

# Asymptomatic Brugada syndrome: Navigating implantable cardioverter-defibrillator implantation dilemma



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## Introduction

Brugada syndrome (BrS) is an inherited disease that heightens the risk of developing ventricular arrhythmias (VAs) and sudden cardiac death (SCD) in individuals with structurally normal hearts. Although patients presenting with aborted SCD or documented spontaneous sustained ventricular tachycardia (VT) have a clear indication for an implantable cardioverter-defibrillator (ICD),<sup>1</sup> arrhythmic risk stratification and management of asymptomatic patients or those with syncope remain challenging. An implantable loop recorder (ILR) may have a significant role in this subgroup of patients.

## Case report

A 50-year-old man, a professional truck driver, was diagnosed with asymptomatic spontaneous type 1 BrS (Figure 1). His genetic test revealed a variant of uncertain significance in the SCN5A gene (NP\_932173.1:p.His880Asp, NM\_198056.2:c.2638C>G, NC\_000003.11:g.38627331 G>C) in heterozygosity. He had no family history of SCD or BrS. His Shanghai score was 3.5. His transthoracic echocardiography showed a nondilated left ventricle with preserved ejection fraction (57%) and no other abnormalities. Cardiac magnetic resonance was remarkable for a right ventricle with dimensions within the superior level (indexed end-diastolic volume 110 mL/m<sup>2</sup>), with normal ejection fraction (50%) and dyskinesia of the apical segment of the free

## KEY TEACHING POINTS

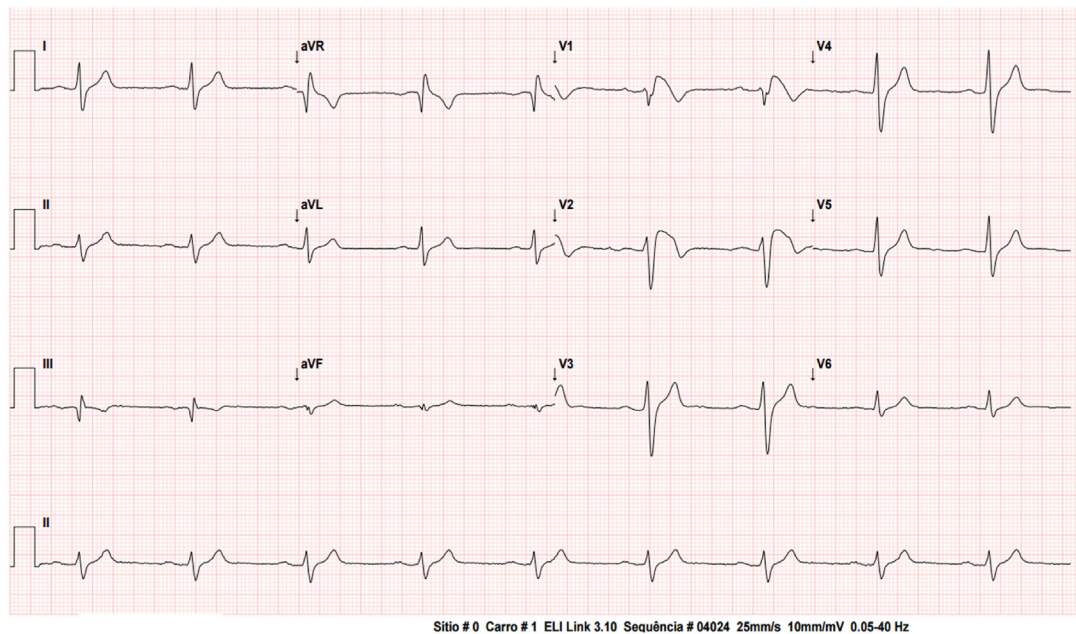
- Risk stratification and management of patients with asymptomatic Brugada syndrome (BrS) remain challenging.
- Although implantable loop recorders (ILR) are recommended for unexplained syncope, their role in asymptomatic patients is less clear; they may assist in identifying patients at higher risk for sudden cardiac death, thereby guiding treatment decisions.
- The ILR's value in detecting otherwise missed arrhythmic events is highlighted in a case where an ILR revealed a significant arrhythmic event in a patient with asymptomatic BrS who had a positive genetic test, leading to the timely implantation of an implantable cardioverter-defibrillator.
- This case underscores the lack of validated tools for risk assessment in patients with asymptomatic BrS; the importance of coupling several arrhythmic risk factors; and the significance of employing a comprehensive approach, incorporating ILR monitoring, for assessing arrhythmic risk in individuals with BrS exhibiting intermediate risk levels.

**KEYWORDS** Asymptomatic Brugada syndrome; Ventricular arrhythmia; Implantable cardioverter-defibrillator; Implantable loop recorder; Sudden cardiac death

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wall. There was no evidence of late gadolinium enhancement. Twenty-four-hour Holter monitoring showed sinus rhythm with first-degree atrioventricular block and no VAs. The treadmill stress test was unremarkable, with no VAs. Considering all the above, an electrophysiological study (EPS) was initially proposed, but the patient refused. After



**Figure 1** Electrocardiogram revealing sinus rhythm, heart rate 51 beats/min, first-degree atrioventricular block, ST-elevation in V<sub>1</sub> and V<sub>2</sub> and fragmented QRS in V<sub>1</sub> and aVF, compatible with type 1 Brugada pattern.

discussing the options with the patient, he agreed to an ILR implantation (Reveal Linq; Medtronic, Minneapolis, MN).

The patient remained asymptomatic after having an ILR for 20 months. However, during remote telemonitoring, a 9-second run of a very fast polymorphic VT was detected (Figure 2). On questioning, the patient admitted to feeling light-headed during the event while resting in an upright position. As a result, a transvenous single-chamber ICD was implanted (RESONATE EL ICD VR DF4; Boston Scientific, Marlborough, MA).

This case highlights the difficult decision to perform ICD implantation in the context of primary prevention in patients with BrS and the potential role of the ILR in the selection of patients who may benefit from it. The importance of the ILR in this case is worth noting, given that the VT was short duration and the patient reported only light-headedness, which could have been easily disregarded.

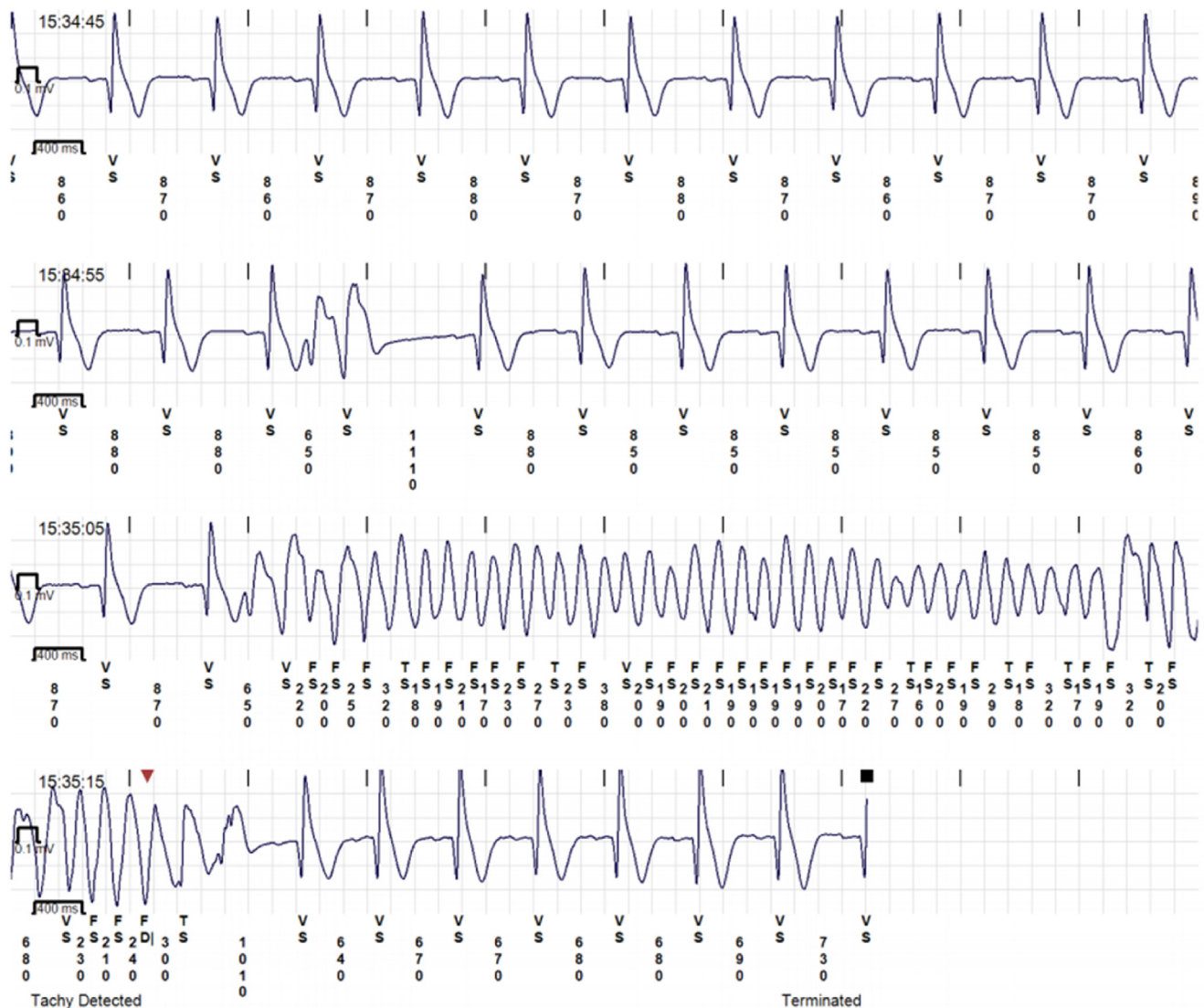
## Discussion

BrS is an inherited disorder that predominantly affects males, with a lifelong incidence of life-threatening VAs estimated at approximately 5%–10%, often occurring as the initial manifestation of the condition.<sup>2,3</sup> Although most patients (approximately 63%) are asymptomatic at the time of diagnosis, major arrhythmic events can develop at a rate of 12% over 10 years.<sup>4</sup> Fatal arrhythmias typically manifest during periods of rest or sleep, indicating a potential connection with bradycardia or vagal events. Precisely identifying and treating individuals at an elevated risk of SCD pose significant challenges in their clinical care. Several risk factors for arrhythmic

events have been identified, but the most robust predictors are a spontaneous type 1 Brugada electrocardiogram pattern and presumed arrhythmogenic syncope.<sup>2,5</sup>

Although ICD implantation for SCD prevention is recommended in patients with BrS who experienced aborted SCD or have documented spontaneous sustained VT (class I recommendation),<sup>1</sup> risk stratification and treatment management of asymptomatic patients or those with syncope remain challenging.<sup>6</sup> Several risk scores for predicting arrhythmic events in BrS exist,<sup>2,7,8</sup> however, none allows stratifying those with intermediate risk.<sup>9</sup> An increase in the cumulative Shanghai score was found to be generally associated with a heightened risk of life-threatening arrhythmias, with no malignant events occurring if scoring <3.5.<sup>8</sup> Nonetheless, there are currently no recommendation of ICD implantation based on a Shanghai score cutoff because even low- to moderate-risk patients may have VAs, such as our patient. The Predicting Arrhythmic Event score was recently created and validated and found to be useful in predicting major arrhythmic events for primary prevention in patients with BrS.<sup>4</sup> Despite its wider inclusion of several risk factors and its better performance in predicting arrhythmic events compared with other scores, it needs further validation studies.

Drug-provocation and exercise tests have been suggested to improve risk stratification in asymptomatic patients with BrS, but there is no consensus or guideline recommendation for their routine use in assessing arrhythmic risk. Ajmaline and flecainide are commonly used, but procainamide is the only option in some countries. However, it has been found that the outcome of the pharmacologic test was significantly influenced by the drug used, with ajmaline more likely to provoke a type 1 Brugada pattern compared with procainamide,



**Figure 2** Implantable loop recorder telemonitoring sheet revealing a short run of polymorphic ventricular tachycardia (9 seconds).

raising concerns about the diagnostic accuracy of these tests,<sup>10</sup> with nearly 25% of them yielding false-negative results.<sup>3</sup> In contrast to drug-provocative testing, there are limited data on the role of exercise testing in BrS.<sup>11</sup> A study identified the following 3 independent predictors of increased arrhythmic risk in asymptomatic patients with spontaneous type 1 BrS: (1) increased S-wave upslope duration ratio in peak exercise; (2) augmentation of the J-point during late recovery in lead aVR, but not conventional precordial leads; and (3) delayed heart rate recovery during late recovery.<sup>11</sup> In addition, augmentation of ST-segment elevation during early recovery from exercise testing was found to be a strong predictor of spontaneous ventricular fibrillation, especially for asymptomatic patients or patients with syncope.<sup>12</sup>

Electrophysiological testing's value in arrhythmic risk assessment is controversial. It may identify asymptomatic patients at risk and aid in investigating syncope unrelated to VAs.<sup>13,14</sup> Asymptomatic patients with spontaneous type

1 Brugada pattern and positive EPS have been found to have significantly higher event rates than patients with negative EPS.<sup>15</sup> However, evidence suggests that symptomatic patients may develop arrhythmias more easily during EPS,<sup>6,16</sup> which is an independent predictor of shock occurrence, and a negative EPS has a negative predictive value for VAs in patients with BrS with syncope.<sup>17</sup> Expert consensus and guidelines neither strongly encourage nor discourage testing for BrS, suggesting consideration of an ICD in cases of inducible VAs.<sup>1</sup> In our case, the patient refused EPS, which could have led to earlier ICD implantation.

Syncope is common in BrS, affecting nearly one-third of patients. However, defining the arrhythmic origin of syncope is challenging because it may result from both bradyarrhythmias and tachyarrhythmias, and relies on the patient's description of the event.<sup>18</sup> Although often, vasovagal syncope, or syncope due to orthostatic hypotension,



has a good prognosis,<sup>3,6</sup> it remains an indisputable risk factor, especially when associated with type 1 BrS. Type 1 BrS with unexplained syncope or asymptomatic spontaneous type 1 pattern carries moderate VA risk.<sup>19</sup> Guidelines recommend ICD implantation for type 1 Brugada pattern with arrhythmic syncope due to significantly increased risk compared with asymptomatic patients (class IIa recommendation).<sup>1</sup>

Given the uncertainty around syncope or near-syncope in these patients, ILRs are advocated for investigating symptoms like palpitations in high-risk individuals when comprehensive evaluation has not revealed a cause or led to treatment.<sup>6</sup> Although in low-risk patients with asymptomatic SCD, ILR implantation has been found to offer only modest benefits, given the low rate of detected arrhythmias (0.5%)<sup>15,18</sup>; in low-risk patients with symptomatic SCD, ILRs play a crucial role in linking symptoms to suspected VAs (1.9% of VAs in patients with syncope).<sup>5,6,17,19,20</sup> Arrhythmia detection changes management for 20%–57% of patients with BrS with unexplained syncope or palpitations,<sup>3,5,6,18</sup> with VAs being detected in only 7% of cases, leading to ICD implantation in 8% of symptomatic patients and in 1% of asymptomatic patients. Detecting arrhythmias associated with these symptoms before SCD is vital, and ILRs aid in ruling out VAs as the cause of atypical syncope, potentially leading to reconsidering and suspending ICD implantation.<sup>5,19,20</sup> Therefore, the existing evidence reinforces current guideline recommendations favoring early ILR implantation in the assessment of unexplained syncope in patients with BrS (class IIa recommendation).<sup>1</sup> However, there are no recommendations regarding ILR implantation in asymptomatic patients, considering their apparently low risk of developing SCD; yet it might be considered when coupled with high-risk arrhythmic features, such as a family history of SCD,<sup>5</sup> older age,<sup>18</sup> positive EPS, and positive genetic testing, mainly presence of SCN5A gene variants,<sup>21,22</sup> such as in our patient. This approach can detect asymptomatic short runs of VAs that might otherwise go unnoticed<sup>23</sup> and prompt ICD implantation.

In our case, the implantation of the ILR played a pivotal role in detecting VT, which was particularly noteworthy as it occurred when the patient was upright and reported only near syncope. This underscores the potential for misdiagnosing this event as vasovagal syncope, highlighting the importance of the ILR in accurate diagnosis.

Interestingly, the median time from implantation to actionable events can range from 1 to 68 months,<sup>6,19,20</sup> similar to what happened in our patient at 20 months. This suggests that in some cases prolonged monitoring may be necessary,<sup>6</sup> further strengthening ILR value.

Considering all the above, selecting asymptomatic patients for primary prevention ICD implantation in BrS poses challenges, considering potential complications. Indeed, inappropriate ICD interventions and device-related issues can lead to significant morbidity.<sup>13,24</sup>

Besides ICDs, drugs, and lifestyle changes to prevent arrhythmias, ablation has been suggested as a possible thera-

peutic option, with some studies indicating that identifying and eliminating the arrhythmic electrophysiological substrate, often located in the right ventricular anterior wall and outflow tract, can normalize the electrocardiogram and prevent arrhythmias.<sup>25</sup> However, there is currently no role for substrate ablation in asymptomatic patients.<sup>1</sup>

Our patient was a professional truck driver, yet he has a disease with an increased risk of SCD. Due to the potential for decompensation while driving, many jurisdictions impose driving restrictions for patients with ICDs. However, there are no legal considerations regarding professional driving in patients without ICD with certain diseases associated with an increased risk of sudden cardiac events. This is a matter of political and ethical concerns for which there is currently no universal legislation.

Our patient had a spontaneous type 1 Brugada pattern, QRS fragmentation, a type 1 pattern in peripheral leads, and the presence of a SCN5A gene variant, all of which may contribute to a moderate arrhythmic risk. However, because he was asymptomatic, an EPS was initially proposed, which the patient refused, and the decision to proceed to ILR implantation was not completely clear. Although ILR implantation should be considered in patients with BrS with unexplained syncope, its role in asymptomatic patients is less clear. Yet, it may aid in risk re-stratification by detecting brief episodes of potentially fatal VAs, which could otherwise be missed in asymptomatic patients with BrS with arrhythmic risk factors,<sup>23</sup> such as positive genetic testing.

## Conclusion

Although current guidelines suggest ILRs in many borderline situations, a more extensive and timely use of these devices should be advisable to obtain a more reliable arrhythmic risk stratification in asymptomatic patients with BrS,<sup>23</sup> especially in those with arrhythmic risk factors.

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