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ENDOCARDIAL ABLATION OF VENTRICULAR ECTOPIC BEATS ARISING FROM THE BASAL INFERO-SEPTAL PROCESS OF THE LEFT VENTRICLE

Short title: Ventricular ectopics from the LV infero-septal process

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ABSTRACT

Background

Idiopathic VE shows predilection to sites within the left ventricular base such as the outflow tract/aortic sinuses, LV summit and adjacent to the aorto-mitral continuity. We characterize VE arising from the inferior septum of the LV base that were successfully managed by LV endocardial ablation from the infero-septal recess of the LV.

Objectives

To determine the incidence, electrocardiographic, electrophysiological findings and anatomical features associated with ventricular ectopy (VE) arising from the basal infero-septal process of the left ventricle (ISP-LV) ablated using an LV endocardial approach via the infero-septal recess of the left ventricle.

Methods

425 consecutive patients undergoing VE ablation between 2012-16 at 3 centers were evaluated. Demographics, ECG and procedural data were analyzed for patients with ISP-LV VEs.

Results

7(1.5%) had a site of origin from the ISP-LV. Common ECG findings were a RBBB concordant/atypical LBBB early transition pattern suggestive of a basal origin with a left superior axis, biphasic QRS in aVR and small s wave in V6. Earliest activation was seen in an area below the outflow tract accessed from the infero-septal recess inferior to the His bundle. In 3 cases, transient junctional rhythm was seen during ablation. All cases were ablated successfully with no complications.

Conclusions

Ventricular ectopy arising from the ISP-LV represents a distinct subset of idiopathic arrhythmia and can be successfully treated by endocardial catheter ablation from the infero-septal recess. They share common surface ECG and electrophysiological findings with special anatomical features that need recognition for successful catheter ablation.

Keywords

Ventricular ectopics; left ventricular ostium; catheter ablation; infero-septal process; left ventricular outflow tract.

Introduction

Ventricular tachycardia (VT) and ventricular ectopy (VE) are known to display predilection for well-described anatomical locations that are amenable to catheter ablation. Ventricular ectopic beats originating from the left ventricular base have been described to exit from anatomically distinct sites, such as the aortic valvular sinuses, areas adjacent to the aorto-mitral continuity, and the so-called LV summit.

In a recent report, Santangeli and colleagues describe 5 patients with a novel site of origin of VE from the basal LV infero-septum, an area referred to as the 'posterior-superior process' of the LV. They described their successful elimination by catheter ablation from the right atrium after prior unsuccessful attempts.[1] This region of the left ventricle is best described, however, using an attitudinally correct term, namely the infero-septal process of the left ventricle (ISP-LV).

In this study, we describe the incidence, electrophysiological findings and anatomical features associated with idiopathic VE arising from the ISP-LV, and define an LV endocardial approach for their ablation via the infero-septal recess of the LV.

Methods

We assessed all consecutive patients seen at our institutions between January 2012 and December 2016 undergoing VE ablation. All patients underwent baseline 12-lead ECG and 24-hour ambulatory ECG. Evaluation for structural

heart disease was based on either transthoracic echocardiography or gadolinium enhanced cardiac magnetic resonance imaging (MRI). All anti-arrhythmic drugs were discontinued for at least 5 half-lives prior to the procedure. This study was approved by the Institutional Review Board or Research Ethics Committee at each institution.

Electrophysiological study and Ablation

Having obtained informed written consent, electrophysiological study was performed under local anesthesia in the post-absorptive state. Surface ECG leads were applied in conventional locations, and standard multi-electrode catheters were placed in the coronary sinus and right ventricle. Mapping was performed using a 3.5 mm, open saline-irrigated RF ablation catheter (Thermocool, Biosense-Webster, Inc, Diamond Bar, CA, USA), and in one case, a contact force enabled catheter (Thermocool SmartTouch, Biosense-Webster, Inc, Diamond Bar, CA, USA). Mapping was performed via the retrograde aortic approach, and via the trans-mitral approach when necessary. Unfractionated Heparin was used to maintain the ACT between 300-400 seconds.

In each case, a 3D electro-anatomical map was constructed using either CARTO (Biosense-Webster, Inc, Diamond Bar, CA, USA) or Ensite Velocity (St. Jude Medical, Inc, St. Paul, MN, USA). If VE was not present at baseline, isoproterenol infusion (2-5 mcg/min) was administered to achieve at least a 25% increase in sinus rate. Detailed mapping was undertaken in the aortic valvular sinuses, the LV outflow tract, the basal LV septum, and at the septal RV/RVOT. Bipolar pace-

mapping was performed at just above capture threshold at a cycle length determined by the coupling interval of the clinical VE.

Ablation was performed at the earliest site of activation and excellent pace-map match (defined as ≥11/12 leads or >90% as measured using template matching software on Labsystem Pro (BARD Electrophysiology, Lowell, MA, USA)). Radiofrequency ablation 25-35W was performed for up to 120 seconds, followed by a waiting period of up to 30 minutes.

ECG analysis

Analysis of 12-lead ECGs was performed using electronic calipers on the EP recording software at 100 mm/s speed. Data on bundle branch morphology, frontal plane axis, QRS duration and maximum deflection time (MDT) were analyzed. Maximum deflection index (MDI) was derived by dividing the MDT by the QRS duration. The QRS duration was measured from the earliest onset of the QRS deflection in any lead to the latest offset in any lead and the MDT from QRS onset to the largest amplitude positive or negative deflection in the precordial leads.[2]

Follow up

Subsequent to the procedure, patients were followed with ambulatory ECG, echocardiography and clinic visits at 3, 6 and 12 months.

Results

During the study period, 425 consecutive patients underwent VE ablation at the centers in the United Kingdom, Egypt, and the United States of America. A total of 459 distinct VE were targeted. Of these, 210 (46%) originated from the RVOT, 31 (7%) from the RV body, 70 (15%) from the LV body, and 161 (35%) related to the so-called “LV ostium”. Of those related to the LV base, 37 (8%) arose from the region adjacent to the aorto-mitral continuity between the hinges of the aortic and mitral valves, 75 (16%) from the aortic sinuses, 31 (7%) from the crest of the LV myocardial cone (LV summit), 2 (0.4%) from the para-Hisian LV, 9 (2%) mitral annular, while 7 (1.5%) had a site of origin mapped to the ISP-LV.

Patient characteristics

We identified 7 patients, 5 of whom were male, with a mean age 60 (SD 14), who underwent ablation of a VE originating from the ISP-LV. Table 1. All patients had frequent VEs, with a mean burden of 23% (SD 9), despite medical therapy with ≥1 antiarrhythmic drug and a mean symptom duration of 20 months (SD 6). Their mean left ventricular ejection fraction was 54% (SD 4). Only 1 patient had ischemic heart disease, but with preserved LV function and no evidence of ischemia on stress testing.

Electrocardiography

The typical 12-lead ECG morphology of the VE is shown in Figure 1. All VEs were monomorphic, with fixed coupling intervals. The mean QRS duration of VE originating from the ISP-LV was 152 ms (SD 14). The clinical VE was

characterized by a RBBB concordant pattern, or an atypical LBBB pattern with early transition by V2, a left superior axis, and a small s wave in V6. The morphology in aVR was either biphasic, or showed a small r wave. Mean MDI was 0.52 (SD 0.03).

Mapping and ablation

Activation and pace-mapping were performed in all patients. The right and left sides of the basal septal region were mapped. LV access was via a retrograde or trans-mitral approach. Mean earliest local activation at the successful ablation site was 28 ms (SD 4) pre-QRS and >90% pacemap match was achieved at corresponding sites. The right atrium was mapped in one patient with no earlier signals. Activation times on the RV aspect of the septum and the coronary sinus were universally later than those obtained from the endocardial LV. In sinus rhythm, no delayed potentials or His/Purkinje potentials were seen at the site of successful ablation. In all cases, the site of earliest activation was inferior and basal to the location of the His bundle electrogram on the LV septum. Furthermore, no areas of abnormal endocardial voltage were seen in the vicinity of the exit site. Representative mapping data are shown in Figures 2 and 3. In 3 cases, transient junctional rhythm with 1:1 AV relation was seen during ablation, similar to the response seen during slow pathway modification. A mean of 4 lesions (range 2-9) was required to abolish ectopic activity, delivering 25-35 W for up to 120 seconds. In 6 cases, the site of origin was reached by retroflexion of the catheter beneath the aortic valve. In one case, the retrograde approach only

suppressed the VE, and the trans-mitral approach (Figure 3) was required to abolish the VE.

Follow up

There were no instances of heart block or new conduction abnormalities. Patients were followed up for a mean of 287 days (SD 233) with 24-hour Holter monitoring showed no recurrence of the clinical VE. In one, the emergence of a second low burden VE of different morphology was noted.

Discussion

Idiopathic VE arising from the ISP-LV represented 1.5% of those observed in this large cohort of patients. All were successfully treated by radiofrequency catheter ablation from the endocardial aspect of the infero-septal recess of the LV. Our series confirms common features of a RBBB positive concordance or atypical LBBB morphology with transition by V2, indicating a basal origin, with a left superior axis and small terminal negative (s) wave in V6.

The so-called ‘aortic vestibule’, was first described by Francis Sibson as the component of the LV outflow tract into which the leaflets of the aortic valve fall in diastole, and which remains open in systole by virtue of its partially fibrous walls.[3–5] Subsequently labelled ‘Sibson’s Vestibule’ by Henry Gray [6], this vestibule is contiguous with the infero-septal recess of the left ventricle. (Figure 4). It is possible, through the infero-septal recess, to approach the leftward part of the basal segment of the ventricular cone, which was defined by McAlpine as the “posterior-superior” process. The myocardial process itself extends almost to the

crux of the heart, being bounded on its right side by the epicardial tissues of the inferior pyramidal space. It was detailed dissections made by Wallace McAlpine that revealed the salient interrelationships between these components.[6] (Figures 4 and 5) In his atlas, McAlpine stressed the importance of demonstrating the various cardiac structures as they are seen within the body, a concept that he christened attitudinally appropriate anatomy. It is paradoxical, therefore, that when describing components that remain incompletely understood, he reverted to the inappropriate approach of describing the heart as seen as if removed from the body and positioned on its apex. It is only when the heart is considered in this "Valentine" position that the component of the ventricular myocardial cone described by McAlpine occupies a "posterior-superior" location. When viewed in an attitudinally correct fashion, this "posterior-superior" process is an inferior and septal.

In the series of 5 patients presented by Santangeli et al., 3 had undergone prior unsuccessful ablations from the endocardial aspect. Successful abolition of the VE could only be achieved by ablation from the infero-medial component of the right atrium. In that study, the ECG morphology of the clinical VE appeared heterogenous, with 3 having a LBBB morphology, and 2 with a left inferior axis. These finding could be explained by different exit sites from the basal LV infero-septum. In our series, patients had a more homogenous ECG morphology, and appeared similar to the fourth and fifth patients in the series reported by Santangeli and colleagues. The finding that the earliest site of activation pre-QRS was consistently mapped to the LV endocardium, combined with their successful elimination, suggests closer proximity of the site of origin to the LV

endocardium. As such, it was not necessary to pursue mapping and ablation in the RA.

Although no complication was seen in the series reported by Santangeli and his associates, it is important to note the close proximity of the AV node, and the AV nodal artery, to the epicardial aspect of the muscular boundary of the infero-septal recess, which forms the myocardial floor of the triangle of Koch. The application of radiofrequency energy at this site may increase the risk of atrioventricular block. A left-sided endocardial approach may reduce the risk of such inadvertent damage to the conduction system by avoiding the AV nodal artery (Figure 5). The anatomical target site at the LV endocardium is juxtaposed to the compact AV node along the superior smooth-walled basal septum and lies inferior to the proximal conduction system. The penetrating AV bundle is found at a higher site, immediately inferior to the junction of the right and non-coronary sinuses in the sub-aortic outflow tract. At the site of successful ablation, there was a notable absence of Purkinje potentials, excluding exit from fascicular conduction tissue. During ablation, nonetheless, brief periods of junctional rhythm were seen in 3 patients, suggesting proximity to AV nodal-type tissue. In our series, no evidence of abnormal AV conduction, nor new conduction abnormality, was seen. Great care and careful monitoring of anterograde conduction during ablation was necessary owing to the recording of a His bundle electrogram at a site superior to the site targeted for ablation.

Programmed stimulation in our cases did not induce ventricular tachycardia. VE frequency, however, significantly increased with intravenous isoproterenol

infusion or became more prominent during the washout phase after infusion termination. These observations are in keeping with a probable triggered activity response as has been reported for outflow tract VE.[7]

Para-Hisian VE can arise near the basal LV infero-septum. Due to its more superior location, dominant R waves can be seen in the inferior leads, and are most prominent in lead II.[8] The basal inferior crux has also been reported as a distinct site of origin, with a similar incidence of VE (1.8%).[9] Although basal crux VE have a similar frontal plane axis to those of VE arising from the ISP-LV, they almost exclusively show a LBBB morphology, have higher MDI values (0.62 vs. 0.52), and QS complexes in the inferior limb leads, lead II in particular, suggestive of an epicardial origin. In contrast, ISP-LV VE exhibit small r waves in the inferior leads and small s waves in V6, suggestive of an endocardial origin.[10] Furthermore, basal crux VE are eliminated from the proximal middle cardiac vein or coronary sinus. Although basal crux arrhythmias have surface ECG features that are morphologically distinct from the endocardial LV-ISP arrhythmias, it is possible that they represent an additional arrhythmia morphology with a site of origin from the LV-ISP. The crux of the heart represents a region where all four cardiac chambers come into maximal proximity inferiorly. The pyramidal space, however, is not a muscular structure, but rather an area sandwiched by the muscular boundaries of the four cardiac chambers. Arrhythmias, therefore, cannot arise from the space itself, but rather from the structures forming its boundaries. We believe the term "crux arrhythmias" represents a subset of LV-ISP arrhythmias that originate from the most postero-inferior and epicardial segment of the LV-ISP, and which can be accessed through the coronary sinus.

Conclusions

Ventricular ectopic beats arising from the basal infero-septal process of the LV constitute a distinct clinical entity of idiopathic ventricular arrhythmia. They can be safely ablated endocardially from the infero-septal recess. This anatomical region, when assessed in an attitudinally appropriate orientation is best described as being “infero-septal”, and not “posterior-superior”. It should be carefully mapped in patients with basal morphology, RBBB positively concordant/atypical LBBB early transition and left superior axis ventricular ectopy.

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Tables

Table 1: Patient demographics and ECG parameters

Patient	1	2	3	4	5	6	7
Gender	M	M	F	M	F	M	M
Age (y)	74	48	43	52	81	66	57
LVEF (%)	55	56	54	50	49	52	60
CMRI	Focal antero-apical LGE	Not done	Not done	Mild impairment, no LGE	Mild impairment, no LGE	Basal lateral mid myocardial LGE	Not done
VE Burden (%)	32	11	14	21	31	30	19
Prior ablation	None	None	None	None	None	tAVNRT	None
QRSd (ms)	150	168	152	166	132	159	136
MDI	0.48	0.54	0.49	0.54	0.55	0.53	0.54

LVEF, left ventricular ejection fraction; CMRI, cardiac magnetic resonance imaging; VE, ventricular ectopic; QRSd, QRS duration; MDI, maximum deflection index; LGE, late gadolinium enhancement; tAVNRT, typical atrioventricular nodal re-entrant tachycardia.

Figure legends

Figure 1. **Electrocardiography:** Ventricular ectopic morphology from the 7-patient series. Note RBBB/atypical LBBB pattern morphology, a left superior axis with a small s wave in the lateral precordial leads and biphasic aVR. In the case of atypical LBBB pattern, early transition in the precordial leads is seen.

Figure 2: **Trans-aortic Mapping:** Panel A - RAO projection of a 3D electro-anatomical activation map of successful ablation site with ablation lesions (red tags) and His bundle electrogram (yellow tag). Activation pattern is consistent with focal activation. Panel B - Representative fluoroscopic images in RAO 30° and LAO 40°. The ablation catheter lies in a basal and septal position just beneath the aortic valve. Panel C - Successful ablation site electrogram 35ms pre-QRS. Note absence of high frequency Purkinje pre-potential. Map 1 (unipolar), Map 1-2 bipolar distal ablation signal, Map 3-4 bipolar proximal signal. Panels D and E: Schematic cross-sectional representations of the LV in corresponding RAO and LAO orientations showing the path of the retroflexed catheter (Black arrow) reaching the basal infero-septal LV process (Black asterisk) via the infero-septal recess (Sibson vestibule). Images used with permission from the UCLA Cardiac Arrhythmia Center - Wallace A. McAlpine Collection.

RAO, right anterior oblique; LAO, left anterior oblique; CT, Crista Terminalis; IVC, inferior vena cava; CS, coronary sinus; RA, right atrium; SVC, superior vena cava; P, posterior aortic sinus; L, left aortic sinus; L.A.App, left atrial appendage; P, posterior (non-coronary) aortic sinus; L, left aortic sinus; R.V., Right ventricle; L.V., left ventricle; LA, left atrium; T.V. tricuspid valve; M.V. Mitral valve; J, junction of the anterior mitral leaflet and membranous septum.

Figure 3: Panel A – **Trans-septal Mapping:** Right lateral projection of a 3D electro-anatomical activation map of the successful ablation site (blue tag) and the His bundle electrogram (yellow tag). Panel B – Orthogonal fluoroscopic images in RAO and LAO showing a trans-mitral approach the area outlined in white denotes the mapped region. Panel C – Successful ablation site electrogram 27ms pre-QRS. Panels D and E - Schematic cross-sectional representations of the LV in corresponding RAO and LAO orientations showing the path of the trans-septal catheter (Black arrow) reaching the basal infero-septal LV process (Black asterisk) via the infero-septal recess (Sibson vestibule). Images used with permission from the UCLA Cardiac Arrhythmia Center - Wallace A. McAlpine Collection.

RAO, right anterior oblique; LAO, left anterior oblique; CT, Crista Terminalis; IVC, inferior vena cava; CS, coronary sinus; RA, right atrium; SVC, superior vena cava; P, posterior aortic sinus; L, left aortic sinus; L.A.App, left atrial appendage; P, posterior (non-coronary) aortic sinus; L, left aortic sinus; R.V., Right ventricle; L.V., left ventricle; LA, left atrium; T.V. tricuspid valve; M.V. Mitral valve; J, junction of the anterior mitral leaflet and membranous septum.

Figure 4: Cross-Sectional Attitudinal Anatomy of the Basal Infero-Septal process of the Left Ventricle. Coronal section of the heart through the aortic sinuses viewed from a posterior (left panel) and anterior (right panel) perspective with corresponding schematics (bottom panels) demonstrating salient anatomical features. This shows that the aforementioned “posterior-superior process” is in fact an inferior and septal process (white and black asterisks). Images used with permission from the UCLA Cardiac Arrhythmia Center - Wallace A. McAlpine Collection.

CT, Crista Terminalis; IVC, inferior vena cava; CS, coronary sinus; RA, right atrium; SVC, superior vena cava; P, posterior (non-coronary) aortic sinus; L, left aortic sinus; R, right aortic sinus; L.A.App, left atrial appendage; R.V., Right ventricle; L.V., left ventricle; T.V. tricuspid valve; M.V. Mitral valve; P.A., pulmonary artery.

Figure 5: Anatomical specimens demonstrating the relationship of the atrial aspect of the myocardial boundary of the basal infero-septal process of the LV (asterisks) to critical structures. Top panel: Right posterior oblique view with the right atrium removed showing the course of the AV nodal branch of the right coronary artery (white arrow) overlying the myocardial boundary of the basal infero-septal process of the LV. Bottom panel: Left posterior oblique view with both atria removed. Yellow beads indicate exit of the proximal conduction tissue inferior to the junction of the right and non-coronary aortic sinuses. Red beads indicate the boundary of the septal wall anteriorly and inferiorly. White arrows indicate the LV endocardial approach to the basal infero-septal process via the infero-septal recess and the approach from the infero-medial RA. Images used with permission from the UCLA Cardiac Arrhythmia Center - Wallace A. McAlpine Collection.

TV, Tricuspid valve; LV, Left ventricle.

Figures

Figure 1: Electrocardiography

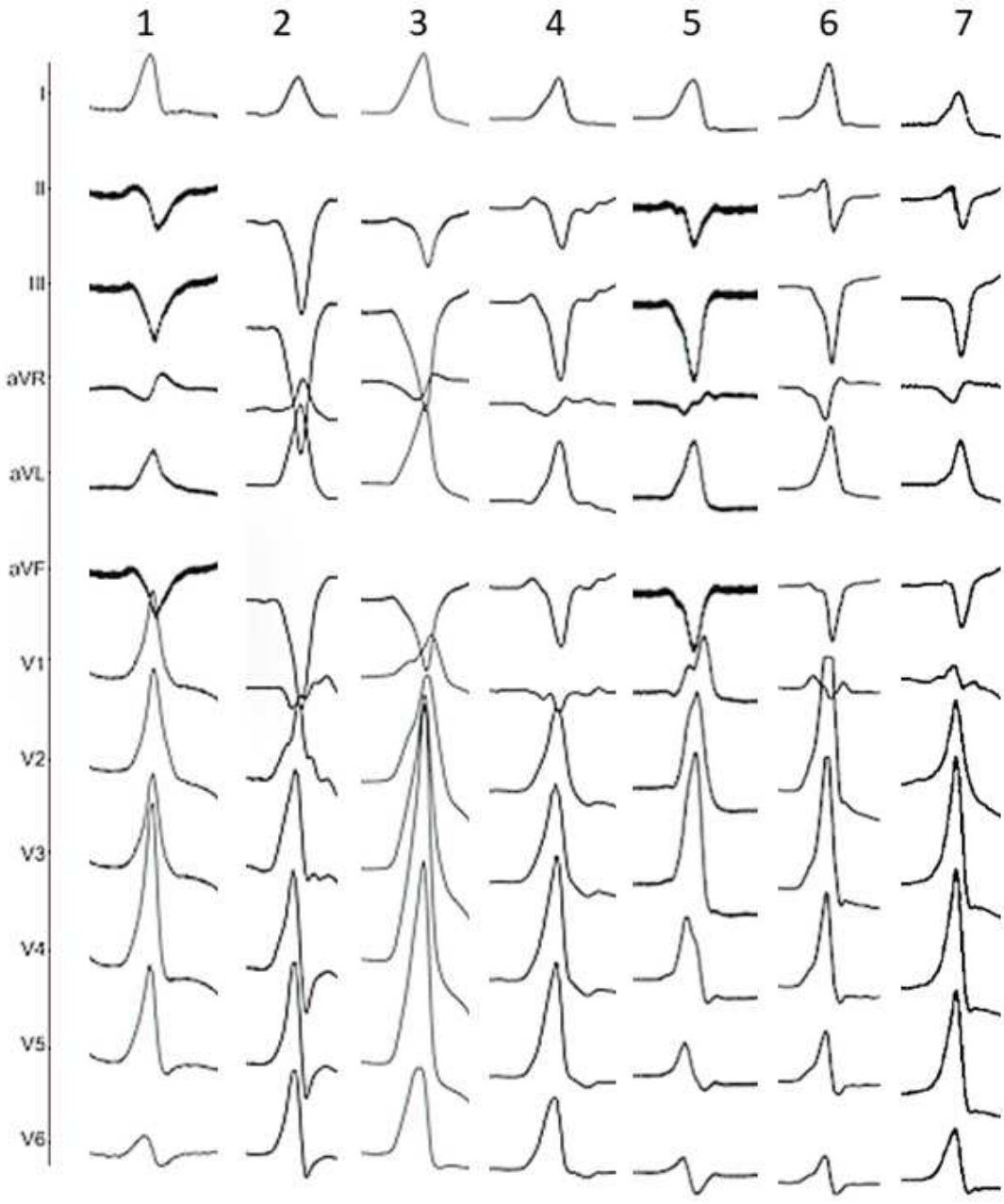

Figure 2: Trans-aortic Mapping of the Infero-septal Process of the LV base.

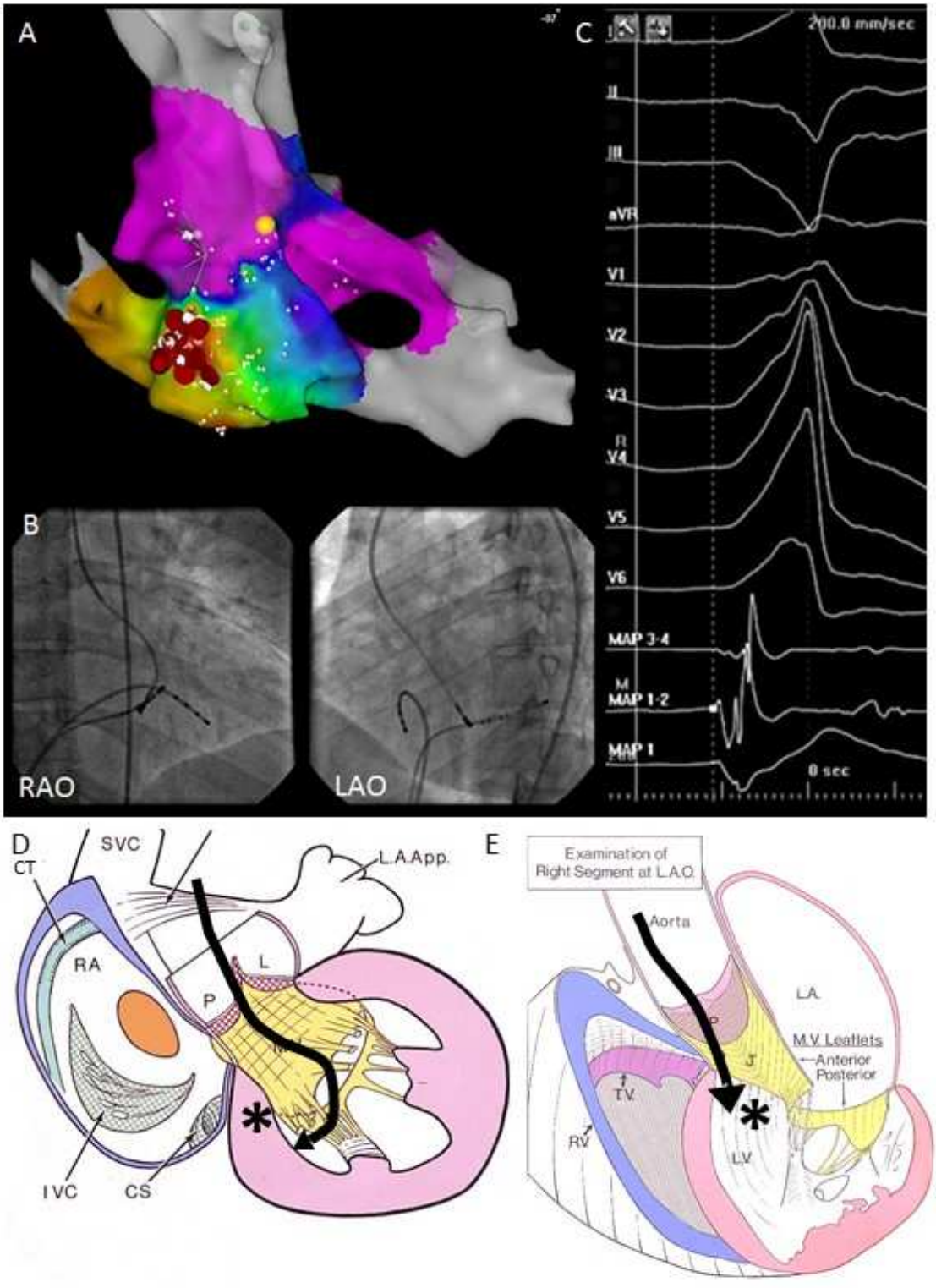

Figure 3: Trans-Septal Mapping of the Basal Infero-Septal Region of the LV

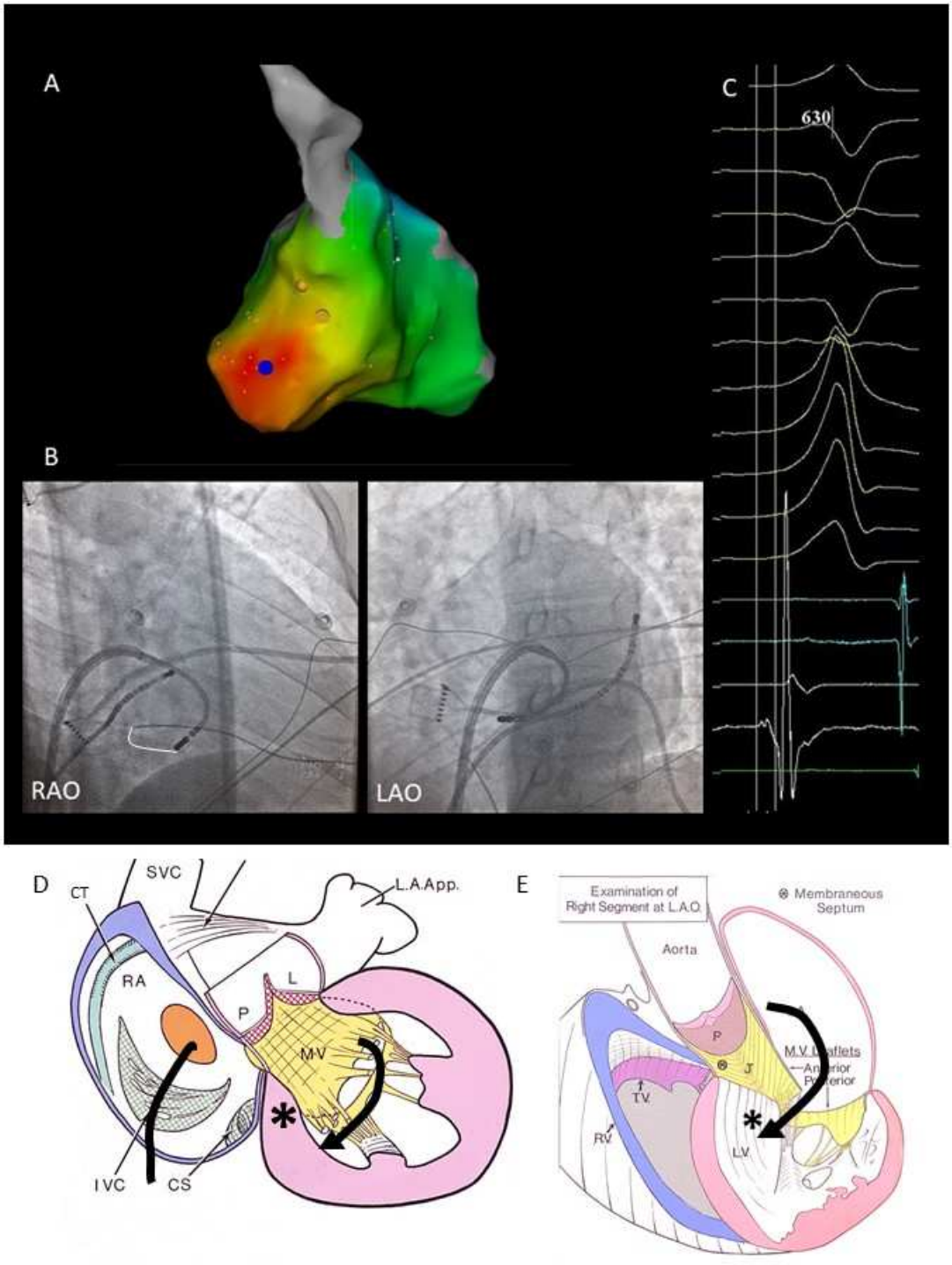

Figure 4: Cross Sectional Attitudinally Oriented Anatomy of the Basal Infero-Septal Process of the Left Ventricle.

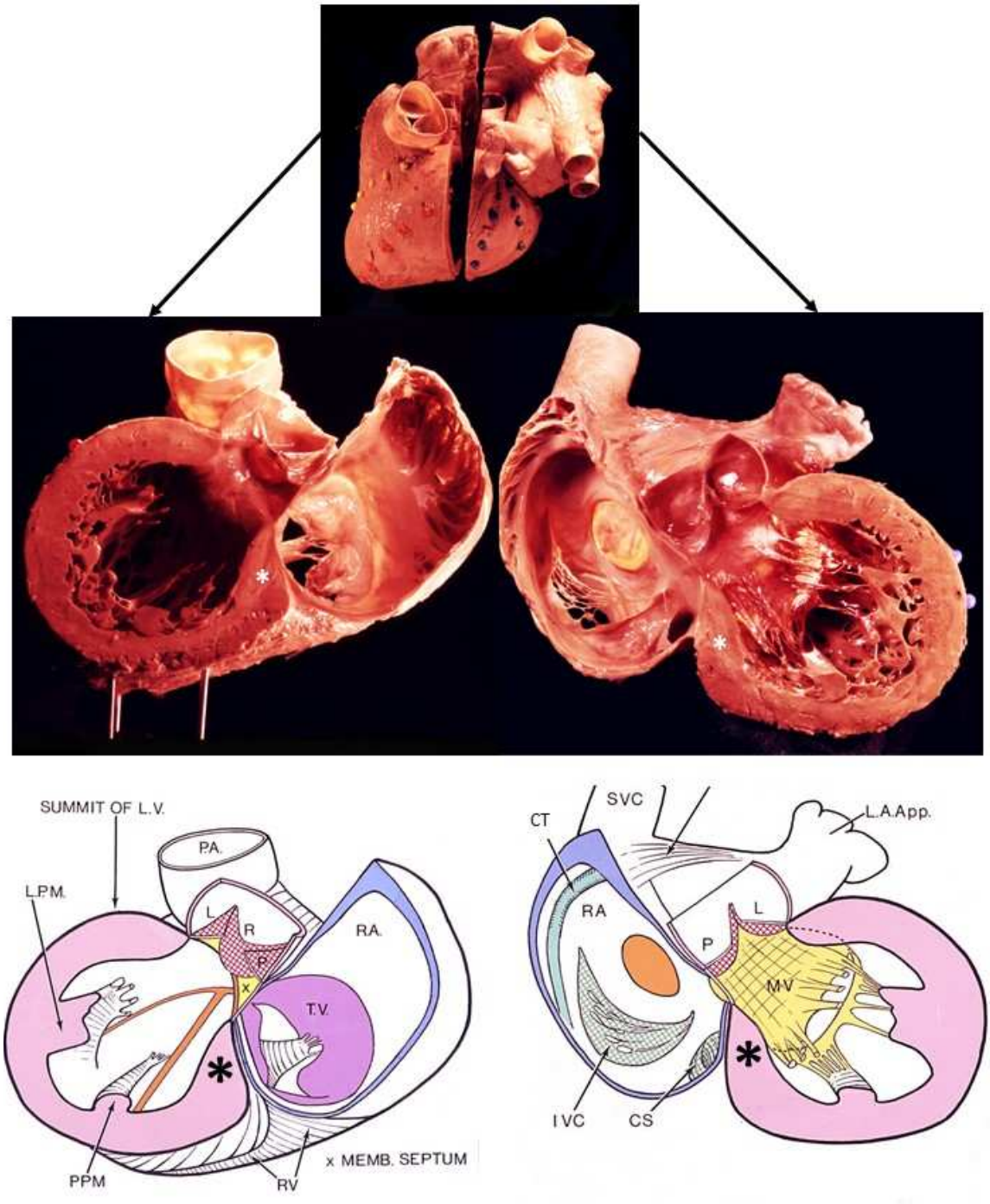

Figure 5: Relationship of the Basal Infero-Septal Process of the Left Ventricle to Critical Structures.