Focal ventricular arrhythmias originating from the left ventricle adjacent to the membranous septum

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Aims
We report the features of focal ventricular arrhythmias (VAs) arising from the left ventricle (LV) adjacent to the membranous septum.

Methods and results
We studied eight patients (five men, 65 ± 10 years) with n = 2 or without structural heart disease (n = 6) who had ventricular tachycardia (n = 4) or premature ventricular contractions (n = 4) originating from the LV septum underneath the aorta. Ventricular arrhythmias exhibited a focal activation pattern, left (n = 4) or right bundle branch block (n = 4), respectively, left superior (n = 4) or inferior axis QRS morphology (n = 4), negative QRS polarity in lead III and early or no precordial transition in all. During all of these VAs, far-field electrograms in the His bundle (HB) region preceded the QRS onset. In all patients, ventricular pre-potentials were recorded during VAs while late potentials were recorded in sinus rhythm at the border of a localized low-voltage area underneath the aorta. Radiofrequency catheter ablation at the presumed sites of origin successfully eliminated VAs in five patients and was abandoned in the remaining three because the HB electrogram was recorded at that site.

Conclusion
Focal VAs may arise from the LV adjacent to the membranous septum as a part of the LV ostium, and broadens the spectrum of LV ostium VAs.

Keywords
Focal • Ventricular arrhythmia • Left ventricle • Membranous septum • Radiofrequency catheter ablation

Introduction
The left ventricular outflow tract (LVOT) forms a part of the ostium of the left ventricle (LV) and is known to be one of the major sources of focal ventricular arrhythmias (VAs).1–6 Anatomically, the LVOT consists of the aortic root and the sites below the aortic valve including the aorto-mitral continuity that is located at a lateral site in the LVOT. It has been reported that the aortic root is the most common location of VA origins in the LVOT, followed by the aorto-mitral continuity.4,6 However, VAs arising from other sites in the LVOT have not been described. In this report, we describe a distinct subgroup of focal VAs that arise from the LV septum underneath the aortic valve.

Methods
The study subjects consisted of eight consecutive patients with symptomatic VAs refractory to at least one antiarrhythmic drug with a focal mechanism that originated from the LV septum underneath the aortic valve. The baseline characteristics of these patients, including their age, gender, LV ejection fraction, presence of structural heart disease, nature of the clinical arrhythmia, and electrocardiogram during the VAs, were recorded. Each patient gave written, informed consent, and all antiarrhythmic drugs were discontinued for at least five half-lives prior to the study.

Electrophysiological study
For mapping and pacing, standard multielectrode catheters were introduced from the right femoral vein and placed in the coronary sinus, His bundle (HB) region, and right ventricular apex. When few premature ventricular contractions (PVCs) were observed at the beginning of the electrophysiological study, induction of the ventricular tachycardia (VT) or PVCs was attempted by programmed electrical stimulation with one, two, and three extra-stimuli introduced after an 8-beat drive train and burst pacing from the right ventricular apex (to a cycle length as short as 300 ms), with the infusion of isoproterenol if necessary. During

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procedures in the LV, intravenous heparin was administered to maintain an activated clotting time >250 s.

Mapping and ablation

Non-fluoroscopic electroanatomic mapping in the ventricles was performed with a 7.5-French quadrupolar deflectable 3.5-mm-tip external-irrigated ablation catheter (Navistar ThermoCool™, Biosense Webster, Diamond Bar, CA, USA) via the femoral vein and artery or the transseptal approach with a 11.5-French deflectable sheath (Agilis NxT™, St. Jude Medical, AF Division, Minnetonka, MN, USA) in addition to fluoroscopy as previously reported. Activation mapping was performed in all cases to identify the earliest site of ventricular activation during VT or PVCs. Pace mapping was also performed at a pacing cycle length of 500 ms and stimulus amplitude of 1 mA greater than the late diastolic threshold. Ventricular pacing was also performed adjacent to the right ventricular HB region with a stimulus current of 20 mA to capture both the right ventricle (RV) and HB. The score for the pace mapping was determined to as high as 50 W, with the goal being able to achieve a decrease in the incidence of VT or PVCs within 300 ms. Post-procedure follow-up included clinic visits and telephone calls to all patients and their referring physicians.

Results

Baseline characteristics

The baseline characteristics of the eight patients are shown in Table 1. There were five men and three women between the ages of 48 and 79 years (mean age 65 ± 10 years). Two patients had a history of ischaemic heart disease with severely reduced LV systolic function, but one of them had suffered from the same morphology of VAs before the onset of ischaemic heart disease. One of them had developed complete AV block and had an implantation of a cardiac resynchronization therapy defibrillator. In the other six patients, echocardiography demonstrated normal LV systolic function and no evidence of structural heart disease. The presenting clinical arrhythmia was sustained VT in two patients, non-sustained VT in two, and frequent (>10 000 beats/24 h) PVCs without runs of non-sustained VT in four. One patient noted that his symptoms markedly worsened with exertion. None of the eight patients suffered from cardiac arrest or syncope. The duration of symptoms prior to the study ranged between 2 weeks and 12 years. Antiarrhythmic drugs which failed to control the VAs included beta-blockers in six patients, sotalol in two, amiodarone in two, mexiletine in one, and flecainide in one.

Electrocardiographic and electrophysiological characteristics

The electrocardiographic and electrophysiological characteristics of the eight patients are shown in Figures 1 and 2 and Tables 1 and 2.

Table 1 Baseline and arrhythmia characteristics of the study patients

<table>
<thead>
<tr>
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<td>Beta-blocker, flecainide</td>
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<td>RBBB/LSA</td>
<td>RBBB/LSA</td>
<td>RBBB/LSA</td>
<td>LBBB/LIA</td>
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<td>147</td>
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<td>V1–V2</td>
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<td>&lt;V1</td>
<td>&lt;V1</td>
<td>V1–V2</td>
<td>V2–V3</td>
<td>V1–V2</td>
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AADs, antiarrhythmic drugs; CAVB, complete AV block; CHF, chronic heart failure; ICM, ischaemic cardiomyopathy; LBBB, left bundle branch block; LIA, left inferior axis; LSA, left superior axis; LV, left ventricular; MI, myocardial infarction; NSVT, non-sustained ventricular tachycardia (VT); PVCs, premature ventricular contractions; RBBB, right bundle branch block; SHD, Structural heart disease; SVT, sustained VT.
Figure 1 Twelve-lead electrocardiograms of ventricular tachycardia (VT) and pace maps in Case 1. Note that pacing from the His bundle (HB) catheter with a higher output exhibited a narrow QRS complex by direct capture of the HB whereas that with a lower output exhibited a wide QRS complex by capture of only the local myocardium in the right ventricle (RV). Also note that pacing from the successful ablation site (ABL) reproduced an excellent match to the QRS complex of VT whereas pacing from the other sites near the HB exhibited a later precordial transition and could not reproduce a negative polarity of QRS complex in lead III. RCC, the right coronary cusp.

Figure 2 Twelve-lead electrocardiograms of ventricular arrhythmias in Cases 2–6.
The VAs exhibited either a left or right bundle branch block QRS morphology in four and four patients, respectively, and left superior or inferior axis in four. However, the VAs with an inferior axis QRS morphology exhibited a negative polarity of the QRS complex (Qr, rS, or QS pattern) in lead III. In all patients, the VAs exhibited a QS pattern in lead aVR and an upright R-wave in lead aVL. The mean QRS duration during the VT or PVCs was 167 ± 21 ms (range; 145–206 ms). The precordial transition zone was observed between leads V1 and V2 in four patients and between leads V2 and V3 in one, and there was no precordial transition in three patients.

During the electrophysiological study, the clinical VAs occurred spontaneously in six patients and were induced by programmed ventricular stimulation with or without isoproterenol infusion in the other two patients. No sustained VT was induced in any patients and attempts to entrain the arrhythmia by burst pacing were not feasible.

### Mapping and catheter ablation

The average procedure time was 81 ± 22 min. The results of the mapping and catheter ablation are summarized in Table 2. In seven of the eight patients, activation mapping during the VAs was available. In all of those patients, the far-field electrogram from the HB region exhibited the earliest right ventricular activation in the LV septum underneath the aortic valve (Figure 1). It was noted that pacing from the RCC always exhibited a positive polarity of the QRS complex in lead III and pacing from the RV and HB always exhibited a later precordial transition than the VAs in all patients. Pacing from the non-coronary cusp (NCC) could not capture the ventricular myocardium but did capture the atrial myocardium in all patients. In the one patient for whom only pace mapping was available, a late ventricular potential was also observed during sinus rhythm at the site of an excellent pace map. Though the transaortic approach was used to position the ablation catheter at the LV septum underneath the aortic valve in seven patients, the transseptal approach was required in one patient (Figure 4A, B, and C). In the transaortic approach, the ablation catheter was positioned at the site straight down through the valve in six patients, and retrogradely by deflecting the loop of the ablation catheter in one patient (Figure 4A, B, and C). In all six patients with the straight down transaortic approach, a HB electrogram was recorded from at least either the distal or proximal electrode pair of the ablation catheter positioned at the site of earliest ventricular activation and best pace map (Figure 3) whereas it was not in the other two patients. The voltage map revealed that in all but one patient (who had ischemic cardiomyopathy), there was a localized area with a low-voltage (<1.5 mV) underneath the aortic valve and the presumed site of the VA origin was located at the border between the localized area with a low voltage underneath the aortic valve and that with a high voltage (>1.5 mV) in the LV (Figure 4A, B, and C). In Case 2 with a history of inferior myocardial infarction, the voltage map revealed that the area with a low voltage in the inferior wall of the LV that was associated with the myocardial infarction was separate from the localized area with a low voltage underneath the aortic valve (Figure 4A).

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
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<td>NSVT</td>
<td>PVCs</td>
<td>PVCs</td>
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<td>PVCs</td>
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<td>(+)</td>
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<td>(+)</td>
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<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
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<td>22</td>
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<td>23</td>
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<td>20</td>
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<tr>
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<td>(−)</td>
<td>(+)</td>
<td>(+)</td>
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<td>None</td>
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</table>

### Table 2 Electrophysiological findings and results of catheter ablation

EPS, electrophysiological study; HB, His bundle; ISP, isoproterenol; N/A, not applicable; No., number; PES, programmed electrical stimulation; RF, radiofrequency; Spont., Spontaneous; SR, during sinus rhythm; V-QRS, the local ventricular activation time relative to the QRS onset. The other abbreviations are as in Table 1.
In five of the eight patients, successful catheter ablation was achieved with one RF application at the site of earliest ventricular activation in the LV septum underneath the aortic valve. No junctional rhythm occurred during the RF applications in any patient. However, RF catheter ablative energy was not applied in the remaining three patients because of concern for the safety of the AV conduction system as a large amplitude of HB electrogram was recorded at the site of earliest ventricular activation during the VTs. During the follow-up period (8 ± 2 months) after the ablation, the five patients undergoing ablation remained free of any VTs without any antiarrhythmic drugs. No complications occurred.

Discussion

Previous studies have revealed that VTs with a focal mechanism can arise from various sites in the LV.1–6,10–14 Those VTs may be classified into several distinct subgroups by their mechanism and by having a distinct anatomical site of origin. This study presents VTs with a focal mechanism characterized by: (i) male dominance; (ii) a tendency for PVCs rather than sustained VT; (iii) a tendency for an early precordial transition; (iv) a left inferior axis with a negative polarity of the QRS complex in lead III or left superior axis QRS morphology; (v) a site of origin in the LV septum underneath the aortic valve in close proximity to the HB; and (vi) presence of pre-potentials during the VTs and late potentials during sinus rhythm at the site of origin.

Ventricular arrhythmias with a focal mechanism may arise from the LV with and without structural heart disease.10 However, VTs originating from the LVOT are usually idiopathic1–6,10 and these idiopathic VTs may occur even in hearts with structural heart disease. In fact, in the two patients with structural heart disease in this study, the VTs were likely to be idiopathic because the onset of the VTs preceded the onset of the ischaemic cardiomyopathy in one patient and the site of the VT origin was located away from the area of myocardial infarction in the other patient. Therefore, this study may present a distinct subgroup of idiopathic VTs arising from the LV septum underneath the aortic valve.

In all the cases in this study, the site of the VT origin was located in the LV septum close to the recording site of the HB electrogram and at the border of the localized area with a low voltage underneath the aortic valve. Anatomically, the posterior part of the RCC is adjacent to the central fibrous body, which carries within it the penetrating portion of the HB.15 Anteriorly, the RCC is related to the bifurcating atrioventricular bundle and the origin of the left bundle branch. The NCC lies superior to the central fibrous body. The HB penetrates through the central fibrous body and continues as the atrioventricular conduction bundle that then passes to the crest of the muscular ventricular septum, immediately beneath the membranous septum. Therefore, the VTs in this study were considered to originate from the LV adjacent to the membranous septum. The aortic and mitral valves are in direct apposition and form two attachments to an elliptical opening at the base of the LV known as the LV ostium.6,16 Although VTs arising from this region are being increasingly recognized as targets for catheter ablation,9 to the best of our knowledge, this is the first report describing VTs originating from the LV membranous septum.
LV adjacent to the membranous septum as a part of the LV ostium and broadens the spectrum of LV ostium VAs. In fact, the VAs in this study exhibited pre-potentials during the VAs and late potentials during sinus rhythm, a finding that is relatively common in LV ostium VAs although the presence was much more frequent in the VAs in this study than in the other LV ostium VAs.3,5,6,11

Previous studies reported that VAs can originate from the vicinity of the HB such as the right ventricular HB region, RCC, and NCC and they can exhibit similar electrocardiographic characteristics regardless of whether they have a right- or left-sided origin.15,17,18 However, VAs originating from the LV adjacent to the membranous septum may be easily differentiated from VAs originating from the RCC by the electrocardiograms because RCC VAs always exhibit upright R-waves in all the inferior leads whereas no VAs in this study did. In fact, the previous study reported VAs originating from the site similar to the site of the

![Figure 4](image-url)

**Figure 4** (A) Fluoroscopic images (left panels), activation map (right upper panel), and voltage map (right lower panel) exhibiting the successful ablation site in Case 2. The red tags indicate the successful ablation site. In the voltage map, the purple, and red indicate the areas with a voltage of the local bipolar electrogram ≥ 1.5 and ≤ 0.5 mV, respectively. Ao, aorta; LAO, left anterior oblique view; RAO, right anterior oblique view. (B) Fluoroscopic images (left panels), activation map (right upper panel), and voltage map (right lower panel) exhibiting the successful ablation site in Case 3. The electroanatomic maps were created by adding the activation and voltage data during the PVCs onto the three-dimensional left ventricular anatomical shells which were reconstructed with real-time integration of the intracardiac echocardiography. The red and orange tags indicate the successful ablation site during the PVCs and sinus rhythm, respectively. The three-dimensional anatomical shells of the RV and aorta were reconstructed with real-time integration of the intracardiac echocardiography during sinus rhythm. Note that the successful ablation site was located at the LV septum underneath the aortic valve. LV, left ventricle. (C) Fluoroscopic images (left panels) and voltage map (right panel) exhibiting the successful ablation site in Case 1. MA, mitral annulus; RL, right-lateral. The other abbreviations are as in the previous figures.
VA origin in this study. Although the previous study suggested that those VAs might originate from the LVOT underneath the aortic valve, we believe that those VAs originated from the RCC for several reasons. First, those VAs exhibited upright R-waves in all the inferior leads which could never be reproduced at any other sites near the HB than the RCC in this study. Second, that report had been written before the concept of VAs that can be ablated above the aortic valve was established and no methods such as aortography and echocardiography were attempted in order to identify the exact site of VA origin. The electrocardiographic characteristics of the VAs in this study were very similar to those of the VAs originating from the right ventricular HB region in the previous studies. However, this study suggested that the comparison of the preordial transition between the VAs and pace maps from the RV and HB may be helpful for predicting a VA origin in the LV adjacent to the membranous septum in each patient. The previous study suggested that when far-field electrograms preceding the near-field electrograms are recognized in the right ventricular HB region during the VAs, they may be an indicator of the VA origin being in the RCC or NCC. However, this study suggested that the LV adjacent to the membranous septum also should be considered in the differential diagnosis of the site of the VA origins when those findings are obtained. It may not be reasonable to describe a new category of VAs from the electrocardiographic point of view of this study because the VAs exhibited variable QRS axes and morphologies. However, it was reported that VAs originating from the antero-septal (HB region) and mid-septal portions of the tricuspid annulus which are located opposite the site of the VA origin in this case series exhibited variable QRS axes and morphologies (even a right bundle branch block pattern in lead V1 was observed in one case). Therefore, we believe that we can describe this new category of VAs based on the site of the origin. Variations in the anatomy and local and transseptal conduction around the VA origins may be associated with those variable QRS axes and morphologies during the ventricular septal VAs.

This study addressed several practical problems in the mapping and catheter ablation of VAs originating from the LV adjacent to the membranous septum. First, mapping at the LV septum underneath the aortic valve may be challenging in some cases. In those cases, a retrograde transaortic approach by deflecting the loop of the ablation catheter or transseptal approach may be helpful. Second, catheter ablation at the LV septum underneath the aortic valve may cause the risk of inadvertent damage to the normal AV conduction system. For example, catheter ablation of the AV junction can be reliably achieved using RF energy delivered in the LV when the conventional right-sided approach is unsuccessful. Therefore, meticulous mapping should be performed in order to avoid such complications in the catheter ablation of VAs originating from the LV adjacent to the membranous septum.

Conclusions

This report describes VAs with a focal mechanism that arise from the LV adjacent to the membranous septum as a part of the LV ostium, and broadens the spectrum of LV ostium VAs. The electrocardiographic and electrophysiological characteristics of these VAs are very similar to those of VAs originating from the other sites near the HB such as the right ventricular HB region, RCC, and NCC. The LV adjacent to the membranous septum also should be considered in the differential diagnosis of the site of the VA origins when the electrocardiographic and electrophysiological findings suggest that they may arise from the vicinity of the HB.

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