JOURNAL OF CARDIOVASCULAR ELECTROPHYSIOLOGY

Mapping and Ablating Ventricular Premature Contractions that Trigger Ventricular Fibrillation: Trigger Elimination and Substrate Modification

Journal:	*Journal of Cardiovascular Electrophysiology*
Manuscript ID:	JCE-140601.R1
Wiley - Manuscript type:	Techniques, Technology, and Innovations
Date Submitted by the Author:	n/a
Complete List of Authors:	Nogami, Akihiko; University of Tsukuba, Cardiology
Key Words:	Clinical: Catheter ablation – ventricular tachycardia, Clinical: Cardiac mapping – electrogram analysis, Clinical: Electrophysiology – cardiac arrest/sudden death, Clinical: Non-invasive techniques – Holter/event recorders, Clinical: Implantable devices – ventricular tachycardia/fibrillation

"Techniques, Technology, and Innovations in EP" Section in the *Journal of the Cardiovascular Electrophysiology*

Mapping and Ablating Ventricular Premature Contractions that Trigger Ventricular Fibrillation: Trigger Elimination and Substrate Modification

AKIHIKO NOGAMI, M.D., Ph.D.

From the Cardiovascular Division, University of Tsukuba, Tsukuba, Ibaraki, Japan

Brief title: VF Ablation

Address for correspondence:

Akihiko Nogami, M.D., Ph.D., the Cardiovascular Division, University of Tsukuba, 1-1-1 Tennodai Tsukuba, Ibaraki, 305-8575, Japan.

Tel: +81-29-853-3142

Fax: +81-29-853-3143

E-mail: akihiko-ind@umin.ac.jp

Abstract: 239 words, Text: 3200 words; 4 figures, 5 references.

Abstract

Mapping and Ablating the Trigger of Ventricular Fibrillation.

Ventricular fibrillation (VF) is a malignant arrhythmia, usually initiated by a ventricular premature contraction (VPC) during the vulnerable period of cardiac repolarization. Ablation therapy for VF has been described and increasingly reported. Targets for VF triggers are VPC preceded Purkinje potentials or the right ventricular outflow tract (RVOT) in structurally normal hearts, and VPC triggers preceded by Purkinje potentials in ischemic cardiomyopathy. The most important issue before the ablation session is the recording of the 12-lead ECG of the triggering event, which can prove invaluable in regionalizing the origin of the triggering VPC for more detailed mapping. In cases where the VPC is not spontaneous or inducible, ablation may be performed by pacemapping. During the session, mapping should be focused on the earliest activation and determining the earliest potential is the key to a successful ablation. However, a modification of the Purkinje network might be applied when the earliest site cannot be determined or is located close to the His-bundle. Furthermore, the electrical isolation of the pulmonary artery (PA) can suppress RVOT type polymorphic ventricular tachycardia in some patients with rapid triggers from the PA. Suppression of VF can be achieved by not only the elimination of triggering VPCs, but also by substrate modification of

possible reentry circuits in the Purkinje network, or between the PA and RVOT. Further studies are needed to evaluate the precise mechanisms of this arrhythmia.

Key words

catheter ablation, right ventricular outflow tract, polymorphic ventricular tachycardia, Purkinje network, trigger beat, ventricular fibrillation

Introduction

While previous studies have shown that ventricular fibrillation (VF) is perpetuated by reentry or spiral waves, recent data suggest the role of specific sources triggering this arrhythmia. Haïssaguerre et al. [1] reported that idiopathic VF could be suppressed by catheter ablation of those triggers originating from the Purkinje system or right ventricular outflow tract (RVOT) and the ablation therapy for VF has been increasingly reported during the last decade. In general, this ablation appears to have a high success rate and is relatively easy to perform, although precise mapping is required. However, little is known about the initiating mechanism of VF. Further, whether the mechanism of the ablation effect is due to the suppression of the trigger or substrate modification is also unclear. The objective of this review was to summarize the strategies we have incorporated into our catheter ablation procedures for VF, especially in difficult and complicated cases.

Twelve-lead Recording of Triggering VPCs

Most cases of VF appear to originate from the Purkinje system, and some cases report initiating events that are distinct from the cardiac conduction system such as the RVOT [1]. Recording of the 12-lead ECG of the triggering event can prove invaluable in regionalizing the origin of the triggering VPC for

more detailed mapping, and an effort to record such a trigger should be routine. The target site can be speculated with the 12-lead ECG documentation: RVOT, right distal Purkinje, left posterior Purkinje, or left anterior Purkinje system. In the patients without ectopy, the putative source of the VPC can be ablated in sinus rhythm based on pace mapping followed by radiofrequency (RF) energy delivery. In the patients with multifocal VPCs, the true triggering VPC that initiates VF or nonsustained polymorphic ventricular tachycardia (VT) has to be confirmed. It is essential that there is accurate documentation of the triggering VPC, with a 12-lead ECG.

Figure 1 shows ECGs from a 59-year-old female patient with early repolarization associated with VF [2]. Each panel shows the QRS complexes during sinus rhythm and the VPC. In the emergency room, significant J-ST elevation in the infero-lateral leads and VPC bigeminy with a right bundle branch block (RBBB) configuration and superior axis were observed after the spontaneous termination of polymorphic ventricular tachycardia (VT) (Fig. 1A). One month after the implantation of a defibrillator (ICD), a triggering VPC ablation was performed due to frequent ICD shocks. During the ablation session, frequent monofocal VPCs were observed (Fig. 1B), and Purkinje potentials on the posterior left ventricular septum preceded the onset of the VPC by 65 ms. An RF energy application at that site immediately eliminated the

VPC. However, a few days after the session, VF recurred. A 12-lead Holter recording could record the initiation of the VF (Fig. 1C). The "true" triggering VPC was similar to the ablated VPC, but different (especially lead aVR). Interestingly, while J-ST elevation was recorded in the emergency room and during the VF recurrence, it was not observed during the ablation session. There was a possibility that the true triggering VPC appeared only during the J-ST elevation. The patient did not prefer to undergo a re-ablation session and the oral administration of disopyramide successfully suppressed the VF recurrence.

In the intensive care unit, a synthesized 12-lead ECG from the signals recorded using three to five electrodes is sometimes used. In our experience, the limb leads in the synthesized 12-lead ECG are similar to the Mason-Likar lead configuration, in which the limb lead electrodes are placed on the torso rather than the distal extremities, and can be used for the morphology analysis of VPCs. However, the chest lead information in the synthesized ECG is less useful because of its inaccuracy. Twelve-lead Holter monitoring also uses a Mason-Likar lead configuration similar to the limb leads and the real six chest electrodes for the chest leads, and appears to be highly reliable and useful for the diagnosis of "true" triggering VPCs.

Substrate Modification of the Purkinje Network

The Purkinje system is the most frequent site of initiation of VF. Recent work has demonstrated that the Purkinje network is critical in the triggering and maintenance of VF in animal experiments and patients. Catheter ablation targeting the Purkinje potentials responsible for triggering VF has been shown to be possible and efficacious in a number of conditions such as idiopathic VF (short-coupled variant of torsade de pointes), ischemic VF, and chronic myocarditis. What is still undetermined is whether the mechanism of the ablation effect is due to the suppression of the trigger or substrate modification.

During activation mapping of the triggering VPC, attention should be paid to the preceding sharp Purkinje-like signals. Mapping should be focused on the earliest activation of this potential, and determining the earliest potential is the key to a successful ablation. However, the potential may sometimes be seen to occur with intra-Purkinje block to the myocardium, and not produce a VPC. This means that there is the possibility that not only the elimination of the triggering VPC, but also conduction block in the Purkinje network can suppress the triggering VPC and VF. In fact, dissociated firing from the Purkinje network is sometimes seen after a successful ablation. The following case is an example of the successful suppression of VF by the modification of the Purkinje network

[3].

A 54-year-old man with idiopathic VF (short-coupled variant of torsade de pointes) underwent catheter ablation for frequent episodes of ICD shocks. Nonsustained polymorphic VT with the same QRS morphology as the clinical polymorphic VT was repeatedly inducible by atrial pacing after an intravenous administration of cibenzoline (Fig. 2A). There was no change in the QRST complexes in any of the electrograms after the intravenous administration of cibenzoline. The first VPC (VPC1) had an RBBB configuration with right-axis deviation and the second one (VPC2) had an RBBB pattern with a northwest axis. The coupling interval of VPC1 to the preceding normally conducted QRS complex was 250 ms. During the polymorphic VT, diastolic and presystolic Purkinje potentials were recorded from an octapolar electrode catheter with 1.25-mm electrode widths and 2-mm inter-electrode spacings placed on the left ventricular septum (Fig. 2A and Fig. 2B). Diastolic Purkinje potentials were recorded earlier from the proximal than distal electrodes, and fused presystolic Purkinje potentials were recorded earlier from the distal than proximal electrodes. During sinus rhythm, recording at the same site demonstrated fused Purkinje potentials before the onset of the QRS. Because the earliest Purkinje activation site before VPC1 could not be determined and seemed to be a more proximal site than the site of electrodes 7-8, RF energy was

delivered to the site of electrodes 3-4. A Purkinje potential from this site preceded the onset of VPC1 by 15 ms and VPC2 by 60 ms. The intracardiac electrograms recorded after the ablation showed the abolition of the local Purkinje potentials at the middle portion and a slight delay in the occurrence of the local ventricular electrogram during sinus rhythm (Fig. 2C). The polymorphic VT became noninducible and only an isolated VPC was inducible. The morphology of this isolated VPC differed from the previous triggering VPCs (VPC1 or VPC2). Further, Purkinje firing was observed before this VPC and intra-Purkinje block occurred. Holter monitoring after the ablation revealed no VPCs. He was followed up without any drugs or episodes of syncope or VF recurrences during a follow-up period of 14 years. These observations suggest that the VF initiation was caused by activity from the Purkinje tissue. However, the suppression of the VF was achieved with catheter ablation of the Purkinje network, not of the earliest Purkinje activation of the initial triggering beat in this patient. If the early phase of VF is perpetuated by variable reentrant loops within the Purkinje network, the mechanism of VF suppression in this patient can be explained by intra-Purkinje block.

In the report by Haïssaguerre et al. [1] electrocardiograms recorded after ablation showed the abolition of the local Purkinje potentials and a slight delay in the occurrence of the local ventricular electrogram. However, they did not

determine how much of the complex Purkinje network was involved in each patient and the issue of multiple foci versus differing activation routes from limited foci remains unsolved. In our case, catheter mapping revealed that the constantly changing polymorphic QRS morphology resulted from the changing propagation in the Purkinje arborization and the polymorphic VT became noninducible after the catheter ablation of the Purkinje network. We did not ablate the earliest site of the Purkinje activation, and the isolated VPC with diastolic Purkinje activation was still inducible after the catheter ablation.

Of course, the earliest activation site of the Purkinje activation during the triggering VPC should be searched and ablated; however, a modification of the Purkinje network might be applied when the earliest site cannot be determined or is located close to the His-bundle. In my experience, the right-sided triggers usually arise from the distal right bundle branch and the most proximal site of the origins on the left side was the bifurcation of the left anterior and posterior fascicles. If the earliest site is located proximal to the bifurcation, ablation of just the distal site is recommended for the initial application. It is possible to create substrate modification and eliminate the origin nearby because the Purkinje network can be easily ablated.

Because the Purkinje network in humans is mostly localized to the subendocardium, a transmural lesion creation is not needed. Further, the

ventricular myocardium of the culprit Purkinje network in idiopathic VF is usually healthy. This differs from ischemic VF, in which the ventricular myocardium at the culprit Purkinje network usually has a low-voltage and is located near a scar-border. During the Purkinje network modification, the creation of bundle-branch block or hemi block is not required. While some change in the frontal axis has been observed in some patients after the ablation during a left septal Purkinje ablation, the QRS width remains almost the same. Catheter manipulation sometimes produces transient bundle-branch block. As a result, peripheral Purkinje potentials no longer precede the local ventricular activation in sinus rhythm, and it make mapping of the Purkinje network difficult. For this reason the creation of bundle branch block should be avoided.

Substrate Modification for RVOT Type Polymorphic VT

The RVOT is the most common origin of monomorphic VT in structurally normal hearts and it is also the origin for triggers of polymorphic VT, which rapidly degenerates into VF. This type of ablation is essentially no different than the ablation of idiopathic RVOT-VPCs or VT. The ablation targets the site of earliest activation and pacemapping in the RVOT [4]. The following case

demonstrates an unusual patient with the suppression of polymorphic VT by conduction block between the pulmonary artery (PA) and the RV.

A 56-year-old female with multiple episodes of syncope was referred to our hospital, and Holter monitoring revealed frequent episodes of polymorphic VT (Fig. 3A). The mean cycle length of the VT was 220 ms and the morphologies of the first three QRS complexes of the polymorphic VT were always the same. Electroanatomical mapping was performed and the propagation map of the first VPC had a centrifugal pattern from the posterior attachment of the RVOT. From that site, pace mapping was performed. Interestingly, pacing at a cycle length of 300 ms created the exact same polymorphic QRS configurations as those during the clinical polymorphic VT (Fig. 3B and Fig. 3C). After several RF energy applications to the posterior RVOT, the repetitive VPCs disappeared. However, isolated VPCs with a slightly different QRS morphology and longer coupling interval remained. Therefore, mapping in the PA was performed. From the PA, a delayed PA potential was recorded during sinus rhythm and that potential preceded the onset of the QRS during the VPC that remained (Fig. 4A). Between the PA and RVOT potentials, a tiny bridging potential was recoded. RF energy was delivered at this site in the PA. Just after the RF energy application, the PA potential disappeared (Fig. 4B). Repetitive firing from the PA was observed; however, there were no VPCs. These findings indicate there

was bidirectional conduction block between the PA and RVOT. In this case, the site-of-origin of the triggering beat was in the PA, and the multiple exits or non-uniform conduction to the RVOT might create the polymorphism of the VT. In fact, the change in the QRS configuration was reproduced by pacing at a relatively long cycle length. In this case, the electrical isolation of the extracardiac vessel, i.e. PA, suppressed the fibrillatory arrhythmia in the connecting heart chamber, i.e. RV. Interestingly, it is quite similar to the relationship between the pulmonary vein and left atrium in the mechanism of paroxysmal atrial fibrillation.

It has now been clearly established that myocardial sleeves extend into the great arteries for variable distances. These myocardial sleeves commonly extend fairly symmetrically crossing each of the 3 pulmonary valve cusps. The extensions can vary from a few mm up to more than 2 cm into the pulmonary artery [5]. The outflow tract artery junction is complex both in terms of its development and histologically with multiple tissue types interfacing in this region. The precise mechanism of the polymorphic changes in the QRS complex cannot be clarified from our results. However, based on our results [4] and previously reported data [5], the functional block or delayed conduction by rapid firing due to triggered activity or micro-reentry arising from a single focus led to chaotic conduction, causing polymorphic VT/VF without an organic

delayed conduction zone. In the presented case, burst pacing from the earliest activation site could reproduce several initial QRS complexes identical to the documented polymorphic VT. This reproducibility suggested that the polymorphic VT from the RVOT occurred from a single focus by triggered activity or micro-reentry with multiple myocardial exits to the RV and the development of polymorphic QRS waves. In addition, we recently demonstrated the shorter coupling interval (CI) index (CI / preceding R-R) in the patients with polymorphic VT than in those with monomorphic VT and the shorter CI index during VT than isolated VPCs in the same patients with polymorphic VT [4]. These might result from complexes that are impinging on the ventricular refractoriness (producing dispersion of refractoriness) or may be related to a triggered mechanism of initiation. In the presented case, the repetitive VPCs disappeared after several RF applications to the posterior RVOT. A residual isolated VPC had a slightly different QRS morphology and longer CI and originated from the PA.

Conclusion

VF is a lethal arrhythmia that may be present in patients with or without structural heart disease. RF catheter ablation of VF is feasible and can be used as a bailout therapy for drug-refractory electrical storms. Suppression of VF can

be achieved by not only the elimination of triggering VPCs, but also the creation of conduction block between the PA and RVOT, or of the Purkinje network. Further studies are needed to evaluate the precise mechanisms of this arrhythmia.

References

1. Haïssaguerre M, Shoda M, Jais P, Nogami A, Shah DC, Kautzner J, Arentz T, Kalushe D, Lamaison D, Griffith M, Cruz F, Paola A, Gaïta F, Hocini M, Garrigue S, Macle L, Weerasooriya R, Clementy J: Mapping and ablation of idiopathic ventricular fibrillation. Circulation 2002; 106; 962-967.
2. Haïssaguerre M, Derval N, Sacher F, Jesel L, Deisenhofer I, de Roy L, Pasquié J-L, Nogami A, Babuty D, Yli-Mayry S, De Chillou C, Scanu P, Mabo P, Matsuo S, Probst V, Le Scouarnec S, Defaye P, Schlaepfer J, Rostock T, Lacroix D, Lamaison D, Lavergne T, Aizawa Y, Englund A, Anselme F, O'Neill M, Hocini M, Lim KT, Knecht S, Veenhuyzen GD, Bordachar P, Chauvin M, Jais P, Coureau G, Chene G, Klein GL, Clémenty J: Sudden cardiac arrest associated with early repolarization. N Eng J Med 2008, 358: 2016-2023.
3. Nogami A, Sugiyasu A, Kubota S, Kato K: Mapping and ablation of idiopathic ventricular fibrillation from Purkinje system. Heart Rhythm 2005; 2: 646-649.
4. Igarashi M, Tada H, Kurosaki K, Yamasaki H, Akiyama D, Sekiguchi Y, Kuroki K, Machino T, Murakoshi N, Nakata Y, Kuga K, Nogami A, Aonuma K: Electrocardiographic Determinants of the Polymorphic QRS Morphology in Idiopathic Right Ventricular Outflow Tract Tachycardia. J Cardiovasc Electrophysiol 2012; 23: 521-526.

5. Asirvatham SJ: Correlative anatomy for the invasive electrophysiologist: outflow tract and supravalvar arrhythmia. J Cardiovasc Electrophysiol 2009; 20: 955-968

Figure Legends

Figure 1. Surface 12-lead ECGs from a female patient with early repolarization associated with VF.

(A) In the emergency room, significant J-ST elevation in the infero-lateral leads; and VPC bigeminy with an RBBB configuration and superior axis were observed after the spontaneous termination of polymorphic ventricular tachycardia (VT). (B) During the ablation session, frequent monofocal VPCs with an RBBB configuration and superior axis were observed. (C) A 12-lead Holter recording could record the VF recurrence. The "true" triggering VPC is similar to the ablated VPC, but is different (especially lead aVR) (arrowhead). Interestingly, while J-ST elevation was recorded in the emergency room and during the VF recurrence (arrows), it was not observed during the ablation session.

Figure 2. Catheter mapping during polymorphic VT in a male patient with a short-coupled variant of torsade de pointes [3].

(A) During the polymorphic VT which was induced by rapid atrial pacing after the administration of intravenous cibenzoline, diastolic Purkinje potentials and presystolic Purkinje potentials were recorded from the left

ventricular septum. During sinus rhythm, fused Purkinje potentials were recorded before the onset of the QRS. (B) Representation of an octapolar electrode catheter placed on the left ventricular septum. (C) Intracardiac electrograms recorded after ablation showing the abolition of the local Purkinje potential (P) at the middle portion and a slight delay in the occurrence of the local ventricular electrogram during sinus rhythm (arrow). The polymorphic VT became noninducible and only an isolated VPC was inducible. The morphology of this VPC differed from the previous triggering VPC and intra-Purkinje block was also observed before this VPC (arrowhead).

HBE = His-bundle electrogram; HRA = high right atrium; LAO = left anterior oblique view; LV = left ventricle; P = Purkinje potential; RAO = right anterior oblique view; S_A = atrial pacing stimulus. (*From Nogami A, Sugiyasu A, Kubota S, et al. Mapping and ablation of idiopathic ventricular fibrillation from Purkinje system. Heart Rhythm 2005, 2: 646-649. With permission.*)

Figure 3. Surface 12-lead ECGs in a female patient with an RVOT type polymorphic VT.

(A) Holter monitoring revealed frequent episodes of polymorphic VT. The mean cycle length of the VT was 220 ms and the morphologies of the first

three QRS complexes of the polymorphic VT were always the same. (B) Polymorphic VPC couplets were recorded during the ablation session. (C) Pacemapping at the earliest activation site in the RVOT reproduced the exact same polymorphic QRS configurations as those during the clinical polymorphic VT.

Figure 4. Successful ablation in the pulmonary artery.

(A) From the pulmonary artery (PA), a delayed PA potential was recorded during sinus rhythm (arrow head) and this potential preceded the onset of the QRS during the remaining VPC (arrow). Between the PA and RVOT potentials, a tiny bridging potential was recorded. (B) Just after the RF energy application in the PA, the PA potential (arrow heads) disappeared. Repetitive firing from the PA was observed (arrow); however, there were no VPCs. These findings indicate that bidirectional conduction block occurred between the PA and RVOT.

HBE = His-bundle electrogram; HRA = high right atrium; PAP = pulmonary artery potential; RF = radiofrequency energy.

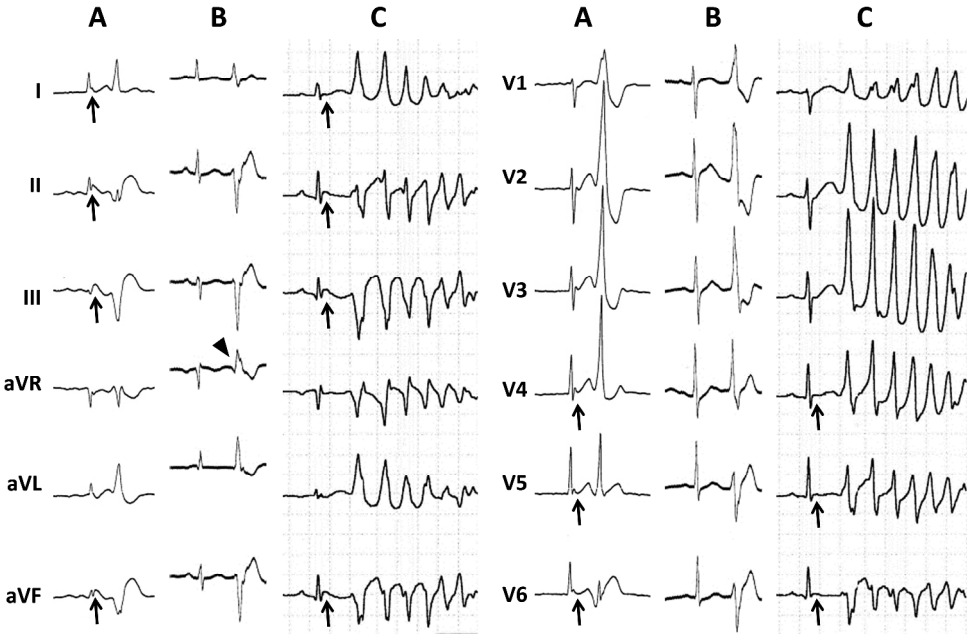

Figure 1. Surface 12-lead ECGs from a female patient with early repolarization associated with VF. (A) In the emergency room, significant J-ST elevation in the infero-lateral leads and VPC bigeminy with an RBBB configuration and superior axis were observed after the spontaneous termination of polymorphic ventricular tachycardia (VT). (B) During the ablation session, frequent monofocal VPCs with an RBBB configuration and superior axis were observed. (C) A 12-lead Holter recording could record the VF recurrence. The "true" triggering VPC is similar to the ablated VPC, but is different (especially lead aVR) (arrowhead). Interestingly, while J-ST elevation was recorded in the emergency room and during the VF recurrence (arrows), it was not observed during the ablation session.

1719x1190mm (96 x 96 DPI)

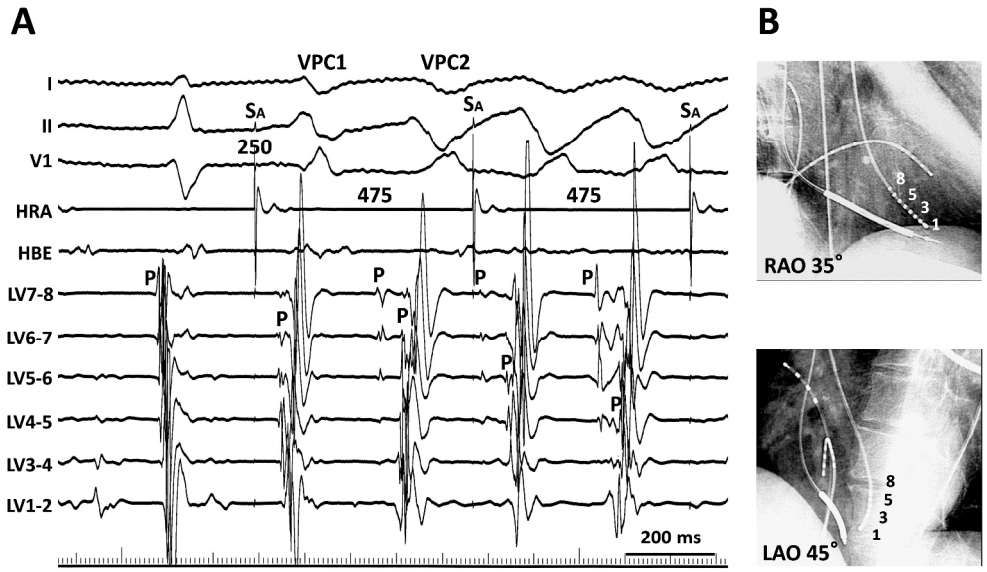

Figure 2AB. Catheter mapping during polymorphic VT in a male patient with a short-coupled variant of torsade de pointes [3].
(A) During the polymorphic VT which was induced by rapid atrial pacing after the administration of intravenous cibenzoline, diastolic Purkinje potentials and presystolic Purkinje potentials were recorded from the left ventricular septum. During sinus rhythm, fused Purkinje potentials were recorded before the onset of the QRS. (B) Representation of an octapolar electrode catheter placed on the left ventricular septum.
1719x1190mm (96 x 96 DPI)

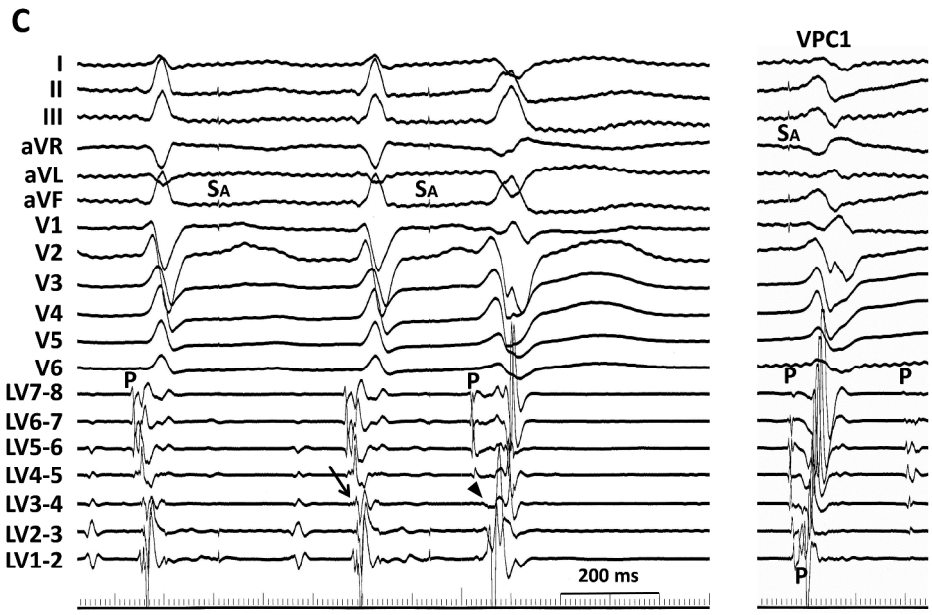

Figure 2C. Catheter mapping during polymorphic VT in a male patient with a short-coupled variant of torsade de pointes [3].
(C) Intracardiac electrograms recorded after ablation showing the abolition of the local Purkinje potential (P) at the middle portion and a slight delay in the occurrence of the local ventricular electrogram during sinus rhythm (arrow). The polymorphic VT became noninducible and only an isolated VPC was inducible. The morphology of this VPC differed from the previous triggering VPC1 and intra-Purkinje block was also observed before this VPC (arrowhead).
HBE = His-bundle electrogram; HRA = high right atrium; LAO = left anterior oblique view; LV = left ventricle; P = Purkinje potential; RAO = right anterior oblique view; SA = atrial pacing stimulus. (From Nogami A, Sugiyasu A, Kubota S, et al. Mapping and ablation of idiopathic ventricular fibrillation from Purkinje system. Heart Rhythm 2005, 2: 646-649. With permission.)

1719x1190mm (96 x 96 DPI)

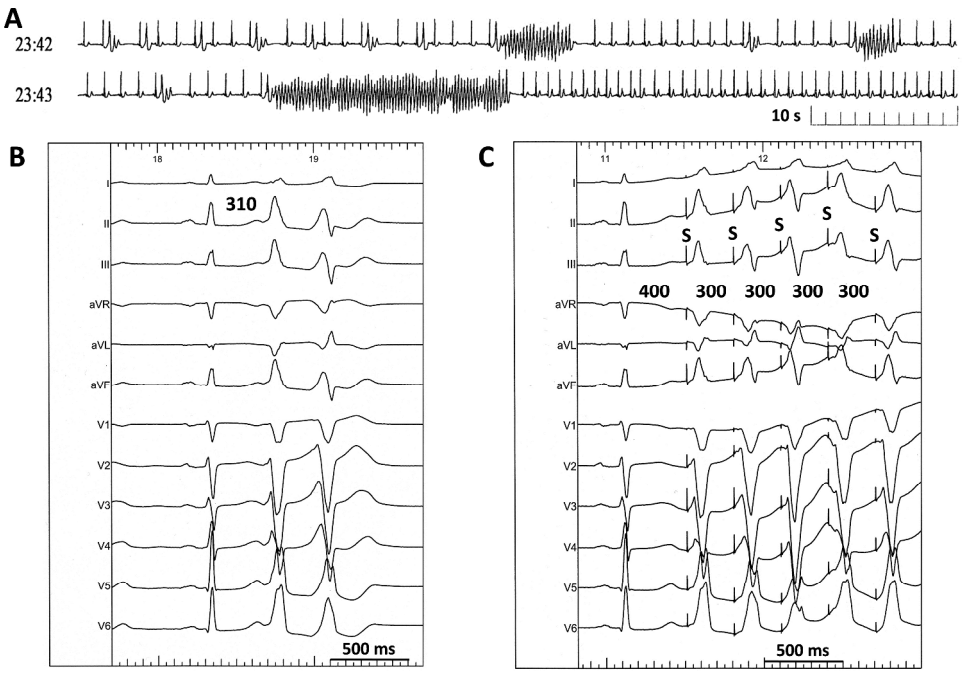

Figure 3. Surface 12-lead ECGs in a female patient with an RVOT type polymorphic VT.
(A) Holter monitoring revealed frequent episodes of polymorphic VT. The mean cycle length of the VT was 220 ms and the morphologies of the first three QRS complexes of the polymorphic VT were always the same. (B) Polymorphic VPC couplets were recorded during the ablation session. (C) Pacemapping at the earliest activation site in the RVOT reproduced the exact the same polymorphic QRS configurations as those during the clinical polymorphic VT.

1719x1190mm (96 x 96 DPI)

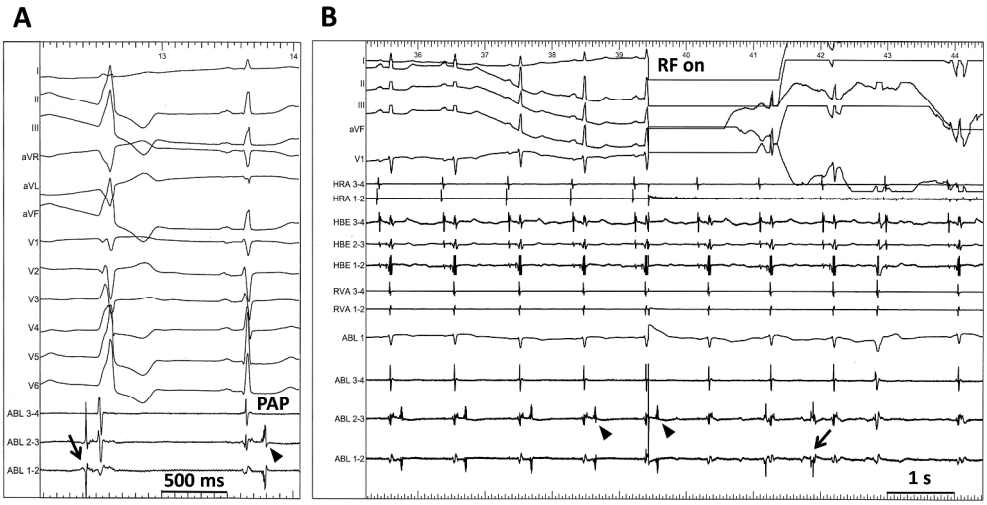

Figure 4. Successful ablation in the pulmonary artery.
(A) From the PA, a delayed PA potential was recorded during sinus rhythm (arrow head) and this potential preceded the onset of the QRS during the remaining VPC (arrow). Between the PA and RVOT potentials, a tiny bridging potential was recorded. (B) Just after the RF energy application in the PA, the PA potential (arrow heads) disappeared. Repetitive firing from the PA was observed (arrow); however, there were no VPCs. These findings indicate that bidirectional conduction block occurred between the PA and RVOT.
HBE = His-bundle electrogram; HRA = high right atrium; PAP = pulmonary artery potential; RF = radiofrequency energy.
1719x1190mm (96 x 96 DPI)