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Potential triggering of repetitive nonreentrant ventriculoatrial synchrony by loss of atrial capture

Asli Inci Atar MD[1] | Ilyas Atar MD[2]

[1]Department of Cardiology, Ankara City Hospital, Ankara, Turkey

[2]Department of Cardiology, Ankara Guven Hospital, Ankara, Turkey

Correspondence
Asli Inci Atar, Ankara City Hospital, Universiteler Mahallesi, 1604 Cadde, No:9 Çankaya, Ankara, Turkey.
Email: asliatar@gmail.com

Abstract

Background: Data on the factors that trigger repetitive nonreentrant ventriculoatrial synchrony (RNRVAS) are limited. We hypothesize that loss of atrial capture may trigger RNRVAS. We aimed to use an atrial threshold test to observe the development of RNRVAS upon loss of atrial capture in patients with implantable cardiac electronic devices (CIED).

Methods: Patients with DDD mode CIEDs [177 patients, 67.5 ±14.8 (70) years; 70 women] were included. Atrial threshold test was done in DDD mode at a rate at least 10 beats above the basal heart rate, with an AV delay of 300 ms (range 250–350). A multivariable logistic regression model was used to assess the independent predictors of RNRVAS.

Results: RNRVAS was observed in 69 of the 177 patients (39.0%) during atrial threshold test. In patients with VA conduction, incidence of RNRVAS increased to 76.7%. In univariate analysis, younger age ($p = .038$) and the presence of VA conduction ($p < .001$) were associated with an increased risk of RNRVAS, whereas complete AV block or any AV node conduction defect ($p < .001$) and the ventricular pacing ratio ($p = .001$) were inversely related to the risk of RNRVAS occurrence after loss of atrial capture. In multivariate analysis complete AV block ($p = .009$) and ventricular pacing ratio ($p = .029$) appeared as independent factors inversely related to the risk of RNRVAS development.

Conclusion: In this study, we demonstrated that loss of atrial capture results in RNRVAS in one-third of patients with a CIED in DDD mode, and in three-fourths of those with VA conduction under certain predisposing CIED settings.

KEYWORDS
atrial capture test, cardiac implantable electronic device, endless loop tachycardia, loss of atrial capture, repetitive nonreentrant ventriculoatrial synchrony

1 | INTRODUCTION

Endless loop tachycardia (ELT) (Barold, 1991; Barold & Levine, 2001) and repetitive nonreentrant VA synchrony (RNRVAS) (Barold, 1991; Barold & Levine, 2001) are the two types of pacemaker-mediated tachycardias that are seen in patients with retrograde ventriculoatrial (VA) conduction. Thanks to ever-improving technology and algorithms associated with the implantable cardiac electronic

devices (CIED), it is possible to prevent or stop ELT, which is a well-studied and characterized condition. The data on RNRVAS is limited due to its lower occurrence rates, however, studies suggest that RNRVAS may trigger atrial fibrillation (Barold et al., 2012; Gjermeni et al., 2021; Kaufman et al., 2012; Sharma et al., 2016).

Atrial fibrillation, atrial tachycardia and related atrial rhythms recorded by CIEDs are classified as 'atrial high-rate events' (AHRE) and increased rate of strokes were shown to correlate with the presence of AHRE during CIED controls (Bertaglia et al., 2019; Healey et al., 2012; Kaufman et al., 2012). However, some studies have shown that RNRVAS incidences are misinterpreted as AHRE attacks by the CIED which leads to the underdiagnosis of RNRVAS occurrences.

Data on the factors that trigger RNRVAS are limited. (Barold, 1991, 1997; Barold & Levine, 2001; Sharma et al., 2016) The underlying mechanisms of RNRVAS and ELT are similar, therefore we think that the triggers may be similar too and RNRVAS may actually be more frequent and more significant than it is reported. Atrial premature beats and atrial capture problems are known to trigger ELT. We hypothesized that under certain predisposing conditions loss of atrial capture during atrial threshold test, as well as increased atrial threshold or an atrial premature beat causing the atrial pace stimulus to fall in the myocardial refractory period may result in VA conduction, triggering RNRVAS as a result. In order to test this hypothesis, we planned to do atrial threshold test in DDD mode and evaluate if RNRVAS develops upon loss of capture in patients with DDD pacemakers, DDD implantable Cardioverter-defibrillators (ICD) and cardiac resynchronization therapies (CRT).

2 | METHODS

2.1 | Patients

Out of 420 patients with DDD pacemakers who were admitted to cardiology outpatient clinics of two participating hospitals for elective device control between October 7th, 2021 and December 31st, 2021, 177 [mean age, 67.5 ±14.8 (70) years; 107 men, 70 women] were included in this study. A total of 420 patients with pacemakers, ICDs and CRTs were evaluated. Those with VVI/VDD mode devices, atrial fibrillation/flutter/tachycardia, lead dysfunction or uninterpretable atrial threshold test were excluded and the remaining 177 patients were included in the study.

All patients signed informed consent forms. Patients with atrial fibrillation, atrial tachycardia, very frequent atrial premature beats preventing healthy evaluation of the atrial threshold test, patients in whom pacing continued after the lowest threshold value, patients with higher than measurable threshold values, patients with inconclusive threshold test results, patients with atrial or ventricular lead malfunction were excluded.

Out of 177 subjects, 105 had pacemakers, 20 had ICDs and 52 had CRTs. Overall, 77 patients had Abbott - St Jude Medical, 70 had Medtronic, 20 had Boston -Scientific, 7 had Biotronik and 3 patients had LivaNova - Sorin devices. Demographical and clinical features of the patients, indications for CIED implantation and details of the devices were recorded to be analyzed in this study.

2.2 | Evaluation of VA conduction

The ventricular threshold test was performed in VVI mode, while recording surface ECG and/or atrial EGM with the relevant programmer device. VA conduction was accepted as 'present' if all ventricular stimuli were retrogradely conducted to the atria. This VA conduction test was done at the same pace rate with the atrial threshold test.

2.3 | Atrial threshold test

In order to demonstrate that loss of atrial capture may trigger RNRVAS, a specific atrial threshold test was designed. Atrial threshold test was done in DDD mode at a rate at least 10 beats above the basal heart rate (maximum 80–100 bpm), with an AV delay of 300 ms (range 250–350) in all but LivaNova - Sorin devices, which were set to DAO mode as the closest possible setting. The pace amplitude was decreased every 4 to 10 beats, while the pulse width was kept constant in all devices.

The PVARP settings of the patients were not changed during atrial threshold tests. Only in case of PMT induction during atrial threshold test, PVARP duration was increased.

Upon the loss of atrial capture, the EGM recordings were examined for appearance and duration of RNRVAS as explained below. Loss of atrial capture was confirmed with loss of P waves on surface ECG or loss of atrial signal after pace stimulus on ECM as recorded by the programmer device. In case of development of ELT with loss of atrial capture, PVARP was lengthened, and the test was repeated.

2.4 | Diagnosis of RNRVAS

We described in detail the flow of events in Figure 1 as basis of our RNRVAS diagnosis. Diagnosis of RNRVAS was confirmed only after the flow of events described in Figure 1 were fulfilled as modified from Barold (1991) and Barold & Levine (2001) (Figure 2).

2.5 | Statistical analysis

The statistical package SPSS, version 20.0 (SPSS, Chicago, IL, USA) was used for statistical analyses. Continuous variables are expressed as means ± standard deviation (median). All continuous variables were checked with Kolmogorov – Smirnov normality test to show their distributions. All our continuous variables showed abnormal distributions, therefore Mann–Whitney U test was used to compare all of them. Chi-square test was used to compare categorical variables. *P*-values were considered statistically significant if smaller than 0.05. Subgroup analysis was done for the 104 patients with pacemakers.

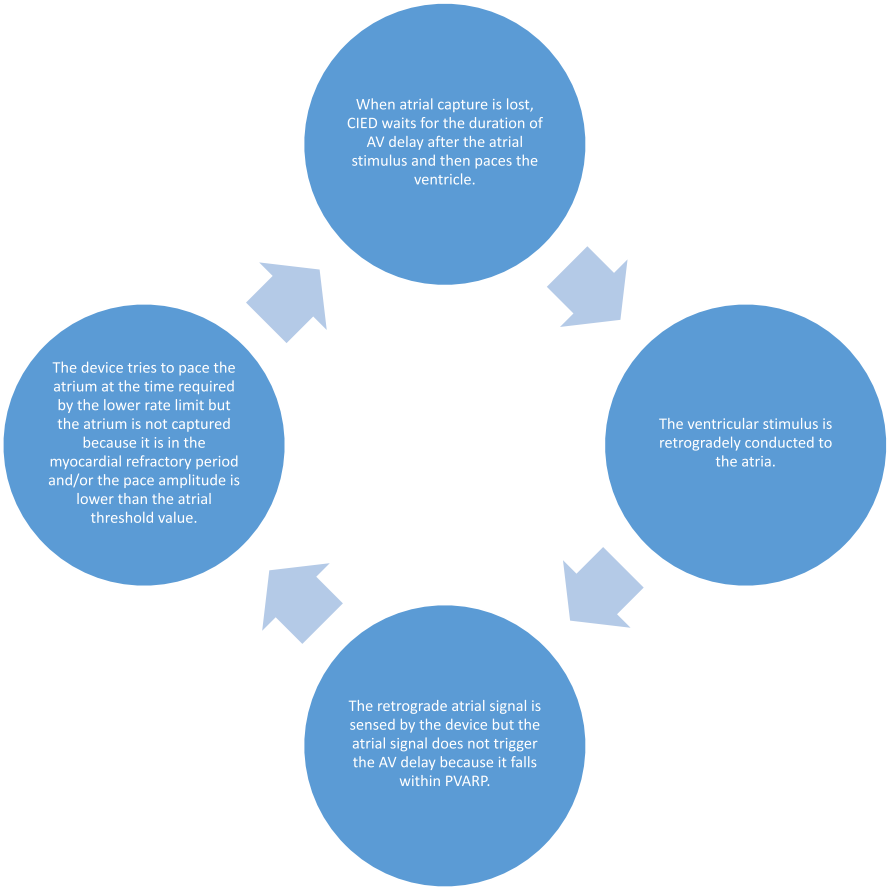


FIGURE 1 Description of flow of events leading to triggering of RNRVAS

We determined the sample size for the test by power/sample size formulas. The power analysis of binary logistic regression analysis at 80% power and at a 0.05 significance level required sample size of 150.

A multivariable logistic regression model was used to assess the independent predictors of RNRVAS. The alternative test hypothesis was built as two-sided for each statistical analysis. The tests were independent and so the experiment-wise Type 1 error did not exceed 0.05 alpha levels. All parameters in Table 1 were assessed using univariate analysis except for the presence of VA conduction which is mandatory for RNRVAS development. Significant univariate variables with p .05 were included in the multiple logistic regression analysis for odds ratios and 95% confidence intervals.

3 | RESULTS

3.1 | All patients

We observed RNRVAS in 69 of the 177 patients (39.0%) during atrial threshold test. Except age, history of a complete AV block, any AV node conduction defect and VA conduction (Table 1), the baseline clinical characteristics of patients with and without RNRVAS were similar. The patients with RNRVAS were younger than those without it ($p = .038$). History of complete AV block ($p < .001$) or any AV nod conduction defect ($p < .001$) was significantly more prevalent, and VA conduction ($p < .001$) significantly less in patients without RNRVAS than in patients with RNRVAS. In univariate analysis, younger age ($p = .038$) and the presence of VA conduction ($p < .001$) were associated with an increased risk of RNRVAS, whereas complete AV block or any AV node conduction defect ($p < .001$) and the ventricular pacing ratio ($p = .001$) were inversely related to the risk of RNRVAS occurrence after loss of atrial capture. In multivariate analysis, complete AV block (OR 0.15, 0.03–0.61; 95%CI, $p = .009$) and ventricular pacing ratio (OR 0.98, 0.96–0.99; 95%CI, $p = .029$) appeared as independent factors inversely related to the risk of RNRVAS development. (Table 2).

Information on CIED is given in Table 1 When patients with and without RNRVAS were compared, more patients with ICDs displayed RNRVAS compared to the patients with pacemakers ($p = .003$). Our results indicate that the presence of CRTs did not make a significant difference in the occurrence of RNRVAS. ELT was more frequently triggered during the atrial threshold test in patients with RNRVAS ($p = .003$). Ventricular pace ratio was significantly lower in patients with RNRVAS ($p = .001$). Atrial pace ratio was similar in patients with or without RNRVAS.

3.2 | Patients with pacemakers

The results of patients with pacemakers compared to data collected from all patients are presented in Table 1. In patients with a history

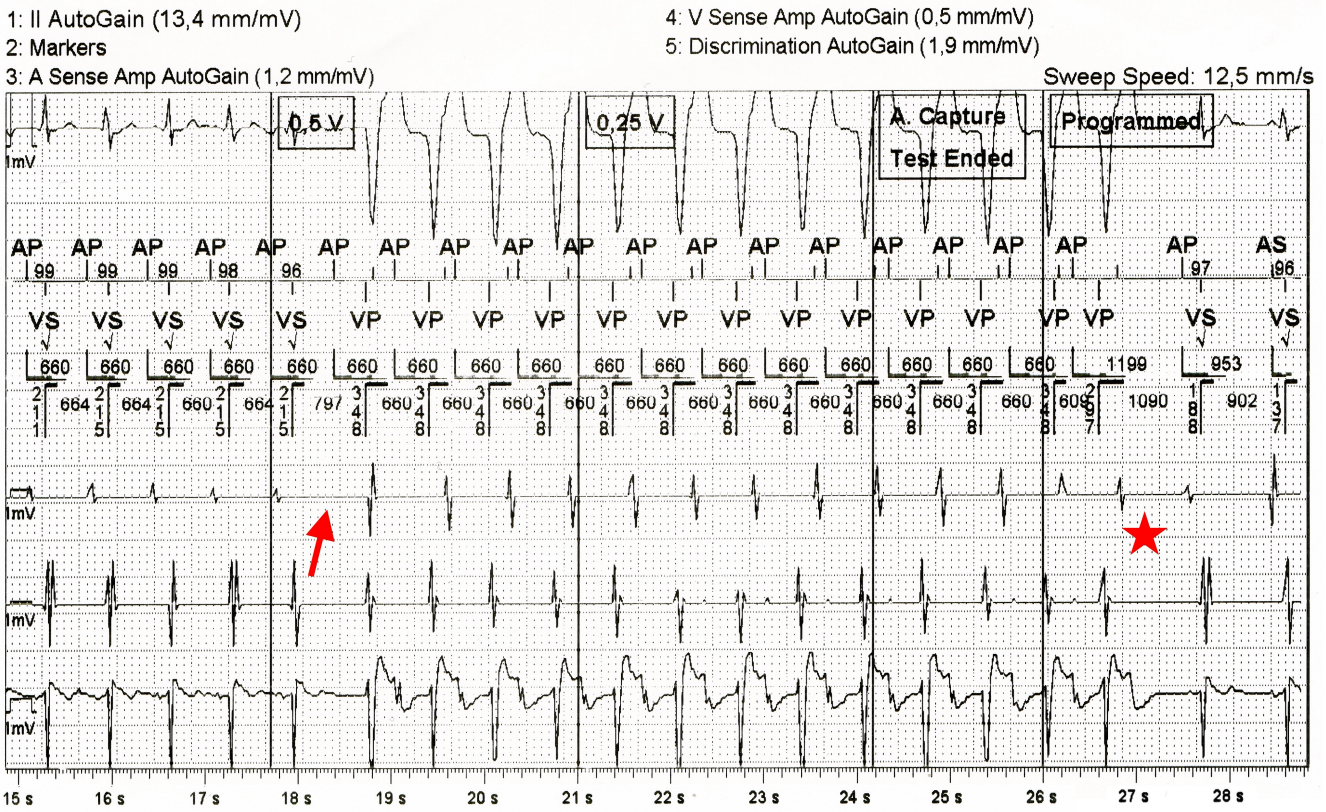


FIGURE 2 Recording from St Jude medical device demonstrating commencement of RNRVAS during atrial threshold test with loss of atrial capture. Red arrow points to where atrial capture is lost and RNRVAS starts. Red stars point to atrial threshold test end and RNRVAS terminated. From top to bottom: (1) DII surface ECG, (2) marker channel and intervals, (3) atrial EGM, (4) near field ventricular EGM, (5) far field ventricular EGM. Recording sweep speed 12.5 mm/s. RNRVAS, repetitive nonreentrant ventriculoatrial synchrony; AP, Atrial pace; AS, Atrial sense; VS, ventricular sense; VP, ventricular pace; Ab, Atrial activity in Post ventricular atrial blanking period; AR, Atrial activity sensed in PVARP; BV, Biventriküler pace; Ar, atrial activity sensed in PVARP; bV, Biventriküler pace; PAC, Premature atrial contraction; RVS, Right ventricular sense; RVP, Right ventricular pace; LVS, Left ventricular sense; LVP, Left ventricular pace

of complete AV block ($p < .001$) or any AV nodal conduction defect ($p < .001$), RNRVAS was seen significantly less frequently. In the patients with RNRVAS, presence of VA conduction ($p < .001$) and sinus node disease ($p = .001$) were more frequent compared to patients without RNRVAS. ELT induction during atrial threshold test ($p < .001$), a high atrial pace ratio ($p = .030$) and a low ventricular pace ratio ($p < .001$) were significantly more frequent in patients with RNRVAS.

3.3 | RNRVAS

When all patients were analyzed, the incidence of RNRVAS was 39%. However, if we consider the patients with only VA conduction, then the incidence of RNRVAS increases to 76.7% (69 of 90 patients). Out of 66 patients who displayed AV block, 5 developed RNRVAS (7.6); however, this proportion went up to 35.7% (5 of 14 patients) in the presence of VA conduction. The RNRVAS incidence was 84.2% (64 of 76 patients) in patients who had VA conduction in the absence of AV block.

In 66 of the 69 patients with RNRVAS, the cycle ended when heart rate decreased at the end of the atrial threshold test (Figure 2). In 3 patients, RNRVAS converted to ELT after the atrial threshold test ended. (Figure 3).

One patient who was implanted a DDD pacemaker 17 months ago, for severe sinus node dysfunction, was found to be in RNRVAS at a heart rate of 60 bpm (Figure 4) and presented with pacemaker syndrome-like symptoms. When the device was interrogated, atrial pacing threshold was found to be increased to 2.5 V/0.4 s. As the atrial pace amplitude was previously set to 2.5 V/0.4 s, increased atrial threshold resulted in intermittent loss of atrial capture leading to RNRVAS at a low heart rate (50 bpm) (Figure 5a,b).

4 | DISCUSSION

4.1 | Main findings

In this study, patients with two chamber pacemakers, ICDs and CRT devices were evaluated for development of RNRVAS during atrial threshold test upon loss of capture under certain predisposing CIED settings. We demonstrated that loss of atrial capture results

TABLE 1 Baseline clinical and CIED features of all patients and subgroup of patients with pacemakers

	All patients			Patients with pacemakers		
	Patients without RNRVAS *N*: 109	Patients with RNRVAS N: 69	*p* value	Patients without RNRVAS N: 74	Patients with RNRVAS N: 31	*p* value
Age, (years)	69.1 ±14.8 (71)	65.1 ±14.6 (65)	.038	70.6 ±15.6 (65)	68.6 ±18.1 (64)	.858
Female, *n* (%)	42 (38.9)	28 (40.6)	.875	39 (52.7)	17 (54.8)	1.0
Complete AV block, *n* (%)	61 (56.5)	5 (7.2)	<.001	52 (70.3)	4 (12.9)	<.001
Any AV node conduction defect, *n* (%)	86 (79.6)	18 (26.1)	<.001	64 (86.5)	9 (29)	<.001
SND, *n* (%)	21 (19.4)	20 (29)	.149	18 (24.3)	19 (61.3)	.001
CAD, *n* (%)	58 (53.7)	35 (50.7)	.758	33 (44.6)	9 (29.0)	.190
Heart failure, *n* (%)	40 (37)	31 (44.9)	.346	9 (12.2)	0	.055
LVEF, %	46.5 ±17.1 (55)	44.9 ±16.4 (50)	.576	55.3 ±10.8	58.2 ±5.2	.397
Atrial fibrillation, *n* (%)	36 (33.3)	14 (20.3)	.086	24 (32.4)	11 (35.5)	.822
Hypertension, *n* (%)	82 (75.9)	50 (72.5)	.601	57 (77.0)	22 (71.0)	.621
Diabetes mellitus, *n* (%)	25 (23.1)	19 (27.5)	.593	14 (18.9)	7 (22.6)	.790
LBBB, *n* (%)	35 (32.4)	27 (39.1)	.420	7 (9.5)	2 (6.5)	1.0
VA conduction, *n* (%)	21 (19.3)	69 (100)	<.001	12 (16.2)	31 (100)	<.001
Type of device						
Pacemaker, *n* (%)	74 (68.5)	31 (44.9)	.003	–	–	–
ICD, *n* (%)	6 (5.6)	14 (20.3)	.003	–	–	–
CRT, *n* (%)	28 (25.9)	24 (34.8)	.238	–	–	–
Rate response mode active, *n* (%)	29 (26.9)	17 (24.6)	.861	23 (31.1)	13 (41.9)	.368
ELT in threshold test, *n* (%)	1 (0.9	8 (11.6)	.003	0	6 (19.4)	< .001
Atrial pace ratio, %	35.6 ±33.5 (23.0)	39.2 ±35.2 (30.0)	.928	37.7 ±33.8 (18.5)	55.8 ±29.9 (35.6)	.030
Ventricular pacing ratio, %	78.5 ±37.8 (99.0)	44.9 ±45.4 (22.5)	.001	74.9 ±35.6 (98)	22.0 ±33.4 (3.8)	< .001

Abbreviations: RNRVAS, repetitive nonreentrant ventriculoatrial synchrony; AV, atrioventricular; SND, sinus node disease; CAD, Coronary artery disease; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; VA, ventriculoatrial; ICD, implantable cardioverter-defibrillator; CRT, cardiac resynchronization therapy; ELT: Endless loop tachycardia.

in RNRVAS in more than one-third of patients with a CIED in DDD mode, and in more than three-fourths of those with VA conduction. To the best of our knowledge, this is the first study in the literature demonstrating the relationship between loss of atrial capture and systematic RNRVAS development.

Several clinically important results were revealed by this study:

1. In patients with DDD pacemakers/ICDs and CRTs, RNRVAS developed in 39% during atrial threshold test. When patients with VA conduction were considered, RNRVAS was observed in 76.7%.
2. The presence of AV block or a high ventricular pacing ratio are independent predictors of low RNRVAS observance.
3. VA conduction was present in 21.2% of patients with AV block 7.6% of whom developed RNRVAS during atrial threshold test.
4. In univariate analysis, age, presence of ELT, the device being DDD pacemaker or ICD were related to the detection of RNRVAS. However, in multivariate analysis these parameters were not independent predictors of RNRVAS.
5. In one patient with severe sinus node dysfunction and nodal rhythm, loss of atrial capture was observed to trigger RNRVAS even in very low heart rates (50–60 bpm) and caused pacemaker syndrome-like symptoms. This finding suggests that RNRVAS may be more frequent and more easily triggered than previously reported.

TABLE 2 Factors statistically significantly associated with RNRVAS: Multivariable analysis

Variable	OR	95% CI	*p* value
Age	1.01	0.95–1.08	.714
Complete AV block	0.15	0.03–0.61	.009
Any AV node conduction defect	0.23	0.02–2.27	.208
ELT	3.27	0.28–38.13	.345
Pacemaker	0.31	0.03–3.21	.327
Ventricular pacing ratio	0.98	0.96–0.99	.029

Abbreviations: RNRVAS, repetitive nonreentrant ventriculoatrial synchrony; AV, atrioventricular; ELT, Endless loop tachycardia.

In our study, we showed that in the presence of predisposing conditions such as long AV delay, short lower rate interval and presence of VA conduction; RNRVAS can be triggered easily with loss of atrial capture. This is the first study demonstrating this finding in the literature.

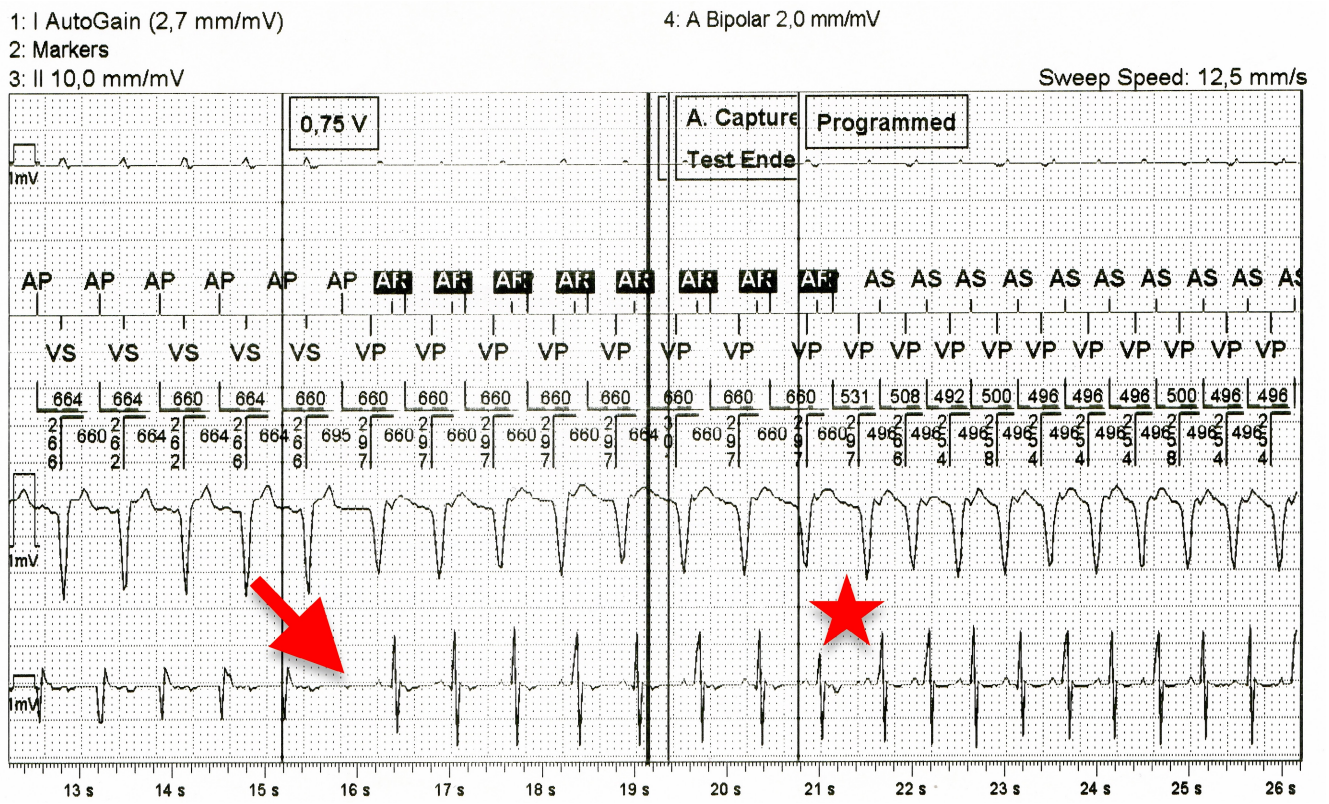


FIGURE 3 Recordings demonstrating commencement of RNRVAS and ELT during atrial threshold test with loss of atrial capture. Red arrow points to where atrial capture is lost and RNRVAS starts. Red stars point to atrial threshold test end and RNRVAS terminated and ELT started. Recording from St Jude Medical device showing from top to bottom: (1) D1 surface ECG, (2) Marker channel and intervals (3) D2 surface ECG (4) Atrial EGM. Recording sweep Speed 12.5 mm/s. RNRVAS, repetitive nonreentrant ventriculoatrial synchrony; ELT, Endless loop tachycardia; AP, Atrial pace; AS, Atrial sens; VS, ventricular sens; VP, ventricular pace

4.2 | The mechanism of RNRVAS and predisposing factors

RNRVAS was first described by Barold (1991). Several studies showed that in two-chamber devices, long AV delay, long PVARP, short lower rate interval, presence of VA conduction and long VA conduction periods were predisposing factors of RNRVAS (Barold, 1991, 2017; Barold & Levine, 2001). A few studies described ventricular ectopic beats and retrograde atrial conduction after ventricular pacing as a trigger mechanism for RNRVAS (Barold, 1991; Sharma et al., 2016). Andric et al. described a patient with DDD Pacemaker implanted for AV block after mitral valve replacement (Andric et al., 2018). The patient was admitted for decompensated heart failure caused by ELT and RNRVAS with increased atrial threshold. In this case report, the induction of RNRVAS due to increased atrial threshold was not demonstrated, but was suggested as the possible cause. There are no other cases in the literature with evidence showing the relationship between increased atrial threshold and RNRVAS.

In this study, we show that the absence of VA conduction accompanied by the presence of AV block decreases the risk of RNRVAS development in both univariate and multivariate analyses.

VA conduction is mandatory for development of RNRVAS, and AV block is frequently accompanied by VA block. We showed that only 21.2% of the patients with AV block had VA conduction. This number is consistent with the findings of Richter et al. (2013).

The absence of VA conduction in the remaining 78.8% explains why patients with AV block experience RNRVAS less. Av block results in increased ventricular pacing ratio which was an independent predictor of absence of RNRVAS development in univariate and multivariate analyses in this study.

4.3 | Possible mechanisms of RNRVAS development as a result of atrial capture problem

In this study, we demonstrated that RNRVAS is triggered as a result of atrial capture failure. This may be due to the following situations:

1. A lower rate limit set to a high heart rate or sensor rate response result in atrial pacing at high heart rates. This increases atrial pacing rate with atrial capture loss and increases the probability of triggering RNRVAS.
2. During atrial threshold test in devices that automatically measure threshold periodically, loss of capture may trigger RNRVAS.
3. After an atrial ectopic beat, pace stimulus in atrium may fall in the myocardial refractory period causing noncapture, and this may trigger RNRVAS.

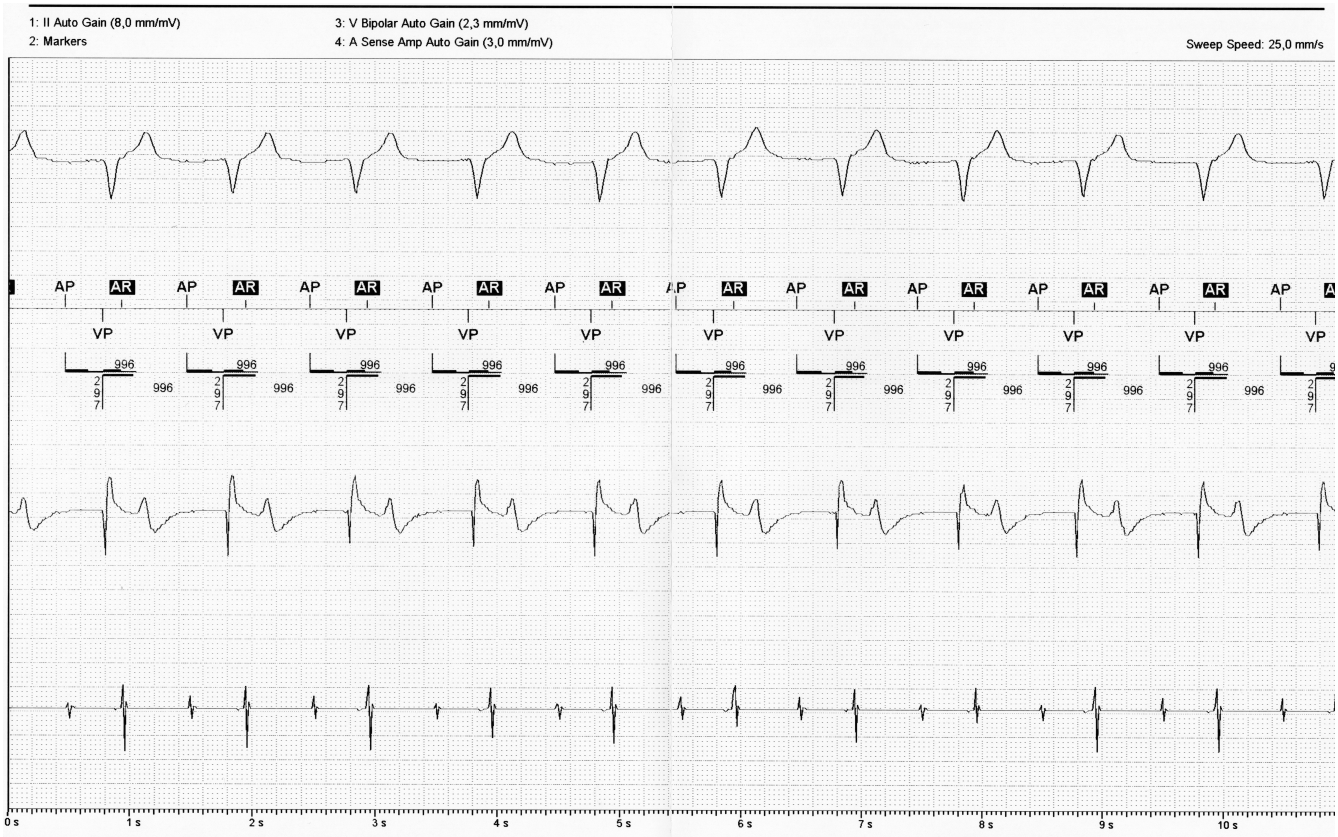


FIGURE 4 Recording from a patient who was in RNRVAS when his pacemaker was interrogated during routine pacemaker control. Recording from St Jude Medical device showing from top to bottom: (1) DII surface ECG (2) Marker channel and intervals (3) Ventricular EGM (4) Atrial EGM. Recording sweep Speed 25 mm/s. RNRVAS, repetitive nonreentrant ventriculoatrial synchrony; AP, Atrial pace; AR, Atrial activity sensed in PVARP; VP, Ventricular pace

After a noncaptured atrial pace stimulus, the device waits during the AV delay duration and paces the ventricle. Because the atrium is not captured, the AV node is not refractory when ventricle is paced, so the signal is conducted retrogradely to the atrium. This retrograde atrial signal falls into PVARP; therefore, it is sensed, but does not trigger AV delay. The device waits until the lower rate limit is reached and tries to pace the atrium, but the atrium is in the refractory period or atrial threshold is high so it is not captured. This continues in a loop leading to RNRVAS which ends if VA conduction is somehow blocked or atrium is captured.

4.4 | RNRVAS, AHRE, atrial overdrive pacing

The study of Kohno et al. (2011) evaluated AHRE recordings for diagnosis of atrial tachyarrhythmias. Our results support their findings. They studied 39 patients with St. Jude DDD pacemakers for 16.7 ±9.8 months. In half of the patients, atrial overdrive pace (AOP) algorithm was turned on and the patients were followed. AHRE was observed in 20 of 39 patients (51%) and among these 257 AHRE, 148 were AF and 109 were RNRVAS. There was a total of 257 AHRE attacks among 51% of the 39 patients, where 148 of the attacks were AF and 109 were RNRVAS. In this study, patients with RNRVAS or RNRVAS and AF were all in the group assigned to AOP "ON" ($p = .0020$). In all the patients who developed RNRVAS, atrial pacing ratio was significantly higher (92.2% vs. 49.9%, $p < .0001$).

In our study, atrial pacing ratio was significantly higher in the subgroup of patients with pacemakers ($p = .030$) compared to patients with patients with ICDs, although this was not statistically significant in the whole study population ($p = .928$). The reason for the atrial pacing ratio being lower in our study may be because patients with ICDs and CRTs were also included. Both in the ASSERT sub study (Hohnloser et al., 2012), and the study by Kohno et al. (2011), RNRVAS was four times more frequent in patients with AOP turned on.

In general practice, in case of atrial premature beats, AOP is activated to prevent induction of atrial fibrillation. If some atrial premature beats are not sensed during AOP, then loss of atrial capture may be seen resulting in RNRVAS in presence of VA conduction.

In the ASSERT study(Kaufman et al., 2012), which included 2343 patients with DDD pacemakers, erroneous AHRE recordings were numerous mostly due to the presence of RNRVAS (13.9%). These data prove RNRVAS is underreported and in fact more frequently encountered than currently estimated. In the ASSERT study, all the pacemakers were of St Jude Medical and atrial arrhythmia recognition algorithms of St Jude Medical devices are thought to be more sensitive in recognizing RNRVAS (Barold, 2017; Barold & Stroobandt, 2012; Kaufman et al., 2012). In St Jude Medical devices, AHRE algorithms use both sensed and paced atrial signal for recognition, therefore RNRVAS attacks are recorded as AHRE (Barold, 2017). The actual incidence of RNRVAS is unknown due to the absence of specific algorithms for recognizing RNRVAS in CIEDs. However, in the patient who experiences RNRVAS at low heart rates, like in the case of our patient (Figure 5), SJM algorithms are unable to diagnose the problem.

4.5 | Clinical significance of RNRVAS

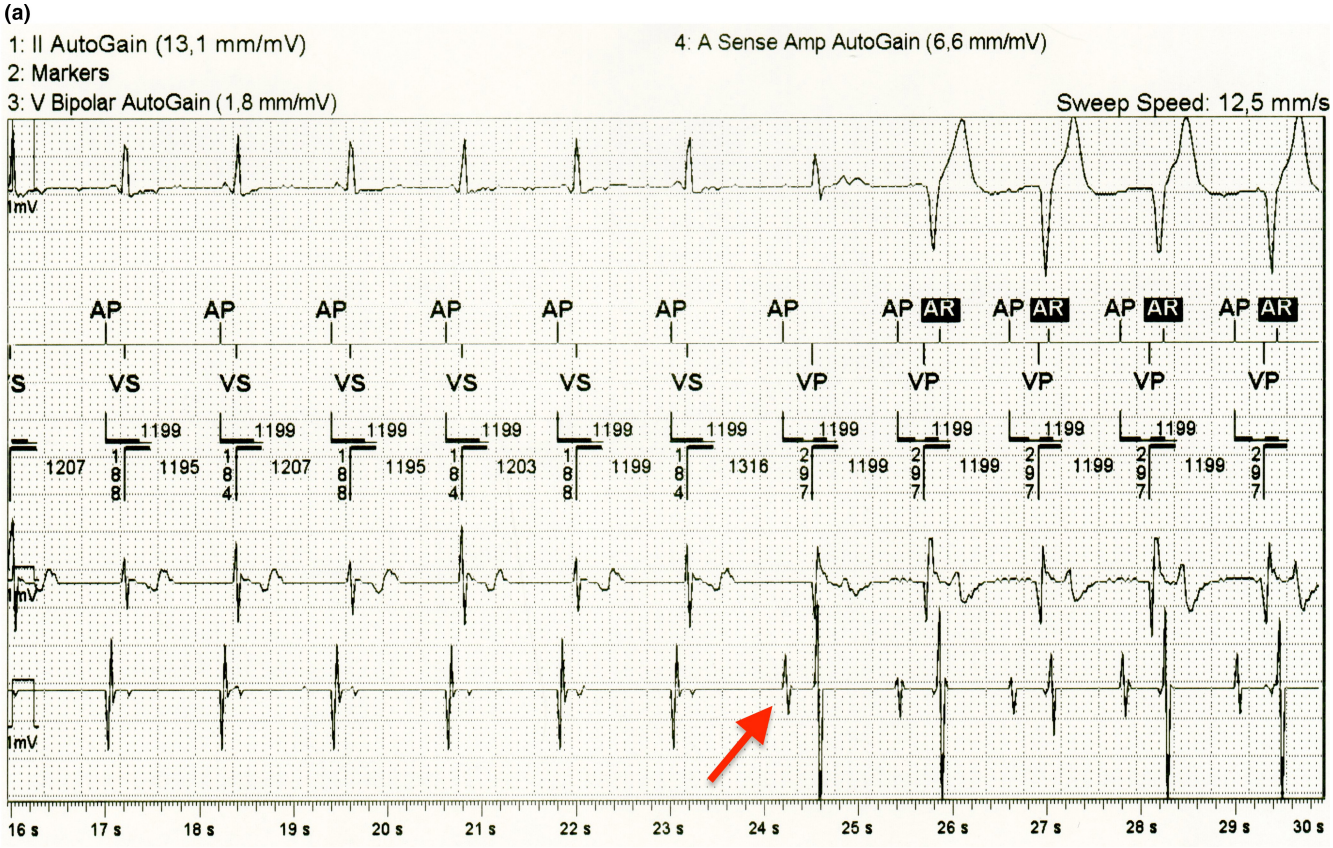
RNRVAS attacks are triggered by sensor driven heart rate increase, as in our patient who experienced RNRVAS at low heart rates (Figure 4) (Healey et al., 2012; Kaufman et al., 2012; Kohno et al., 2011). The fact that RNRVAS is triggered very easily during atrial threshold tests necessitates reevaluation of the general approach to RNRVAS. Sharma et al. (Sharma et al., 2016) propose four clinical scenarios in case of RNRVAS: (i) pacemaker syndrome as a result of loss of AV synchronization, (ii) unnecessary increase in ventricular pacing ratio, (iii) false AHRE diagnosis, (iv) mode switch due to false AHRE diagnosis and pro-arrhythmia. In the same study, the possibility that false AHRE diagnosis may lead to unjustified anticoagulant use and device programming is underlined. False AHRE diagnosis may also lead to unnecessary antiarrhythmic medicine usage and ablations.

4.6 | Treatment and device programming to avoid RNRVAS

To the best of our knowledge, there are no algorithms specifically for detection or termination of RNRVAS in the devices available today. Certain adjustments in device programs may prevent or terminate RNRVAS (Barold, 1991, 2017; Barold & Levine, 2001; Sharma et al., 2016) and we recommend that as many of these modifications as possible be included in the upcoming device algorithms. (i) Decreasing lower rate limit, (ii) short AV delay or automatically shortening AV delay, (iii) decreased sensor indicated upper rate or turning off R mode, (iv) shortening PVARP or programming a rate dependent PVARP; (v) programming non-competitive atrial pacing, (vi) programming ventricular pacing decreasing algorithms when the patient's AV conduction is functional (MVP, AAI-SafeR, or RhythmIQ). Medtronic

FIGURE 5 Recordings demonstrating commencement of RNRVAS during loss of atrial capture. (a) Development of RNRVAS with loss of atrial capture, (b) Activation of SIR response with loss of atrial capture and the start of RNRVAS. Red arrow points to where atrial capture is lost. Red stars point to SIR response. Recording from St Jude Medical device showing from top to bottom: (1) DII surface ECG, (2) Marker channel and intervals, (3) Ventricular EGM (4) Atrial EGM. Recording sweep Speed 25 mm/s. RNRVAS, repetitive nonreentrant ventriculoatrial synchrony; SIR, Sensor – indicated rate; AP, Atrial pace; AR, Atrial activity sensed in PVARP; VS, ventricular sens; VP, Ventricular pace

(a)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3: V Bipolar AutoGain (1,8 mm/mV)
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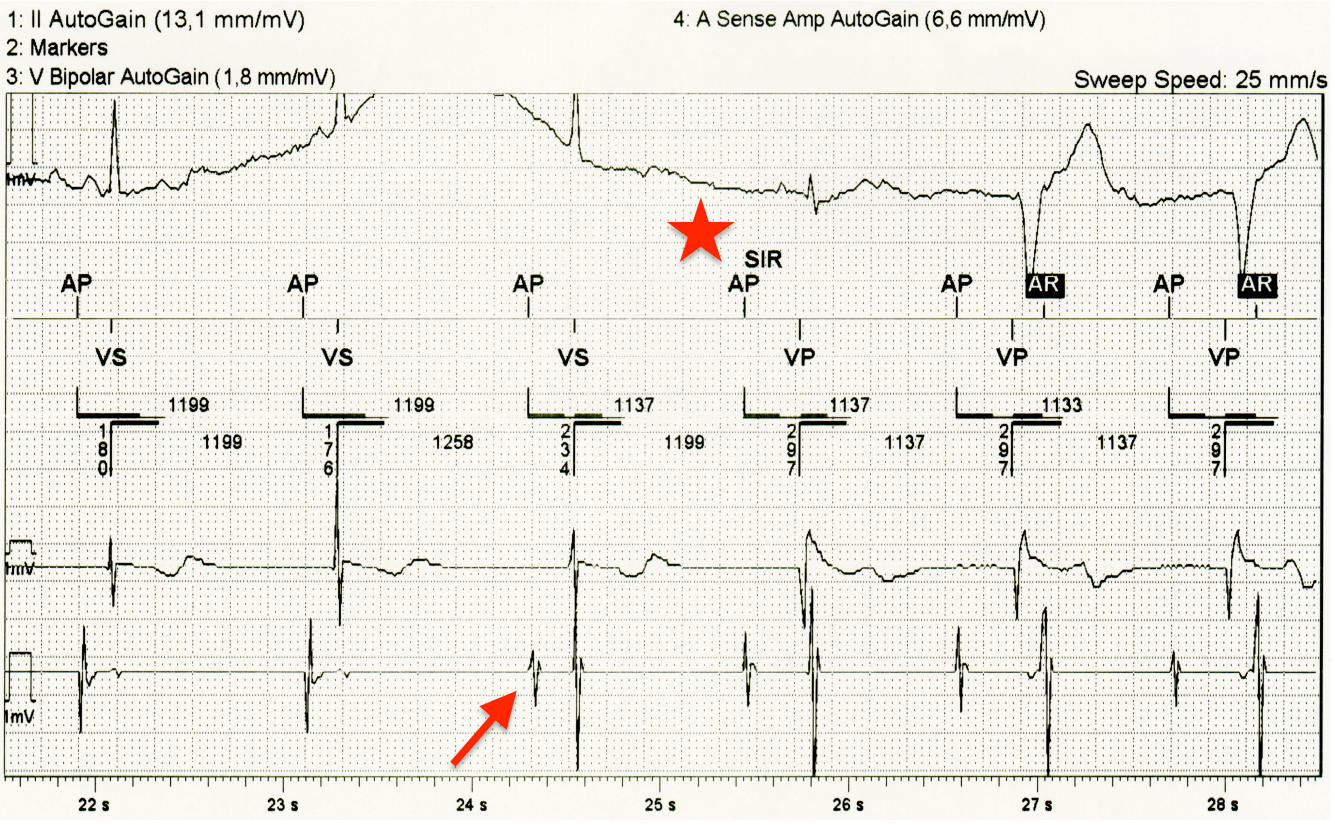
16 s 17 s 18 s 19 s 20 s 21 s 22 s 23 s 24 s 25 s 26 s 27 s 28 s 29 s 30 s

(b)


1: II AutoGain (13,1 mm/mV)
2: Markers
3: V Bipolar AutoGain (1,8 mm/mV)
4: A Sense Amp AutoGain (6,6 mm/mV)
Sweep Speed: 25 mm/s
1mV
SIR
AP AP AP AP AP AR AP AR
VS VS VS VP VP VP
1199 1199 1137 1137 1133
1199 1258 1199 1137 1137
22 s 23 s 24 s 25 s 26 s 27 s 28 s

devices have noncompetitive atrial pacing algorithm which is programmable and may eliminate RNRVAS (Bertaglia et al., 2019). We also recommend meticulous measurement of atrial threshold and programming the pace amplitude considering safety margins to prevent loss of capture.

4.7 | Study limitations

In this study, we were not able to evaluate the relationship between real-life incidence of RNRVAS occurrence and loss of atrial capture due to the lack of algorithm capabilities. In this study, atrial threshold test was specifically designed to demonstrate the relationship between loss of atrial capture and RNRVAS. The settings used in the atrial threshold test are different from the real-life settings of the participants. Our results prove that when predisposing conditions are present, RNRVAS is easily induced. The observed frequency of RNRVAS in our study may be a lot higher than clinical frequency because the specific predisposing settings of the atrial threshold test are different from the regularly used settings of the patients. Further studies are needed to evaluate the relationship between RNRVAS inducibility with atrial threshold test and RNRVAS incidence in AHRE recordings.

5 | CONCLUSIONS

In this study, we showed that under predisposing device settings, loss of atrial capture has a high likelihood of triggering RNRVAS in DDD pacemakers/ICDs and CRTs of five different manufacturers. We also demonstrated that in the presence of sinus node dysfunction, RNRVAS may be seen even at very low heart rates. The incidence of RNRVAS may be a lot higher than previously reported. Our findings may help explain the reason behind presence of RNRVAS as a reason for erroneous AHRE recordings. In patients with VA conduction, we recommend avoiding RNRVAS predisposing settings. New algorithms for diagnosis and prevention/suppression of RNRVAS seem to be required in current devices.

AUTHOR CONTRIBUTIONS

Both authors made substantial contributions to the conception and design of the work. Both actively participated in data acquisition. Ilyas Atar was responsible for analysis and interpretation of data. Asli Inci Atar was responsible for drafting the article and revising it critically for important intellectual content. Ilyas Atar made the final approval of the version to be published.

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CONFLICT OF INTEREST

None of the authors has associations that might pose a conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

ETHICS STATEMENT

The study protocol was approved by the Institutional Committee on Human Research and Ethics. The study was conducted in compliance with the Declaration of Helsinki.

ORCID

Asli Inci Atar https://orcid.org/0000-0002-2653-0048

REFERENCES

Andric, S., Tesic, D., Somer, D., Srdanovic, I., Miljkovic, T., Jakovljevic, D. G., & Velicki, L. (2018). Ventriculoatrial synchrony induced heart failure. *Acta Clinica Belgica*, *73*, 439–443.

Barold, S. S. (1991). Repetitive reentrant an non-reentrant ventriculoatrial synchrony in dual-chamber pacing. *Clinical Cardiology*, *14*, 754–763.

Barold, S. S. (1997). Pacemaker induced repetitive nonreentrant ventriculoatrial synchrony: Initiation and termination by ventricular extrasystole. *Pacing and Clinical Electrophysiology*, *20*, 989–992.

Barold, S. S. (2017). A review of the atrial upper rate algorithms of St. Jude Medical (Abbott) cardiac implantable electronic devices: Incidence of repetitive nonreentrant ventriculoatrial synchrony (RNRVAS). *Herzschrittmachertherapie & Elektrophysiologie*, *28*, 320–327.

Barold, S. S., & Levine, P. A. (2001). Pacemaker repetitive nonreentrant ventriculoatrial synchronous rhythm: A review. *Journal of Interventional Cardiac Electrophysiology*, *5*, 45–58.

Barold, S. S., & Stroobandt, R. X. (2012). Erroneous automatic pacemaker arrhythmia diagnosis. Is it malfunction or a design limitation? *Heart Rhythm*, *9*, 998–1001.

Barold, S. S., Stroobandt, R. X., & Van Heuverswyn, F. (2012). Pacemaker repetitive nonreentrant ven- triculoatrial synchrony. Why did automatic mode switching occur? *Journal of Electrocardiology*, *45*, 420–425.

Bertaglia, E., Blank, B., Blomström-Lundqvist, C., Brandes, A., Cabanelas, N., Dan, G. A., Dichtl, W., Goette, A., de Groot, J. R., Lubinski, A., Marijon, E., Merkely, B., Mont, L., Piorkowski, C., Sarkozy, A., Sulke, N., Vardas, P., Velchev, V., Wichterle, D., & Kirchhof, P. (2019). Atrial high-rate episodes: Prevalence, stroke risk, implications for management, and clinical gaps in evidence. *Europace*, *21*, 1459–1467.

Gjermeni, E., Doering, M., Richter, S., Hindricks, G., & Bode, K. (2021). Novel pacemaker-mediated arrhythmia without Ventriculoatrial conduction can induce atrial fibrillation. *JACC Clinical Electrophysiology*, *7*, 1–5.

Healey, J. S., Connolly, S. J., Gold, M. R., Israel, C. W., van Gelder, I., Capucci, A., Lau, C. P., Fain, E., Yang, S., Bailleul, C., Morillo, C. A., Carlson, M., Themeles, E., Kaufman, E. S., Hohnloser, S. H., & ASSERT Investigators. (2012). ASSERT investigators. Subclinical atrial fibrillation and the risk of stroke. *The New England Journal of Medicine*, *366*, 120–129.

Hohnloser, S. H., Healey, J. S., Gold, M. R., Israel, C. W., Yang, S., van Gelder, I., Capucci, A., Lau, C. P., Fain, E., Morillo, C. A., Ha, A., Carlson, M., Connolly, S. J., & ASSERT Investigators. (2012). Atrial overdrive pacing to prevent atrial fibrillation: Insights from ASSERT. *Heart Rhythm*, *9*, 1667–1673.

Kaufman, E. S., Israel, C. W., Nair, G. M., Armaganijan, L., Divakaramenon, S., Mairesse, G. H., et al. (2012). Positive predictive value of device-detected atrial high-rate episodes at different rates and durations: An analysis from ASSERT. *Heart Rhythm*, *9*, 1241–1246.

Kohno, R., Abe, H., Oginosawa, Y., Tamura, M., Takeuchi, M., Nagatomo, T., & Otsuji, Y. (2011). Reliability and characteristics

of atrial tachyarrhythmias detection in dual chamber pacemakers. *Circulation Journal*, *75*, 1090–1097.

Richter, S., Muessigbrodt, A., Salmas, J., Doering, M., Wetzel, U., Arya, A., Hindricks, G., Brugada, P., & Israel, C. W. (2013). Ventriculoatrial conduction and related pacemaker-mediated arrhythmias in patients implanted for atrioventricular block: An old problem revisited. *International Journal of Cardiology*, *168*, 3300–3308.

Sharma, P. S., Kaszala, K., Tan, A. Y., Koneru, J. N., Shepard, R., Ellenbogen, K. A., et al. (2016). Repetitive nonre-entrant ventriculoatrial synchrony: An underrecognized cause of pacemaker-related arrhythmia. *Heart Rhythm*, *13*, 1739–1747.

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