High Frequency of Early Repolarization and Brugada-Type Electrocardiograms in Hypercalcemia

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Background: J wave, or early repolarization has recently been associated with an increased risk of lethal arrhythmia and sudden death, both in idiopathic ventricular fibrillation and in the general population. Hypercalcemia is one of the causes of J point and ST segment elevation, but the relationship has not been well studied. The aim of this study was to examine the effects of hypercalcemia on J point elevation.

Methods: Electrocardiographic findings were compared in 89 patients with hypercalcemia and 267 age- and sex-matched healthy controls with normocalcemia. The association of J point elevation with arrhythmia events in patients with hypercalcemia was also studied.

Results: The PR interval and the QRS duration were longer in patients with hypercalcemia than in normocalcemic controls. Both the QT and the corrected QT intervals were shorter in patients with hypercalcemia compared with normocalcemic controls. Conduction disorders, ST-T abnormalities, and J point elevation were more common in patients with hypercalcemia than normocalcemic controls. Following the resolution of hypercalcemia, the frequency of J point elevation decreased to a level similar to that noted in controls. During hospitalization, no arrhythmia event occurred in patients with hypercalcemia.

Conclusion: Hypercalcemia was associated with J point elevation.

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hypercalcemia; early repolarization; Brugada syndrome; J wave; J point elevation

J wave, or early repolarization, is characterized by an elevation at the junction between the end of the QRS complex and the beginning of the ST segment (J point) in a 12-lead electrocardiogram (ECG). The presence of J wave has been considered a benign phenomenon for decades.¹ However, there is increasing evidence that early repolarization is associated with an increased risk of ventricular fibrillation and sudden cardiac death.^{2–4}

J wave has been linked to various biological conditions, such as low body temperature and ischemia.^{5,6} Furthermore, hypercalcemia, which may alter cardiac electrophysiology, is another cause of J wave.^{7–9} However, the relationship among hypercalcemia and J point and ST segment elevation has been described primarily in case reports, with the exception of one case series^{7,10–18} but has not been studied in detail.

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Furthermore, the association of hypercalcemia with fatal arrhythmias has been described in only a few case reports and is not well understood.^{13,16} Therefore, this study aimed to investigate the role of hypercalcemia in both J point elevation and arrhythmia.

METHODS

Study Population

We conducted a retrospective chart review of the electronic records of patients in our hospitals between 2005 and 2013 to identify patients with hypercalcemia, which was defined as a serum Ca^{2+} level, corrected for serum albumin, >12 mg/dL. Patients with sinus rhythm as determined in ECGs recorded at the time of their hypercalcemia who did not have structural heart disease were eligible for the analysis. Patients with other causes of J point elevation, including hypercalcemia ($\text{K} > 5.5$ mEq/L), acidosis ($\text{pH} < 7.35$), and hypothermia, were excluded.

Control subjects with sinus rhythm and normocalcemia, defined as a corrected serum Ca^{2+} level from 8.0 to 10.0 mg/dL, were selected from 86,068 consecutive ECGs stored within the ECG database of Niigata University Medical and Dental Hospital. The subjects were matched to patients with hypercalcemia based on both age and sex (patient: control ratio, 1:3). Subjects with either renal dysfunction or structural heart disease were excluded.

Electrocardiographic Measurements

ECG findings were compared between patients with hypercalcemia and normocalcemic controls. The corrected QT (QTc) interval was calculated using Bazett's formula.¹⁹ "J point elevation" was defined as an elevation of the J point, either as a QRS slurring or a notching ≥ 0.1 mV in ≥ 2 consecutive leads of a 12-lead electrocardiogram.²

Statistical Analysis

The data are presented as the medians (25th and 75th percentiles), or numbers (%). The continuous variables were compared using either the unpaired Student's *t*-test or the nonparametric Mann-Whitney's U-test between groups, or via either the paired *t*-test or the nonparametric Wilcoxon

Table 1. Clinical Characteristics of Hypercalcemic Patients

Characteristic	Patients, n = 89
Male sex, no. (%)	34 (38)
Age (years) ^a	64 (54-72)
Etiologies of hypercalcemia	
Hyperparathyroid (primary and secondary)	36 (40)
Cancer	34 (38)
Overdose of vitamin D	10 (11)
Sarcoidosis	4 (4)
Others	5 (6)
Hypertension, no. (%)	25 (28)
Diabetes mellitus, no. (%)	15 (17)
Heart diseases, no. (%)	5 (6)
Medication, no. (%)	26 (29)
β -Blocker, no. (%)	4 (4)
Antiarrhythmic drugs, ^b no. (%)	2 (2)
Ca^{2+} channel blocker, no. (%)	20 (22)

^aMedian (interquartile range); ^bOne patient had pilsicainide and another had amiodarone.

rank-sum test between different serum Ca^{2+} levels, as appropriate. The categorical variables were compared using the chi-square test in between groups, or McNemar test between different serum Ca^{2+} levels. The effects of covariates on J point elevation among hypercalcemic patients were analyzed using multivariate logistic regression models. A two-sided P value of less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 21.0 (IBM Inc., Armonk, NY, USA). The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agreed with the manuscript as written.

RESULTS

Among the 532 patients with hypercalcemia who were treated at our institutions, we identified 89 patients with 12-lead ECGs (34 male [38%]; median age, 64 years) with findings consistent with hypercalcemia (Table 1). Common causes of hypercalcemia included malignancy ($n = 35$ [39%]), primary hyperparathyroidism ($n = 25$ [28%]), and renal dysfunction ($n = 18$ [20%]). Among the ECG findings, both the PR interval and the QRS duration were longer in patients with hypercalcemia compared with age- and sex-matched normocalcemic controls (Table 2). Both the QT and the corrected QT intervals

Table 2. Comparison of Electrocardiographic Characteristics in Hypercalcemia Patients and Normocalcemia Controls

	Hypercalcemia, n = 89	Normocalcemia Control, n = 267	P Value
Heart rate (bpm) ^a	76 (66–89)	68 (61–76)	<0.001
PQ interval (ms) ^a	160 (145–185)	148 (137–164)	<0.001
QRS duration (ms) ^a	99 (92–108)	92 (86–99)	<0.001
QT interval (ms) ^a	354 (332–372)	378 (361–397)	<0.001
Corrected QT interval (ms) ^a	396 (378–417)	407 (391–419)	0.01
Conduction disorder, no. (%)	22 (25)	10 (4)	<0.001
Prolonged PR interval, no. (%)	12 (13)	8 (3)	<0.001
Right bundle branch block, no. (%)	4 (4)	2 (0.7)	0.04
Left anterior hemiblock, no. (%)	10 (11)	4 (1)	<0.001
Left bundle branch block, no. (%)	1 (1)	0 (0)	0.25
ST segment/T wave abnormality, no. (%)	29 (33)	12 (4)	<0.001
J point elevation, no. (%)	27 (30)	23 (9)	<0.001
Location of J point elevation			
Inferior leads, no. (%)	9 (10)	10 (4)	0.03
Lateral leads, no. (%)	4 (4)	9 (3)	0.74
Right precordial leads, no. (%)	7 (8)	1 (0.4)	<0.001
Multiple locations, no. (%)	7 (8)	3 (1)	0.003

^aMedian (interquartile range). CI, confidence interval.

were shorter in patients with hypercalcemia than in normocalcemic controls. Conduction disorder and ST-T abnormalities were each more common in patients with hypercalcemia compared with normocalcemic controls. J point elevation was more common in patients with hypercalcemia (n = 27 [30%]) than in normocalcemic controls (n = 23, [9%]).

After exclusion of the patients who had abnormal serum electrolyte levels or antiarrhythmic drugs, both of which may affect ECG findings analysis was repeated in 50 patients with hypercalcemia and 150 controls (Table S1). We replicated similar results that hypercalcemia was associated with conduction disorder, ST segment/T wave abnormality, and J wave.

Although the causes of hypercalcemia were various, majority of patients had hyperparathyroidism or cancer. Therefore, we compared ECG findings between patients with hyperparathyroidism and those with cancer (Table S2). The frequency of conduction disorder, ST segment/T wave abnormality, and J wave were similar between two groups.

The clinical and ECG characteristics of the 27 patients with hypercalcemia who had early repolarization, and the representative ECGs characterized by J point elevation, are included in Table 3 and Figure 1, respectively. J point elevation was noted in the inferior leads in 9 patients (10%), in the lateral leads in 4 patients (4%), and the right precordial leads in 7 patients (8%). J point elevation

was noted at multiple locations in 7 patients (8%). There were three morphologies of J point elevation, including a "scooped appearance" J point and ST segment elevation without a distinct T wave (n = 5),¹⁸ Brugada-type ECG findings (n = 5),²⁰ and an early repolarization pattern without ST segment elevation (n = 17).

Among the 89 patients with ECGs recorded in the setting of hypercalcemia, there were no differences in the ages, sex, serum electrolyte levels, and causes of hypercalcemia between patients with J point elevation and those without J point elevation (Table 4). Both the QT interval and the corrected QT interval were shorter in patients with J point elevation compared with those without J point elevation, whereas the heart rate, PQ interval, and QRS duration were similar between the two groups. The frequency of conduction disorder including prolonged PR interval, right bundle branch block, left anterior hemiblock, and left bundle branch block was similar between two groups. ST segment/T wave abnormality was more common in patients with J point elevation compared with those without J point elevation.

In univariate models, among ECG findings, shortening of QT interval (odds ratio, 0.986; 95% confidence interval, 0.972–1.000; P = 0.046) and ST segment/T wave abnormality (odds ratio, 4.286; 95% confidence interval, 1.633–11.246; P = 0.003) were associated with the presence of early repolarization in patients with hypercalcemia.

Table 3. Clinical and Electrocardiographic Characteristics of Hypercalcemia Patients with J Point Elevation

No.	Sex	Age (year) ^a	Etiology of Hypercalcemia	Ca ²⁺ Levels (mg/dL) ^a	Heart Rate (bpm) ^a	PR Interval (ms) ^a	QRS Duration (ms) ^a	QT Interval (ms) ^a	QTc Interval (ms) ^a	Conduction Disorder	ST Segment/T Wave Abnormality	Location of J Point Elevation
1	M	47	Primary hyperparathyroidism	12.1	70	160	112	350	379	-	ST elevation in I II V ₆	I II V ₆
2	F	35	Over dose of Vitamin D	14.2	71	153	81	354	385	-	-	V ₃₋₆ , I II
3	F	48	Primary hyperparathyroidism	13.0	67	143	87	350	370	-	-	IaVL V ₅₋₆
4	F	78	Hepatocellular cancer	13.9	48	227	94	402	363	Prolonged PR	-	I II aVL V ₅₋₆
5	M	50	Squamous cell cancer	15.0	117	157	93	273	382	-	-	II aVF V ₆
6	M	64	Esophageal cancer	13.2	80	155	106	391	450	-	ST elevation in II III aVF	II III aVF
7	M	67	Laryngeal cancer	12.2	60	212	88	392	302	Prolonged PR	-	II III aVF
8	F	59	Primary hyperparathyroidism	12.0	62	187	113	362	370	-	-	II III aVF
9	F	60	Secondary hyperparathyroidism	13.7	63	193	90	387	397	-	-	III aVF
10	F	65	Sarcoidosis	12.9	69	131	106	368	397	-	-	II III aVF
11	F	65	Ovarian cancer	15.6	89	175	86	320	391	-	ST elevation in V1-2	II III aVF
12	F	68	Primary hyperparathyroidism	12.9	91	173	100	320	395	-	-	II III aVF
13	M	35	Primary hyperparathyroidism	12.0	62	147	112	340	348	-	ST elevation in I II V ₃₋₆	II III aVF ₆
14	M	72	Primary hyperparathyroidism	12.7	68	141	100	357	380	-	-	I II aVF V ₄₋₆

(Continued)

Table 3. Continued

No.	Sex	Age (year) ^a	Etiology of Hypercalcemia	Ca ²⁺ Levels (mg/dL) ^a	Heart Rate (bpm) ^a	PR Interval (ms) ^a	QRS Duration (ms) ^a	QT Interval (ms) ^a	QTc Interval (ms) ^a	Conduction Disorder	ST Segment/T Wave Abnormality	Location of J Point Elevation
15	M	62	Oropharyngeal cancer	14.4	89	128	88	372	452	–	–	I II aVF V ₆
16	F	55	Primary hyperparathyroidism	13.4	58	168	100	365	361	–	–	I,II aVF,V ₆
17	M	27	Primary hyperparathyroidism	15.0	61	178	102	386	388	LAH	ST elevation in V ₁₋₃	V ₁₋₃
18	M	57	Non-Hodgkin's lymphoma	16.9	66	167	107	362	381	–	ST elevation and T wave inversion in V ₁₋₂	V ₁₋₃
19	M	59	Non-Hodgkin's lymphoma	17.3	87	210	114	337	408	Prolonged PR	ST elevation in V ₁₋₂	V ₂₋₃
20	M	69	Unknown	12.6	75	196	110	335	375	–	ST elevation in V ₁₋₃	V ₁₋₃
21	F	64	Squamous cell cancer	13.8	100	208	96	354	456	–	ST elevation in V ₁₋₂	V ₁₋₂
22	F	73	Buccal mucosa cancer	15.8	78	145	98	336	384	–	ST elevation in V ₁₋₂	V ₁₋₂
23	F	80	Overdose of vitamin D	13.2	71	325	120	338	369	Prolonged PR	ST elevation in V ₁₋₃	V ₁₋₂
24	M	58	Primary hyperparathyroidism	12.5	55	183	115	362	348	–	ST elevation in I II V ₁₋₆	I II V ₄₋₆ , V ₁
25	F	84	Tongue cancer	15.2	89	174	165	370	452	LBBB	ST elevation in I aVL V ₂₋₅	I II aVL V ₁₋₅
26	M	64	Overdose of vitamin D	15.5	79	216	90	352	403	Prolonged PR	ST elevation in V ₂₋₃ , ST depression in V ₅₋₆	II III aVF V ₂₋₃
27	M	64	Overdose of vitamin D	15.2	86	157	108	329	395	–	ST elevation in V ₁₋₃	II III aVF V ₁₋₃
Total	M:14 F:14 (55–68)	64 (55–68)		13.7 (12.7–15.2)	71 (62–87)	173 (153–196)	100 (90–112)	354 (337–370)	384 (370–397)	Yes: 7	Yes: 15	inferior: 9, lateral: 4, right precordial: 7, multiple : 7

^aMedian (interquartile range). LAH, left anterior hemiblock; LBBB, left bundle branch block.

Figure 1. Representative 12-lead ECGs recorded in hypercalcemic patients showing early repolarizations. (A) Patient 1; (B) Patient 3; (C) Patient 13; (D) Patient 12; (E) Patient 14; (F) Patient 16; (G) Patient 19; (H) Patient 20; (I) Patient 24. Patient numbers correspond to those listed in Table 3. The arrows indicate J point elevation.

Multivariate models adjusted for sex, age, and all covariates revealed that shortening of corrected QT interval (odds ratio, 0.985; 95% confidence interval, 0.971–1.000; $P = 0.045$) and ST segment/T wave abnormality (odds ratio, 4.091; 95% confidence interval, 1.486–11.261; $P = 0.01$) were associated with the presence of early repolarization in patients with hypercalcemia (Table 5).

ECGs were recorded in both a hypercalcemic state (serum Ca^{2+} levels, 14.3 ± 1.4 mg/dL) and a normocalcemic state (serum Ca^{2+} levels, 9.4 ± 0.5 mg/dL) in 28 patients. In these patients, both the PQ interval and the QRS duration were longer, and the QT interval was shorter in the setting of hypercalcemia compared with normocalcemia, whereas the heart rate was not

Table 4. Comparison of Characteristics in Hypercalcemia Patients with J Point Elevation and Those without J Point Elevation

Characteristic	J Point Elevation (+) n = 27	J Point Elevation (-) n = 62	P Value
Age (years) ^a	64 (55–68)	64 (54–73)	0.46
Male sex, no. (%)	14 (52)	20 (32)	0.08
Etiology of hypercalcemia			
Hyperparathyroidism, no. (%)	10 (37)	26 (42)	0.67
Cancer, no. (%)	11 (41)	23 (37)	0.75
Overdose of vitamin D, no. (%)	4 (15)	6 (10)	0.34
Sarcoidosis, no. (%)	1 (4)	3 (5)	0.65
Others, no. (%)	1 (4)	4 (6)	0.52
Diabetes mellitus, no. (%)	5 (16)	10 (16)	0.50
Hypertension, no. (%)	6 (22)	19 (31)	0.42
Serum Ca ²⁺ (mg/dL) ^a	13.7 (12.7–15.2)	13.1 (12.4–14.0)	0.13
Serum K ⁺ (mEq/L) ^a	3.9 (3.5–4.4)	4.3 (3.7–4.5)	0.53
Serum creatinine (mg/dL) ^a	1.1 (0.7–2.2)	1.1 (0.7–2.2)	0.69
Ca ²⁺ channel blocker, no. (%) ^a	5 (19)	15 (24)	0.56
Heart rate (bpm) ^a	71 (62–87)	77 (66–91)	0.29
PQ interval (ms) ^a	173 (153–196)	156 (143–181)	0.08
QRS duration (ms) ^a	100 (90–112)	98 (92–107)	0.56
QT interval (ms) ^a	354 (337–370)	353 (329–374)	0.94
Corrected QT interval (ms) ^a	384 (370–397)	400 (382–420)	0.02
Conduction disorder, no. (%)	7 (26)	15 (24)	0.86
Prolonged PR interval, no. (%)	5 (19)	7 (11)	0.27
Right bundle branch block, no. (%)	0 (0)	4 (6)	0.23
Left anterior hemiblock, no. (%)	1 (4)	9 (15)	0.13
Left bundle branch block, no. (%)	1 (4)	0 (0)	0.30
ST segment/T wave abnormality, no. (%)	15 (56)	14 (23)	0.002

^aMedian (interquartile range).**Table 5.** Association of ECG Findings with J Point Elevation in Hypercalcemia

Effect	Odds Ratio	95% CI	P Value
Male sex	0.481	0.172–1.348	0.16
Age	0.998	0.964–1.034	0.93
Corrected QT interval	0.985	0.971–1.000	0.045
ST segment/T wave abnormality	4.091	1.486–11.261	0.01

Models were adjusted for all covariates.
Abbreviations as in text.

different between the two states (Table 6). Among the 11 patients with J point elevation in the setting of hypercalcemia who had repeated ECG recording after hypercalcemia was resolved, J point elevation was disappeared after hypercalcemia was resolved in eight patients (73%), and the frequency of J point elevation became similar to that in controls (Fig. 2; $P = 0.30$). During hospitalization, no arrhythmia event occurred in patients with hypercalcemia.

DISCUSSION

In this study, we found that the frequency of J point elevation was increased in patients

with hypercalcemia. Furthermore, hypercalcemia was associated with the prolongation of both the PR interval and the QRS interval, and with the shortening of the QT interval. In spite of these ECG changes, no arrhythmia event occurred in patients with hypercalcemia.

Hypercalcemia alters ionic current kinetics in cardiomyocytes and may induce ECG abnormalities such as the shortening of QT interval and the prolongation of both the PR interval and the QRS duration.^{7–9} Hypercalcemia was associated with QT interval shortening and delayed cardiac conduction; these ECG changes were restored when serum Ca²⁺ levels returned to the normal range.

Table 6. Comparison of Electrocardiographic Characteristics between Hypercalcemic State and Normocalcemic State in 28 Patients

	Hypercalcemia	Normocalcemia	P Value
Heart rate, (bpm) ^a	73 (66–85)	70 (65–80)	0.21
PQ interval (ms) ^a	176 (154–206)	155 (142–173)	<0.001
QRS duration (ms) ^a	106 (94–116)	99 (89–107)	0.004
QT interval (ms) ^a	354 (337–391)	392 (376–414)	0.004
Corrected QT interval (ms) ^a	396 (381–415)	429 (399–446)	0.002
Conduction disorder, no. (%)	12 (43)	10 (36)	0.50
Prolonged PR interval, no. (%)	7 (25)	3 (11)	0.13
Right bundle branch block, no. (%)	3 (11)	3 (11)	1.00
Left anterior hemiblock, no. (%)	6 (21)	4 (14)	0.50
Left bundle branch block, no. (%)	1 (4)	1 (4)	1.00
ST segment/T wave abnormality, no. (%)	13 (46)	5 (18)	0.04
J point elevation, no. (%)	11 (39)	4 (14)	0.04
Location of J point elevation			
Inferior leads, no. (%)	2 (7)	1 (4)	1.00
Lateral leads, no. (%)	1 (4)	2 (7)	1.00
Right precordial leads, no. (%)	6 (21)	1 (4)	0.06
Multiple locations, no. (%)	2 (7)	0 (0)	–

^aMedian (interquartile range).

Abbreviations as in text.

Furthermore, hypercalcemia has been linked to J point elevation,^{7,10–18} and we found J point elevations with various morphologies, including a J point with a scooped appearance and ST segment elevation, as well as Brugada-type ECG findings and early repolarization, which were present in 30% of patients with hypercalcemia. The frequency of J point elevation was not different among causes of hypercalcemia. A previous case series study described 16 patients with hypercalcemia due to various diseases who exhibited a J point with both a characteristic scooped appearance and ST segment elevation.¹⁸ In this study, 6% of patients with hypercalcemia exhibited the scooped appearance. Brugada-type ECG findings have been reported in the right precordial leads in the setting of hypercalcemia, in two case reports,^{13,14} and were found in 6% of patients with hypercalcemia in this study. Furthermore, this study demonstrated that hypercalcemia was also associated with early repolarization, as was the case in previous case reports.^{16,21} The evidence that the J point elevation resolved following the resolution of hypercalcemia supports our hypothesis.

J point elevations including early repolarization and Brugada-type ECG are associated with an increased risk of ventricular tachyarrhythmias and sudden cardiac death.^{2,22} Furthermore, ventricular tachyarrhythmias have occasionally been reported in patients with hyperparathyroidism

who have J point elevation in the setting of hypercalcemia.^{7,10–18,23} However, although J point elevation was frequently found in patients with hypercalcemia due to various diseases, no fatal arrhythmia was observed during short periods of hospitalization in this study. The number of patients and observation periods in this study may not be enough to observe the association of J point elevation with the risk of arrhythmia. Ventricular tachyarrhythmias have developed in patients without J point elevation in the setting of hypercalcemia due to hyperparathyroidism,²⁴ and ventricular tachyarrhythmia may be a complication of hyperparathyroidism, and J point elevation in the setting of hypercalcemia may not be directly associated with an increased risk of ventricular tachyarrhythmia.

Hypercalcemia is associated with various electrophysiologic changes, including shortening of QT interval, decreased cardiac conduction, and J point elevation, all of which can create a substrate for arrhythmia.^{2,7–9,25,26} However, ventricular tachyarrhythmias have occurred only rarely in patients with hypercalcemia, based on the findings of this study and those of previous reports, suggesting that hypercalcemia may also exert proarrhythmic effects.^{8,16} In experimental studies, elevated extracellular Ca²⁺ exerts a stabilizing effect on the membrane and decreases excitability.^{27,28} Although dispersion of QT interval, which indicates an

Figure 2. Representative 12-lead ECGs in both hypercalcemic (left side) and normal calcium states (right side). (A) Patient 10; (B) Patient 18; (C) Patient 25; (D) Patient 27. Patient numbers correspond to those listed in Table 3. The arrows indicate J point elevation. Serum Ca⁺⁺ level was corrected using the serum albumin level.

arrhythmogenic substrate, is increased in patients with short QT syndrome, hypercalcemia does not increase QT interval dispersion, despite a shortened QT interval.^{29–31}

The mechanism by which hypercalcemia induces J point elevation is unclear. Data from our study and from other studies suggest that J point

elevation likely occurs in the setting of a shortened QT interval.^{2,32,33} The frequency of early repolarization is elevated in patients with short QT syndrome and asymptomatic subjects with a short QT interval.³³ The QT interval is mildly short, and abnormally short repolarization periods have been identified in the inferolateral area of the

left ventricle in patients with early repolarization syndrome.^{2,32} Brugada-type ECG findings may occur in the settings of various pathophysiologic conditions, and hypercalcemia may unmask J point elevation. However, this can explain our findings only in a fraction of patients because Brugada syndrome is a rare disease.²⁰ Actually, sodium channel blocker challenge, a provocative test for Brugada syndrome, is negative at normocalcemic state in a patient with hypercalcemia-induced Brugada type ECG,¹³ and it is positive after parathyroidectomy in another patient with hypercalcemia-induced Brugada type ECG.³⁴

Hypercalcemia-induced J point elevation may be explained by transmural differences in the magnitude of the action potential notch, which has been proposed as one of the mechanisms for early repolarization and Brugada type ECG.³⁵ Decreased inward Na^+ - Ca^{2+} exchanger current is one of the major changes in ionic currents caused by hypercalcemia.^{8,28} Because of the heterogeneous expression of the Na^+ - Ca^{2+} exchanger throughout the myocardium, the change in inward Na^+ - Ca^{2+} exchanger current may be more pronounced in the epicardium of the ventricles compared with the endocardium, possibly resulting in increased transmural differences in the action potential notch and the appearance of J point elevation.³⁶

This study had several limitations. As discussed above, it is unknown whether hypercalcemia-induced J point elevation increases the risk of ventricular tachyarrhythmias or not. The number of patients included in this study may have been too small to detect the relationship between J point elevation and the risk of arrhythmia in the setting of hypercalcemia. Only a small number of patients had follow-up ECG recordings after hypercalcemia was resolved. Holter ECG monitoring was not performed and we could not assess the frequency of nonsustained ventricular tachyarrhythmias and premature complexes. The precise mechanism by which hypercalcemia induces early repolarization or Brugada-type ECG is unknown. This was a retrospective study; prospective studies are warranted to investigate the role of early repolarization in the prediction of arrhythmia in patients with various diseases that may cause hypercalcemia.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web site:

Table S1. Comparison of Electrocardiographic Characteristics in Hypercalcemia Patients (Who Had Normal Na and K Levels without Any Medicine Affecting Ion Channels) and Normocalcemia Controls.

Table S2. Comparison of Characteristics between Hypercalcemia Patients with Hyperparathyroidism and Those with Cancer.