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Late elimination of challenging idiopathic ventricular arrhythmias originating from left ventricular summit by anatomical ablation

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ABSTRACT

Ablation of premature ventricular complexes (PVCs) originating from left ventricular outflow tract (LVOT)/left ventricular summit (LVS) is challenging with considerable rate of failure. Recently, in a novel approach to ablation of these arrythmias, application of radiofrequency energy to anatomically opposite sites of presumed origin of arrythmia, has been associated with moderate procedure success. Although late elimination of PVCs that are persistent following an ablation procedure has been previously reported, this observation has not been studied sufficiently. In this report, firstly, we present three cases of lately eliminated LVS PVCs, then, we discuss possible mechanism of this observation and conclude that after an initial failed attempt of anatomic ablation, operators may choose a period of watchful waiting before attempting a redo procedure.

1. Introduction

Premature ventricular contractions (PVC) are common ventricular arrhythmias (VA) occurring in patients both with and without structural heart disease. Idiopathic PVC occur due to mechanisms unrelated to structural heart disease. The common origins of idiopathic PVCs are right ventricular outflow tract (RVOT) and left ventricular outflow tract (LVOT) structures such as aortic root, aortomitral continuity (AMC) as well as epicardial structures such as left ventricular summit (LVS) [1]. LVS is a structure bounded by left anterior descending (LAD) and left circumflex (LCx) arteries, with an imaginary arch from first septal artery to left atrioventricular groove. LVS is bisected by great cardiac vein (GCV)/anterior interventricular vein (AIV) into superior and inferior regions (Fig. 1). Superior (basal) region of LVS was initially considered to be inaccessible for radiofrequency catheter ablation due to close proximity of coronary arteries and/or thick epicardial fat pads [2]. Recently, it has been demonstrated that, ablation of anatomically opposite sides of a focus that is either inaccessible or unsafe for ablation irrespective of local electrogram timing can result in complete elimination of LVS PVCs in selected cases [3]. The effect of this 'anatomical ablation' on late cure of PVCs from these sites has not been studied sufficiently. Herein, we report three cases of initially unsuccessful elimination of PVCs originating at LVS and ablated by anatomic ablation strategy, that were found to be eliminated lately at follow-up visits.

2. Methods and case descriptions

2.1. Study population

The reported three cases were drawn from 21 consecutive symptomatic patients who underwent cardiac mapping and ablation for idiopathic PVCs originating from LVS at the Ankara University, Department of Cardiology, Electrophysiology Unit between July 2015 and August 2017.

2.2. Electrophysiological study, mapping and ablation

Patients were taken to the cardiac electrophysiology laboratory

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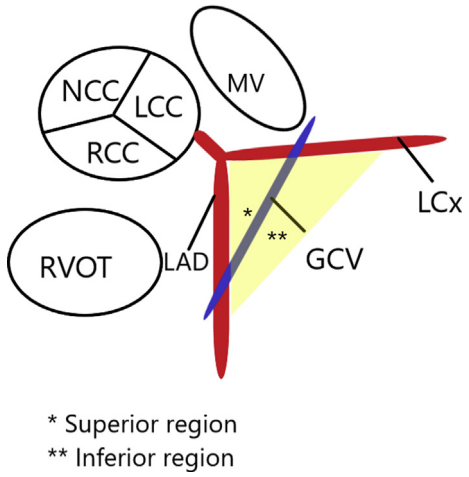

Fig. 1. Schematic representation of left ventricular summit (LVS, yellow triangle), and anatomically close structures. LVS is divided into superior and inferior regions. GCV: Great Cardiac Vein, MV: Mitral valve, LAD: Left anterior descending artery, LCC: Left coronary cusp, LCX: Left circumflex artery, NCC: Non-coronary cusp, RVOT: Right ventricular outflow tract.

in a fasting state and conscious sedation was utilized whenever necessary. Antiarrhythmic medications were discontinued ≥5 half-lives before the study. Vascular accesses were obtained through right femoral vein/artery and/or right jugular veins and initially a 6-French quadripolar catheter and a 6-French decapolar catheter was placed in the right ventricle for pacing and coronary sinus, respectively. Twelve lead surface ECGs and intracardiac electrograms were recorded simultaneously by an electrophysiology system (EP Tracer, CardioTek B.V., Maastricht, The Netherlands). If clinical ventricular arrythmia was not spontaneously present at baseline, burst pacing and programmed stimulation from right ventricle/right atrium with/without intravenous isoproterenol infusion (2–10 μg/min) were performed for provocation.

Mapping and ablation were performed with a 3D electroanatomic mapping system (Carto 3, Biosense-Webster, Diamond Bar, CA, USA) and a 3.5-mm-tip irrigated mapping and ablation catheter (SmartTouch, Biosense Webster, Diamond Bar, CA, USA). A long guiding sheath (Preface, Biosense Webster, Diamond Bar, CA, USA) was used to support the ablation catheter whenever it deemed necessary. Intravenous unfractionated heparin was administered to maintain an activated clotting time >250 s. Electroanatomic mapping and ablation method have been previously described.[3, 14] Briefly, point-by-point activation mapping was performed to create electro anatomic maps of the RVOT, supra- and infravalvular LVOT, AMC and GCV/AIV and available branches in patients with spontaneously induced idiopathic ventricular arrhythmia (IVA)'s. The local activation time was measured by annotating the earliest local bipolar activation time compared with surface QRS of the IVA. Earliest ventricular activation was color-coded in each chamber and pace-mapping utilizing PASO software of Carto 3 system was used with thresholds just above local capture whenever possible. When the local ventricular activation time preceded the surface QRS onset ≥20 ms and pacing from this site produced an excellent match, the catheter ablation was attempted with a temperature-controlled mode with a target temperature of 43 °C, maximum power set to maximum 40W with a flow rate of 17 ml/min in RVOT, LVOT and AMC. If the ablation was to be performed inside the GCV/AIV, the maximum power was set to 25W with a flow rate of 30 ml/min in a power-controlled mode. The impedance limit in radiofrequency generators was disabled in cases with high pre-delivery impedance levels.

In patients with earliest local activation < −20 ms ablation of earliest activation site, along with anatomically opposite/close sites, as per anatomical ablation protocol was performed. Detailed activation sites and ablation targets are described for each reported case separately. Coronary angiography was always performed prior to ablation in all cases in order to assess the distance from the major epicardial coronary arteries. Ablation was not attempted at sites with a distance < 5mm.

2.3. Case descriptions

In 15 of 21 patients, PVCs were eliminated at the end of the procedure. All 6 remaining patients who had persistent PVCs following the procedure were followed clinically. During follow-up 24-h ambulatory ECG was recorded in all patients, irrespective of symptoms. In three patients, late elimination of PVCs was observed.

Following are the detailed case descriptions of these patients, with summary of clinical features presented in Table 1.

2.3.1. Case 1

A 72-year old female patient with history of hypertension was referred to our clinic with symptoms of palpitation and dizziness. Her complaints were accentuated by physical activity. She had no prior history of heart disease. Routine ECG revealed frequent PVCs characterized by right bundle branch block (RBBB), inferior axis morphology, R in V1, Rs in lead I, Q wave amplitude in aVR > aVL, and maximum deflection index (MDI, defined as earliest time to maximum deflection in any precordial lead divided by the total QRS duration, > 0.55 indicating epicardial origin) of 0.54. A 24-h ambulatory ECG was performed revealing a PVC burden of 28.409. Echocardiography revealed no structural heart disease, and coronary angiography demonstrated insignificant, non-obstructive coronary artery disease (CAD). After unsuccessful drug therapy with metoprolol and consequently verapamil, the catheter ablation was planned. Activation and pace mapping was performed using Carto 3 electroanatomic mapping system as described in the methods.

RVOT, LVS, LVOT and AMC regions were accessed and mapped in detail. Activation and pace-mapping revealed the earliest activation site at proximal AIV with −19msec and 11/12 pacemapping score

Table 1
Clinical features of patients with late elimination of premature ventricular complexes.

Patient	ECG Features	PVC Burden	Earliest activation site	Sites of RF energy delivery	Post-ablation antiarrhythmic treatment
Patient #1	RBBB, inferior axis, MDI = 0.54	28 409/day	AIV (−19msec)	AIV, LCC, AMC, RVOT	None
Patient #2	IVCD, inferior axis, MDI = 0.62	36 783/day	GCV (−14msec)	AMC, AIV, GCV, LCC, RVOT	Metoprolol 50mg/day, stopped 30 days following the procedure
Patient #3	IVCD, inferior axis, MDI = 0.56	29 638/day	LCC(-15msec)	LCC, AIV, AMC, RVOT	Metoprolol 50 mg/d

AIV: anterior interventricular vein, AMC: aorto-mitral continuity, GCV: great cardiac vein, LBBB: left bundle branch block, LCC: left coronary cusp, MDI: maximum deflection index, PVC: premature ventricular complex, RBBB: Right bundle branch block, RF: radiofrequency RVOT: right ventricular outflow tract.

and, simultaneous coronary angiography revealed no coronary artery in close proximity. Acquired signals were low frequency, far-field signals. Irrigated radiofrequency energy (Rf) delivery at 20Watts-30mL/min for 60 seconds transiently suppressed the PVCs but eventually failed. Then, additional sequential unipolar Rf ablations were delivered at supra and subvalvular left coronary sinus of Valsalva, AMC and eventually RVOT at 40W for 2 minutes at every site. At the end of the procedure (115 minutes), PVCs persisted despite extensive anatomic ablation attempts. However, at 80-day follow-up visit, the patient, while not receiving any anti-arrhythmic therapy, was completely asymptomatic and 24-h ambulatory Holter monitor revealed 130 PVCs. She reported to feel completely asymptomatic 2 weeks after the procedure. Fig. 2A demonstrates the PVC ECG, the complex anatomy of the region and consequent irrigated ablation lesions at the CARTO 3 electro-anatomic mapping system.

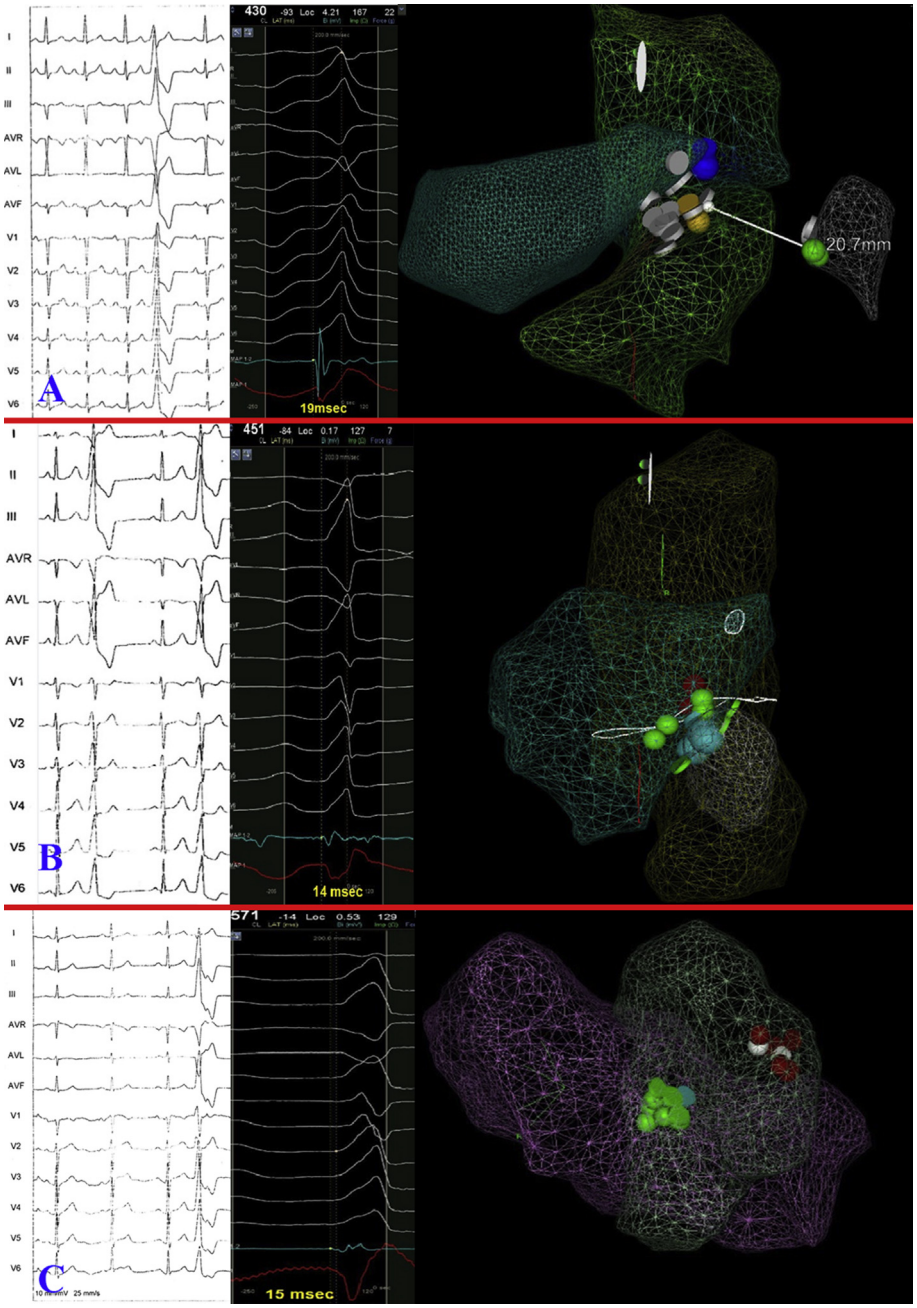

Fig. 2. A. *(Left)* 12-lead surface electrogram of the PVC; *(Middle)* local signal at the earliest site (proximal AIV); *(Right)* 3D "mesh" electroanatomic map of the PVC. Green mesh denotes: LVOT and AMC, blue mesh: RVOT, gray mesh: AIV. The white dots represent ablation tags while colored spots denote the earliest site at each region. **B.** *(Left)* 12-lead surface electrogram of the PVC; *(Middle)* local signal at the earliest site (septal branch of GCV); C- 3D "mesh" electroanatomic map of the PVC. Green mesh denotes: LVOT and AMC, blue mesh: RVOT, gray mesh: GCV septal branch. The green dots represent ablation tags while blue and red spots denote the earliest site at each region. Note the close proximity of septal branch to posterolateral RVOT. White line denotes the aortic annulus. **C.** *(Left)* 12-lead surface electrogram of the PVC; *(Middle)* local signal at the earliest site (subvalvular LCC); *(Right)* 3D "mesh" electroanatomic map of the PVC. Purple mesh denotes LVOT and AMC; and gray mesh denotes RVOT. Because the Smart-touch catheter could not be advanced distally, a non-irrigated catheter was utilized for ablation inside the AIV and the mesh anatomy of AIV could not be integrated to the figure. The green and red dots represent ablation tags while blue and white spots denote the earliest site at each region.

2.3.2. Case 2

A 24-year old female patient with no history of heart disease presented to our clinic with complaint of irregular pulse, palpitations and dizziness. She had experienced near-syncope one week before the presentation. Frequent PVCs were evident on ECG which was otherwise normal. PVCs showed interventricular conduction defect (IVCD) morphology with inferior axis, rS in V1, transition before V3, Qr in lead I, and aVL/aVR Q wave amplitude ratio of 1.9, and MDI of 0.62. No signs of structural heart disease were present on echocardiographic examination. 24-hour PVC burden was 36.783. Patient was unwilling for medical therapy so catheter ablation was performed. Activation and pace mapping, performed using Carto 3 electroanatomic ablation system, suggested an intramural site beneath LVS. The local activation was −14msec at GCV septal branch, −12msec at AMC, −10msec at LCC and −5msec at posterolateral RVOT. The pacemapping was not more than 10/12. Sequential unipolar irrigated Rf ablations were delivered starting from AMC (40W, 2 minutes), which were not successful. Then anatomically opposing sites were targeted starting from AIV and GCV septal branch (25W, 2 minutes), LCC (40W), and RVOT (40W, 1minute). At each site, Rf energy transiently diminished the PVCs, but PVCs persisted at the end of the procedure (90minutes) with decreased frequency. The patient was given metoprolol 50mg once daily. However, at 30-day follow-up visit, patient reported to be completely asymptomatic and 24-h ambulatory Holter monitor revealed no PVC. Metoprolol was stopped and subsequent Holter monitor 1-month later revealed 0 PVC again with no symptoms. Fig. 2B demonstrates the PVC ECG, the anatomy of the region and consequent irrigated ablation lesions at the CARTO 3 electroanatomic mapping system.

2.3.3. Case 3

A 56-year old male patient with severe hypertension who had a long history of symptomatic PVCs underwent unsuccessful medical treatment including bisoprolol, metoprolol, propafenone, and diltiazem. Echocardiographic examination revealed no structural heart disease. Coronary angiography performed 6 months ago at another center had revealed non-obstructive minimal CAD. 24-hour PVC burden was 29,638. PVCs had IVCD morphology with inferior axis, RS in V1, S wave in V6, rs in lead I, precordial transition before V3, aVL/aVR Q wave ratio of ≈1.0 and MDI of 0.56. Catheter ablation was planned. The activation and pace mapping was performed with Smart-touch catheter in RVOT, AMC and LVOT using Carto 3 mapping system, and a non-irrigated Rf catheter (Marinr Multicurve Ablation Catheter, Medtronic, USA) had to be utilized in distal coronary sinus because Smart touch catheter could not be advanced distally. Activation time did not reach 20 msec at any site, suggesting an intramural site beneath LV summit. The earliest site found at subvalvular LCC (−15msec), 2 cm inferior to left main coronary artery and AIV was the second earliest site (−14msec), posterolateral RVOT was −10 msec. Rf at 40W for 3 minutes at subvalvular LCC had no effect on PVCs. Thereafter, irrigated Rf lesions were delivered targeting the closest spots to this earliest site starting from AIV (non-irrigated catheter; 15Watts for 1 minute due to significant pain despite fentanyl and high impedance), left aortic sinus of Valsalva, AMC (40 Watts for 2 minutes at each site), and finally posterolateral RVOT (40W for 2 minute), but all of those eventually failed to eliminate the PVCs which persisted at the end of the procedure with diminished frequency. The patient was discharged the next day with metoprolol 50mg once daily. At 3rd month follow-up visit, the 24-h PVC burden at Holter monitor was 108/day and the patient was completely asymptomatic. Fig. 2C demonstrates the PVC ECG morphology, the anatomy of the region and consequent irrigated ablation lesions at the CARTO 3 electroanatomic mapping system.

3. Discussion

Ablation of PVCs originating from LVS is particularly challenging because LVS is an epicardial structure and is bounded by important anatomical structures such as major coronary arteries. Difficult access of this region by endocardial approach has favored epicardial approach either by sub-xiphoid pericardial access or by distal coronary venous system [4]. Progressive evolution in our understanding of cardiac anatomy has led to new potential targets for ablation of these PVCs. LCC, RCC, AMC and RVOT structures are in direct anatomical relationship with LVS (Fig. 1). Recent studies have pointed to PVCs thought to be originating from intramural sites between these structures and LVS [5]. In most recent studies, it has been proposed that transmural lesions created at aforementioned endocardial sites can result in successful elimination of PVCs [3,6]. Our data supports that this approach could precede percutaneous epicardial approach to ablation, as previously proposed by Santangeli et al. [6].

Anatomic ablation can be summarized as following: Irrigated radiofrequency energy is applied at the earliest ventricular activation site when it precedes the QRS onset by at least 20 ms or shows an excellent pace map (≥11/12) in the endocardial sites or distal coronary sinus. If Rf could not be delivered at a site because of a risk of collateral damage or if the first attempt was unsuccessful, subsequent Rf energy was delivered at anatomically opposite sides (endocardial versus epicardial or above versus below the aortic valve) to the first ablation site (anatomic catheter ablation). When there were multiple opposite sides, a Rf ablation was delivered first at the site that was located at the shortest distance from the first site or demonstrated an earliest ventricular activation or best pace map among those sides. If the sequential endocardial and epicardial ablation were unsuccessful in eliminating the PVCs despite an appropriate radiofrequency energy delivery at left sided chambers, the lower posterolateral RVOT was also mapped considering the close anatomical proximity to left ventricular summit and some recent reports of successful ablation of LVS PVCs from RVOT [7] and Rf energy was also delivered at this site with the shortest distance to the earliest activation on the left side, provided that this distance was less than 15mm, aiming complete abolition of PVCs.

Radiofrequency ablation (RA) lesions result from resistive and conductive heat transfer to the tissue. Although effects of RA are more pronounced during the period of energy delivery delayed effects have been demonstrated [8]. Histopathological lesions are characterized by coagulation necrosis surrounded by an area of inflammation [8,9]. The surrounding inflammation and microcirculatory damage [8] may result in lesion expansion leading to delayed effects. These delayed effects have been reported to occur as late as 30 days after the ablation [10]. Late success due to delayed effects of RA has been reported to occur in various ventricular arrhythmias [3,11,12].

In a previous report by Yamada et al., anatomic ablation was eventually successful in 60% of LVOT ventricular arrhythmias, 20% of which was actually late success (4 out of 22 patients) [3]. We hypothesize that in the anatomical approach to ablation of PVCs originating from LVS, the necessity of achieving transmural lesion for complete suppression of the arrhythmia may be an important factor for success. The second mechanism of suppressing VAs may be the creating circumferential conduction block in the exit sites of VA if RA cannot produce transmurality or sites are not approachable due to anatomic obstacles or RA has to be abandoned due to close proximity to coronary arteries. Late expansion and maturation of Rf lesions could also be an important factor in completing the gaps between the lesions. Quantification of late lesion progression after RA is probably the next important step in and eventually new insights may lead to alternation of duration and quantity of energy

levels required to be delivered to achieve procedural success at a late stage. In our cases, we delivered considerably higher energy levels for longer durations. It remains to be seen whether late success is sustained at much longer follow-up and whether the technique could be performed with good reproducibility.

Simultaneous unipolar and/or bipolar RA are other methods that require additional and custom technical equipment can also be utilized in the ablation of challenging PVCs from LVS. We did not perform these techniques. However, potential for damage to left coronary circulation, which may be even more pronounced due to proximity of major coronary vessels in this region, is an important limiting factor for wide adoption of this method [13]. Patient-specific anatomy may be an important factor in applicability of bipolar RA for LVS PVCs.

Two of the reported patients had received anti-arrhythmic medications (metoprolol) following the procedure. Although medical treatment may have contributed in elimination of PVC, it should be noted that one of the patients has previously undergone unsuccessful trial of beta blocker (including metoprolol) treatment. Also, after stopping of metoprolol, there was no reoccurrence of PVCs in the other patient. Finally, various factors may have theoretically contributed to elimination of PVCs and larger studies are necessary for confirmation of our observation.

4. Conclusion

PVCs originating from LVS are challenging arrhythmias with considerable failure rates. Whenever the RA at initially suitable sites fails to eliminate PVCs, the earliest sites at anatomically opposite sides can be targeted with moderate level of late success. Therefore, after an initial failed attempt of anatomic ablation, operators may choose a period of watchful waiting before attempting a redo procedure.

Declaration of interest

The authors report no conflict of interest.

Conflicts of interest

None.

Author contributions

BC, EB and CE designed and prepared the manuscript. BC, EB, FC, KV, ST, TA, and OA performed the procedures. VD and NO collected the data. HG and CE reviewed the manuscript draft.

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