Masked premature ventricular contractions and intradevice interaction causing ventricular fibrillation

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Introduction

Implantable cardioverter-defibrillators (ICD) are indicated for patients with cardiomyopathies to reduce their risk of sudden cardiac death from both ventricular tachycardia (VT) and ventricular fibrillation (VF). ICDs and biventricular ICDs can, however, be proarrhythmic, especially when pacing into a scar. We describe 2 cases of patients with frequent premature ventricular contractions (PVCs) who developed recurrent polymorphic VT/VF due to interaction between PVC timing and blanking periods, leading to R-on-T ventricular pacing following pseudo-pseudofusion.

Case report

Case 1

A 53-year-old woman with dual-chamber ICD (Fortify Assura DR2357-40Q, St. Jude [Abbott] Medical, St. Paul, MN) presented to the emergency department following 2 presyncopal events with ICD shocks.

She had nonischemic cardiomyopathy with left ventricular ejection fraction (LVEF) of 30% secondary to myocarditis (LVEF was 50% 1 year prior when she first developed symptoms). She had frequent PVCs, for which a PVC ablation was attempted 5 months prior at an outside institution but was unsuccessful owing to inadequate frequency following sedation. She was diagnosed with sinus node dysfunction following recurrent syncope on beta blockers; a dual-chamber pacemaker was implanted (Assurity MRI 2272; St. Jude Medical, St Paul, MN).

She was first encountered within our institution 1 month prior and diagnosed with myocarditis by cardiac magnetic resonance imaging and positron emission tomography–computed tomography. Endomyocardial biopsy was nondiagnostic. She was treated with pulse dose methylprednisolone followed by prednisone 40 mg daily. Her pacemaker was upgraded to a dual-chamber ICD with unchanged pacing parameters of DDD 60–130 beats per minute, paced/sensed AV delay (AVD) 250/225 ms, ventricular intrinsic preference (VIP) algorithm enabled with AVD extension of 100 ms.

During the current presentation, her 12-lead electrocardiogram showed sinus rhythm with chronic right bundle branch

KEY TEACHING POINTS

- The post–atrial pacing ventricular blanking period (PAVB) and crosstalk detection window (CDW) are timing intervals used to prevent ventricular asystole due to crosstalk. Ventricular safety pacing (VSP) is utilized by some manufacturers' devices to pace at a shorter AV delay if a ventricular depolarization is detected during the CDW to avoid asystole and R-on-T pacing.
- A premature ventricular contraction can be completely masked within the PAVB when pseudo-pseudofusion occurs, leading to triggered ventricular pacing at the programmed AV delay. This may result in R-on-T pacing and initiation of polymorphic ventricular tachycardia (VT) / ventricular fibrillation (VF).
- Reprogramming of the lower rate limit to avoid pseudo-pseudofusion and/or changing the AV delay to avoid pacing during the vulnerable period after pseudo-pseudofusion can successfully prevent further VT/VF episodes.

KEYWORDS Implantable cardioverter-defibrillator; Intradevice interaction; Pacemaker-induced arrhythmia; Premature ventricular contraction; Ventricular fibrillation

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block, left anterior fascicular block, and occasional PVCs. ICD interrogation showed normal lead parameters including R wave 6.7 mV, with automatic sensitivity setting. There were 2 episodes of polymorphic VT, each terminated by a single ICD shock. The patient was started on intravenous amiodarone. On the following day, a third episode of polymorphic VT occurred. Telemetry showed an atrial pacing spike just after the onset of a PVC with left bundle branch block pattern and inferior axis (pseudo-pseudofusion), followed by ventricular pacing on the T-wave downslope of that PVC initiating polymorphic VT (Figure 1A). ICD interrogation confirmed these findings (Figure 1B).

Careful analysis showed that ventricular sensing of the PVC fell entirely within the nonprogrammable post–atrial pacing ventricular blanking (PAVB) period, causing the PVC to be "masked." Ventricular pacing was then triggered at the programmed interval: 350 ms with VIP activated (250 ms paced AVD + 100 ms VIP extension, first red asterisk in Figure 1B), and 250 ms when VIP was not activated (second red asterisk in Figure 1B). Pacing at an AVD of 250 ms occurred during the vulnerable repolarization period of the PVC, while pacing at an AVD of 350 ms occurred outside the vulnerable period (Figure 1A and 1B).

Repeat analysis of the 2 prior episodes (Figure 1C and 1D) revealed similar initiation of VT with the same "masked" PVC. Given minimal pacing requirements and that all 3 episodes initiated when the PVC occurred at the same coupling interval as atrial pacing, the cycle length of which was somewhat variable, the lower rate limit (LRL) was decreased to 40 bpm. We extended the AVD to 400 ms to avoid pacing within the vulnerable period of the PVC, even if pseudo-pseudofusion occurred. At 1 month post discharge, she developed slow monomorphic VT terminated by antitachycardia pacing. She had no further polymorphic VT/VF episodes at 8 months follow-up.

Case 2

A 47-year-old man with history of aortic coarctation repaired at age 5 years, uncorrected bicuspid aortic valve, and mildly reduced LVEF 40%–45%, received a dual-chamber ICD (Vigilant EL D233; Boston Scientific, Natick, MA) at an outside institution following cardiac arrest with a shockable rhythm at the gym. He began having recurrent VF episodes with ICD shocks 6 weeks after implantation, particularly during exertion. He was treated with mexiletine and multiple beta blockers (carvedilol, metoprolol, atenolol, betaxolol), but he self-discontinued each owing to side effects.

Following his fourth ICD shock (7 months after ICD implantation), he was started on propranolol and amiodarone at an outside hospital. He presented to our institution after his fifth ICD shock. Twelve-lead electrocardiogram showed sinus rhythm with right bundle branch block, left anterior fascicular block, first-degree AV block with PR interval 220 ms, and occasional PVCs. ICD interrogation showed pacing settings DDDR with LRL 60 bpm, upper tracking/sensor rate of 105/145 bpm, paced/sensed

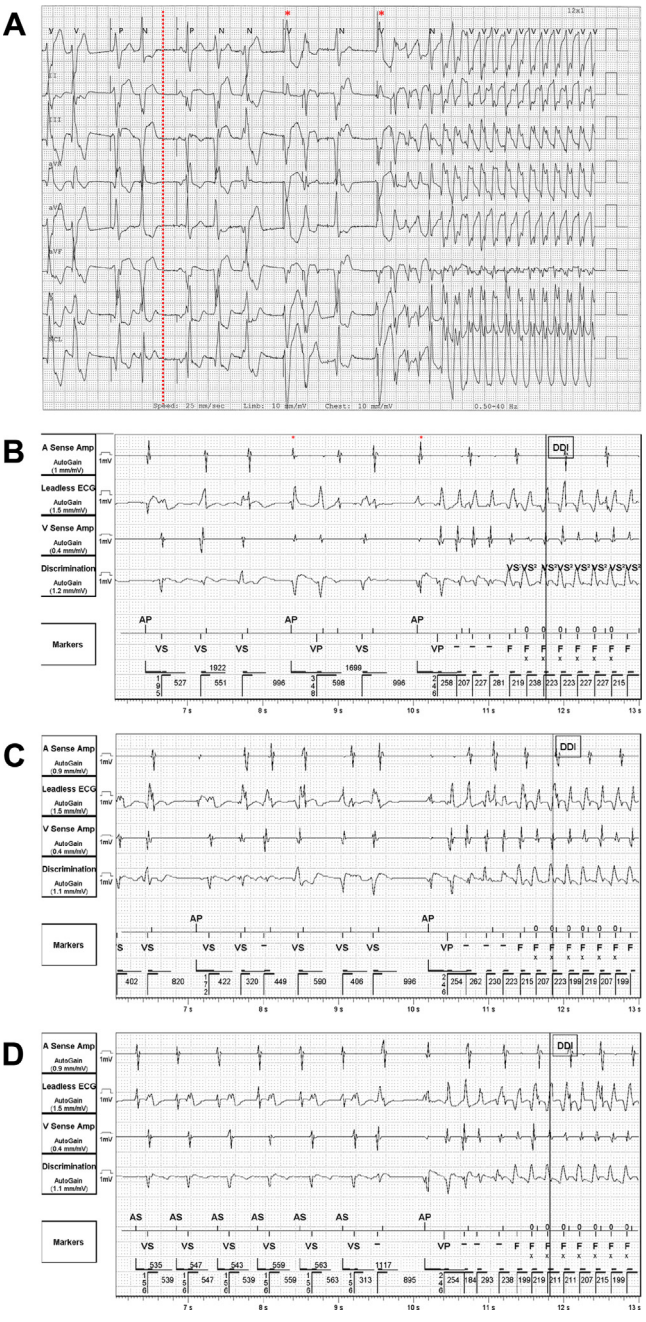

Figure 1 Pseudo-pseudofusion triggered ventricular pacing leading to polymorphic ventricular tachycardia (VT) in patient 1. **A:** Initiation of polymorphic VT captured on 7-lead continuous electrocardiogram (ECG). The red vertical line corresponds to the beginning of the implantable cardioverter-defibrillator (ICD; Fortify Assura DR2357-40Q; St. Jude [Abbott] Medical, St. Paul, MN) interrogation shown in panel **B**. Pacing mode was DDD 60–130 beats per minute, paced AV delay 250 ms, ventricular intrinsic preference (VIP) on. Frequent multifocal premature ventricular complexes (PVCs) were present. Pseudo-pseudofusion occurs during 2 PVCs (*red asterisk*). The PVCs are masked within the post–atrial ventricular blanking and hence ventricular pacing occurs at the programmed AV interval. During the first PVC, VIP with 100 ms extension in the AV delay (AVD) is activated, leading to AVD of 346 ms. During the second PVC, VIP is deactivated and V pacing occurs at the programmed paced AVD of 246 ms, leading to R-on-T pacing and initiation of polymorphic VT. **C, D:** Two earlier episodes where only ICD interrogation was available, demonstrating similar initiation.

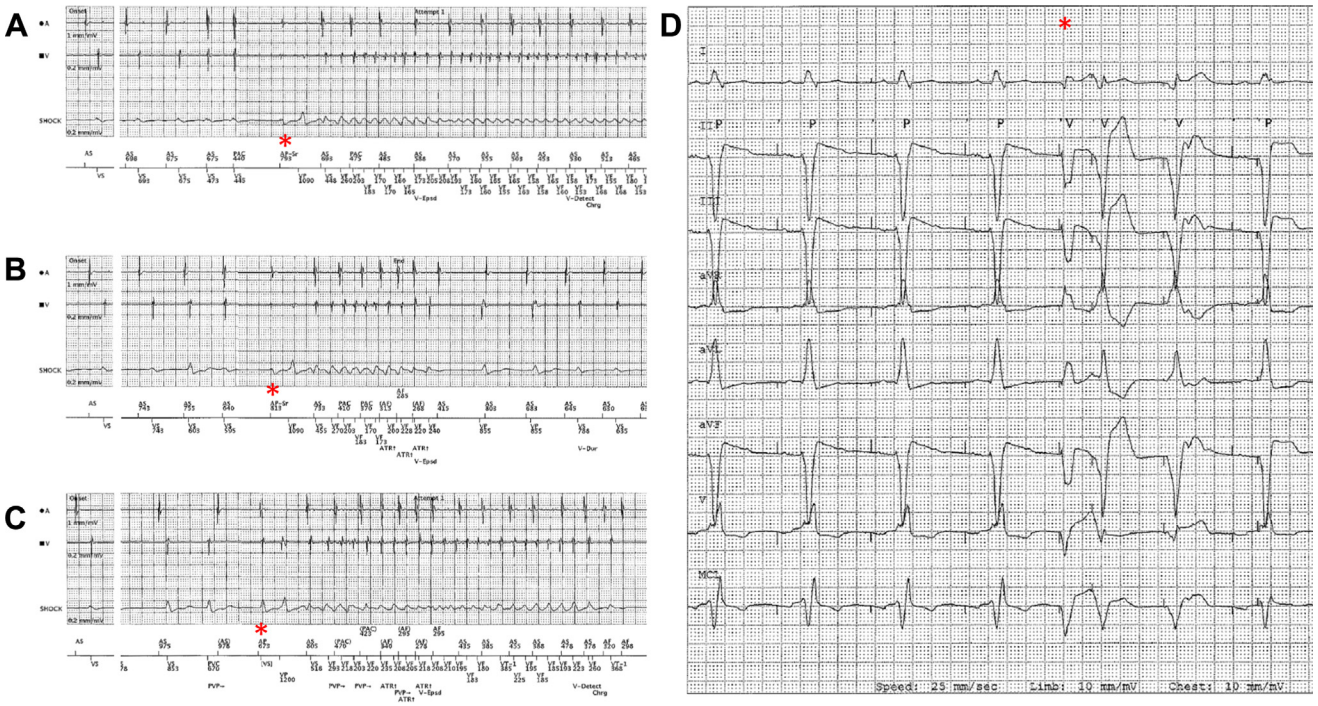

Figure 2 Pseudo-pseudofusion triggered ventricular pacing leading to ventricular fibrillation (VF) in patient 2. **A:** Implantable cardioverter-defibrillator (Vigilant EL D233; Boston Scientific, Natick, MA) interrogation demonstrating sustained VF triggered by pseudo-pseudofusion with a premature ventricular complex (PVC) masked within the post–atrial pacing ventricular blanking period (*red asterisk*). Pacing mode was DDDR 60–105 beats per minute (bpm) with paced AV delay (AVD) 340 ms. **B:** Nonsustained VF triggered by the same mechanism. **C:** A nonsustained VF episode that occurred following initial reprogramming to DDD 55–105 bpm with paced AVD of 400 ms. **D:** A 7-lead continuous electrocardiogram strip showing R-on-T pacing as a result of pseudo-pseudofusion with a masked PVC (*red asterisk*), which did not initiate VF. SHOCK = far-field ventricular electrogram.

AVD of 260–340 ms / 230–300 ms, RHYTHMIQ (AAI with VVI backup) off. All lead parameters were normal, including R-wave sensing >25 mV and ventricular sensitivity of 0.6 mV. He had 5 total VF episodes treated with 1 ICD shock each (Figure 2A), and multiple nonsustained VF episodes (Figure 2B).

Careful review showed "masked" PVCs with pseudo-pseudofusion, and triggered ventricular pacing initiating each sustained and nonsustained VF episode. External monitoring showed triggered ventricular pacing on the T-wave downslope of a PVC, which did not initiate VF (Figure 2D). We initially reprogrammed pacemaker settings to DDD 50–105 bpm, AVD 280–400 ms, with RHYTHMIQ on. However, the patient re-presented 1 week later with presyncope and recurrent nonsustained VF episodes with similar mechanism (Figure 2C). We reprogrammed his pacing settings to DDI 70 bpm (this faster LRL demonstrated no pseudo-pseudofusion) with AVD 400 ms. He underwent an attempted PVC ablation (5.8% burden on 2-week monitor), but this was unsuccessful owing to inadequate PVC frequency during the procedure. The patient has had no further sustained or nonsustained VF episodes over 5 months follow-up off antiarrhythmic medications.

Discussion

We describe 2 cases where intradevice interactions led to a PVC being "masked" within the PAVB interval with pseudo-pseudofusion, triggering ventricular pacing during the vulnerable period of repolarization, and causing recurrent polymorphic VT/VF. In both cases, appropriate reprogramming with changing of the LRL and AVD successfully prevented further VF episodes without more aggressive and unnecessary medical treatments. While VT/VF initiation from pacing during the vulnerable period is known to be possible with asynchronous or DVI pacing, and with ventricular undersensing, it has not been previously reported in DDD mode with normal pacemaker function.[1–3]

Standard pacing programming ensures that each atrial paced beat is followed by a ventricular beat; ventricular safety pacing (VSP) is designed to avoid R-on-T pacing in case of pseudo-pseudofusion. In St. Jude Medical ICD devices, following atrial pacing, there is a nonprogrammable 52 ms PAVB interval, followed by a crosstalk detection window (CDW) of 12 ms. If ventricular sensing occurs in the CDW, VSP is triggered and delivers a ventricular impulse with an AVD of 120 ms. In Boston Scientific ICDs, there is a programmable PAVB (38, 45, 65, or 85 ms), but no CDW or VSP. These cases highlight the potential pitfalls of these programming "safeguards" when an appropriately timed PVC falls completely within the PAVB.

An undetected (masked) PVC leading to R-on-T pacing is likely rare, given the many coincident conditions necessary for it to occur, but also underrecognized. Given the recurrent nature of VT/VF episodes, however, underrecognition may have major treatment implications. Abuissa[4] previously

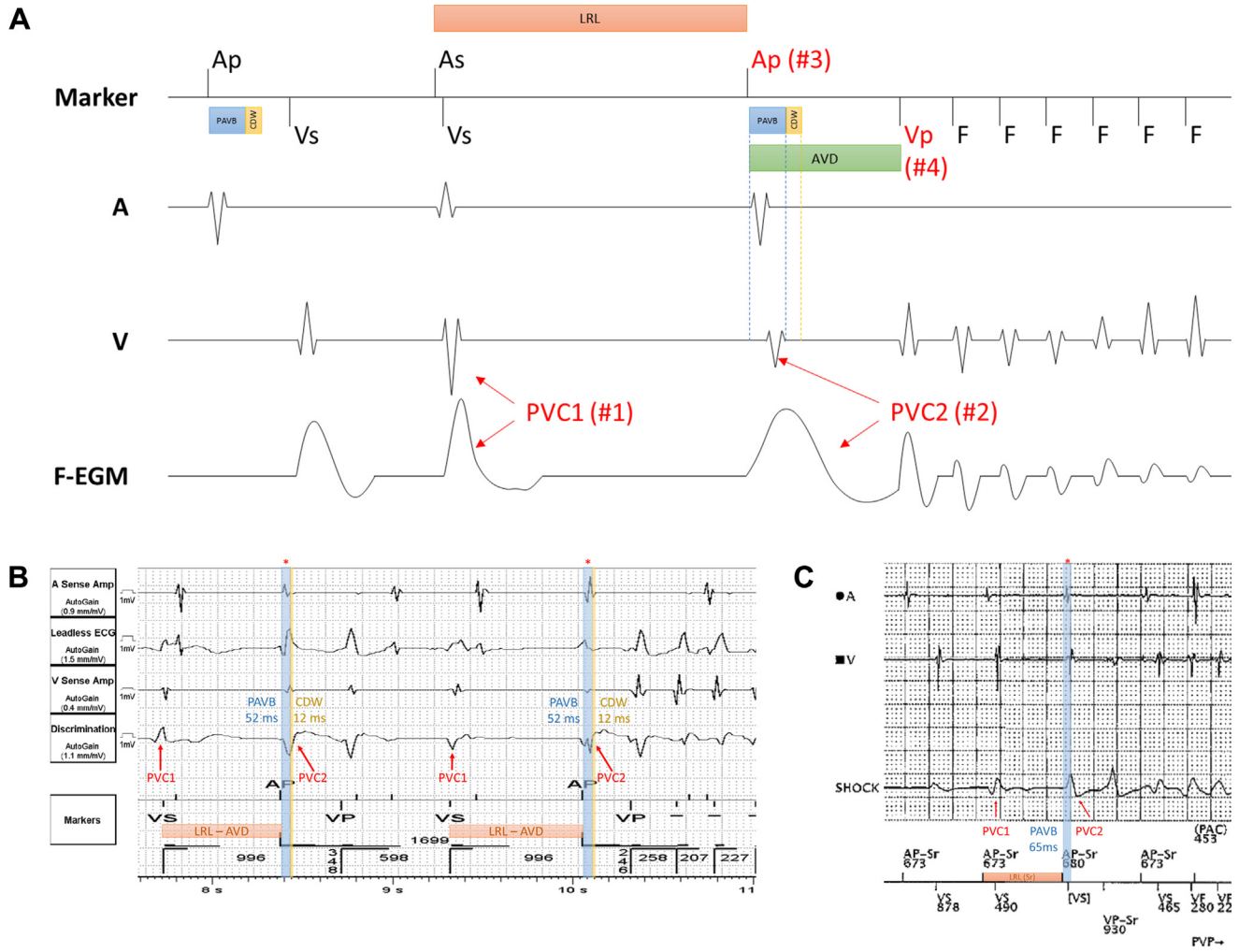

Figure 3 Mechanism of masked premature ventricular complex (PVC) leading to ventricular tachycardia (VT) / ventricular fibrillation (VF) in DDD pacing. Following atrial pacing, the post–atrial pacing ventricular blanking (PAVB) period is initiated, followed by a crosstalk detection window (CDW). Any ventricular sensing during the PAVB is blanked (ie, ignored), whereas sensing during the CDW leads to ventricular safety pacing at a short AV delay (AVD). Note that a CDW does not exist in Boston Scientific ICDs. **A:** The critical events leading to VT/VF in these cases (in red). After a first PVC (#1), a second PVC (#2) occurs at the same time as atrial pacing (#3), as determined by the lower rate limit (LRL), leading to pseudo-pseudofusion. Near-field sensing of the second PVC (#2) falls within the PAVB and is masked. Hence, ventricular pacing is triggered at the programmed AVD (#4), which falls within the PVC repolarization vulnerable period, leading to VF. The coupling interval between the 2 PVCs is long and variable, coinciding with the LRL-determined (or sensor-indicated rate) atrial pacing interval by chance. **B:** The episode in Figure 1B labeled with the critical PVCs and intervals. **C:** The episode in Figure 2C labeled with the critical PVCs and intervals. Ap = atrial paced; As = atrial sensed; ECG = electrocardiogram; F = ventricular fibrillation cycle length detected; F-EGM = far-field electrogram; Vp = ventricular paced; Vs = ventricular sensed.

reported a case of a "masked" PVC in a patient with a Boston Scientific ICD, leading to initiation of monomorphic VT. In that case, ventricular pacing occurred late in the T-wave downslope, suggesting that the mechanism of initiation was unidirectional block following the ventricular paced beat initiating re-entry. Delacretaz[5] reported VF in a patient with temporary epicardial leads and a Medtronic temporary pacemaker, initiated by asynchronous atrial pacing (owing to undersensing of atrial fibrillation), a masked normally conducted QRS complex, and R-on-T ventricular pacing. This phenomenon, however, would not occur with normal lead parameters, as in our 2 cases.

Out of 349 hospitalized patients with dual-chamber ICDs interrogated at our institution between July 2019 and August 2020, of whom 95 had received an appropriate ICD shock for VT/VF, we did not identify any other cases of "masked" PVC leading to R-on-T pacing–triggered VT/VF. PVC-induced VF may appear similarly with pseudo-pseudofusion on some episodes but not others, excluding a "masked" PVC as the primary etiology (Supplemental Figure 1).

Several features present in both cases were likely key in causing this rare phenomenon. Both patients had frequent multifocal PVCs, including couplets with a long coupling interval approximating the LRL, likely due to parasystole (Supplemental Figure 2), allowing for PVCs to occur at the same time as atrial pacing (Figure 3). Both patients also had baseline paced AVD programmed to 250–340 ms to avoid unnecessary right ventricular pacing, which, in turn, coincided with the PVC T-wave downslope when pseudo-pseudofusion occurred. While R-on-T pacing rarely causes

VF, the heart may be significantly more vulnerable after 2 consecutive PVCs owing to elevated sympathetic tone and levels of interstitial norepinephrine.[6]

Multiple programming changes were made in both patients, including extending the AVD to 400 ms and changing the LRL. Changes in both parameters may be necessary. Extending the AVD avoided pacing in the vulnerable period in patient 1, but not patient 2. Raising the LRL was necessary in patient 2 to prevent pseudo-pseudofusion and further episodes. Although the triggering PVC coupling intervals can be highly variable (Supplemental Figure 3), they likely occur within a limited range, which can be avoided with empiric adjustment of the LRL and AVD (atrial pacing cycle length post-PVC = LRL – AVD in devices with ventricular-based timing).

Although not tested in either case, shorter AVD (ie, 150 ms, as in Supplemental Figure 1B) may have prevented VF episodes by pacing during absolute refractoriness of the ventricle even with a "masked" PVC, though unnecessary right ventricular pacing may result. Single-chamber inhibited pacing modes (ie, AAI or VVI) would reliably prevent this problem but were not appropriate in our patients with conduction system disease.

Though both cases presented here were in patients with ICDs, it is possible that the same intradevice interaction can also lead to VF arrest in patients with pacemakers but never come to medical attention if the patient was not resuscitated. We previously showed that intradevice interactions with rate smoothing in Boston Scientific ICDs have led to underdetection of VT, which could lead to sudden death without any documentation of VT.[7] These cases highlight the importance of carefully reviewing the initiation of VF episodes to evaluate potentially reversible or treatable causes, such as a "masked PVC," PVC-induced VF, or torsades de pointes. Enhanced algorithms to differentiate between crosstalk and a PVC are also necessary to prevent such events, given the PAVB is a rudimentary method to avoid crosstalk.

Conclusion

We presented 2 cases of intradevice interaction leading to a PVC being masked within the PAVB with pseudo-pseudofusion, leading to triggered ventricular pacing during the vulnerable period and polymorphic VT/VF. In both cases, lengthening the AVD to 400 ms and changing the LRL (lowered in 1 case and increased in the second) resulted in complete elimination of the VT/VF episodes. These cases highlight the potential pitfalls of the simple PAVB algorithm to avoid crosstalk.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://10.1016/j.hrcr.2020.11.002.

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