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Review

Modern mapping and ablation of idiopathic outflow tract ventricular arrhythmias

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Abstract

Outflow tract (OT) premature ventricular complexes (PVCs) are being recognized as a common and often troubling, clinical electrocardiographic finding. The OT areas consist of the Right Ventricular Outflow Tract (RVOT), the Left Ventricular Outflow Tract (LVOT), the Aortomitral Continuity (AMC), the aortic cusps and the Left Ventricular (LV) summit. By definition, all OT PVCs will exhibit an inferior QRS axis, defined as positive net forces in leads II, III and aVF. Activation mapping using the contemporary 3D mapping systems followed by pace mapping is the cornerstone strategy of every ablation procedure in these patients. In this mini review we discuss in brief all the modern mapping and ablation modalities for successful elimination of OT PVCs, along with the potential advantages and disadvantages of each ablation technique.

Keywords: premature ventricular contractions; ablation; 3D mapping systems

1. Introduction

Premature ventricular complexes (PVCs) are being recognized as a common and often troubling, clinical electrocardiographic finding. It is well known that a significant proportion of these arrhythmias usually originate from the outflow tract of either the right or the left ventricle (RVOT or LVOT). PVC-induced cardiomyopathy (PVC-CM), defined as the development of LV dysfunction caused by a high burden of PVCs (usually $\geq$10% of the total number of QRS complexes), has also been recognized as a clinical entity in consensus statements from both the European Heart Rhythm Society (EHRA) [1] and the American Heart Association (AHA) [2]. PVC treatment with catheter ablation is nowadays the proposed treatment for symptomatic patients suffering from PVC-CM [1,2]. In this mini-review, we will describe some of the novel mapping and ablating modalities in idiopathic outflow tract (OT) PVCs. Basic anatomical considerations and relationships between OT structures, are reviewed and novel differentiation ECG algorithms are provided, in order to help with PVC localization. Moreover, we provide a thorough description of mapping techniques, catheters and contemporary 3-dimensional systems used and finally summarize on some of the most commonly used ablation techniques.

2. Basic anatomical considerations

In order to accurately pinpoint the location of an OT PVC with the use of the electrocardiogram (ECG), we must first obtain a comprehensive knowledge on the exact anatomic relation between the right and left OTs. The RVOT is located anteriorly to the LVOT, directed cephalad to the left shoulder, with the pulmonic valve located anteriorly and leftward, relative to the aortic valve. Conversely, the LVOT is situated posterior to the RVOT, with a cephalad direction to the right shoulder [3]. The aortic valve consists of three coronary cusps, the left coronary cusp, the right coronary cusp and the non-coronary cusp. The aortomitral continuity (AMC) is a fibrous band of tissue that extends between the anterior mitral leaflet and the left and non-coronary cusps of the aortic valve. The right coronary cusp (RCC) is located anteriorly, the non-coronary cusp (NCC) posteriorly and the left coronary cusp (LCC) posteriorly and to the left. A very important information is that the RCC is situated right posterior to the posteroseptal part of the RVOT, while the NCC is the lowest coronary cusp and in close proximity with the interatrial septum. The aortic cusps are frequent sites of successful ablation in OT PVCs [4]. Letsas *et al.* [4] recently reported a successful ablation rate of 46.7% in the aortic cusps, 4.9% in the AMC and 36.2% in the RVOT, for OT PVCs [4].

The left ventricular (LV) summit is the most superior epicardial segment of the LV and is defined as the triangular

area formed by the left anterior descending (LAD) artery, the left circumflex artery (LCx) and the first septal perforator branch. The great cardiac vein (GCV) and its continuum, the anterior interventricular vein (AIV), transect and divide the LV summit into two parts (Fig. 1): (1) the inferior part, which is considered an "accessible area", suitable for catheter ablation and (2) the superior part, also termed as the "unaccessible area" and unsuitable for catheter ablation, due to the presence of the epicardial arteries and epicardial fat [5–7].

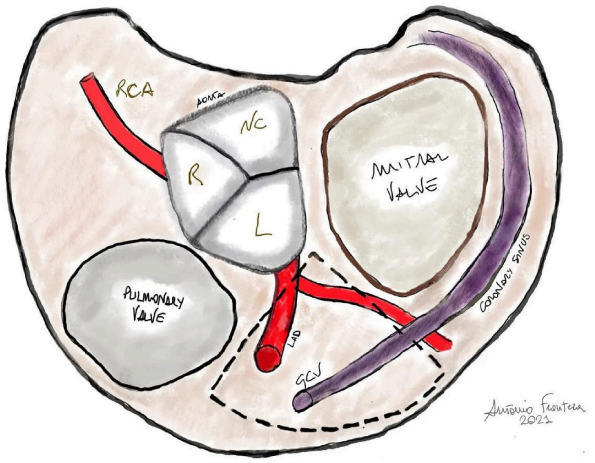

Fig. 1. Schematic representation of the LV summit and its relationship with the great cardiac vein (GCV) and the left anterior descending artery (LAD) in Left anterior oblique (LAO) view. L, Left coronary cusp; R, Right coronary cusp; NC, Non-coronary cusp.

3. How to pinpoint the origin of the PVC using the electrocardiogram

OT PVCs represent the majority of idiopathic PVCs. The OT areas consist of the RVOT, the LVOT, the AMC, the aortic cusps and the LV summit. By definition, all OT PVCs will exhibit an inferior QRS axis, defined as positive net forces in leads II, III and aVF. Several ECG differentiation algorithms have been published using stepwise approaches to pre-define the successful ablation area, guide initial vascular access (RVOT or LVOT/femoral vein or artery approach) and limit complications, given the close anatomical relationship between the RVOT and LVOT [8–15]. The most likely origin of PVCs with left bundle branch block (LBBB) morphology in precordial lead V1 and precordial transition (first precordial lead with R>S in the PVC morphology) after lead V3 (leads V4–6) is the RVOT. Conversely, in cases where the precordial transition is located in lead V1 or V2, the most likely origin is the LVOT [8].

When the precordial transition in sinus rhythm precedes the precordial transition of the OT PVC (the PVC QRS exhibits later precordial transition than the QRS in sinus rhythm), the most likely origin is the RVOT [10]. For OT PVCs with precordial transition in lead V3, one of the easiest applicable algorithms is the V2S/V3R index [12]. It is calculated as the S-wave amplitude in lead V2 divided by the R-wave amplitude in lead V3 during the OT PVC. Values $\leq$1.5 predict LVOT origin with 89% sensitivity and 94% specificity. Recently, Efremidis *et al.* [15] published a novel differentiation algorithm for OT PVCs with precordial transition in V3, the RV1–V3 transition ratio, with higher sensitivity (94%) and less specificity (73%), using a cutoff value of $\geq$0.9 to predict LVOT origin. The most important published algorithms for differentiation of OT PVCs successful ablation location are summarized in Table 1 (Ref. [8–15]).

4. Mapping the arrhythmia

Withdrawal of antiarrhythmic drugs for a period of at least 5 half-lives (preferably longer in cases of amiodarone) is of critical value prior to any ablation procedure for OT PVCs. Sedation is often avoided, because It may suppress the spontaneous PVC. However, mild sedation with intravenous propofol and fentanyl may be necessary. High density activation mapping using any of the contemporary 3-dimensional mapping systems (Carto 3 from Biosense Webster, Ensite NavX from St Jude Medical or Rhythmia from Boston Scientific) is the preferred modality, as it allows rapid, simultaneous and anatomically accurate acquisition of several activation points during the PVC, with the use of multipolar catheters with close coupled electrodes (Pentaray©, HD Grid© and Orion© mapping catheters).

The Orion© catheter consists of 64 small sized electrodes, with a small interelectrode spacing of 2.5 mm, which provide faster simultaneous mapping with better near-field signal quality. This catheter combined with the Rhythmia© mapping system and Its automated intelligent annotation module, provides an accurate and very fast mapping of any PVC. However, due to its size and shape, its handling may be difficult in a small sized ventricle. The Pentaray© catheter consists of 20 electrodes distributed in 5 soft and flexible, 3-French branches. When combined with the novel Carto Prime© system mapping module, It can substantially improve ablation safety and efficacy, using features like Parallel mapping© (simultaneous 3D activation mapping of different morphology PVCs, from the same cardiac chamber) and LAT Hybrid© (providing an association of the PVC Local Activation Time information to Its corresponding normal sinus rhythm location). Finally the Ensite X© system from Abbott with Its AutoMap and TurboMap features, when combined with the Advisor HD Grid© catheter (16 electrodes), allows for fast and ultra high density mapping of any PVC, with the best signal to noise ratio. Fig. 2 exhibits a typical example of a 3D reconstruction model of both left and right ventricular heart chambers during activation mapping of a septal intramural PVC, using the Carto Prime module. Multipolar catheters are very

Table 1. Common published ECG differentiation algorithms for successful localization of OT PVC origins.

ECG FINDINGS	DEFINITION	RESULTS	COMMENTS
Transition in precordial leads [8]	1st precordial lead with R>S	V1 or V2→LVOT origin V4 and after→RVOT origin	Cardiac rotation affects reliability
R wave duration index in leads V1 or V2 [9]	Percentage of longer R wave duration in V1 or V2 to QRS complex duration	R wave duration index $\geq$50% suggestive of a left-sided origin	Discriminates RVOT vs aortic sinus cusp origins
V2 transition ratio [10]	Percentage of R wave during PVC $(R/R+S)_{VT}$ in V2 divided by the percentage of R wave in sinus rhythm $(R/R+S)_{SR}$	Values $\geq$0.6 predict left origin (**91% accuracy**)	Used only if PVC precordial transition in lead V3
Transition Zone index (TZ index) [11]	TZ score of PVC minus TZ score of sinus rhythm	If TZ index $<$0, predictive of left sided origin with **88% sensitivity and 82% specificity**	
V2S/V3R index [12]	S wave in V2 divided by R wave amplitude in V3 during PVC	Values $\leq$1.5 predict left sided origin with **89% sensitivity and 94% specificity**	It can be applied irrespective of precordial transition
V4/V8 ratio [13]	Ratio of PVC R wave in V4 to PVC R wave in V8	Values $>$3 suggestive of left sided origins with **88% sensitivity and 77% specificity**	V8 lead located at the inferior tip of the left scapula
V4/V8 index [13]	Ratio of PVC R wave V4/V8 divided by R wave V4/V8 in sinus rhythm	Values $>$2.28 suggestive of left-sided origins with **67% sensitivity and 98% specificity**	V8 lead located at the inferior tip of the left scapula
V3R/V7 index [14]	R wave amplitude in lead V3R during PVC, divided by R wave amplitude in lead V7 during PVC	V3R/V7 $\geq$0.85 predictive of LVOT origin with **87% sensitivity and 96% specificity**	V3R located at the right correspondent place of V3 and V7 at the left posterior axillary line at 5th intercostal space
The RV1–V3 transition ratio [15]	$(RV1+RV2+RV3)_{PVC}/(RV1+RV2+RV3)_{SR}$	Values $\geq$0.9 predict LVOT origin with 94% sensitivity and **73% specificity**	Only for OT PVCs with precordial transition in lead V3

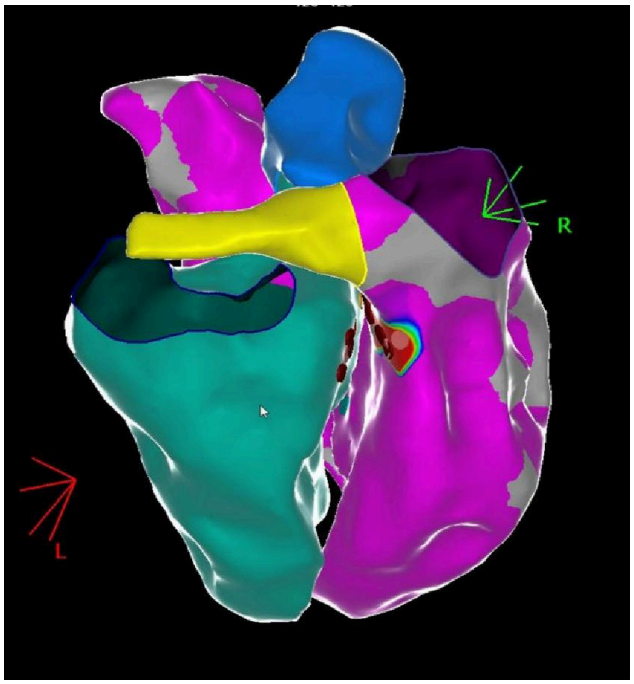

Fig. 2. 3D reconstruction of the left and right ventricle using the Carto 3 mapping system during activation mapping of an intramural PVC which was successfully ablated in the basal septum from both the left and right ventricle (sequential ablation). Purple: Right Ventricle, Green: Left Ventricle, Yellow: Coronary Sinus, red and pink dots: ablation tags in the area with the earliest activation of the PVC.

useful in patients with high and even low PVC burdens, as they substantially accelerate the mapping procedure and limit the X-ray exposure for both the patient and operator.

However, these systems cannot entirely substitute person-reviewed electrogram analysis as an integral part of the mapping procedure. As all these systems are based on specific algorithms in order to time-reference the acquired intracardiac electrograms (EGMs) onto the 3D activation map, they are prone to error. In order for the 3D activation map of the PVC to be reliable, each activation point should ideally be reviewed carefully by the technician and the physician, in both the 3D module and the EP recording system. On the other hand, ultra high density maps acquired with catheters like Orion or Pentaray contain thousands of EGMs and manual review of each single EGM is practically impossible. The automatic QRS morphologic filtering algorithms incorporated in these systems might also exceed the physician's ability to visually identify the mapped PVC. Finally, the EGM filter settings should be also set correctly (ideally 30–500 Hz for bipolar electrograms and 0.05–500 Hz for unipolar electrograms) in order to exclude any noise and maximize the quality of the recorded intracardiac signals.

After the initial 3D map has been acquired with a multipolar catheter, further mapping is advised with the ablation catheter, to accurately delineate the area of interest. Ideally, with adequate catheter-tissue contact (contact force of 5–10 grams), the ablation catheter should record a local bipolar EGM with a near field sharp component that precedes the QRS onset (pre-potential) by at least 20 msec and a synchronous unipolar EGM with a steep QS morphology (sharp downward slope), preferably with the presence of a notch [16,17], especially in patients without previous extensive ablation [18]. The presence of a notched unipolar electrogram on the downstroke deflection has been reported to identify a distribution area of 0.8 ± 0.4 cm^2 with an ablation success rate of 98.4% [17]. Unfortunately, the broadly used open-irrigated ablation catheters, due to their distal tip diameter of 3.5 mm and the 1 mm distance to their proximal bipole, seem to record a bipolar electrogram of a far greater underlying tissue area, with a diameter of 3.5 to 5.5 mm, depending on the angle of contact between catheter and tissue. Mini-electrode mapping improves mapping resolution (constructing "micro-bipolar" maps) and overcomes this obstacle especially in low voltage areas, therefore improving the ablation endpoint [19,20]. Mapping and identification of very-low voltage areas in sinus rhythm (mean amplitude of 0.2 ± 0.1 mV) also seem to characterize the arrhythmogenic substrate in RVOT PVCs and may guide successful catheter ablation, when combined with pace mapping [21].

In patients with infrequent PVCs during 3D mapping despite aggressive stimulation protocols and intravenous isoprenaline (up to 40 μgr/min), pace mapping along with voltage mapping in sinus rhythm can be useful [21]. While previous reports have stressed that pace mapping is inferior to activation mapping, concerning the success of the ablation procedure [22], more contemporary data point out that pace mapping in patients with low intraprocedural burden of idiopathic OT PVCs can lead to comparable results regarding ablation efficacy, when it is executed under a certain protocol (ideally pace map correlation $>$90% with 2 mA pacing output, 2 msec pulse width and contact force $\geq$10 gr) [23]. In any case, pace mapping should always be attempted in combination with activation mapping (whenever it is possible), at the site of earliest ventricular activation. In RVOT PVCs, where initial ablation is ineffective, the pulmonary cusps, pulmonary artery and right coronary cusp should always be mapped afterwards [24–26]. The use of a long sheath (SR0 or SL1) to improve stability and maneuverability, along with pulmonary artery angiography may be useful to accurately determine the exact location of the ablation catheter [27].

5. The role of intracardiac echocardiography (ICE)

Intracardiac echocardiography has emerged as an effective tool in PVC ablation, as it can clearly help in the identification of the right ventricular inflow and outflow tract, the aorta, coronary ostia and the proximal course of

the left main artery, obviating the need for coronary angiography, especially in cases with PVCs ablated from the left coronary cusp. As a result, it enables real time visualization of the ablation catheter stability in the aorta, limiting complications and radiation exposure [28–30]. Furthermore, steam pops, thrombus formation and pericardial effusion can be immediately identified and treated during the procedure, while ensuring the perpendicular catheter-tissue orientation, for optimal ablation results [31].

6. Ablation modalities

Irrigated ablation catheters have ultimately replaced the conventional, temperature-regulated, non-irrigated catheters, as they can create a more effective ablation lesion, avoiding the overheating phenomenon at the catheter-tissue interface. Irrigated catheters allow greater amounts of ablation energy to be delivered in the tissue, especially in areas with low blood flow, without any additional safety cost [32–34]. Ablation at a site with satisfactory near field prematurity in the bipolar EGM and steep negative (QS) unipolar EGM, as mentioned earlier, will usually suppress and cure the OT PVC. However, if the PVC origin is deeper (intramurally or epicardially, e.g., at the LV summit), endocardial catheter ablation is unlikely to suppress and cure the arrhythmia. In these cases, there are alternative ablative approaches, which will be discussed next.

If the activation mapping does not reveal any significant prematurity (<20 msec, far field local electrograms, absence of QS unipolar EGM at the earliest site, suboptimal pace maps, no or late suppression with immediate recurrence after ablation, equal activation times between septal RVOT and LVOT), that means that the PVC origin is deeper in the tissue that we are trying to ablate. Higher energy titration is the first step, but usually that is not enough. For septal (intramural) PVCs, if sequential unipolar ablation fails (ablation from the one side of the septum and on the exact opposite side, with the same catheter), simultaneous unipolar ablation may be effective in patients with septal PVCs refractory to sequential ablation [35,36]. Simultaneous unipolar ablation is performed with two separate irrigated catheters each one connected to a separate energy generator with separate ground pads and positioned opposite to each other. This type of ablation results in deeper and larger lesions than unipolar sequential ablation [37].

Bipolar ablation is another ablation modality, where 2 ablation catheters are used, where one of them is responsible for the energy delivery and the other acts as a ground pad, connected to the indifferent electrode port. Consequently, the intervening myocardium is subjected to higher current density between the two catheter tips, which results to deeper and more concentrated lesions that simultaneous unipolar ablation (transmural lesions 20–25 mm) [38,39]. The optimal distance between the two catheters should be 15–20 mm. The delivered energy is uniform between the two catheters, in contrast to unipolar simultaneous ablation, where the energy is titrated separately for each catheter. Major drawback is that there is no widely available setting for this setup and that there is no consensus regarding the optimal energy delivery and duration. Fig. 3 depicts catheter positioning in a patient subjected to bipolar ablation for a septal intramural PVC in our lab.

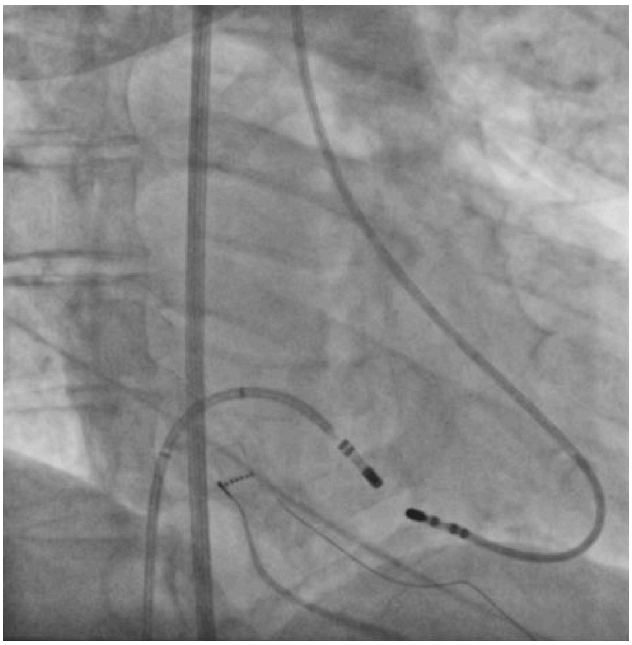

Fig. 3. Right anterior oblique fluoroscopic image of bipolar ablation of a septal PVC in our lab. Irrgated catheter positioned on the septal side of the right ventricle and a 4 mm non-irrigated catheter acting as the indifferent electrode via the septal side of the left ventricle (retrograde aortic approach).

Ablation in distant areas, such as the LV summit can also be performed endocardially, with the use of half normal saline as the irrigant. Half normal saline acts as an insulator to the radiofrequency current, resulting in more tissue energy delivery, when compared with normal saline and larger ablation lesions [40]. Dextrose water as an irrigant produces even larger lesions and increased steam pops in comparison with half saline [40]. Both half saline and dextrose irrigation produces larger ablation lesions, at the expense of increased steam pops especially with catheter forces that exceed 20 gr.

Energy delivery to OT PVCs originating from the LV summit or septal RVOT (via septal collaterals) can also be performed via a novel technique using a guidewire [41]. The 0.014-inch Vision guidewire is advanced into the anterior interventricular vein via an Inquiry Luma-Cath. Since the wire unipolar recording exhibits greater prematurity than the other sites, radiofrequency ablation can be applied through its body (titrated up to 20W) using the Smartablate generator (Biosense Webster) and with its proximal end in a saline bath. Coronary angiography is mandatory before en-

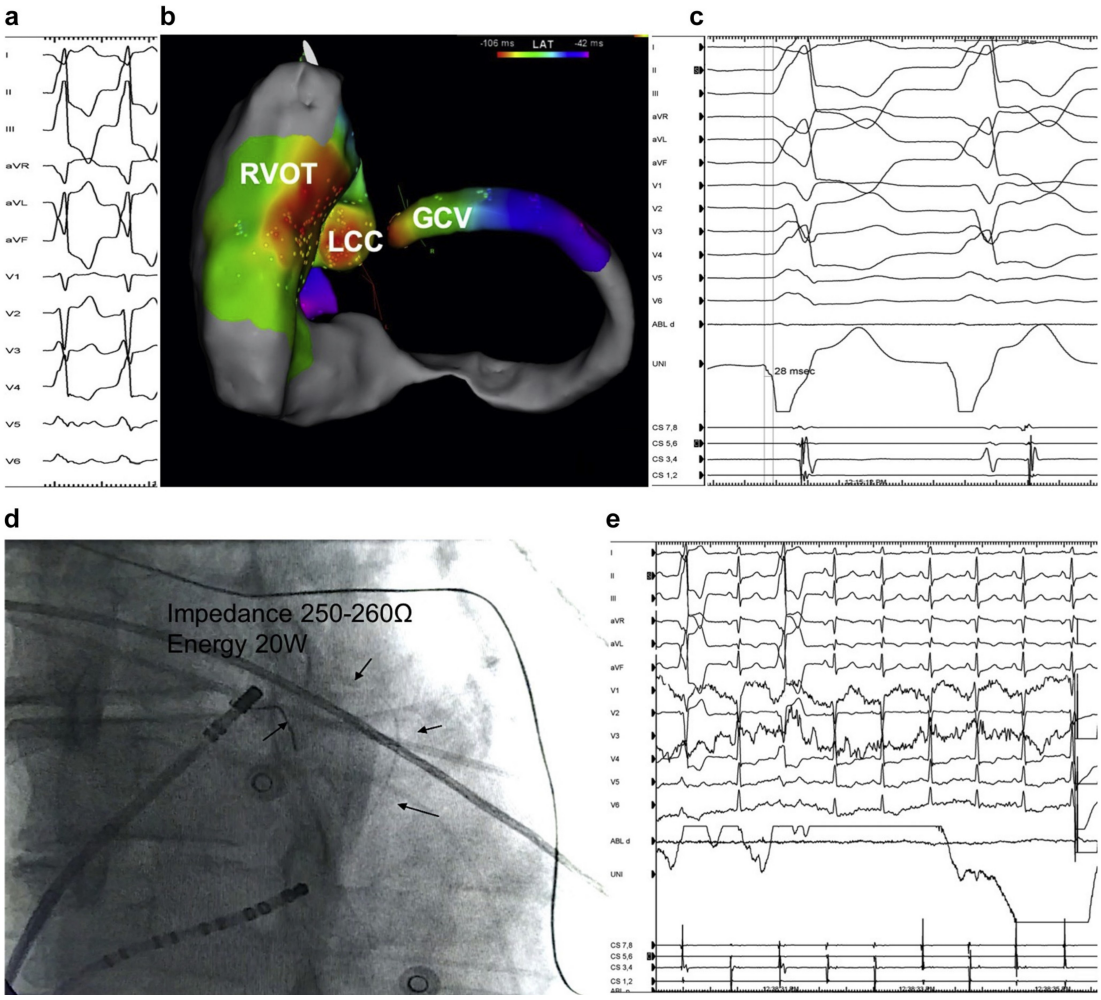

Fig. 4. LV summit PVC ablation technique via an insulated guidewire (Vision© guidewire). (a) 12-lead ECG showing the OT PVC. (b) 3D activation mapping of the RVOT, coronary venous system and left aortic cusp. (c) unipolar recording via the 0.014-inch guidewire with the earliest signal in the anterior interventricular vein (AIV). (d) LAO view showing the wire course at the proximal AIV. (e) PVC abolition with RF energy delivery up to 20W. RVOT, Right Ventricular Outflow Tract; GCV, Great Cardiac Vein; LCC, left coronary cusp. Reproduced with permission from Efremidis *et al.* [41].

ergy delivery, in order to delineate coronary artery anatomy. Fig. 4 (Ref. [41]) depicts the wire position and recordings in a female patient suffering from OT PVCs, who was referred for catheter ablation to our electrophysiology lab.

Other novel techniques for intramyocardial PVCs include catheter ablation via a specially designed 27-G needle tip, which except of energy delivery, it can also pace and record intracardiac electrograms [42]. Energy delivery is greatly augmented via saline irrigation through the needle [43]. Temperature controlled radiofrequency energy is limited to 60 °C for 1–2 minutes. Intracoronary ethanol injection using an over-the-wire angioplasty balloon has been repeatedly performed for PVCs refractory to radiofrequency ablation, despite the risk of possible collateral damage after ethanol leak and backflow [44,45]. Mapping of septal branches of the anterior interventricular vein (AIV) via a miniaturized multielectrode catheter or via an angioplasty wire, is always performed beforehand. Finally, epicardial ablation is also an alternative for LV summit PVCs.

7. Conclusions

The ventricular outflow tracts represent common ablation sites for idiopathic premature ventricular contractions and radiofrequency catheter ablation is an effective therapeutic strategy for these patients. Comprehensive knowledge of the ECG characteristics of OT PVCs and the exact anatomic relations between the LVOT and RVOT are of essential value in order to successfully treat these arrhythmias. Whenever standard ablation techniques prove ineffective, different strategies can be utilized to improve the procedural success rates.

Abbreviations

AHA, American Heart Association; AIV, Anterior Interventricular Vein; AMC, Aortomitral Continuity; CM, Cardiomyopathy; ECG, Electrocardiogram; EHRA, European Heart Rhythm Society; GCV, Great Cardiac Vein; LAD, Left Anterior Descending Artery; LBBB, Left Bundle Branch Block; LCC, Left Coronary Cusp; LCx, Left Circumflex Artery; LV, Left Ventricular; LVOT, Left Ventricular Outflow Tract; NCC, Non Coronary Cusp; OT, Outflow tract; PVC, Premature Ventricular Complex; PVCs, Premature Ventricular Complexes; RCC, Right Coronary Cusp; RVOT, Right Ventricular Outflow Tract.

Author contributions

SD—was the main author of this article. KV and AF—provided the images and tables. PM, AS, AZ, MEZ and MK—performed the online article search and provided the reference pool. NK, KPL and ME—conceived and designed the article layout.

Ethics approval and consent to participate

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Conflict of interest

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