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STATE-OF-THE-ART REVIEW

Exercise and Exercise Stress Testing in Brugada Syndrome

Diagnostic, Prognostic, and Safety Implications

Pattara Rattanawong, MD,[a,b] Narathorn Kulthamrongsri, MD,[b,c] Eugene H. Chung, MD, MPH[d]

ABSTRACT

Brugada syndrome is a cardiac channelopathy associated with sudden cardiac death caused by ventricular arrhythmias. Although pharmacologic Na^+ channel blocker testing remains central to diagnosis, the role of exercise stress testing (EST) in Brugada syndrome is increasingly recognized. Evidence indicates that peak exercise may unmask rate-dependent depolarization abnormalities capable of provoking arrhythmias, whereas the early recovery phase—marked by abrupt sympathetic withdrawal and parasympathetic rebound—more commonly reveals repolarization abnormalities, unmasking the type-1 Brugada pattern and triggering ventricular arrhythmias. Exercise-induced premature ventricular contractions and ST-segment changes during early recovery may serve as clinically meaningful markers of arrhythmic risk. Despite rare case reports of exercise-triggered ventricular arrhythmias, EST appears generally safe when performed with appropriate monitoring and may enhance diagnostic accuracy, particularly when paired with high precordial lead placement or drug provocation. Optimizing EST protocols and integrating recovery-phase markers may improve individualized risk stratification in Brugada syndrome. (JACC Asia. 2026;6:848-859) © 2026 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Brugada syndrome (BrS) is an inherited arrhythmia syndrome associated with an increased risk of sudden cardiac death (SCD).[1,2] It is one of the most prevalent inherited arrhythmia syndromes with an estimated incidence of approximately 0.05%. The condition is significantly more common in Asian populations, particularly among individuals of East and Southeast Asian descent.[3-6] Although significant advancements have been made in pharmacologic diagnostic strategies, particularly with Na^+ channel blocker provocation testing,[7,8] less is known about the impact of physical exertion and the role of exercise stress testing (EST) in BrS. This review aims to explore the potential value and limitations of EST in the diagnosis and risk stratification of BrS while also examining the current understanding of exercise safety in this population. We summarize the existing literature, identify knowledge gaps, and offer perspectives on future directions in this emerging area of clinical relevance.

GENETIC BASIS AND PATHOPHYSIOLOGY

BrS is thought to follow an autosomal dominant inheritance model with incomplete penetrance, although most cases are sporadic.[9] Currently, numerous genes have been linked to this condition, with *SCN5A* being the most prevalent, found in up to 28% of patients.[9,10] The *SCN5A* 1795insD sequence

From the [a]Pali Momi Medical Center, Hawai'i Pacific Health, Aiea, Hawaii, USA; [b]Department of Cardiovascular Medicine, Mayo Clinic, Phoenix, Arizona, USA; [c]Department of Medicine, University of Hawai'i at Mānoa John A Burns School of Medicine, Honolulu, Hawaii, USA; and the [d]Demoulas Center for Cardiac Arrhythmias, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA.

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HIGHLIGHTS

- Exercise-related arrhythmic risk in BrS is low but incompletely characterized across exercise phases.
- Exercise stress testing reveals phase-specific ECG changes: VT/PVCs at peak/early recovery and type 1 unmasking during recovery.
- Exercise stress testing is generally safe and should emphasize monitoring during peak exertion and early recovery.
- Future studies should standardize protocols and validate phase-specific ECG markers for individualized risk stratification.

variant reduces sodium current during action potentials by enhancing slow inactivation under depolarized conditions, thereby decreasing channel availability at high heart rates. This may explain BrS phenotype in which J-point elevation emerges during β-adrenergic stimulation. The variant also affects the fast inactivation of sodium current consequently prolonging QT intervals during slower heart rates.[11,12] Some *SCN5A* variants have been suggested to increase risk during exercise, although these mutations have not been linked to clinical outcomes.[11-13] Depolarization abnormalities are increasingly recognized in BrS, including right ventricular outflow tract conduction delay related to localized fibrosis and altered gap-junction coupling. These structural-electrical substrates may become functionally more apparent at higher heart rates during EST, providing a complementary explanation for exercise-phase conduction slowing and arrhythmia susceptibility.

CURRENT DIAGNOSTIC CRITERIA AND CLINICAL MANIFESTATIONS

Electrocardiogram (ECG) patterns and diagnostic criteria for BrS are now well-established.[7,10] The diagnosis requires a specific electrocardiographic type 1 Brugada pattern (BrP), characterized by J-point and ST-segment elevation ≥2 mm with a coved morphology in 1 or more right precordial leads (V_1 and V_2), followed by a symmetric negative T wave. This pattern, either spontaneous or drug-induced, is definitive for a BrS diagnosis.

However, ECG patterns in BrS can be dynamic and often not apparent. Increasing sensitivity for detecting the type 1 pattern includes elevating right precordial leads to the second intercostal space, EST, and using Holter monitoring. BrP can appear continuously, appear intermittently, or remain hidden, becoming apparent through factors that alter transmembrane ionic currents, such as vagal tone, increased body temperature, male sex hormones, and certain medications.[14] Clinical presentations vary widely, from palpitations to syncope, nocturnal agonal respiration, atrial fibrillation, ventricular arrhythmias/resuscitated SCD, or completely asymptomatic cases. However, symptoms are typically observed at rest and under vagal conditions, influenced by shifts in the sympathetic-parasympathetic balance, with hormonal, metabolic, and genetic factors also playing a role.[15-17]

ABBREVIATIONS AND ACRONYMS

BrP = Brugada pattern
BrS = Brugada syndrome
ECG = electrocardiogram/electrocardiography
EST = exercise stress testing
MAE = major arrhythmic event(s)
PVC = premature ventricular contraction
SCD = sudden cardiac death

12-LEAD HOLTER MONITORING WITH HIGH INTERCOSTAL LEAD

The 12-lead Holter/ECG monitor, especially with precordial leads positioned at higher intercostal spaces (second or third), is an increasingly recognized valuable tool for identifying intermittent or concealed type 1 BrP. Given the dynamic nature of BrS, where diagnostic ECG changes may fluctuate based on autonomic tone or circadian influences, continuous ambulatory monitoring offers a noninvasive strategy to improve detection.[18-20] Most recently, Yinadsawaphan et al[21] showed that a greater temporal burden of type 1 BrP—whether paroxysmal, persistent, or permanent—may be associated with a higher arrhythmic risk, reinforcing the value of serial or extended ECG monitoring in BrS. These findings collectively support the use of 12-lead Holter with high intercostal space lead placement as a high-yield diagnostic and prognostic tool in BrS.

METHODS

We conducted a structured literature search of MEDLINE and the Cochrane databases from inception through May 2024 using predefined search terms related to BrS, exercise, physical exertion, sport, and EST (Supplemental Appendix). Eligible studies included original human studies and case reports evaluating exercise or EST in patients with BrS or Brugada electrocardiographic patterns and reporting electrocardiographic, arrhythmic, diagnostic, or safety outcomes. Reviews, editorials, conference abstracts, animal studies, and studies without

relevant exercise-related outcomes were excluded (Supplemental Tables 1 and 2).

Studies were screened in 2 stages (title and abstract screening followed by full-text review) using predefined inclusion and exclusion criteria. Full-text papers were excluded if they did not involve patients with BrS or Brugada ECG patterns, did not include an assessment of exercise or EST, or did not report predefined outcomes of interest, including ECG changes, type 1 Brugada pattern unmasking, ventricular arrhythmias, syncope, or sudden cardiac arrest/death. The study selection process is summarized in a PRISMA flow diagram (Supplemental Figure 1), and a detailed list of full-text exclusions with corresponding reasons is provided in the Supplemental Appendix.

EXERCISE IN BrS

BRUGADA PATTERN IN ATHLETES. The necessity of ECG cardiac screening for athletes before sports participation remains unsettled in the medical community. The American Heart Association advises athlete screening through comprehensive history and physical examination without routinely using ECG.[22-25] In contrast, the European Society of Cardiology (ESC) strongly advocates for preparticipation ECG screening for athletes, supported by data from an Italian screening experience.[26,27]

"Athlete's heart" is characterized by increased wall thickness, left ventricular mass, and left ventricular diastolic cavity dimension. These characteristics arise from electrical and structural remodeling of the heart caused by prolonged sports training and autonomic modifications, which can frequently result in ECG abnormalities.[28-30]

Early repolarization often appears as an ST-segment upward displacement in precordial/inferior leads. Right precordial early depolarization, type 2, and type 3 BrP are commonly seen in trained athletes without clinical significance, attributed to hypervagotonia from athletic training adaptation.[28,31-33]

Some studies[34] suggest that acetylcholine can depress the action potential plateau in the isolated right ventricular epicardium by decreasing calcium current and/or increasing I_K current, causing an "upsloping" and "concave" ST-segment elevation that is reversible with atropine.[35] However, acetylcholine alone is unlikely to cause a loss of the action potential dome in vivo, as seen in the ventricular epicardium of BrS patients.[34] These findings may explain why early repolarization patterns in trained athletes do not progress to a coved-type BrS and are not associated with an increased risk of SCD.[31]

Although an ECG finding of right precordial ST-segment elevation in trained athletes may raise suspicion of BrS, it is crucial to focus on the differential diagnosis. Baseline ECG evaluations can reveal patterns such as early repolarization or an r'-wave on right precordial leads, making the exclusion of BrS both interesting and challenging.[29,32]

Zorzi et al[36] proposed criteria distinguishing the 2 conditions based on ST-segment elevation at the J point (STJ) and 80 ms after the J point (ST80). They found that 100% of BrS patients had a downsloping ST-segment (STJ/ST80 >1), while an upsloping ST-segment configuration (STJ/ST80 <1) showed high sensitivity (97%), specificity (100%), and diagnostic accuracy (98.7%) for early repolarization. This study only included athletes with type 1 BrP.

Additionally, healthy athletes may show an r'-wave in right precordial leads. In such cases, considering differential diagnoses for type 2 BrP is necessary as well. One assessment[37,38] is the "base of the triangle" criterion for athletes with r'-wave in V_1-V_2, showing high sensitivity (95.6%) and specificity (85%) for BrS recognition. They defined the "base of the triangle" at 0.5 mV of the r'-wave apex, considering type 2 BrP for a base duration ≥160 ms. These criteria provide useful ECG differentiation when an r'-wave is present in healthy athletes.

AUTONOMIC AND ELECTROPHYSIOLOGIC MECHANISMS OF EXERCISE AND RECOVERY IN BrS. SCD during sports often results from an interaction between underlying heart disease ("substrate") and transient acute abnormalities ("triggers") such as sympathovagal imbalance, electrolyte abnormalities, hemodynamic changes, myocardial ischemia, or emotional stress.[39]

Because BrS involves the loss of the action potential dome in the ventricular epicardium, leading to ST-segment elevation and creating a vulnerable window for VA,[35] particularly at rest, Matsuo et al[15] suggested that increased nocturnal vagal activity and withdrawal of sympathetic activity may play an important role in the arrhythmogenesis of BrS, explaining the circadian pattern of VA.

Miyazaki et al[40] also found that beta-adrenoceptor stimulation with isoproterenol reduces ST-segment elevation, whereas muscarinic stimulation with edrophonium increases it. These effects may explain why ST-segment elevation occurs only in 1.0% of patients during exercise but in more than 25.5% of patients during recovery or vagal reactions.[35,41-43] The augmentation during peak exercise is most consistent with rate-dependent depolarization delay in patients with limited Na^+ channel reserve, rather

than a dominant repolarization-worsening effect. Recovery from exercise, marked by a vagal reaction, especially in highly trained athletes, can enhance vagal tone,[44] increasing ST-segment elevation by decreasing heart rate or inhibiting the calcium current. Therefore, heart rate during EST can be a useful parameter for evaluating cardiovascular autonomic function.[42,45,46]

The arrhythmic events associated with BrS occur most often at night or at rest, unlike the majority of arrhythmias responsible for SCD, which are precipitated by a surge in sympathetic activity, suggesting a link between BrS and the autonomic nervous system (ANS).[15] BrS patients, particularly those in Thailand,[47] showed higher parasympathetic activation during exercise recovery compared with baseline, a smaller level of sympathetic activation during recovery than control subjects, and significantly lower peak heart rates, heart rate recovery, and peak oxygen consumption.

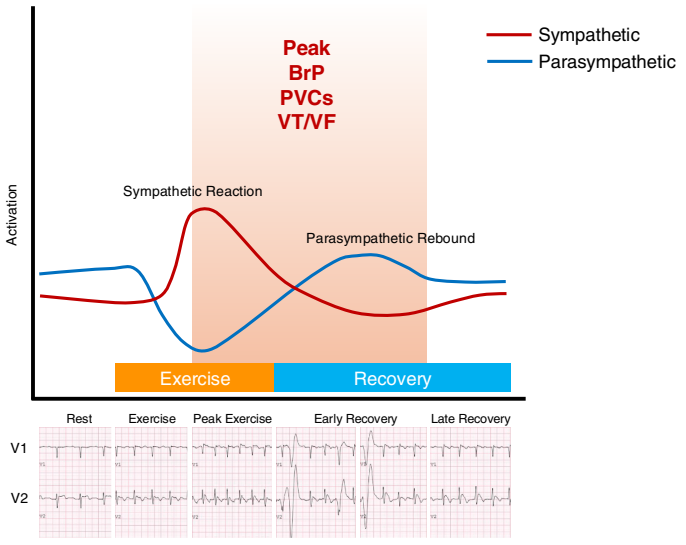
Moreover, the electrocardiographic pattern of BrS is attenuated by exercise or isoproterenol but may be unmasked or intensified by antiadrenergic pharmaceuticals or alpha-adrenergic receptor stimulation. Noninvasive radionuclide techniques have revealed that ANS dysfunction is an important contributor to the electrical instability of BrS.[48] However, studies of heart rate variability, a noninvasive marker of cardiac autonomic tone, have yielded conflicting results.[48]

Miyazaki et al[40] also shows that the electrocardiographic characteristics of BrS fluctuate over time and are influenced by exercise and pharmacological interventions that interact with cardiac autonomic activity. However, Behar et al[49] found that ANS modulation analysis did not identify sensitive predictors of arrhythmic events in BrS patients, but noted greater sinus node response fluctuations in symptomatic patients.

Pichara et al[43] reported similar findings on the effectiveness of using EST during the recovery phase to unmask type 1 Brugada pattern, particularly with high lead placement in the supine position. This rapid restoration of parasympathetic activity and reduced sympathetic response postexercise (**Figure 1**) highlight the complexity of using EST for risk stratification and diagnosis in BrS, warranting further investigation (**Central Illustration**).

EXERCISE-INDUCED ARRHYTHMIC EVENTS AND SAFETY OF EST IN BrS. As previously noted, major arrhythmic events (MAE) (defined as sustained ventricular tachycardia [VT], ventricular fibrillation [VF], or any undocumented rhythm leading to SCD) in BrS occur at rest. However, there have been several reports of syncope and MAE occurring during exercise in BrS patients: a 30-year-old endurance cyclist experiencing episodes of syncope during exercise[50]; a 20-year-old man presenting with sudden cardiac arrest while running[51]; a 20-year-old man presenting with monomorphic VT and syncope during exercise[52]; an 18-year-old man with spontaneous type 1 BrP presenting with sudden cardiac arrest requiring cardiopulmonary resuscitation during exercise, who underwent an EST and developed sustained monomorphic VT during stage 3 of exercise, initiated by a premature ventricular contraction (PVC), which resolved after exercise was terminated[53]; and a 41-year-old man developing type 1 BrP and sustained monomorphic VT during exercise phase which resolved spontaneously.[54] There is also a report of a pediatric BrS patient, an 11-year-old boy with type 2 BrP with syncope during exercise: EST exhibited type 1 BrP at stage 4 of the Bruce protocol and resulted in

FIGURE 1 Autonomic Balance During Exercise and Recovery in Brugada Syndrome



This schematic illustrates the dynamic interplay between sympathetic and parasympathetic activity during the exercise stress test and highlights the 2 distinct arrhythmogenic windows in Brugada syndrome. During peak exercise, strong sympathetic activation typically attenuates the surface type 1 Brugada pattern (BrP); yet, a subset of patients may develop rate-dependent depolarization delay (eg, S-wave upslope prolongation), which can precipitate ventricular arrhythmias despite the overall J-ST suppression. In contrast, the early recovery phase (first 1-3 minutes) is marked by abrupt sympathetic withdrawal and a surge in parasympathetic tone, leading to accentuated J-ST elevation, increased repolarization heterogeneity, and vulnerability to premature ventricular contractions (PVCs), phase 2 re-entry, and ventricular fibrillation (VF). Together, these mechanisms demonstrate that both peak exertion and early recovery carry arrhythmic potential, driven by distinct electrophysiologic and autonomic factors. The black arrow marks the start of the exercise stress test. The black arrow indicates the start of the exercise stress test. VT = ventricular tachycardia.

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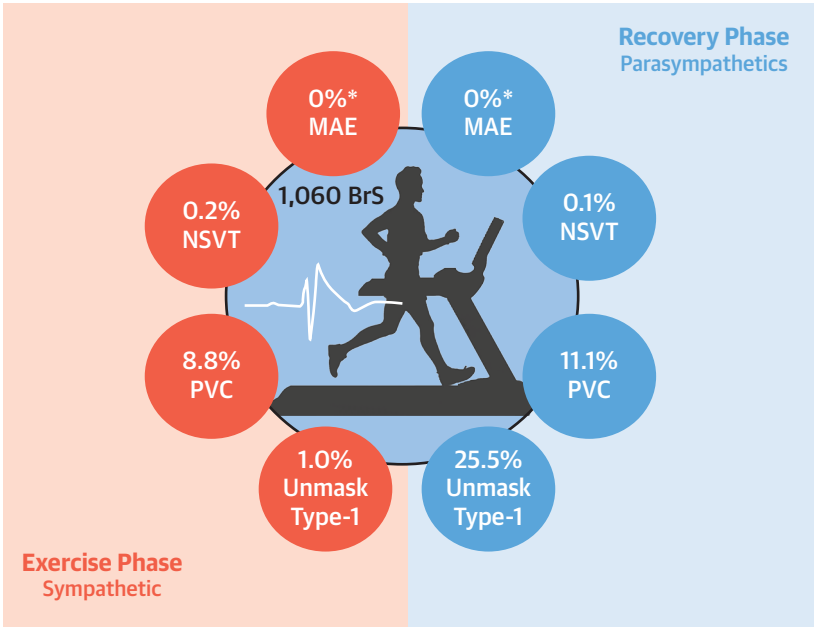
CENTRAL ILLUSTRATION **Autonomic Modulation of Brugada Electrocardiographic Patterns During Exercise and Recovery**



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Exercise stress testing may unmask type 1 Brugada electrocardiographic patterns and provoke arrhythmias during 2 distinct windows: 1) peak exertion, where rate-dependent depolarization delay can reveal conduction vulnerability; and 2) early recovery, where abrupt vagal rebound and repolarization abnormalities can accentuate J-ST elevation and increase arrhythmogenic risk. The illustration highlights these phase-specific mechanisms and summarizes the key diagnostic and prognostic implications of exercise stress testing in Brugada syndrome (BrS). (*Several case reports have described major arrhythmic events during peak exercise and early recovery). MAE = major arrhythmic events; NSVT = nonsustained ventricular tachycardia; PVC = premature ventricular contraction.

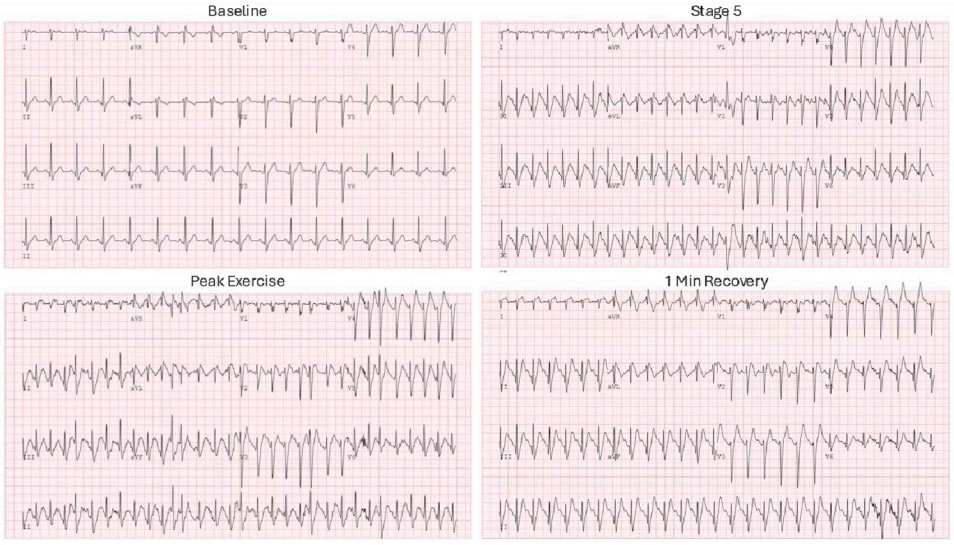
sustained pleomorphic VT. Genetic testing confirmed an *SCN5A* variant.[55]

In addition, BrS can overlap with idiopathic VT or VF. A 33-year-old man, initially diagnosed with idiopathic VT at age 13 years, was successfully treated with RF ablation and remained VT free for 20 years. At age 33 years, he presented with palpitations and an EST-induced monomorphic VT along with unmasking of a type 1 Brugada pattern. A pilsicainide challenge confirmed the BrS diagnosis.[56] This case suggests that EST may be beneficial in identifying BrS in similar situations.

Among 1,060 patients combined from 13 observational studies, no MAE (0%) were reported during EST.[42,43,45,47,49,57-63] Only 2 cases of nonsustained VT occurred at peak exercise (0.2%),[43] and 1 case (0.1%) was observed during early recovery. However, MAE were documented in 7 case reports,[53-56,64-66] suggesting that while rare, life-threatening arrhythmias can occur in certain high-risk individuals during the peak of exercise or during the early recovery phase (**Central Illustration**). These intervals represent the critical risk windows during EST in BrS and should therefore be closely monitored. Peak exercise events likely reflect rate-dependent depolarization/conduction vulnerability, whereas early recovery events are more strongly tied to repolarization augmentation and vagal rebound. This autonomic imbalance likely contributes to arrhythmogenesis in BrS and underscores the importance of vigilant monitoring at peak exercise and throughout early recovery in high-risk patients.

Although EST can induce ventricular arrhythmias, VF is uncommon. Sympathetic predominance during exercise, together with the gradual cool-down phase of standard protocols, may limit abrupt autonomic shifts and reduce repolarization heterogeneity, thereby decreasing the likelihood of arrhythmic degeneration. Notably, no major arrhythmic events were observed during EST across the included observational cohorts; however, this finding should be interpreted with caution, because the absence of observed events does not exclude a small but

FIGURE 2 **Type 1 Brugada Electrocardiographic Pattern Unmasked During Exercise Stress Testing**



Example of a type 1 Brugada electrocardiographic pattern unmasked during an exercise stress test. A coved-type ST-segment elevation in the right precordial leads emerged and peaked during the early recovery phase. This highlights the value of monitoring the recovery phase to detect concealed Brugada patterns in suspected cases.

nonzero risk. The upper confidence limit for rare events cannot be assumed to be zero, and clinically meaningful risk may still exist, particularly in the setting of limited sample sizes and heterogeneous study designs.

UNMASKING TYPE 1 BrP WITH EXERCISE. EST has been recognized as a valuable tool for unmasking the type 1 BrP, with cases reported during both[67-68] the exercise phase[54-56,69-72] and the recovery phase.[50,64,66-67,73-79] However, accumulating evidence suggests that the early recovery phase is the most critical period for revealing BrP (**Figure 2**). Makimoto et al[42] studied 93 patients with BrS who underwent an EST and found that ST segments were augmented in 37% of the patients during the early recovery phase, but none of the patients had ST-segment augmentation during exercise. EST with high lead placement during the passive recovery phase in the supine position has been shown to increase the detection of the type 1 Brugada ECG pattern by 32%.

Among 1,060 BrS patients included across the observational studies summarized in **Table 1**, only 1.0% exhibited a type 1 Brugada pattern (BrP) during exercise, with this estimate derived from 3 cohorts.[45,47,60] In contrast, a significantly higher proportion, 25.5%, had type 1 BrP unmasked during the recovery phase, based on 4 cohorts.[41-43,60] Notably, all patients who demonstrated type 1 BrP during exercise also exhibited the pattern in the early recovery phase.[54,56,69-72] These findings highlight the postexercise period as the optimal window for detecting BrP (**Figures 1 and 2**). For each descriptive aggregate estimate of major arrhythmic events and type 1 BrP unmasking, the contributing cohort studies and case reports are listed in **Tables 1 and 2**.

The mechanism underlying these findings appears to be linked to autonomic regulation. Recent findings by Chanavirut et al[47] further support this autonomic influence, demonstrating that BrS patients exhibit a more rapid restoration of parasympathetic tone and reduced sympathetic activation during the recovery period compared with control subjects. This enhanced parasympathetic rebound may explain why type 1 BrP is more frequently unmasked during early recovery than during exercise.

During the early recovery phase, a sudden shift from sympathetic to parasympathetic dominance may increase J-point elevation, making type 1 BrP more apparent.[50] This autonomic imbalance in BrS patients likely contributes to arrhythmogenic risk during the first 2 minutes of recovery, a period when most arrhythmias are reported. Given this strong autonomic influence, EST[43] should prioritize early recovery phase monitoring, because it provides the highest diagnostic yield for BrS detection (**Figure 1**).

TABLE 1 Summary and Baseline Characteristics of 13 Observational Cohort Studies and 21 Reports (22 Cases)

First Author, Year	Design	n	Age, y	Male	Symptomatic	Syncope	SCA/SCD/VF	Spontaneous Type 1 at Baseline
Amin et al,[45] 2009	Retrospective	50	42.5 ± 2.6	50 (100)	20 (40)	15 (30)	2 (4)	9 (18)
Behar et al,[49] 2016	Prospective	118	46.1 ± 13.7	89 (75.4)	40 (34)	23 (58)	8 (20)	39 (33.1)
Chanavirut et al,[47] 2016	Cross-sectional	11	50 ± 6	11 (100)	11 (100)	0 (0)	11 (100)	11 (100.0)
Furuhashi et al,[60] 2001	Prospective	6	50.2 ± 6	6 (100)	0 (0)	0 (0)	0 (0)	3 (50.0)
Leong et al,[59] 2021	Prospective	25	NA	19 (76)	11 (44)	0 (0)	15 (60)	3 (12)
Makimoto et al,[42] 2010	Prospective	93	46 ± 14	91 (97.8)	57 (61.3)	35 (37.6)	22 (23.7)	73 (78.5)
Morita et al,[41] 2020	Prospective	307	45 ± 12	299 (97.4)	88 (28.7)	75 (24.4)	13 (4.2)	219 (71.3)
Pichara et al,[43] 2023	Prospective	74	49 ± 14	57 (77)	11 (14.9)	5 (6.7)	3 (4.1)	58 (78.4)
Pospiech et al,[61] 2015	Prospective	46	49 ± 14	40 (87)	18 (39)	9 (19.6)	0 (0)	26 (56.5)
Romero et al,[62] 2020	Prospective	110	44.64 ± 13.66	82 (74.5)	25 (22.7)	14 (13)	11 (10.0)	34 (30.9)
Subramanian et al,[63] 2017	Prospective	75	49.1 ± 15.4	68 (90.7)	0 (0)	0 (0)	0 (0)	75 (100)
Tachibana et al,[57] 2017	Cross-sectional	110	NA	108 (98)	40 (36.4)	39 (35)	13 (12)	91 (82.7)
von Hafe et al,[58] 2021	Cross-sectional	35	53.9 ± 1	25 (71.4)	20 (57.1)	10 (28.6)	11 (31.4)	20 (57.1)
Case reports	Retrospective	21 reports (22 cases)	40.2 ± 14.9	20 (100)	10 (50)	2 (10)	1 (5.0)	3 (15.0)

Values are mean ± SD or n (%).
SCA = sudden cardiac arrest; SCD = sudden cardiac death; VF = ventricular fibrillation.

Of note, patients where a spontaneous type 1 BrP is only observed with high lead placement, standard lead positions during EST may unmask the pattern during the recovery phase.[74]

TRANSITION FROM SYMPATHETIC TO PARASYMPATHETIC. The dynamic nature of the type 1 BrP, especially during transition of sympathetic and parasympathetic balance, has been highlighted by a number of case reports. Power et al[80] reported a major arrhythmic event in a BrS patient who experienced sudden lightheadedness during basketball practice, attempted to sit down, and then lost consciousness. An athletic trainer promptly administered cardiopulmonary resuscitation, and an automated external defibrillator successfully restored sinus rhythm on the first attempt. The automated external defibrillator's stored electrogram recorded polymorphic VT deteriorating into VF. Similarly, Garcia-Borbolla et al[65] described a 38-year-old man who underwent an EST for chest pain evaluation. In this case, sustained monomorphic VT occurred during the early recovery phase, immediately after peak exertion, when sympathetic stimulation declined. The authors suggested that autonomic fluctuations, particularly the abrupt shift to vagal predominance, may have contributed to the development of arrhythmia. Ozeke et al[66] also reported an asymptomatic patient in whom type 1 BrP was unmasked, PVCs were observed, and sustained VT was induced during the early recovery phase of EST, further supporting the significance of this transition period in arrhythmogenesis.

In another case,[78] a patient with intermittent spontaneous type 1 BrP had less prominence of the pattern during exercise but saw it re-emerge with increased ST-segment elevation during early recovery.

Notably, all MAE during exercise occurred at peak exertion, whereas events during recovery were within the first 3 minutes of recovery. This pattern aligns with the underlying autonomic dysregulation in BrS, where the sudden shift from sympathetic activation to parasympathetic dominance during early recovery plays a key role in triggering PVCs and VT, which may degenerate into VF (**Figure 1**, **Central Illustration**).

Autonomic modulation is a critical determinant of arrhythmogenesis in BrS. During exercise, sympathetic stimulation enhances Na^+ and Ca^{2+} channel activity, which typically suppresses the surface expression of the type 1 BrP. This attenuation of J-ST elevation occurs in the majority of patients; however, a small subset (~1.0%) demonstrate ST/J augmentation during peak exercise, likely caused by rate-dependent depolarization abnormalities. In contrast, the abrupt parasympathetic rebound during recovery may reduce Na^+ channel availability, increasing repolarization heterogeneity and facilitating phase 2 re-entry, a well-established mechanism for VF initiation in BrS patients.

Pospiech et al[61] explored the impact of exercise on the V_1 β angle in BrS, highlighting its potential role in distinguishing BrS from incomplete right bundle branch block. In healthy individuals, the β angle exhibited a dynamic response, with a significant reduction at peak exercise followed by a rapid return to baseline during recovery. In contrast, BrS patients displayed a less pronounced β angle reduction during

exercise, along with a postexercise "latency" effect, where the β angle remained elevated compared with incomplete right bundle branch block, even though the postexercise increase was not statistically significant. These findings suggest that β angle dynamics during and after exercise may serve as a novel diagnostic marker, further refining the distinction between BrS and incomplete right bundle branch block in challenging cases.[61]

MECHANISMS OF EXERCISE VS RECOVERY ARRHYTHMIAS. In BrS, arrhythmias provoked during exercise and those triggered during the early-recovery phase arise from distinct electrophysiologic mechanisms. Ventricular arrhythmias occurring during exercise are thought to reflect rate-dependent depolarization abnormalities, where heightened sympathetic activation and increased heart rate unmask Na^+ channel dysfunction and exacerbate conduction delay in the right ventricular outflow tract.[41,42] In contrast, arrhythmias arising in the early-recovery phase appear more strongly linked to abrupt sympathetic withdrawal and parasympathetic rebound, which can intensify epicardial-endocardial heterogeneities and re-entrant vulnerability. Early recovery has been identified as a particularly arrhythmogenic window in BrS, with ST-segment augmentation and exercise-induced type 1 BrP frequently observed.[45,46] Taken together, these findings support a mixed depolarization-repolarization framework[81,82] for exercise-related ECG changes in BrS, operating in a phase-specific manner across peak exertion and early recovery. Recognizing these divergent mechanisms may have important implications for risk stratification, interpretation of EST, and counseling regarding exertion-related triggers in BrS.

GENOTYPE AND EST RESPONSE IN BrS. Although genetic testing provides important diagnostic and prognostic information in BrS, current evidence does not demonstrate a consistent genotype-phenotype relationship with respect to ECG behavior during EST. The only study directly evaluating genotype during EST showed that *SCN5A*-positive patients exhibited greater conduction slowing at higher heart rates, manifested as more pronounced QRS widening.[45] However, this conduction difference did not translate into predictable variation in the characteristic EST response and our reviews similarly highlight the absence of such evidence. Taken together, these data suggest that while *SCN5A* variants may influence myocardial conduction reserve, current literature does not support a clinically meaningful genetic effect on the BrP's modulation during EST.

PROGNOSTIC VALUE OF EST IN BrS. Symptomatic and asymptomatic BrS patients exhibit significantly different ventricular depolarization dynamics, particularly during exercise and even more prominently in the recovery phase.[62] Amin et al[45] demonstrated the aggravation of augmenting type 1 BrP during an EST. EST, when combined with drug challenge testing, may serve as a valuable tool for improving diagnostic accuracy, particularly in ruling out BrS. This was demonstrated in a 54-year-old asymptomatic male *SCN5A* variant carrier who underwent a flecainide challenge test, which yielded negative results. Subsequent EST also failed to reveal ST-segment elevation or unmask a type 1 BrP, further supporting its role in excluding a BrS diagnosis in certain cases.[55] Makimoto et al[42] found that augmentation of ST-segment elevation during early recovery was a significant and independent predictor of cardiac events and concluded that this phenomenon is specific to patients with BrS and may serve as a marker of poor prognosis.

A greater heart rate recovery during EST was observed exclusively in patients with a history of VF, suggesting a potential link between autonomic function and arrhythmic risk.[49] Early heart rate recovery is primarily driven by parasympathetic reactivation, indicating that these patients may have either heightened parasympathetic activity or an increased sensitivity to vagal stimulation during recovery. An important study by Morita et al[41] investigated 307 BrS patients who underwent EST to assess the occurrence of PVCs across different phases—rest, exercise, and recovery. Over a follow-up period of 92 ± 68 months, 30 patients experienced VF. PVCs were observed in approximately 27% of patients, occurring most frequently during exercise (20%), followed by 9% within 0 to 1.5 minutes postexercise, 6% during the early recovery phase (1.5-3.0 minutes), and 4% during late recovery (3.0-5.0 minutes). Notably, only PVCs arising during the early recovery phase (1.5-3.0 minutes)—and not those immediately after exercise—were independently associated with future VF events on multivariable analysis. These findings underscore the importance of autonomic rebound during early recovery and suggest that PVCs in this window may serve as a clinically meaningful marker for risk stratification in BrS, helping to identify patients at higher risk for MAE.[41]

A study on EST in asymptomatic type 1 BrP patients identified key predictors of MAE, including SCD and VF, over a 77.9 ± 28.9-month follow-up. Multivariate analysis found 3 independent risk factors, one of which was a >30% increase in S-wave upslope duration at peak exercise, indicating rate-

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TABLE 2 22 Case Reports Describing Type 1 Brugada Pattern or Ventricular Arrhythmias During Exercise or Recovery

First Author	Year	Sex	Age, y	Symptomatic	Spontaneous Type 1	Previous MAE	Family History	Type 1 at Peak	Type 1 at Recovery
Drug-induced type 1									
Aboyme et al[69]	2022	Male	24	NR	NR	NR	R	R	NR
Archontakis et al[73]	2011	Male	43	NR	NR	NR	NR	NR	R
Burkle et al[64]	2016	Male	46	R	NR	NR	R	NR	R
Garcia-Fuertes et al[74]	2016	Male	19	NR	NR	NR	NR	NR	R
Goto et al[54]	2015	Male	41	R	NR	NR	NR	R	NR
Grimster et al[75]	2008	Male	33	NR	NR	NR	NR	NR	R
Guevara-Valdivia et al[70]	2003	Male	38	R	NR	NR	R	R	NR
Jayasuriya et al[76]	2011	Male	34	R	NR	NR	NR	NR	R
Ozeke et al[66]	2009	Male	59	NR	NR	NR	NR	NR	R
Papadakis et al[67] (A)	2009	Male	36	NR	NR	NR	R	R	R
Papadakis et al[67] (B)	2009	Male	56	NR	NR	NR	R	NR	R
Safabakhsh et al[68]	2021	Male	46	NR	NR	NR	NR	R	R
Stroker et al[71]	2016	Male	49	R	NR	NR	NR	R	NR
Tan et al[55]	2016	Male	21	R	NR	NR	NR	R	–
Tijskens et al[72]	2019	Male	52	NR	NR	NR	NR	R	NR
Yuasa et al[56]	2014	Male	33	R	NR	R	NR	R	NR
Zou et al[77]	2021	Male	50	R	NR	NR	R	NR	R
Spontaneous type 1									
Batra et al[53]	2019	Male	18	R	R	R	NR	–	–
Esperer et al[50]	2007	Male	30	R	R	NR	NR		R
Garcia-Borbolla et al[65]	2007	Male	38	NR	R	NR	R	–	–
Guevara-Valdivia et al[78]	2001	Male	28	R	R	NR	NR		R
Ishibashi et al[79]	2017	Male	51	NR	R	NR	R		R

TABLE 2 Continued

First Author	VT/VF at Peak	VT/VF at Recovery	PVC/NSVT at Peak	PVC/NSVT at Recovery	Drug-Induced Type 1	Drug-Induced PVC/VT	Inducible VT/VF	VT/VF at Follow-up
Drug-induced type 1								
Aboyme et al[69]	NR	NR	NR	NR	–	–	–	–
Archontakis et al[73]	NR	NR	NR	NR	R	NR	–	NR
Burkle et al[64]	NR	NR	NR	R	R	R	R	NR
Garcia-Fuertes et al[74]	NR	NR	NR	NR	R	NR	R	–
Goto et al[54]	R	NR	NR	NR	R	NR	R	NR
Grimster et al[75]	NR	NR	NR	NR	–	–	–	–
Guevara-Valdivia et al[70]	NR	NR	NR	NR	–	–	NR	NR
Jayasuriya et al[76]	NR	NR	NR	NR	–	–	R	–
Ozeke et al[66]	NR	R	NR	R	–	–	NR	NR
Papadakis et al[67] (A)	NR	NR	NR	NR	R	NR	–	–
Papadakis et al[67] (B)	NR	R	NR	NR	R	NR	–	–
Safabakhsh et al[68]	NR	NR	NR	NR	R	NR	–	–
Stroker et al[71]	NR	NR	NR	R	R	NR	–	NR
Tan et al[55]	R	–	NR	–	–	–	–	–
Tijskens et al[72]	NR	NR	NR	NR	R	NR	NR	NR
Yuasa et al[56]	R	NR	R	NR	R	R	R	–
Zou et al[77]	NR	NR	NR	R	NR	NR	R	R
Spontaneous type 1								
Batra et al[53]	R	NR	NR	NR	–	–	R	–
Esperer et al[50]	NR	NR	NR	NR	–	–	R	NR
Garcia-Borbolla et al[65]	NR	R	NR	NR	–	–	NR	NR
Guevara-Valdivia et al[78]	NR	NR	NR	NR	–	–	R	NR
Ishibashi et al[79]	NR	NR	NR	NR	–	–	R	NR

MAE = major arrhythmic event; NR = no reported; NSVT = nonsustained ventricular tachycardia; R = reported; PVC = premature ventricular contraction; VT = ventricular tachycardia.

dependent depolarization delay during peak exertion. In the same study, repolarization abnormalities and autonomic dysfunction were reflected by J-point elevation in aVR >2 mm during late recovery and delayed heart-rate recovery, emphasizing that both peak exercise and the early-recovery phase contribute meaningful prognostic information and reinforce the value of EST in BrS risk stratification.[63] These predictors illustrate that EST captures both depolarization-based vulnerability at peak exercise and repolarization/autonomic vulnerability during recovery. This autonomic imbalance could contribute to arrhythmogenesis in BrS, reinforcing the need for careful monitoring at peak and postexercise in high-risk individuals (**Figure 1**, **Central Illustration**).

STUDY LIMITATIONS. Exercise-induced type 1 BrP can be challenging to interpret, particularly in patients with multiple comorbidities, such as coronary artery disease or vasospasm.[83] Therefore, interpretation should be made cautiously on a case-by-case basis. Most cases of type 1 BrP caused by other etiologies, or Brugada phenocopy, can be distinguished through a drug challenge test. If an EST reveals a BrP, but type 1 BrP fails to appear with Na^+ channel-blocking drug challenge testing, the most likely explanation is underlying coronary artery[84,85] disease or vasospasm.[86]

Last, the aggregate estimates from our review should be interpreted with caution, as they represent descriptive pooling across heterogeneous studies rather than results from a formal meta-analysis. Exercise protocols, ECG lead placement, recovery-phase monitoring, and outcome definitions varied across cohorts, which may have influenced the observed event rates.

CONCLUSIONS

EST in BrS appears to be a useful *adjunctive* tool for diagnostic evaluation and risk assessment, particularly for unmasking the type 1 Brugada pattern during the early recovery phase, when autonomic fluctuations—especially parasympathetic rebound—may contribute to arrhythmogenesis. Observational studies suggest that several exercise-related parameters, assessed at peak exercise and during early recovery, are associated with an increased risk of major arrhythmic events, including prolonged S-wave upslope duration at peak exercise (a marker of rate-dependent depolarization delay), J-point elevation in lead aVR >2 mm, delayed heart-rate recovery, and PVCs during early recovery, which may reflect repolarization abnormalities and autonomic imbalance.

Importantly, PVCs during early recovery have been identified in observational cohorts as a potential marker of heightened arrhythmic vulnerability, possibly related to increased repolarization heterogeneity and phase 2 re-entry mechanisms. These findings underscore the importance of continued ECG monitoring during the recovery phase, because clinically relevant arrhythmic manifestations may not be apparent during exercise alone.

Although exercise-induced ventricular arrhythmias are uncommon, isolated case reports describe sustained VT or VF during exertion in selected high-risk individuals, highlighting the need for individualized clinical assessment. In addition, EST may aid in distinguishing BrS from incomplete right bundle branch block and Brugada phenocopies, particularly when interpreted alongside sodium-channel blocker challenge testing. Modified protocols, including high precordial lead placement and passive supine recovery, may further enhance the detection of type 1 Brugada patterns and improve diagnostic sensitivity.

Overall, current evidence suggests that EST may serve as a complementary, noninvasive modality to refine diagnostic assessment and support risk stratification in patients with BrS. For now, its clinical utility should be interpreted in the context of heterogeneous observational data, and prospective, standardized studies are needed to validate these findings and define the role of EST in routine clinical practice.

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ADDRESS FOR CORRESPONDENCE: Dr Pattara Rattanawong, Pali Momi Medical Center, Hawai'i Pacific Health, Aiea, Hawaii 96701, USA. E-mail: pattara.rattanawong@hphmg.org.

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KEY WORDS Brugada, exercise, sudden cardiac death

APPENDIX For a supplemental figure and tables, please see the online version of this paper.