Treatment of complex atrial arrhythmias in Lamin heart disease by use of charge density mapping.

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Abstract

In younger patients Lamin heart disease is an underdiagnosed etiology of complex irregular atrial arrhythmias occurring in the absence of pulmonary vein activity. We describe a novel mapping system in 2 sisters with unusual manifestation of Lamin disease.

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Stefano Caselli, Kurt Mayer and Christine Attenhofer Jost: none to report;

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Introduction

In younger patients Lamin heart disease is an underdiagnosed etiology of complex irregular atrial arrhythmias occurring in the absence of pulmonary vein activity. As these arrhythmias can be impossible to map by serial contact mapping, we describe the use of a novel noncontact mapping array to characterize the septal origin of these atrial flutters, close to the site of conduction system disease in two sisters with Lamin A/C mutation. In addition, very unusual morphological abnormalities such as ventricular noncompaction and abnormal pulmonary vein connection are reported for the first time in Lamin heart disease.

Case report patient A

This female patient was diagnosed with left ventricular non-compaction (Figure1), left ventricular ejection fraction (LVEF 0.52) and frequent (30%) premature ventricular contractions (PVC) at the age of 37years. The MRI did not show any scar nor late enhancement. An electrophysiological study was performed, and the major origin site of the PVC was identified near the aortic valve and was successfully ablated. Nine years later, at the age of 46years, she presented with EF 0.47, frequent episodes of non-sustained ventricular tachycardia, together with frequent and highly symptomatic paroxysmal atrial fibrillation. The patient underwent pulmonary vein isolation and prophylactic ICD implantation. One year later a redo procedure for multiple left atrial flutters was unsuccessful, as contact mapping could not localize the irregular atrial activation patterns. An antiarrhythmic treatment with flecainide was administered and stopped after 2 years because of decrease in EF to 0.35. Then at the age of 50years she underwent a redo procedure for left atrial flutters because a novel noncontact mapping system (AcQmap®, Acutus Medical) had become available (1)11. This system allows a beat-to-beat analysis of the atrial activation (Coulomb/area) simultaneously in the entire atrium to localize irregular activation patterns. The method has been validated against contact mapping in sinus rhythm and atrial fibrillation (2).

There was no activity in any pulmonary vein. A left atrial map showed a flutter with changing activation sequence originating from the interatrial septum region with a cycle length of 270ms. (Figure 2 upper panel left) Therefore also a right atrial map was performed, which showed the trigger at the corresponding site in the right atrial septum. During RFA at the site with very barely visible electrograms (Figure 2 panel A) the flutter slowed to 365msec and converted to Sinus Rhythm only in the right atrium, while the left atrium continued in the arrhythmia (Figure 2 panel B). An additional left atrial map showed again the earliest triggers in the septum and further ablation there led to conversion to Sinus Rhythm (Figure 2 panel C). Afterwards a very long interatrial conduction time of 200ms was observed.

During follow up of 3 years the patient remained free of atrial arrhythmias longer than 2 minutes according to the ICD interrogation, in the absence of any antiarrhythmic drug. However, during follow-up she experienced during follow-up repeated stroke despite anticoagulation with VKA, which were attributed to thromboembolism from the non-compacted ventricular myocardium. Therefore, the anticoagulation was combined with Aspirin.

Case report patient B

This otherwise healthy female patient underwent RFA at the age of 39 years for atrial tachycardia from the right atrial free wall. At the time she had a normal echocardiogram with normale EF, morphology and size of both ventricles and mild biatrial enlargement and mitral regurgitation. At the age of 46 years a pacemaker was implanted for second and third degree Atrioventricular (AV) Block. One year later she had atrial flutter and underwent successful RFA. At the time prolonged atrial conduction times were noted with a transisthmus interval of 320msec and a split potential of 188msec. At the age of 48 the patient presented with incessant pacemaker mediated tachycardia in the presence of complete anterograde AV Block. Therefore, the retrogradly conducting slow pathway had to be ablated.

At the age of 51years the patient had a TIA. Because of symptomatic atypical atrial flutter an EP procedure with AcQmap® Acutus Medical was performed. During contrast injection into the left superior pulmonary vein (LSPV) and abnormal connection to the brachiocephalic vein was found (Figure 3), which was closed later with an Amplatzer cardiac plug.

The pulmonary veins had no activity during an irregular atrial flutter of varying cycle length between 230 and 260ms (figure 3 A). Beat to beat atrial mapping with the Acutus system showed a trigger of about 0.5cm diameter at the anteroseptal left atrium (Figure 3 upper panel). During RFA conversion to sinus rhythm was observed (Figure 3B). No further atrial arrhythmia could be induced with pacing down to 250ms cycle length (Figure 3C). During follow up of 1.5 years the patient remained free of relevant atrial arrhythmia (Atrial fibrillation burden <0.7% in the pacemaker interrogation). An upgrade to an ICD was done in 2021 after pacemaker battery depletion, because the Lamin Mutation hat been diagnosed.

Genetic Testing .

Because of the positive family history genetic testing was performed, which revealed a heterozygotous mutation in the Exon 6 of the LMNA gene c.1129C>T(p.Arg377Cys) rs397517889 in the sisters and in the two cousins with DCM. The same mutation was found in an asymptomatic 18-year-old son of Patient A with nonsustained VT. For primary prevention he underwent prophylactic ICD implantation.

Discussion:

These are the first case reports of complex irregular atrial flutters mapped with a novel noncontact mapping system (AcQmap®, Acutus Medical) in Lamin heart disease. Contact mapping had not been successful because of irregular and varying atrial conduction patterns. Instead beat to beat analysis of the simultaneous activation in the entire heart chamber by the Acutus system showed the origin of arrhythmias without annotation. The electrograms at target sites showed minimal amplitudes at maximum gain, further illustrating the limitations of contact mapping by filtering and subtraction for bipolar EGM. But the visualization of activation wavefronts repeatedly arising from the same regions by AcQmap indicated the true focal origin of these unusual atrial arrhythmias in the absence of any pulmonary vein activity. They arose from the interatrial septum, close to the regions of interatrial and atrioventricular block in otherwise healthy young patients, which is typical for Lamin heart disease (3-5). During follow up of 2 and 3 years no major recurrences have been demonstrated in PM and ICD interrogation, which illustrates the successful mapping and ablation strategy using this novel technology.

Interestingly these two sisters with Lamin A/C mutation demonstrate two unusual morphological features, which have not been described previously in this context: noncompacted left ventricular myocardium leading to recurrent strokes and a vertical vein connection from the LSPV to the SVC. This adds to the clinical spectrum of Lamin heart disease and the diagnosis by genetic testing is important because of worse prognosis and prophylactic ICD implantation has been recommended in many cases (5, 6).

References:

1. Grace Andrew, Willems Stephan, Meyer Christian, Verma Atul, Heck Patrick, Zhu Min, Shi Xinwei, Chou Derrick, Dang Lam, Scharf Christoph, Scharf Gunter, Beatty Graydon: High-resolution noncontact charge-density mapping of endocardial activation. JCI Insight. 2019 Mar 21;4(6):e126422.

2. Shi Rui, Parikh Pras, Chen Zhong, Angel Nathan, Norman Mark, Hussain Waijd, Butcher Charlie, Haldar Shouvik, Wong Tom: Validation of Dipole Density Mapping During Atrial Fibrillation and Sinus Rhythm in Human Left Atrium. JACC Clin Electrophysiol. 2020 Feb;6(2):171-181

3. Captur G, Arbustini E, Bonne G,. Lamin and the heart, Heart 2018;104:468–479

4. Chauvel R, Derval N, Duchateau J, : Persistent atrial fibrillation ablation in cardiac laminopathy: Electrophysiological findings and clinical outcomes Heart Rhythm. 2021 Mar 31:S1547-5271(21)00311-8. doi: 10.1016/j.hrthm.2021.03.040.

5. Hasselberg NE, Haland TF, Saberniak J, Brekke PH, Berge KE, Leren TP, Edvardsen T, Haugaa KH. Lamin A/C cardiomyopathy: young onset, high penetrance, and frequent need for heart transplantation. Eur Heart J. 2018 Mar 7;39(10):853-860. doi: 10.1093/eurheartj/ehx596.

6. van Rijsingen IA , Arbustini E, Elliott PM, Mogensen J, Hermans-van Ast JF, van der Kooi AJ, van

Tintelen JP, van den Berg MP, Pilotto A, Pasotti M, Jenkins S, Rowland C, Aslam U, Wilde AA, Perrot A, Pankuweit S, Zwinderman AH, Charron P, Pinto YM. Risk factors for malignant ventricular arrhythmias in lamin a/c mutation carriers a European Cohort Study . J Am Coll Cardiol 2012;59:493–500.

7. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck KH, Hernandez-Madrid A, Nikolaou N, Norekvål TM, Spaulding C, Van Veldhuisen DJ; ESC Scientific Document Group. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC).Eur Heart J. 2015 Nov 1;36(41):2793-2867. doi: 10.1093/eurheartj/ehv316. Epub 2015 Aug 29.

Figure 1 : echocardiographic examination of patient A at the age of 37 showing highly trabeculated and mildly dilated left ventricle. In Short axis, in end-systole a non compacted / compacted ratio of 2.4 was calculated; this in addition to a borderline ejection fraction of 52% suggested a diagnosis of left ventricular non compaction. The left ventricular diastolic function was normal. The right ventricle was not dilated and showed normal function. No valvular abnormalities were detected.

Figure 2 : electrophysiological examination with AcQmap®, Acutus Medical of Patient 1; for details see text.

Figure 3 : electrophysiological examination with AcQmap®, Acutus Medical of Patient 2; for details see text.

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