Epicardial multi-site conduction blocks detected by equispaced electrode array and omnipolar technology in Brugada Syndrome

Saverio Iacopino, MD, Federico Cecchini, MD, Alberto Tripodi, MD, Paolo Sorrenti, APRN, Gennaro Fabiano, BSc, Andrea Petretta

PII: S2214-0271(22)00193-2
DOI: https://doi.org/10.1016/j.hrcr.2022.09.015
Reference: HRCR 1413

To appear in: HeartRhythm Case Reports

Received Date: 2 June 2022
Revised Date: 21 September 2022
Accepted Date: 26 September 2022


This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2022 Heart Rhythm Society. Published by Elsevier Inc.
Epicardial multi-site conduction blocks detected by equispaced electrode array and omnipolar technology in Brugada Syndrome

Saverio Iacopino*, MD, Federico Cecchini*, MD, Alberto Tripodi§, MD, Paolo Sorrenti*, APRN, Gennaro Fabiano*, BSc, Andrea Petretta*,

* Electrophysiology Unit, Maria Cecilia Hospital - GVM Care and Research, Cotignola, Italy.

§ Department of Cardiovascular surgery, Maria Cecilia Hospital GVM Care and Research, Cotignola, Italy.

Doctors S. Iacopino and F. Cecchini provided equal first-level contribution in the realization of the manuscript

Short title: Omnipolar technology for epicardial pathologic substrate detection in Brugada Syndrome

Keywords: Brugada syndrome; epicardial ablation; mini-thoracotomy; epicardial multi-site conduction blocks; depolarization failure; omnipolar mapping technology; activation map; zero-fluoroscopy

CORRESPONDING AUTHOR:
Dr. Saverio Iacopino,
Electrophysiology Unit, Maria Cecilia Hospital
GVM Care and Research
Via Corriera 1, 48033 Cotignola (RA)
E-mail address: iacopino@iol.it

E-Mail addresses of the other authors: cecchinifederico1989@gmail.com; alberto.tripodi@gmail.com;
fabianogennaro@gmail.com; paolo.sorrenti@alice.it

Conflict of interest: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Dr. Iacopino, Dr F. Cecchini, Dr. A. Tripodi, G. Fabiano, P. Sorrenti, A. Petretta do not have any conflict of interest to disclose.

TOTAL WORD COUNT: 1994
INTRODUCTION

Brugada Syndrome (BrS) is an inherited channelopathy linked to an increased risk of developing malignant ventricular arrhythmias and sudden cardiac death in otherwise healthy individuals\(^1\). Currently, implantable cardioverter defibrillator (ICD) is still the mainstay of treatment for BrS\(^1\) but for patients experiencing recurrent ICD shocks despite optimal medical therapy, radiofrequency transcatheter ablation (RFCA) of the arrhythmogenic substrate is an available option with promising results\(^2-5\). Although there is a generalized consensus in considering the right ventricular outflow tract (RVOT) epicardium as the locus harboring the pathologic substrate, the exact pathogenesis of BrS is still a matter of debate. The earliest theories related the tendency of developing ventricular arrhythmias to an abnormal and inhomogeneous repolarization giving rise to concealed phase 2 re-entry in the epicardium\(^6,7\); however recently, there is more and more evidence that depolarization abnormalities such as slow conduction, conduction blocks and excitation failure, caused by subtle RVOT epicardium fibrosis and gap-junction abnormalities, may play a paramount role in the arrhythmogenesis\(^3,8,9\).

The aforementioned alterations can be unmasked or magnified by sodium channel-blockers (eg. Ajmaline, Flecainide, Procainamide) and electrophysiologically are responsible of well-described electrogram (EGM) abnormalities such as low amplitude epicardial EGMs (< 1 mV) and/or late potentials (> 120 ms) with multiple components (≥ 3) during sinus rhythm (SR)\(^3,4\).

Nowadays identification of complex cardiac arrhythmias sources requires accurate substrate mapping, precise identification of time signal activation and assessment of propagating wavefront. However, traditional bipolar signal recording has several limitations, and the novel omnipolar mapping technology (OT) was proved a helpful tool in complex mapping\(^10\).

CASE REPORT

A 72-year-old man with Brugada Syndrome (BrS) and a previously implanted implantable cardioverter-defibrillator (ICD) was admitted to our clinic because of recurrent and appropriate ICD shocks despite optimal medical therapy.

The patient was diagnosed with BrS at the age of 62. After his 20-year-old son's sudden death during sleep and evidence at the surface 12-lead ECG of type III Brugada pattern (Figure 1 - panel 2, A), he underwent ajmaline test that unveiled a type I BrS ECG pattern (Figure 1 - panel 2, B). In 2012 he underwent ICD implantation because of his family history of sudden cardiac death (SCD) and three past episodes of uninvestigated syncope during rest.

After about nine uneventful years, the patient had a first appropriate ICD shock for ventricular fibrillation (VF) (Figure 1, Panel 1). Invasive coronary-angiography, intracoronary acetylcholine provocation testing and
transthoracic echocardiography turned out to be normal; moreover hematochemical blood tests ruled out electrolyte abnormalities and inflammatory states. Unfortunately, despite antiarrhythmic therapy with Quinidine (500mg 3 times daily), few weeks later, the patient experienced another episode of VF promptly recognized and treated with DC-Shocks by the ICD. He was then re-admitted to our Hospital for epicardial ablation of the arrhythmogenic substrate with the use of an equi-spaced electrode array with omnipolar mapping technology.

After gaining informed consent, the procedure was performed in the hybrid surgical room under general anaesthesia and invasive arterial pressure monitoring. We previously described our 0-fluoroscopy hybrid minithoracotomy approach for BrS epicardial ablation.

Briefly, pericardial access was achieved via left anterior mini-thoracotomy and a skin incision was conducted along the upper edge of the areola, overlying the 3rd left intercostal space. After dissecting the external and internal intercostal muscles, discontinuation of lung ventilation was applied to displace the lung with a tissue retractor, allowing the pericardial space to be visualized and entered over the right ventricle (RV). Simultaneously, two right femoral venous accesses were obtained under echo-guidance by a second independent operator. An Advisor™ HD-grid multipolar mapping catheter (Abbott, Chicago, IL) was used to create a high-density bipolar and omnipolar map of the RV and RVOT endocardium during SR and a quadripolar diagnostic catheter was advanced up to the RV apex.

Following the endocardial map, which demonstrated the presence of healthy tissue, the multipolar mapping catheter was placed on the epicardium through the mini-thoracotomy access and directly manipulated by the physician by holding it with the fingers or a sawtell forceps. The 3D epicardial RVOT surface was then reconstructed with the EnSite™ X (Abbott, Chicago, IL) exploiting its magnetic navigation properties. Bipolar, HD wave, and OT maps were performed in SR, under baseline condition (pre-ajmaline infusion) and during ajmaline infusion/washout (1 mg/kg in 5 minutes).

At baseline, no areas of abnormal EGMs could be detected on the anterior aspect of the epicardial RVOT. During Ajmaline infusion a Brugada type I pattern was unmasked and an area of low amplitude fractionated and late EGMs, expanded along the epicardial RVOT and right ventricular (RV) anterior wall to cover a surface of 17 cm². The analysis of omnipolar maps revealed the appearance of several multi-site conduction blocks in this epicardial pathologic area: conduction blocks were discovered either in central part either in proximity of the border zone between the normal and low-voltage areas (normal and long-fragmented potential) (Figure 2 and Figure 3 Panel 1). The baseline maps were inspected to compare conduction direction and we noted that the line of conduction block appeared after ajmaline infusion were not present before.

All the pathologic electrograms inside the area were tagged and targeted for radiofrequency (RF) ablation carried out with a contact force sensor (TactiCath™, Abbott) in a temperature-controlled mode (Max 43°C) with a power limit of 30 W until reaching a lesion index (LSI) of 5. The total number of RF applications was 35 for a total RF time of 1600 sec.
After ablation, a second Ajmaline administration did not induce type 1 BrS ECG pattern, and the contemporaneous epicardial remap showed abatement of all the abnormal EGMs previously detected, replaced by a large scar area (Figure 3, Panel 2).

A final programmed ventricular stimulation protocol failed to induce any ventricular arrhythmia. The patient was discharged five days after the procedure without complications. After 5 months of follow up, the patient did not experience any arrhythmia recurrence and a further Ajmaline test was negative for type 1 BrS ECG-pattern induction (Figure 1 - Panel 2, C).

DISCUSSION

OT provides electrode orientation–independent cardiac wavefront trajectory and speed at a single location for each cardiac cycle\(^1\). Both unipolar and bipolar signals read by each electrode triplets (omnipole) are used to obtain the true voltage signal, direction and speed of front propagation. An omnipole resolves signals from all possible simultaneous bipoles (from every direction around the mapping location) from the electric field generated by the travelling wave and could provide a definitive assessment of the local cardiac wave properties\(^12\). The latter can be challenging to determine with traditional bipolar methods because ambiguity arises from the orientation and placement of the electrode in the area of interest. Traditional bipolar based substrate maps are heavily influenced by the direction of a wavefront to the mapping bipole. Recently, Porta-Sanchez et al.\(^13\) evaluated high-resolution, orientation-independent peak-to-peak voltage maps obtained with an equi-spaced electrode array and omnipolar EGMs, in the endocardium of ten pigs. Omnipolar EGMs better delineate infarcted and non-infarcted areas than traditional bipolar EGMs from both orientations.

To the best of our knowledge we reported the first visualization of wavefront-fragmentation and conduction blocks in the epicardial BrS arrhythmogenic substrate obtained with a 3D mapping system and omnipolar high-density mapping.

Our omnipolar substrate mapping revealed, under ajmaline administration, several areas of disorganized propagation and conduction block (Figure 2, Panel 1 and supplementary video); interestingly those areas were located either in the center of the pathologic RVOT either at the border between the pathologic and the non-pathologic RVOT areas outlined during ajmaline administration. OT allowed a fast, detailed, and real time assessment of the arrhythmogenic substrate during BrS ablation procedure. Information on direction wavefront (Figure 2, green arrows) pointed out areas of conduction block and areas in which conduction direction drastically changed before and after ajmaline administration (Figure 2, Panel 2). Traditional bipolar maps lack this information that can be useful for a comprehensive characterization of the ablation target. Presence of chaotic depolarization may provide a functional substrate for phase 2 reentry and degeneration of VT into VF. Moreover precise refinement of the pathologic RVOT borders may be crucial and failure to ablate even a small pathological surface could be responsible for arrhythmic relapses during the follow up\(^3,4\).
Our results are in line with the ones reported for RV-RVOT by Lambiase at al. using an intracardiac noncontact mapping array and Isochronal Mapping\textsuperscript{14}. During a ventricular S1-S2 stimulation protocol the authors found a significant conduction delay in the RVOT of BrS subjects, which was not apparent in healthy controls; moreover, the same regions of delayed conduction gave rise to wavefront fragmentation and lines of blocks that led to polymorphic ventricular tachycardia (VT) degenerated into VF in 5 out of 18 patients affected by BrS. This arrhythmogenic behavior has been recently reported also by Haissaguerre et al.\textsuperscript{8} and Nademanee et al.\textsuperscript{15}: localized block occurs at multiple sites from a single premature stimulus or during sodium channel-blocker infusion and could be responsible for VF initiation.

CONCLUSIONS

Omnipolar technology mapping may be a useful tool in BrS ablation to instantly determine and visualize the true signal voltage, its direction and speed of activation with superior efficiency and less ambiguity than the standard bipolar method. The latter information may help clarify the chaotic signal propagation and wave-breaks in BrS together with better delineate the boundary between pathological and non-pathological areas during sodium channel blocker administration. Displaying a beat-to-beat 3D map of signal propagation OT may also help clarify the genesis of ventricular arrhythmias which, up to now, has never been visualized on a epicardial map.


**Figure 1.** Panel 1 shows ventricular fibrillation initiation interrupted by an appropriate ICD Shock. Panel 2 shows basal ECG (A), unmasking of type 1 BrS ECG pattern during Ajmaline infusion (B) and the disappearance of type 1 BrS ECG pattern during a further Ajmaline administration 3 months after epicardial ablation of the arrhythmogenic substrate (C).

**Figure 2.** Panel 1 shows the omnipolar LAT map performed after the infusion of ajmaline with signal propagation through the epicardial BrS substrate (green arrows represent the local direction of signal propagation). Subpanels A and B represent an enlargement of two RVOT areas where conduction block lines (black lines and arrows) appeared after administration of ajmaline. Panel 2 shows the effects of Ajmaline infusion on signal propagation in the BrS substrate. Subpanels C and D depict omnipolar LAT maps performed under baseline conditions while subpanels E and F show the respective changes during ajmaline infusion (black lines and arrows). As a reader you may notice differences in Ajmaline in the direction of signal propagation and the appearance of conduction block lines (black lines and arrows) in the vicinity of the areas with later and fragmented signals (blue-violet areas) and at the border areas (red-white areas).

**Figure 3:** Panel 1 Omnipolar LAT map performed during baseline condition in sinus rhythm (A) and during ajmaline administration (B); the black line represent the pathologic area tagged for ablation. EGM equivalents of wave breaks (multiple deflections separated by isoelectric lines) and slow/anisotropic conduction (long fractioned potentials) over the yellow-outlined area (C). Panel 2 Radiofrequency ablation of the BrS arrhythmogenic substrate: each sphere corresponds to a point-by-point lesion index guided ablation (D). Remap post ablation during ajmaline administration showed complete abolition of the BrS arrhythmogenic substrate (E) and no abnormal EGM could be found during a further Ajmaline administration (F).
KEY TEACHING POINTS

1. Omnipolar mapping technology (OT) provides voltage, timing, and activation direction assessments independent of catheter orientation; it directly enables visualization of wavefronts on a mapping catheter as opposed to mapping a chamber from a collection of local activation times.

2. Slow conduction areas and wave-breaks within the BrS pathologic substrate under ajmaline administration can be precisely detected and visualized by means of OT mapping.

3. The precise identification of the boundaries between pathologic and non-pathologic tissue substrate provided by the novel high density omnipolar mapping may improve ablation efficacy.

4. The detailed identification of the proper BrS substrate boundaries and the development of conduction slow and conduction block under ajmaline administration may help clarify either the chaotic signal propagation either the mechanism of arrhythmias genesis.