ERP for the first time here and reveal that the incidence of ERP was highest in the second decade of life in men and women and decreased thereafter (Table 1). It is possible that the difference in the age distribution of the subjects in the target cohort and the intermittent appearance of ERP may have affected the reported prevalence of ERP. It is also possible that if we used criteria other than the modified criteria of Haïssaguerre and colleagues, we would have found different incidence values.

The incidence of ERP that we observed (Table 1) was  $\approx$ 50 times as high as the incidence reported for Brugada-type ECG (14.3/100 000 person-years),<sup>16</sup> whereas the male/female incidence ratio for ERP (1.95) was about one-fifth that of Brugada-type ECG (8.97),<sup>16</sup> but the incidence of both ERP and Brugada-type ECG is high at a relatively young age. Because our cohort of atomic-bomb survivors did not include subjects who were <12 years of age on July 1, 1958, and the appearance of ERP was intermittent, it is necessary to follow up a large number of the population who are <10 years of age to arrive at a more precise value.

### Prognostic Value of Early Repolarization Pattern

Sinner et al<sup>18</sup> recently reported in a prospective cohort study that ERP was associated with a  $\approx$ 2- to 4-fold increased risk of cardiac mortality, which was determined through the use of death certificates. They did not mention the association

between ERP and unexpected death because cardiac death was assumed in the ninth version of the *International Classification of Diseases* codes 390 to 429 and 798.<sup>18</sup> On the other hand, Haïssaguerre et al<sup>7</sup> reported that ERP in the inferior or lateral leads was more frequent among patients with idiopathic VF than among control subjects. Rosso et al<sup>8</sup> reported a similar association between ERP and idiopathic VF. Those studies were cross-sectional; here, in a prospective cohort study, ERP predicted unexpected death. How ERP did that, however, is unclear. It has been reported that 11% of Brugada syndrome patients show ERP in the inferior-lateral leads and that drug challenge tests provoke a coved pattern in the inferior-lateral leads in 4.6% of Brugada syndrome patients.<sup>19</sup> Those observations suggest that ERP and Brugada syndrome overlap in phenotype and electrophysiological similarities. The presence of a prominent  $I_{to}$ -mediated action potential notch (spike and dome) in the epicardium, but not the endocardium, generates a transmural voltage gradient during the early phase of repolarization, which manifests J-wave and J-point elevation in the surface ECG in both ERP and Brugada syndrome.<sup>20</sup> Heterogeneous loss of the action potential dome produces phase 2 reentry, leading to polymorphic ventricular tachycardia/VF.<sup>20</sup> It is possible that ERP has a vulnerability to arrhythmias that is due to transmural heterogeneity of ventricular repolarization and that ERP is affected by such factors as testosterone and drugs through ion channel activity.

A J-wave manifestation in both inferior and lateral leads was associated with a higher risk of unexpected death. A J-wave manifestation in many leads suggested that electric instability caused by heterogeneity of repolarization was occurring in broad regions of the ventricles. Merchant et al<sup>21</sup>

reported that notching in lateral leads is significantly more prevalent among ERP patients with idiopathic VF, but they did not assess morphological changes over time. In our study, we defined slurring, notching, and slurring and notching, taking morphological changes into account during follow-up, and found that manifestation in both slurring and notching has an important implication for risk stratification.

In this study, ERP cases had a lower risk of cardiac and all-cause mortality. On the other hand, it has also been reported that ERP in the inferior leads is associated with an increased risk of cardiac death, (HR, 1.28; 95% CI, 1.04 to 1.59;  $P=0.03$ ),<sup>10</sup> and ERP in any localization was associated with an increased risk of all-cause death (HR, 1.87; 95% CI, 1.03 to 3.37;  $P=0.038$ ).<sup>18</sup> Thus, the association between ERP and mortality other than unexpected death is still controversial. We proposed a hypothesis that testosterone may modulate cardiac and total mortality in ERP cases. Various reports indicate that testosterone may be associated with ERP and Brugada syndrome. Early repolarization pattern showed male preponderance<sup>7,8,10</sup>; the typical coved-type Brugada ECG disappears after surgical castration for prostate cancer<sup>22</sup>; and male Brugada syndrome cases have significantly higher plasma testosterone levels than age-matched male controls.<sup>23</sup> It has been suggested that testosterone may increase the outward repolarizing potassium currents such as  $I_{K1}$ ,  $I_{Kr}$ ,  $I_{Ks}$  and  $I_{to}$ , inhibiting inward L-type  $Ca^{2+}$  current.<sup>24–26</sup> Such effects help to induce an outward shift of current in the epicardium, aggravate transmural voltage gradient between epicardium and endocardium, and lead to the J-point and ST-segment elevation seen in ERP and Brugada syndrome. These reports suggest that testosterone is associated with ERP and Brugada syndrome through ion channel activity. On the other hand, several studies reported that low serum testosterone level was associated with an increased risk of cardiovascular and all-cause mortality and cardiovascular risk factors in men (abnormal lipid profiles, impaired glucose metabolism, and high blood pressure).<sup>27–29</sup> Thus, elevated serum testosterone level may influence the prognosis of patients with ERP by increasing the risk of sudden death through a more prominent transmural voltage gradient, which leads to phase 2 reentry and ventricular tachycardia/VF, while decreasing the risk of cardiac and all-cause death, probably through protective effects. However, this hypothesis should be supported by more direct evidence of the association between testosterone and ERP.

In the present study, the HR for unexpected death was lower for ERP (1.83) than for Brugada-type ECG (27.15), and may not directly lead to the recommendation of implantable cardioverter-defibrillator treatment. However, because the number of ERP cases (1429) was much larger than the number of Brugada-type ECG cases (24), the unexpected death rate was greater for ERP cases (27 of 76, 35.5%) than for Brugada-type ECG cases (4 of 76, 5.3%), suggesting a greater public health implication for ERP and a careful evaluation of the past history of syncope and the family history of sudden death or syncope. Further epidemiological and electrophysiological studies are needed to clarify what characteristics among the large number of ERP cases are predictive of high risk.

### Study Limitations

In this study, only 1 cardiologist reviewed all the ECG records obtained during follow-up in 5976 subjects. However, the

accuracy of the diagnosis was ensured because all the ECG records ( $12.2 \pm 7.5$  ECG records per subjects) during follow-up were reviewed for each subject. A second cardiologist blindly reviewed all the ECG records obtained during follow-up in 200 subjects (50 with ERP and 150 without ERP) and 194 ERP cases, and the concordance rate was 86.0% for ERP diagnosis, 83.8% for lead location, and 81.3% for morphology.

We could not deny the effect of structural heart diseases on ERP because we did not perform echocardiography and cardiac catheterization in this epidemiological study.

We did not assess the risk of unexpected death by the nature of the manifestation of ERP (intermittent/persistent), because almost all of the ERP cases (98.3%) showed the intermittent course. Because the magnitude of the J point fluctuated over time in ERP cases, the most elevated values of J point were biased, depending on how many times the ECG was recorded. Thus, we did not assess the effects of the magnitude of J point on unexpected death. For the same reason, other ECG characteristics such as QRS duration and QTc interval were not used as covariates in Cox regression analysis.

With respect to Brugada-type ECG, we did not include 10 patients with types 2 and 3 in the Brugada-type ECG group. We cannot deny the possibility that they might have changed into type 1 if they had drug challenge tests, which could not be performed in our cohort study. We observed 3 unexpected deaths among 10 patients with types 2 and 3.

Age at unexpected death was relatively high in both ERP cases and controls. Uncertainty of the cause of sudden or unexplained accidental death without autopsy information, especially for coronary heart disease, may limit the present results, but this possible bias would be equal for ERP cases and controls.

Because the number of unexpected deaths in ERP cases by lead location and morphology subgroup and in Brugada-type ECG cases was small, such data might limit efforts to draw a definitive conclusion about effects of ERP by lead location and morphology subgroup and Brugada-type ECG on unexpected death.

### Conclusions

In this 5-decade population-based study, we described the epidemiology and long-term prognosis of ERP. Early repolarization pattern was a common ECG finding; ERP appeared intermittently, and its location and J-wave morphology changed over time. Early repolarization pattern was associated with an elevated risk of unexpected death and a decreased risk of cardiac and all-cause death. The manifestation of both slurring and notching and the manifestation of the J wave in both inferior and lateral leads were associated with the higher risk of unexpected death. Further clinical and experimental studies are needed to define the characteristics of high-risk ERP cases so that they can be singled out for preventive measures.

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## Disclosures

None.

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## CLINICAL PERSPECTIVE

Recent studies have suggested a potential arrhythmogenicity and a higher risk of cardiac or all-cause death of early repolarization pattern (ERP) in Western populations. But, the incidence and prognosis of ERP in an Asian population have not yet been elucidated. We investigated 5976 atomic-bomb survivors followed up for  $\approx 5$  decades. Early repolarization pattern was a very common finding throughout the survivors' entire lives, yielding a lifetime positive rate of 23.9%, an incidence rate of 715 per 100 000, and male predominance. In this study, ERP patients had an increased risk of unexpected death and a decreased risk of cardiac and all-cause death. The ERP manifestation of both slurring and notching and the manifestation of the J wave in broad leads were associated with unexpected death. The hazard ratio for unexpected death in ERP was lower than that in Brugada-type ECG. However, because ERP is a very common finding, ERP has a greater public health implication.