Late Depolarization Abnormalities Versus Early Repolarization Abnormalities In Sudden Cardiac Death With Macroscopic (Apparent) Normal Hearts: The end of more than ten years old polemic

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Michel Haïssaguerre et al (1) recently described a new mapping data of patients with inferolateral J-wave syndrome (JWS) refractory to pharmacologic treatment using high-density electrogram mapping during the inscription of J wave. These data showed two distinct substrates, late delayed depolarization, and abnormal early repolarization underlie inferolateral JWSs, with significant electrocardiographic, genetic, and therapeutic implications. Based on these data, these authors propose a new simplified mechanistic classification of SCDs without macroscopic structural heart disease (SHD) in two mechanisms. Table 1

Table 1
Late Depolarization Abnormality vs Early Repolarization Abnormality

Early Repolarization Terminology	Erroneous because are caused by delayed depolarized areas: ***Conduction abnormality***. characterized by low-voltage fractionated LPs: VF substrates. It corresponds with Nademanee´s Group 1(3)	Appropriate: voltage gradients at the initial phase of repolarization: ***Repolarization abnormality.*** This mechanism is founded on animal studies in RV or LV wedge preparations demonstrating that J waves can be a consequence of a transmural repolarization gradient due to a differential distribution and function of the I_{to+} or transient outward current, $I_{K\text{-}ATP}$, *or* I_{Ca++}
Appropriate nomenclature for both mechanisms	Inferolateral J wave	Inferolateral J wave
J-wave pattern not influenced by long cycle	Yes	No
Baseline QRS duration	Wider	Less wide
Response of inferior J-wave patterns to isoproterenol	Persistent in 35% of cases (**2**)	Decrease or normalization in 65% of cases (**2.**)

Most genetic association mutation	Na^+ channel, RVOT epicardial and interstitial epicardial fibrosis with focal finger-like projections of collagen into myocardium, increase heart collagen. The RVOT and RV walls have higher collagen content related with the LV. A gradient of decreasing collagen content was seen from the epicardial to endocardial areas in all chambers. Additionally, reduced gap junction protein connexins-43expression ($Cx43^-$) localized to the intercalated disc, and relation with structural proteins (4). Fibrosis may be a feature irrespective of mutation status (4;5)	I_{to+}, $I_{K\text{-}ATP}$, or I_{Ca++}
SHD	Yes: epicardial structural alterations with delayed, prolonged, and fragmented signal in the RVOT electrogram (4;6)	Without
J-wave mayor voltage area	RVOT (4)	No

Typical VF driver's dominant driver regions	Anterior and inferior RV	In inferior septum

SHD: Structural Heart Disease.; LPs: Late Potentials.; RV: Right ventricle.; LV: Left ventricle or left ventricular.; VF: Ventricular Fibrillation

Koonlawee Nademanee et al (3) conducted a multicenter study with ERS or JWS in 52 young adults patients (4 women; median age, 35 years) to evaluate mapping and ablation of VF substrates or VF triggers. Using epicardial electroanatomical mapping of both ventricles during sinus rhythm and VF for localization of triggers, substrates, and drivers. Ablations were performed on VF substrates, defined as areas that had late depolarization abnormalities characterized by low-voltage fractionated late potentials, and VF triggers. Ablations were performed on VF substrates, defined as areas that had late depolarization abnormalities characterized by low-voltage fractionated late potentials, and VF triggers.

Detailed mapping revealed two phenotypes of ERS/J-WS:

- **Group 1** with late depolarization abnormalities predominantly at the RV epicardium (n=40) Group 1A ERS + BrS = JWS with late depolarization abnormality as the underlying mechanism of high-amplitude J-wave elevation that predominantly resides in the RVOF. The anterior RVOT/RV epicardium and the RV inferior epicardium are the major substrate sites for group 1
- **Group 2:** with VF triggers associated with Purkinje sites.

Ablation is effective in treating symptomatic patients with ERS/J-wave syndrome with frequent VF episodes.

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