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ICD Electrograms in Patients with Brugada Syndrome

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Additional information is available at the end of the chapter

Abstract

In patients with Brugada syndrome, implantable cardioverter-defibrillator (ICD) is the only demonstrated treatment that prevents sudden cardiac death. The progress in ICD technology improved the diagnosis and efficacy of implantable devices in the management and treatment of ventricular tachycardia (VT) and ventricular fibrillation (VF). Recording of electrical events just before and after a delivered or aborted ICD therapy permits a more accurate characterization of the rhythm but also provides information on the electrical events preceding the arrhythmia. This chapter aims to gain insight into the mechanism of initiation and termination of spontaneous VF by analyzing intracardiac electrograms (IEGM) in Brugada patients implanted with ICDs. It has two parts: **(1) update on ICD electrograms in Brugada syndrome patients**, where we review the medical literature on ICD electrograms and their use for detecting electrical manifestations of Brugada syndrome, and **(2) examples of ICD electrograms,** from our own database of patients affected by Brugada syndrome.

Keywords: Brugada syndrome, ICD, defibrillation, ventricular fibrillation, premature ventricular contractions, electrophysiological study

1. Introduction

Brugada syndrome is a clinical syndrome associated with ventricular tachycardia (VT) and ventricular fibrillation (VF), in patients who have no structural heart disease. ECG is the most useful tool for the diagnosis and shows right bundle branch block with ST elevation in right precordial leads. Due to the high recurrence rate of ventricular fibrillation, an implantable cardioverter-defibrillator (ICD) is the accepted mode of treatment and it improves the long-term prognosis.

Clinical studies suggest that spontaneous episodes of VF are induced by PVCs originating at the level of right ventricular outflow tract (RVOT). Abnormal electrophysiological features are present in this zone, with fragmented, low amplitude, late potentials. Programed ventricular stimulation at the level of RVOT increases the chance of VF induction compared to RV apex.

The progress in ICD technology improved the diagnosis and treatment efficacy of implantable devices in the management of VT and VF in Brugada syndrome. Recording of electrical events before and after a delivered or aborted ICD therapy permits not only a more accurate characterization of the rhythm but also provides information on the electrical events preceding the arrhythmia.

2. Mode of onset of ventricular fibrillation in Brugada syndrome

In Brugada syndrome, VF episodes can be preceded by PVCs or start suddenly without a preceding premature ventricular contractions (PVC). This classification assumes distinct electrophysiological mechanism for the two types of VF. Although very few PVCs are observed on Holter monitoring, in Brugada syndrome PVCs tend to occur more frequently before the initiation of VF, as well as ST segment elevation in precordial leads [1]. The mechanism that explains the association of the two phenomena is the marked shortening of the action potential in the RVOT which gives the ST elevation, and phase 2 reentry responsible for PVC firing from the same area with short action potential, which initiates VF [2, 3]. Kofune et al. were able to identify the substrate of the Brugada syndrome by high-resolution electroanatomical mapping. In patients with Brugada syndrome, they found that only the right ventricle is affected, the left being spared, and only a small area within the RVOT is responsible for the syndrome. At this level, they found low-voltage potential with fractionated electrograms. The conduction abnormality from the RVOT gives the final phenotypic expression of right precordial ST segment elevation [4]. Previous studies of Antzelevitch et al. demonstrated that at cellular level the action potential dome propagates from the normal epicardial sites to the epicardial site without dome leading to phase 2 reentry. As the reentry fails to propagate to the endocardium, it leads to closely coupled ventricular premature beats [5]. Specific triggers can lead to heterogeneous repolarization: fever or after exercise when the body temperature rises, and specific medication like: ajmaline, flecainide, and propafenone.

In the study of Kakishita et al., frequent PVCs before the onset of VF were recorded in 67% of the patients. The morphology of preceding PVC electrogram (far-field and near-field) was identical to the PVC that initiated VF. Additionally, different VF episodes seen in the same patient were initiated by the same PVC morphology. The rest of 33% of patients had episodes of VF without preceding PVCs.

A long-short sequence is very unlikely to initiate VF in Brugada syndrome and pause-dependent VF is very rare [6].

3. Coupling interval of the VF initiating PVC

It is well known that PVCs occurring near the peak of the T-wave (ventricular vulnerable period) may lead to ventricular fibrillation. However, in Brugada syndrome, the onset of PVCs inducing VF are close to the end of the T-wave. Kakishita et al. found a coupling interval of 388 ms for the PVC initiating VF in patients with Brugada syndrome. Kasanuki et al found a value of > 300 ms coupling interval for the PVC inducing VF. Spontaneous VF is provoked by a single, long >300 ms coupled PVC. Induced VF can be provoked by multiple extrastimuli with shorter coupling interval < 200 ms for VF induced during electrophysiological study [7].

4. Ventricular fibrillation interval (VF interval)

For long time, physicians thought that the amplitude of VF waves ("fine" or "coarse") is suggestive of defibrillation success, but Murakawa et al. demonstrated on dogs [8] that shorter ventricular fibrillation intervals are associated with higher energies for internal defibrillation. VF interval is a parameter that can be measured using the ICD electrograms. Kerber et al. [9] reported that slower polymorphic VT with cycle length >200 ms needs less energy for defibrillation than VF with cycle length of less than 200 ms. Cismaru et al. studied VF cycle length in patients with Brugada syndrome, induced VF during electrophysiology study, and showed that a longer cycle length that progressively increases is a sign of self-terminating VF [10] (**Figures 1** and **2**).
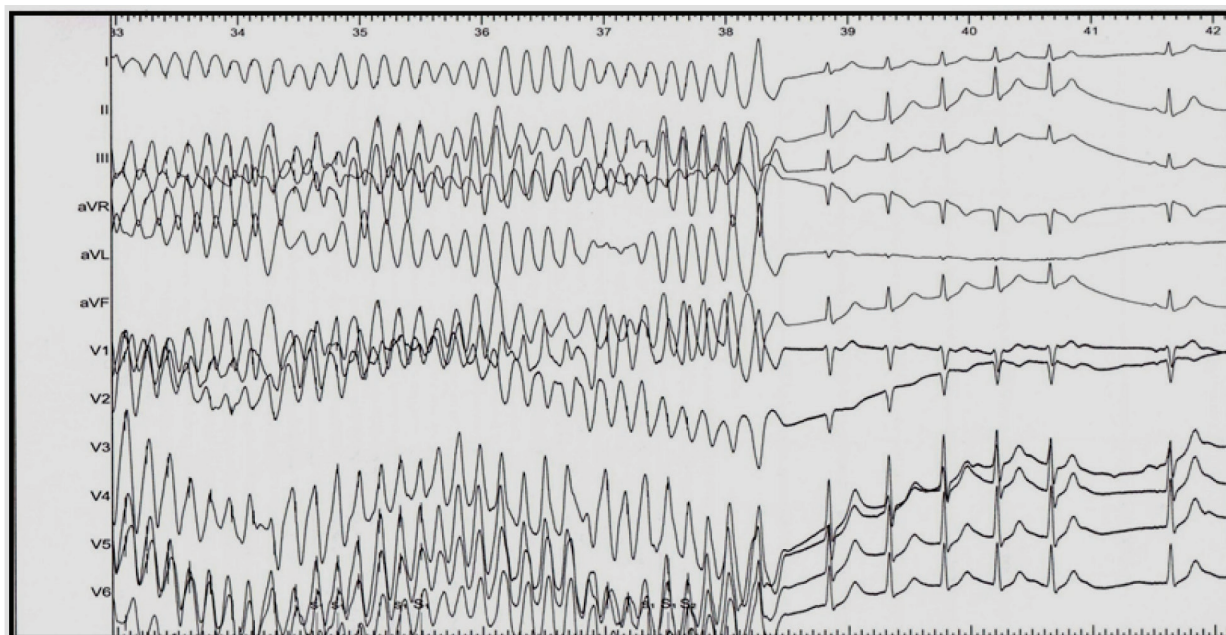

Figure 1. Patient with Brugada syndrome and polymorphic VT induction during electrophysiology study. VT stops spontaneously without any defibrillation.
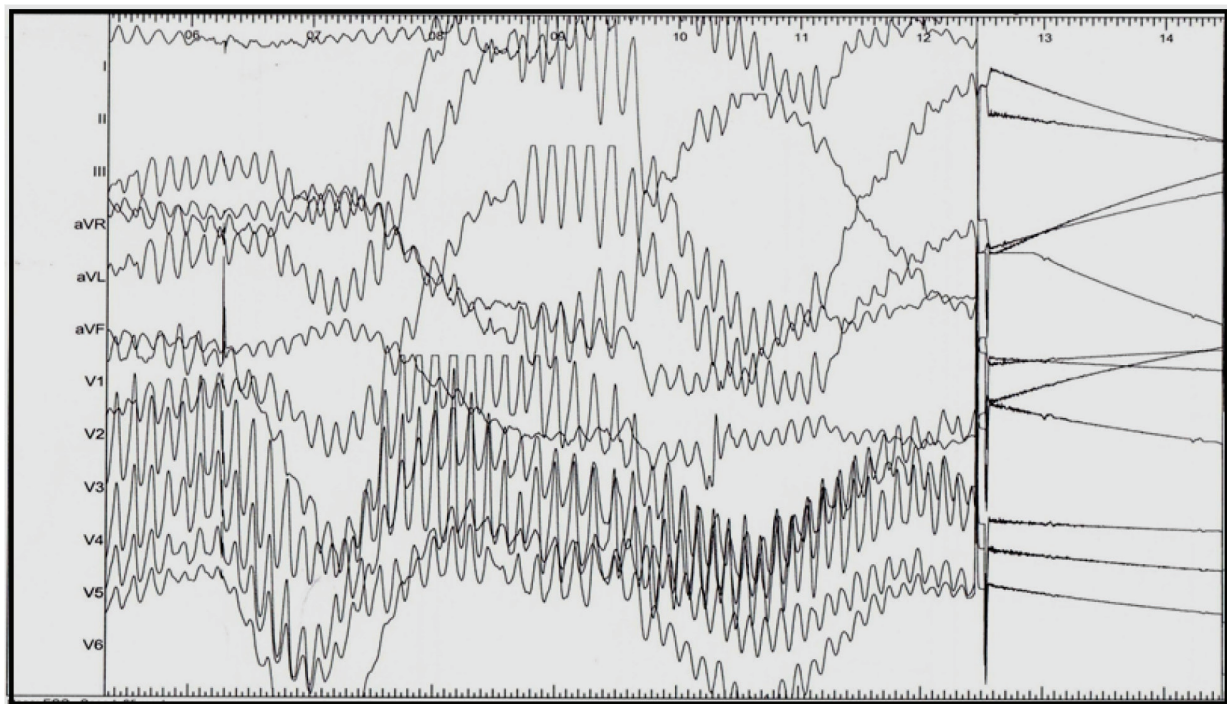
Figure 2. Patient with Brugada syndrome and ventricular fibrillation induction during electrophysiology study. Please note the short VF interval. VF stops after external defibrillation.

Hiratsuka et al. demonstrated that symptomatic patients with Brugada syndrome have significant shorter VF cycle length than asymptomatic patients. The difference is probably given by a different electrophysiological substrate between the two groups [11].

5. Unsuccessful internal defibrillation in Brugada syndrome

Patients with Brugada syndrome have higher rates of unsuccessful internal defibrillation after the implantation of ICD. The study of Watanabe et al. [12] examined the incidence of VF not responding to internal defibrillation and found an incidence of 18%. One explanation could be the origin of the electrical abnormality at the level of RVOT [13] with defibrillation shock delivered between the right ventricular apex and left subclavicular can. Alternative explanation is the short effective refractory period and short ventricular fibrillation interval (FVI) in patients with Brugada syndrome.

6. Intracardiac electrograms (IEGM) compared to morphological changes of an ECG during provocative tests

Probst et al. [14] compared the surface ECG with the intracardiac electrograms (IEGM) from internal defibrillator during an ajmaline test in patients with Brugada syndrome. The ECG morphology changed after ajmaline injection with ST elevation and negative T-waves. The IEGM showed different morphological changes: ST deviation changes with negative T-wave

changes. The changes are in contrast with morphological changes from patients without Brugada syndrome where IEGM correlates to ST segment deviation on ECG. In countries where ajmaline is not available, procainamide can be used for the provocative test.

In the case report of Moore and Kaye, a change of the intracardiac electrogram after an internal defibrillation was compatible with a type 1 Brugada pattern and disappeared 1 min after the electrical shock [15, 16].

7. T-wave alternans in patients with Brugada syndrome

T-wave alternans is the ECG manifestation of action potential repolarization alternans. Beat-to-beat alternation of ventricular action potential in both duration and amplitude reflects the risk of ventricular tachycardia and ventricular fibrillation [16]. T wave alternance (TWA) from ICD electrograms are concordant with TWA from the surface ECG because they measure the same alternans phenomenon [17] (**Figure 3**).

Tada et al. described a patient with Brugada syndrome that presented TWA after administration of a sodium channel blocker (cibenzoline) [18]. Ohkubo et al. also described TWA in a patient with Brugada syndrome after class 1 antiarrhythmic drug (pilsicainide). TWA persisted for 15 min and was followed by microvolt TWA [19].

Tada and colleagues [20] investigated the association between ventricular tachycardia and fibrillation with TWA induced by intravenous pilsicainide (sodium channel blocker). Pilsicainide provoked visible TWA in 17 of 77 Brugada patients. Those with TWA experienced a significantly higher incidence of spontaneous VF (52.9 vs. 8.3%) than those without TWA.
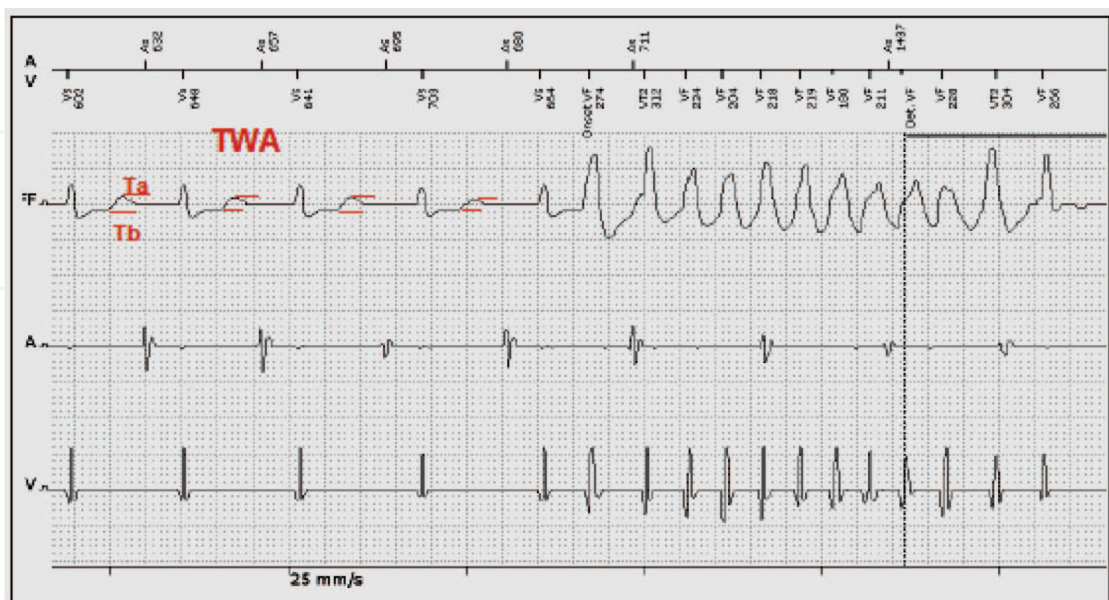

Figure 3. Method for determination of TWA: the amplitude for each T-wave is calculated as the maximum minus the minimum value (horizontal red lines). The difference between the amplitude of the first beat and second beat of each pair is calculated using the formula: TWA = $[(Ta−Tb)_1+(Ta−Tb)_2+…(Ta−Tb)_x]/x$.

8. Use of stored ICD electrograms for catheter ablation of ventricular fibrillation in Brugada syndrome

Stored electrograms can be used for catheter ablation of ventricular fibrillation. Both far-field EGM and near-field EGM are used [21]. First, the EGM that initiates ventricular fibrillation should be captured. This is used as a template for subsequent pacemapping (**Figure 4**). Information regarding the morphology and timing of the EGM are used to search for the best correlation during pacemap. Both spontaneous QRS complex morphology and far-field ICD morphology are used for comparison with the paced morphology. Timing between far-field and near-field ICD electrograms is also used for the template when comparing with the paced beat.

Pacemapping is attempted at the level of RVOT with real-time recording from the ICD electrogram. Both morphology and timing are used to delineate the zone with the best match and that zone will be a target for ablation. The study of Almendral et al. [22] showed spatial resolution of 2 cm² for best match with electrogram morphology and timing. The same resolution was confirmed by Lowery et al. in patients with different types of ventricular fibrillation [21].

Substrate epicardial mapping is initiated in sinus rhythm to identify dense scar <0.5 V and border zone between 0.5–1.5 V. Abnormal electrograms consist in low amplitude–wide duration of >80 ms, with multiple or delayed components outside the end of the surface ECG QRS. The same RVOT zone is remapped after IV flecainide to determine increase in abnormal electrogram area after infusion. Catheter ablation targets the complete elimination of the substrate inside the low-voltage areas [23].
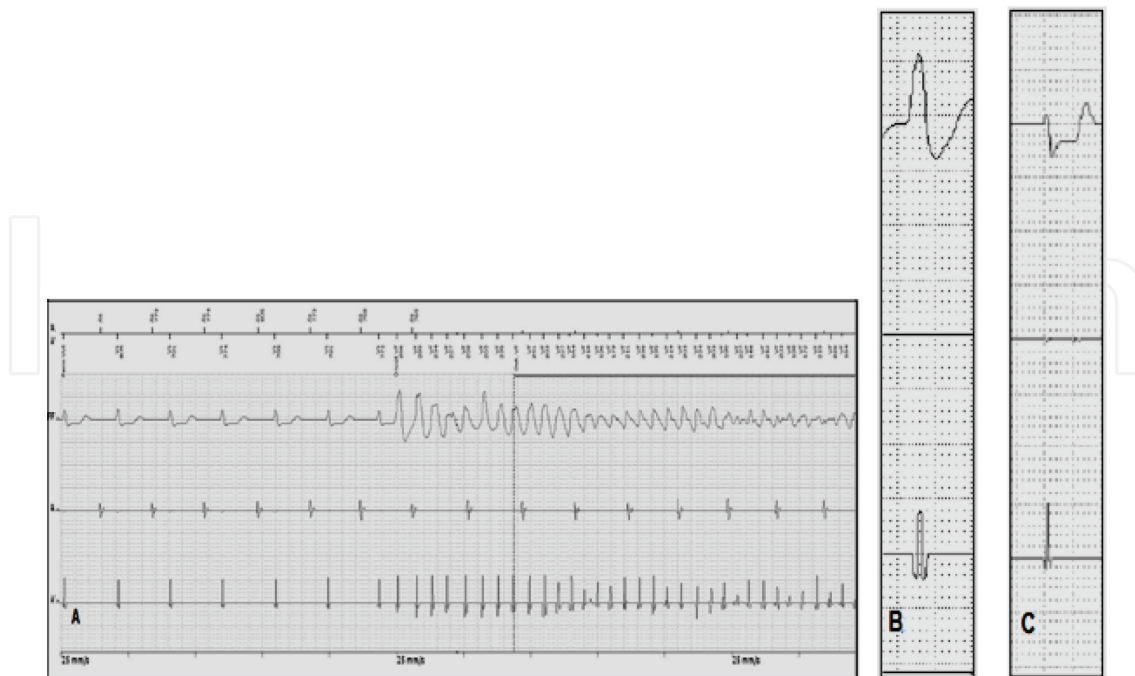

Figure 4. Example of pacemapping of a trigger arising from the RVOT in a patient with Brugada syndrome. Panel A corresponds to the recorded spontaneous PVC inducing VF (A). Panels B and C show near- and far-field electrograms with a bad correlation between the spontaneous RVOT (B) and paced electrogram (C).

9. Examples of ICD electrograms

We present electrograms from our cardiology department in patients with Brugada syndrome:

- Coupling interval of the PVC initiating ventricular fibrillation (**Figures 5** and **6**).
- Safe terminating ventricular tachycardia (**Figures 7** and **8**).
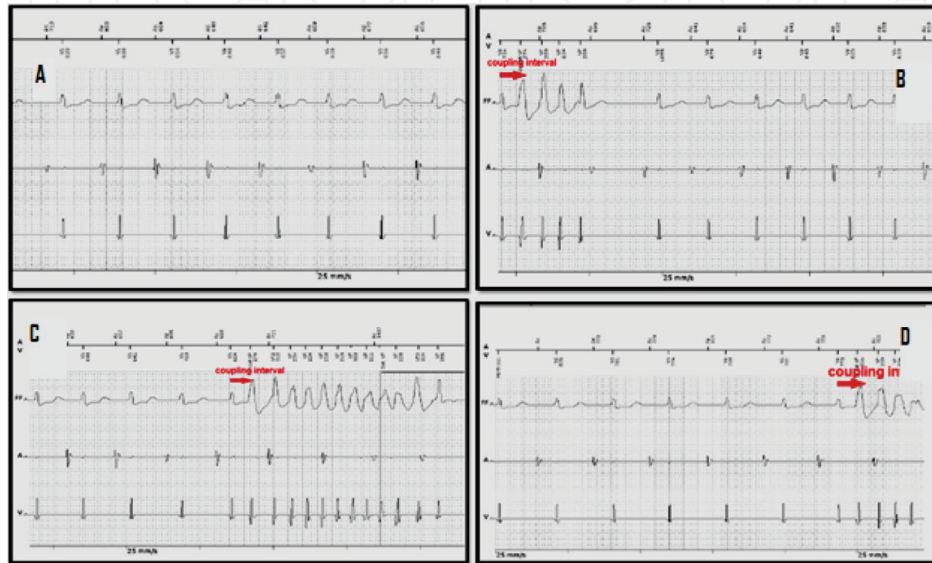- Ventricular fibrillation terminated by an electrical shock (**Figure 9**).

Figure 5. The same coupling interval 330 ms and the same PVC morphology at the initiation of nonsustained VT in a patient with Brugada syndrome. (A) without PVCs; (B) PVC inducing NSVT; (C) same PVC inducing NSVT; (D) same PVC inducing NSVT.

Figure 6. The same coupling interval 322 ms and same morphology at the initiation of nonsustained VT in a patient with Brugada syndrome. (A) PVCs with ventricular trigeminism; (B) same PVC inducing NSVT; (C) same PVC inducing (D) self-terminating VF.
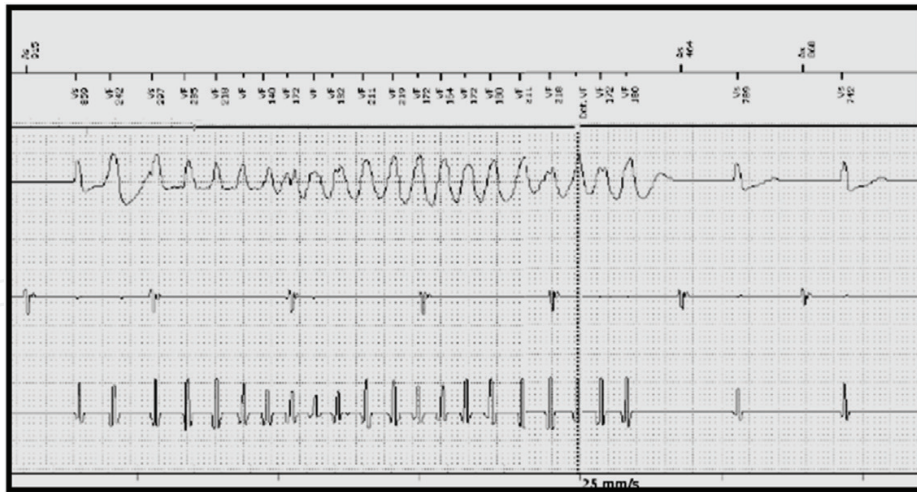
Figure 7. Self-terminating ventricular tachycardia. Please note the long cycle length. Upper electrogram is the far-field ventricular IEGM; in the middle of the strip atrial IEGM; at bottom near-field ventricular IEGM.
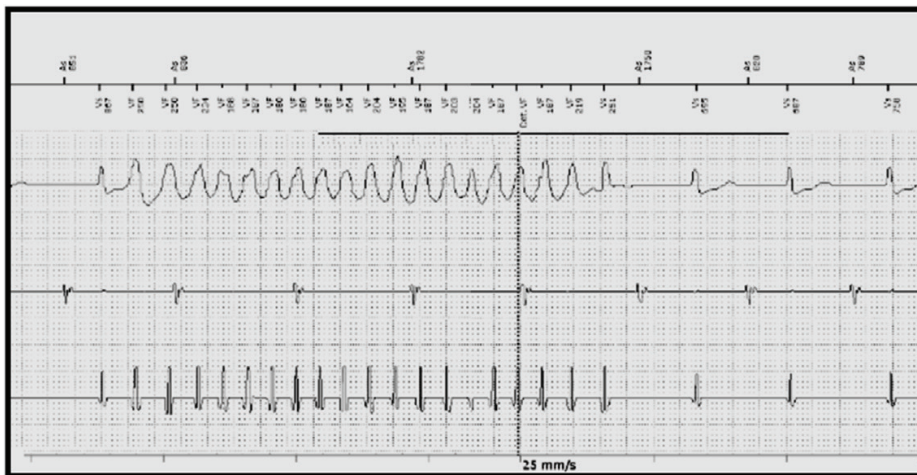

Figure 8. Self-terminating (or nonsustained) ventricular tachycardia. Please note the long cycle length.
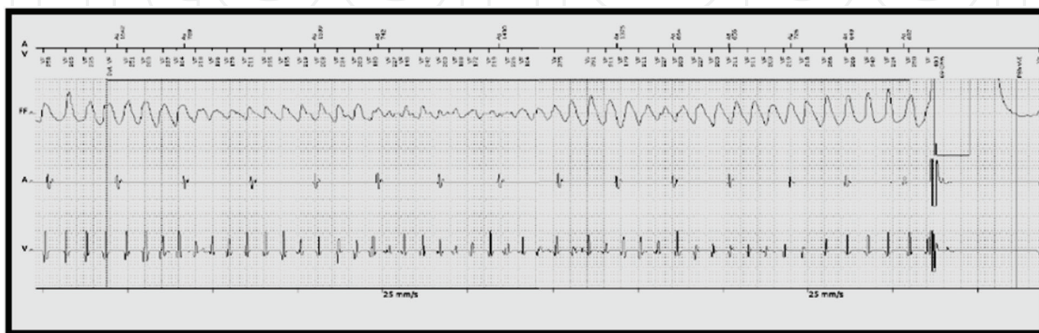

Figure 9. Ventricular fibrillation terminated with an external shock. Please note the short VF interval.

10. Conclusion

Analysis of intracardiac electrograms during episodes of ventricular arrhythmias is effective for clarifying the mechanism of the episode. Many spontaneous episodes of VF are preceded by frequent PVCs. The coupling interval usually is long and reaches the end of the T-wave. Ventricular fibrillation interval is short and may be responsible for failure of internal defibrillation. Longer VF interval values predict spontaneous termination of VF. A catheter ablation technique was described for catheter ablation of PVCs initiating VF in Brugada syndrome and uses the stored IEGMs as template for pacemapping.

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