



Predictive value of notched P wave for life-threatening arrhythmias in patients with Brugada syndrome: Insights from a multicenter prospective study ^e

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ABSTRACT

BACKGROUND Risk stratification for ventricular fibrillation (VF) in Brugada syndrome (BrS) remains a major clinical challenge. Atrial fibrillation is relatively common in BrS, suggesting that atrial conduction abnormalities may be related to arrhythmogenesis. A notched P wave on the surface electrocardiogram (ECG) reflects atrial conduction delay, but its prognostic significance for VF in BrS has not been fully established.

OBJECTIVE This study aimed to evaluate the association between notched P waves and life-threatening arrhythmic events in patients with BrS.

METHODS We analyzed 510 patients with BrS (mean age 51 ± 14 years; 95% men) enrolled in a prospective multicenter registry across 61 hospitals in Japan. Clinical and ECG parameters at enrollment were assessed, and patients were followed for cardiac events (VF, sustained ventricular tachycardia, or sudden cardiac death).

RESULTS During a mean follow-up of 107 ± 62 months, 58 patients (11%) experienced cardiac events. Notched P waves were present in 52 patients (10%). Patients with notched P waves had a significantly higher incidence of cardiac events than those without (27% vs 10%; $P < .001$). Kaplan–Meier analysis demonstrated lower event-free survival in patients with notched P waves ($P < .001$). In multivariable Cox regression, a notched P wave remained an independent predictor of cardiac events (hazard ratio 2.63; 95% confidence interval 1.35–4.78; $P = .006$), along with a history of VF.

CONCLUSION A notched P wave on a standard 12-lead ECG independently predicts life-threatening arrhythmias in BrS and may improve risk stratification by complementing conventional predictors.

KEYWORDS Atrial conduction abnormality; Brugada syndrome; Notched P wave; Risk stratification; Ventricular fibrillation

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Brugada syndrome (BrS) is associated with an increased risk of sudden cardiac death (SCD), most commonly owing to ventricular fibrillation (VF).¹ Implantable cardioverter-defibrillator (ICD) therapy is the standard preventive strategy; however, device-related complications such as inappropriate

shocks, lead failure, and infection remain significant limitations.² Therefore, improving risk stratification is of paramount importance to guide ICD therapy.

Traditionally, BrS has been regarded as a primary ion channelopathy, but recent evidence suggests that structural

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abnormalities, particularly in the right ventricular outflow tract, also contribute to arrhythmogenesis.^{3,4} Moreover, atrial involvement has gained increasing recognition. Atrial fibrillation (AF) occurs in 10%–20% of patients with BrS,⁵ and sodium-channel mutations associated with BrS have been linked to both atrial and ventricular arrhythmias.^{6,7} These findings imply that atrial conduction abnormalities may form part of the broader arrhythmogenic substrate in BrS.

A notched P wave on the surface electrocardiogram (ECG) reflects atrial conduction delay⁸ and has been associated with AF occurrence in the general population.^{9,10} A recent single-center study suggested that notched P waves might also be linked to VF in BrS,¹¹ but the findings were limited by small sample size and retrospective design.

Accordingly, we hypothesized that a notched P wave may serve as a novel marker of arrhythmogenic risk in BrS. Using data from the Japan Idiopathic Ventricular Fibrillation Study, the largest multicenter prospective registry of patients with BrS in Japan,^{12–14} we investigated the clinical utility of notched P waves for VF risk stratification.

Methods

Study population

This study analyzed data from the Japan Idiopathic Ventricular Fibrillation Study, a multicenter prospective registry of patients with BrS. Consecutive patients diagnosed as having type 1 BrS ECG ($n = 523$) between February 2002 and January 2015 were screened. After exclusion of 13 patients owing to inadequate ECG quality, 510 patients (mean age 51 ± 14 years; 95% men) from 61 hospitals were included. Patients were eligible if they demonstrated a spontaneous or drug-induced type 1 Brugada ECG pattern, confirmed by a standard sodium-channel blocker test (pilsicainide or flecainide). All participants had normal findings on physical examination, chest radiography, and echocardiography, and none were taking antiarrhythmic drugs or had electrolyte abnormalities at the time of enrollment. A written informed consent was obtained from all patients, and the study protocol was approved by the ethics committees of participating institutions. All procedures were conducted in accordance with the principles outlined in the Declaration of Helsinki.

Clinical follow-up

Arrhythmic events were prospectively recorded after enrollment, and only events occurring during follow-up were included in the outcome analysis. Patients were followed every 12 months for the occurrence of cardiac events, including SCD, documented VF or sustained ventricular tachycardia (VT) (>200 beats/min), or appropriate

ICD therapy for VF/VT. ICD implantation was performed at the discretion of treating physicians, in accordance with Japanese Circulation Society guidelines.¹⁵ For subgroup analyses, patients without documented VF at enrollment were classified as the “no prior VF” group, regardless of symptom status. For additional analyses, patients were categorized into 3 clinical groups: previous VF, previous malignant syncope without documented VF, and asymptomatic. Syncope was considered malignant (arrhythmic) if it occurred without prodrome or identifiable triggers or if it remained unexplained after evaluation. Patients without a history of malignant (arrhythmic) syncope were defined as asymptomatic; this group included patients with benign vasovagal syncope.

12-lead ECG findings

Standard 12-lead ECGs were obtained at enrollment under stable clinical conditions. Each ECG recording was analyzed at $4\times$ magnification, and P-wave morphology was manually evaluated using a digital vernier caliper (A&D Company). All ECGs were independently reviewed by 2 experienced cardiologists (T.S. and Y.Y.) blinded to clinical data. The interobserver agreement for identifying notched P waves was excellent ($\kappa = 0.87$), with initial disagreement in 14 of 510 cases (2.7%). In cases of initial disagreement, ECGs were jointly re-evaluated in a consensus meeting. If discordance persisted after visual reassessment, peak-to-peak interval and amplitude measurements were repeated using digital calipers at $4\times$ magnification. Remeasurement was performed when interobserver discrepancy in the peak-to-peak interval exceeded 5 ms. Final classification was determined by consensus after remeasurement. No cases required adjudication by a third reviewer. A notched P wave was defined in lead II as an M-shaped morphology with a peak-to-peak interval of >0.04 seconds and accompanied by an amplitude drop of $\geq 10\%$ between peaks (Figure 1). The $\geq 10\%$ amplitude reduction was defined as a relative (percentage-based) decrease between peaks rather than an absolute amplitude cutoff. ECGs were analyzed at $4\times$ magnification using digital calipers with careful attention to baseline stability to minimize measurement variability. ECGs with insufficient quality or extremely low P-wave amplitude were excluded during screening to avoid misclassification. Following the report by Okuyama et al,¹⁶ the evaluation was performed using P-wave morphology in lead II, and based on the findings of Yonezu et al,¹¹ a cutoff value of >0.04 seconds was adopted as the criterion for a notched P wave. Other ECG markers were assessed using established definitions, including r-J interval (>90 ms in lead V_2), corrected QT interval (>420 ms), T-peak–T-end interval (≥ 100 ms in V_2), J waves (≥ 0.1 mV in at least 2 inferior or lateral leads), and fragmented QRS. Late potentials were considered positive when at least 2 of the following 3 criteria were met: filtered QRS duration of >114 ms, root-mean-square voltage of the last 40 ms of <20 μ V, and duration of low-amplitude signals in the terminal portion of the QRS (<40 μ V) of >38 ms.

Abbreviations

AF: atrial fibrillation

BrS: Brugada syndrome

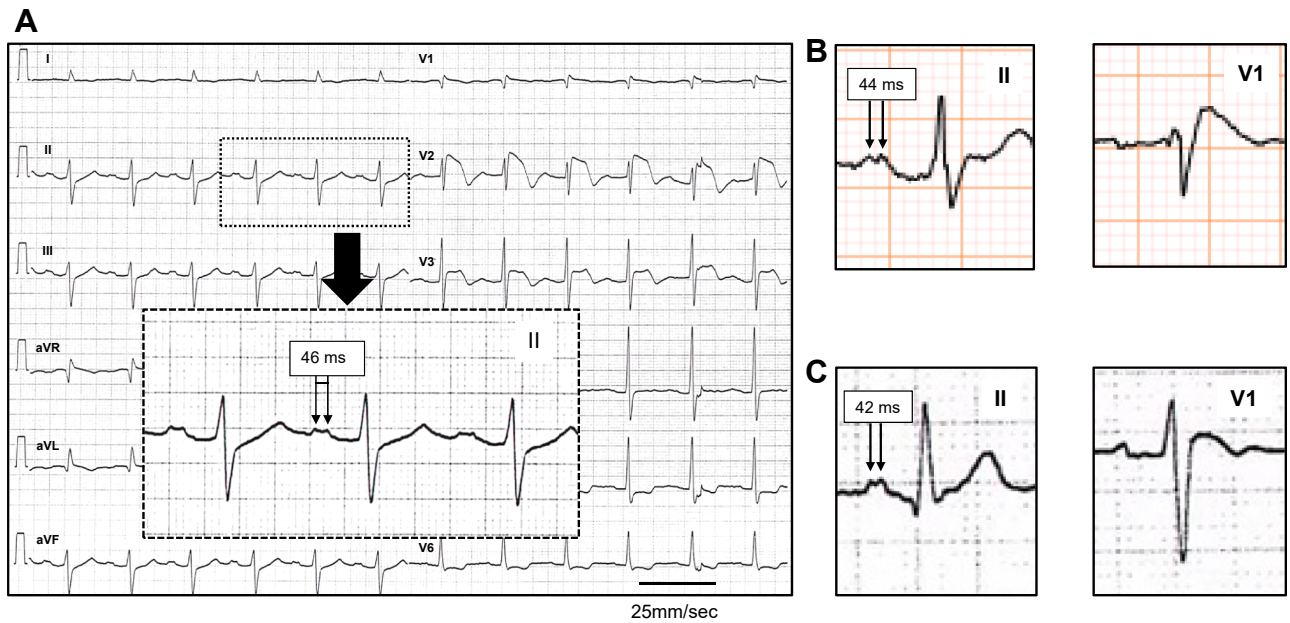
ECG: electrocardiogram

ICD: implantable cardioverter-defibrillator

PES: programmed electrical stimulation

SCD: sudden cardiac death

VF: ventricular fibrillation

**Figure 1**

Representative examples of notched P waves. **A:** Standard 12-lead electrocardiogram showing an M-shaped notched P wave in lead II. **B and C:** Additional representative examples displayed at standard scale, showing lead II with the corresponding V1 lead for reference.

Programmed electrical stimulation

Programmed electrical stimulation (PES) was performed in 420 patients according to a uniform protocol. Stimulation was delivered from the right ventricular apex and outflow tract using 1–3 extrastimuli at drive cycle lengths of 600 and 400 ms, down to a minimum coupling interval of 200 ms. Induction of VF or sustained polymorphic VT requiring direct current shock was defined as positive PES.

Statistical analysis

Continuous variables were expressed as means $\pm$ standard deviations and compared using the Student *t* test or the Mann–Whitney *U* test, as appropriate. Categorical variables were analyzed using Fisher's exact test. Event-free survival was assessed using Kaplan–Meier analysis and compared using the log-rank test. Cox proportional hazards regression was used to identify predictors of cardiac events. Variables with $P < .05$ in univariate analysis were entered into the multivariable model. 2-sided $P < .05$ was considered statistically significant. Statistical analyses were performed using JMP v13.2.1 (SAS Institute).

Results

Baseline clinical characteristics

A total of 510 patients with BrS (mean age 51 ± 14 years; 95% men) were analyzed from 61 participating hospitals (Table 1). A history of VF was present in 99 patients (19%), family history of SCD in 121 (24%), documented AF in 79 (15%), and spontaneous type 1 ECG in 314 (62%). Among patients with drug-induced type 1 ECG ($n = 196$, 38%), 122 (62%) were asymptomatic at enrollment. Among 420 patients who underwent PES, VT/VF was induced in 288 (69%). Additional

ECG findings included J waves in inferolateral leads in 61 patients (12%) and fragmented QRS in 22 (4%).

Notched P-wave prevalence and patient characteristics

A notched P wave on 12-lead ECG was identified in 52 patients (10%). Baseline characteristics were largely comparable between patients with and without notched P waves, except for a trend toward longer P-wave duration in the notched P wave group ($P = .09$). Family history of SCD tended to be less frequent in the notched P wave group ($P = .07$), but no other significant differences were observed in clinical, ECG, or electrophysiological parameters.

Clinical outcomes

During a mean follow-up of 107 ± 62 months, 58 patients (11%) experienced cardiac events (VF, sustained VT, or SCD). Among these patients, 3 experienced cardiac events without ICD implantation, and none of them had a notched P wave. The incidence of cardiac events was significantly higher in patients with notched P waves than those without (27% vs 10%; $P < .001$) (Figure 2A). When patients were stratified according to clinical presentation, event-free survival differed markedly among the 3 categories (Figure 3). Patients with previous VF had the highest incidence of recurrent events, followed by those with previous malignant syncope without documented VF, whereas asymptomatic patients demonstrated the most favorable prognosis. Kaplan–Meier analysis confirmed a stepwise gradient of risk across these groups (log-rank $P < .001$). In contrast, event-free survival was significantly lower in patients with notched P waves than those without ($P < .001$) (Figure 4). In a subgroup analysis restricted to patients without previous VF at enrollment

Table 1 Baseline clinical and electrocardiographic characteristics

Characteristics	All (n = 510)	Notched P wave (n = 52)	Non-notched P wave (n = 458)	P value
Gender (male), n (%)	484 (95)	50 (96)	434 (95)	.66
Age at enrollment (y)	51 ± 14	51 ± 13	51 ± 14	.73
History of VF, n (%)	99 (19)	13 (25)	86 (19)	.28
Family history of SCD, n (%)	121 (24)	7 (13)	114 (25)	.07
History of AF, n (%)	79 (15)	8 (15)	71 (16)	.64
Spontaneous type 1 ECG, n (%)	314 (62)	32 (62)	282 (62)	.98
Inducible VT/VF, n/N (%)	288 of 420 (69)	28 of 35 (80)	260 of 385 (68)	.13
Positive late potentials, n/N (%)	284 of 376 (76)	29 of 38 (76)	255 of 338 (75)	.91
r-J interval in lead V ₂ (ms)	98 ± 14	99 ± 17	98 ± 14	.82
QTc interval in lead V ₂ (ms)	407 ± 44	414 ± 43	406 ± 44	.63
T-peak-to-T-end interval in lead V ₂ (ms)	105 ± 33	115 ± 46	104 ± 30	.16
J wave in inferior and/or lateral leads, n (%)	61 (12)	6 (12)	55 (12)	.92
Fragmented QRS, n (%)	22 (4)	1 (2)	21 (5)	.37
P-wave amplitude in lead II (mV)	0.14 ± 0.14	0.13 ± 0.05	0.14 ± 0.15	.86
P-wave duration in lead II (ms)	107 ± 20	109 ± 15	106 ± 21	.09
ICD implantation, n (%)	328 (65)	32 (62)	296 (65)	.59
Mean follow-up periods (mo)	107 ± 62	95 ± 69	108 ± 61	.16

Comparison of clinical and ECG findings between patients with and without notched P waves.

AF = atrial fibrillation; ECG = electrocardiogram; ICD = implantable cardioverter-defibrillator; QTc = corrected QT; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia.

(n = 411), the incidence of cardiac events remained significantly higher in those with a notched P wave than in those without (12.8% vs 3.5%; $P = .007$) (Figure 2B). Kaplan–Meier analysis in this subgroup similarly demonstrated significantly lower event-free survival in patients with a notched P wave than those without ($P = .005$), as shown in Supplemental Figure 1. However, when the analysis was limited to strictly asymptomatic patients at presentation, no significant association was observed; the incidence of cardiac events was comparable between patients with and without a notched P wave (3.7% vs 2.7%; $P = .76$) (Figure 2C). We evaluated whether the presence of a notched P wave improved the performance of the predicting arrhythmic event (PAT) score, a validated risk model consisting of 8 clinical and ECG parameters with high predictive accuracy for major ventricular arrhythmic events in patients with BrS.¹⁷ When the notched P wave was incorporated into the PAT score, the predictive performance showed a modest improvement, with the area under the curve (AUC) increasing from 0.63 to 0.65 (Figure 5). We further examined potential associations between notched P waves and other established risk markers included in the PAT score. No statistically significant associations were observed between notched P waves and any of the evaluated markers (Supplemental Table 1), including T-peak–T-end interval of >100 ms, arrhythmic or unexplained syncope, VT/VF during drug challenge testing, prolonged PR interval of >200 ms, type 1 ECG pattern in peripheral leads, aVR sign, fragmented QRS, and early repolarization in inferolateral leads.

Predictors of cardiac events

Univariate Cox regression identified younger age, history of VF, spontaneous type 1 ECG, prolonged r-J interval, and

notched P wave as significant predictors of cardiac events. In multivariable analysis, only history of VF (hazard ratio 9.36; 95% confidence interval 5.35–17.0; $P < .001$) and notched P wave (hazard ratio 2.63; 95% confidence interval 1.35–4.78; $P = .006$) remained independent predictors (Table 2).

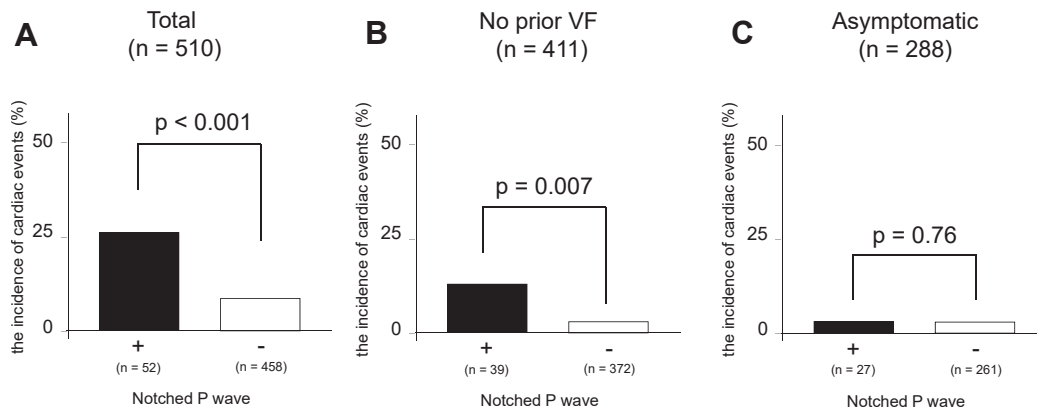
Combined risk factor analysis

When 3 risk factors—history of VF, spontaneous type 1 ECG, and notched P wave—were combined, a stepwise increase in event incidence was observed: 75% in patients with all 3 risk factors, 34% with 2, 7% with 1, and only 1% with none. Kaplan–Meier curves confirmed that event-free survival decreased significantly with increasing number of risk factors ($P < .001$) (Figure 6).

Discussion

Main findings

In this large multicenter prospective registry of patients with BrS, we demonstrated that the presence of a notched P wave on 12-lead ECG was significantly associated with the occurrence of life-threatening arrhythmic events. 3 main findings emerged from the present study. First, patients with notched P waves experienced a higher incidence of VF and related events than those without. Second, multivariable analysis confirmed that a notched P wave was an independent predictor, even after adjusting for established risk markers such as a history of VF and spontaneous type 1 ECG. Third, when integrated into a combined risk model, the notched P wave modestly improved the predictive accuracy for identifying high-risk patients. Importantly, notched P waves were not significantly associated with other established risk markers

**Figure 2**

Incidence of cardiac events in patients with and without a notched P wave. **A:** The incidence of cardiac events was significantly higher in patients with a notched P wave than in those without (27% vs 10%; $P < .001$). **B:** Similarly, in patients without previous VF, the incidence of cardiac events was significantly higher in those with a notched P wave than in those without (12.8% vs 3.5%; $P = .007$). **C:** In contrast, when the analysis was limited to asymptomatic patients, no significant difference was observed between those with and without a notched P wave (3.7% vs 2.7%; $P = .76$). VF = ventricular fibrillation.

included in the PAT score. This suggests that atrial conduction abnormalities reflected by P-wave morphology may represent an electrophysiological dimension distinct from conventional ventricular risk markers. Although the incremental improvement in AUC was modest, the apparent independence of this marker raises the possibility that it captures a different component of arrhythmogenic vulnerability in BrS.

To the best of our knowledge, this is the first multicenter prospective study to establish the clinical significance of P-wave morphology as a marker of arrhythmogenic risk in BrS.

Comparison with previous studies

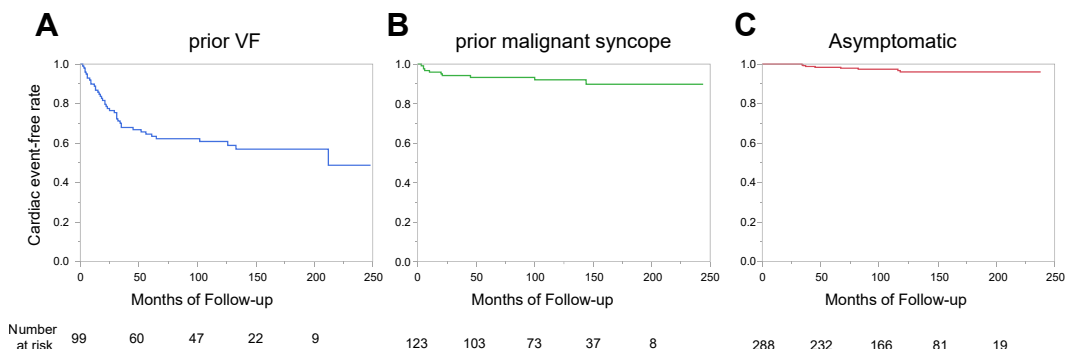
Risk stratification in BrS continues to be difficult, with only a few consistently validated predictors such as a history of VF and spontaneous type 1 ECG.¹ Several ECG markers reflecting ventricular abnormalities (prolonged QRS duration, fragmented QRS, inferolateral J waves, etc) have been proposed,^{12,18–20} but their incremental value remains limited.

In contrast, atrial indices have received little attention. AF is relatively frequent, occurring in 10%–20% of patients. Kusano et al⁵ reported that SCN5A mutations, the most

common genetic variants in BrS, were associated with both VF and AF, supporting the hypothesis that sodium-channel dysfunction extends to atrial myocardium.⁷ Recently, Zanchi et al²¹ investigated whether an artificial intelligence model based on P-wave findings could identify BrS, and demonstrated that artificial intelligence was able to distinguish BrS solely from P-wave features. They concluded that their results support the presence of atrial abnormalities in BrS. Abnormal P-wave morphology, such as prolongation or notching, is a recognized marker of atrial conduction delay and has been linked to AF occurrence in the general population.⁹ Earlier single-center data by Yonezu et al¹¹ suggested a link between notched P waves and VF in BrS, but methodological limitations restricted its significance. The present multicenter prospective registry decisively validates and extends those preliminary findings, establishing notched P waves as a clinically relevant marker for risk stratification in BrS.

Pathophysiological considerations

The association between notched P waves and VF in BrS likely reflects broader atrial involvement in arrhythmogenesis. A notched P wave indicates intra-atrial conduction delay,

**Figure 3**

Kaplan-Meier analysis of cardiac event-free survival according to clinical presentation. **A:** Patients with previous VF. **B:** Patients with previous malignant syncope without documented VF. **C:** Asymptomatic patients, including those with benign vasovagal syncope. Event-free survival differed significantly among the 3 groups, demonstrating a stepwise gradient of risk (log-rank $P < .001$). VF = ventricular fibrillation.

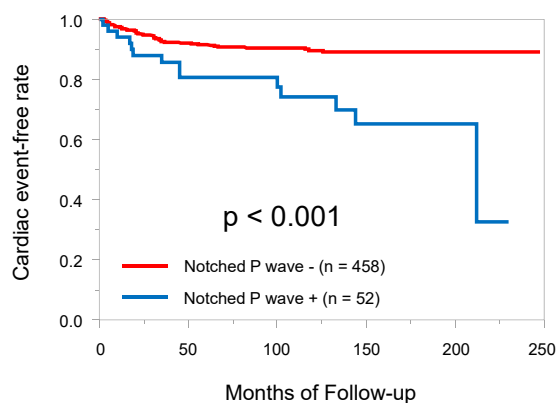


Figure 4

Kaplan-Meier analysis of cardiac event-free survival according to the presence of notched P waves. During follow-up, patients with notched P waves had a significantly lower event-free survival rate than those without ($P < .001$).

which may result from atrial fibrosis, heterogeneous conduction, or sodium-channel dysfunction.²² Autopsy and imaging studies have demonstrated structural abnormalities in both ventricles and atria in BrS, including fibrosis, reduced connexin expression, and conduction slowing.^{23,24} Therefore, P-wave abnormalities may serve as a simple surface marker of diffuse myocardial conduction disease, representing a systemic substrate that predisposes patients not only to AF but also to VF.

It is also possible that atrial conduction abnormalities and ventricular arrhythmogenesis share common mechanisms. Genetic and molecular studies have shown that sodium channelopathies can cause conduction impairment across atrial and ventricular myocardium.^{6,7} Thus, P-wave abnormalities might reflect a more generalized electrophysiological disorder rather than isolated atrial disease. This supports the concept of BrS as an organic heart disease with both atrial

and ventricular involvement, rather than a purely ion channel disorder.^{4,5}

Clinical implications

Our findings have important clinical implications. ICD implantation is the only established therapy for preventing SCD in patients with BrS, but it carries substantial risks, including inappropriate shocks, lead failure, and infections.² Therefore, improved patient selection is essential. The present study suggests that incorporating notched P waves into risk assessment—particularly in combination with a history of VF and spontaneous type 1 ECG—provides incremental predictive value. Patients with all 3 risk factors were at particularly high risk and may derive the greatest benefit from ICD therapy. Conversely, patients without any of these risk factors are regarded as having a relatively low risk, which may allow them to avoid unnecessary ICD implantation.

Recent studies have demonstrated that patients with drug-induced type 1 Brugada ECG generally have a more favorable prognosis than those presenting with a spontaneous type 1 pattern, particularly when asymptomatic at diagnosis.^{25–27} A substantial proportion of our registry consisted of patients with drug-induced type 1 ECG, many of whom were asymptomatic. This clinical context should be taken into account when interpreting the overall event rate observed in our cohort. The low number of cardiac events among patients without ICD implantation likely reflects contemporary clinical practice in Japan, where ICD implantation is widely adopted for individuals assessed as being at intermediate or high risk of arrhythmic events.

To evaluate the incremental prognostic value of P-wave morphology in a clinically relevant subgroup, we performed an additional analysis restricted to patients without previous VF. In this cohort, the presence of a notched P wave remained significantly associated with arrhythmic events. Furthermore, incorporating the notched P wave into an established risk model (PAT score) modestly improved discrimination (AUC

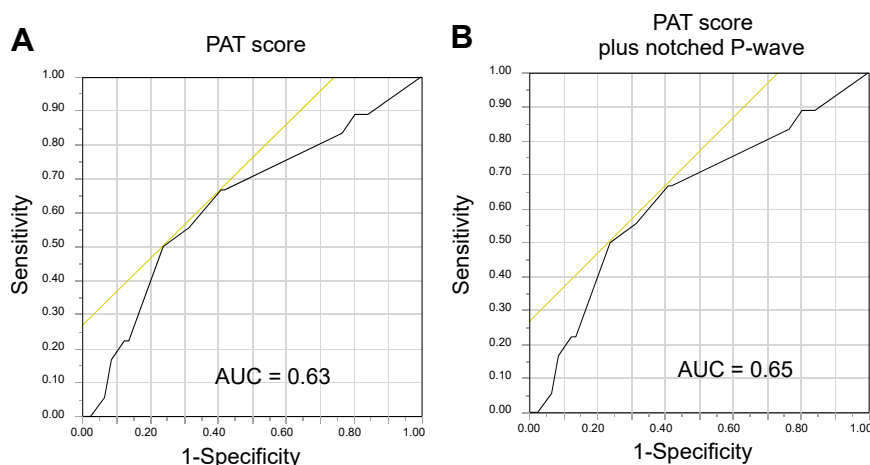


Figure 5

Receiver operating characteristic curve for predicting cardiac events in patients without previous VF (n = 411) at the time of enrollment. A: PAT score. B: PAT score plus notched P wave. AUC = area under the curve; PAT = predicting arrhythmic event; VF = ventricular fibrillation.

Table 2 Univariate and multivariable Cox regression analyses for predictors of cardiac events

Parameters	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	P value	Hazard ratio	95% CI	P value
Men	3.39	0.75–59.8	.13			
Age	0.98	0.96–0.99	.02*	0.99	0.97–1.01	.18
History of VF	10.9	6.32–19.4	<.001 [†]	9.36	5.35–17.0	<.001 [†]
Family history of SCD	0.51	0.41–1.48	.51			
History of AF	1.71	0.88–3.07	.11			
Spontaneous type 1 ECG	2.16	1.20–4.18	.009 [†]	1.93	1.05–3.83	.03*
Inducible VT/VF	0.75	0.43–1.35	.32			
Positive late potentials	2.12	0.91–6.28	.09			
r-J interval of >90 ms in lead V ₂	2.43	1.12–6.32	.02*	1.46	0.66–3.86	.38
QTc interval of ≥420 ms in lead V ₂	1.51	0.85–2.65	.16			
T-peak-to-T-end interval of ≥100 in lead V ₂	0.77	0.44–1.34	.35			
J wave in inferior and/or lateral leads	1.80	0.89–3.34	.10			
Fragmented QRS	1.56	0.47–3.82	.42			
Notched P wave	3.09	1.63–5.49	.001 [†]	2.63	1.35–4.78	.006 [†]

Notched P wave and history of VF emerged as independent predictors of life-threatening arrhythmic events.

AF = atrial fibrillation; CI = confidence interval; ECG = electrocardiogram; QTc = corrected QT; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia.

* $P < .05$.

[†] $P < .001$.

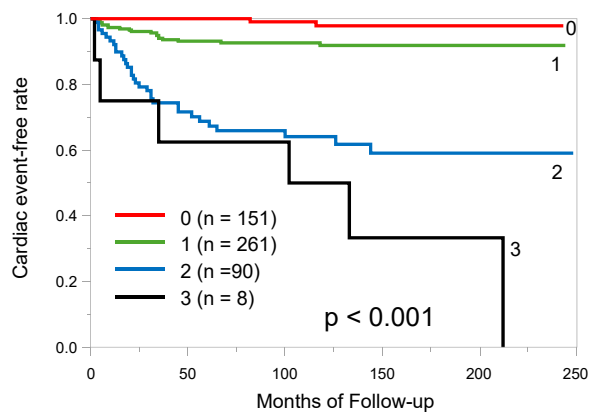
from 0.63 to 0.65), suggesting supplementary value when added to existing risk stratification approaches. However, although the notched P wave retained prognostic relevance in patients without previous VF, it did not discriminate risk among strictly asymptomatic individuals. These findings indicate that identifying reliable markers for risk stratification in truly asymptomatic patients with BrS remains challenging. In particular, in our cohort, none of the 3 patients without ICD implantation who subsequently experienced cardiac events had a notched P wave. This observation underscores

that the notched P wave alone would not have altered management in these specific cases and reinforces that it should not be interpreted as a standalone determinant for ICD implantation in presumed low-risk individuals. Rather, its value seems to lie in complementing established risk markers within a broader risk stratification framework.

Another strength of this marker is its practicality. P-wave analysis is simple, noninvasive, and easily obtainable from routine ECG recordings, unlike genetic testing or invasive electrophysiological studies. This makes it especially valuable in community hospitals or resource-limited settings where advanced diagnostic modalities may not be readily available. Our results also encourage closer monitoring of atrial conduction indices in patients with BrS, with potential implications for AF screening and management.

Study limitations

Several limitations should be acknowledged. First, the definition of a notched P wave was based on visual assessment, which is inherently subject to interobserver variability. Although ECGs were independently reviewed by multiple blinded cardiologists and interobserver agreement was excellent, measurement of peak-to-peak intervals in low-voltage P waves may remain technically challenging despite standardized magnified analysis. In addition, external validation of measurement reproducibility in an independent dataset was not performed and would further strengthen the robustness of this marker. Second, the study population comprised only Japanese patients, and phenotypic differences across ethnic groups have been reported.^{28,29} Therefore, external validation in non-Japanese cohorts will be essential to confirm the generalizability of our findings, and future studies should consider international collaboration to address this limitation. Third, although the follow-up period



Number at risk	0	50	100	150	200
No risk factor	151	126	89	36	3
1 risk factor	261	211	154	79	20
2 risk factors	90	54	38	22	11
3 risk factors	8	6	6	2	1

Figure 6

Cardiac event-free survival according to the number of risk factors. Kaplan-Meier curves stratified by the number of risk factors (history of ventricular fibrillation, spontaneous type 1 electrocardiogram, and notched P wave). Event-free survival decreased stepwise with increasing number of risk factors ($P < .001$).

was relatively long, the number of arrhythmic events remained modest, and larger datasets are needed to further strengthen these findings. Fourth, the relatively high rate of ICD implantation in our cohort likely reflects referral bias to tertiary centers and the long enrollment period during which risk stratification strategies were evolving. Consequently, this population may represent a higher-risk subset of patients with BrS, and the predictive value of notched P waves may differ in lower-risk or community-based cohorts. Fifth, follow-up ECGs were not systematically collected across participating centers, which prevented assessment of temporal changes or inter-ECG variability in P-wave morphology. In addition, the longitudinal stability of notched P waves relative to other established dynamic ECG markers, such as ST-segment variability, could not be assessed. Future prospective studies with standardized ECG acquisition are warranted. Finally, structural and functional atrial assessments, such as cardiac MRI or intracardiac mapping, were not performed, and the mechanistic link between notched P waves and VF remains inferential.

Conclusion

This multicenter prospective study demonstrates that a notched P wave on the standard 12-lead ECG is an independent predictor of life-threatening arrhythmic events in patients with BrS. Incorporating this atrial conduction marker into established risk models may enhance risk stratification and help refine decisions regarding ICD therapy. These findings highlight the role of atrial conduction abnormalities in the arrhythmogenic substrate of BrS and suggest new approaches for improving SCD risk prediction and management.

Appendix

Supplementary Data

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.hrthm.2026.03.004>.

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Disclosures: The authors have no conflicts of interest to disclose.

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