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Arrhythmias and sudden death in heart failure: electrical stratification of risk groups

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ARTICLE INFORMATION

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Acronyms
CMP: cardiomyopathy
HF: heart failure
MVA: malignant ventricular arrhythmias
SD: sudden death
PVC: premature ventricular contractions

ABSTRACT

In this research is presented an overview of heart failure related to arrhythmias and sudden death, which can coexist, worsen, or be cause or consequence of one another. Here are discussed the premonitory electrical signs that allow to stratify risk in patients with previous events, with a possible approach to reality, and in those who have not presented them (most of them, the unprotected ones) and where a prognosis is very difficult, or impossible, to be established. These signs are numerous, elusive, with low specificity and sensitivity, none is absolute or negligible, in order to interpret them, a comprehensive vision is required. Premature ventricular contractions are discussed as predictors and triggers of arrhythmias, sudden death and cardiomyopathy, as well as the usefulness of ablative procedures versus medications. Electrical signs are good for identifying large risk groups but not for identifying high risk individuals inside the large low risk group (the majority).
Keywords: Heart failure, Premature ventricular contractions, Malignant ventricular arrhythmia, Sudden death

Arritmias y muerte súbita en la falla cardíaca: estratificación eléctrica de grupos de riesgo

RESUMEN

Se presenta una panorámica de la falla cardíaca ligada a las arritmias y a la muerte súbita, que pueden coexistir, agravarse, o ser causa o consecuencia una de otra. Se discuten los signos eléctricos premonitorios que permiten estratificar riesgo en pacientes con eventos previos, con posible acercamiento a la realidad, y en quienes no los han presentado (la mayoría, los no protegidos), y resulta muy difícil o imposible establecer un pronóstico. Estos signos son numerosos, esquivos, de baja especificidad y sensibilidad, ninguno es absoluto ni despreciable, para interpretarlos se requiere una visión integral. Se discuten las extrasístoles ventriculares como predictoras y desencadenantes de arritmias, de muerte súbita y de miocardiopatía, y la utilidad de los procedimientos ablativos frente a los medicamentosos. Los signos eléctricos son buenos para identificar grandes grupos de riesgo pero no lo son tanto para, dentro del gran grupo de bajo riesgo (la mayoría), identificar los individuos de alto riesgo.
Palabras clave: *Insuficiencia cardíaca, Complejos ventriculares prematuros, Arritmias ventriculares malignas, Muerte súbita*

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GENERALITIES OF THE VENTRICULAR ARRHYTHMIAS

Malignant ventricular arrhythmias (MVA) are diverse processes of great complexity, which pass between stability and instability; they involve dynamic factors (restitution of the action potential, conduction velocity, short-term memory, electronic currents) in interaction (tissue heterogeneity with greater or lesser risk of MVA) with homogeneity; the isotropy; the anisotropy; the gradients of the action potential; structural (fibrosis, stroke), electrical (hypertrophy, cardiomyopathy [CMP, cardiomyopathy in its original language]) and neurological remodeling; and genetic defects (channelopathies, CMP). Among them, the ventricular fibrillation is a heterogeneous condition with a variety of triggers and mechanisms (**Figure 1**)[1].

Dispersion

The spatial and temporal dispersion is one of the most important premonitory electrical signs between apex and base, septum and free walls, both ventricles (circumferential) and in the myocardial wall [1].

Ventricular Tachycardia

The ventricular tachycardia is one of the major chapters within tachycardia with wide QRS, with multiple mechanisms and electrocardiographic models (**Figure 2**). Its circuit may involve a diastolic common path, entry and exit sites, interior and exterior loops, and dead end contemplative pathways in several locations.

Heart Failure

The 85% of patients with advanced heart failure (HF) has MVA (including the non-sustained) and at the time the high-risk is identified, a cardioverter-defib-

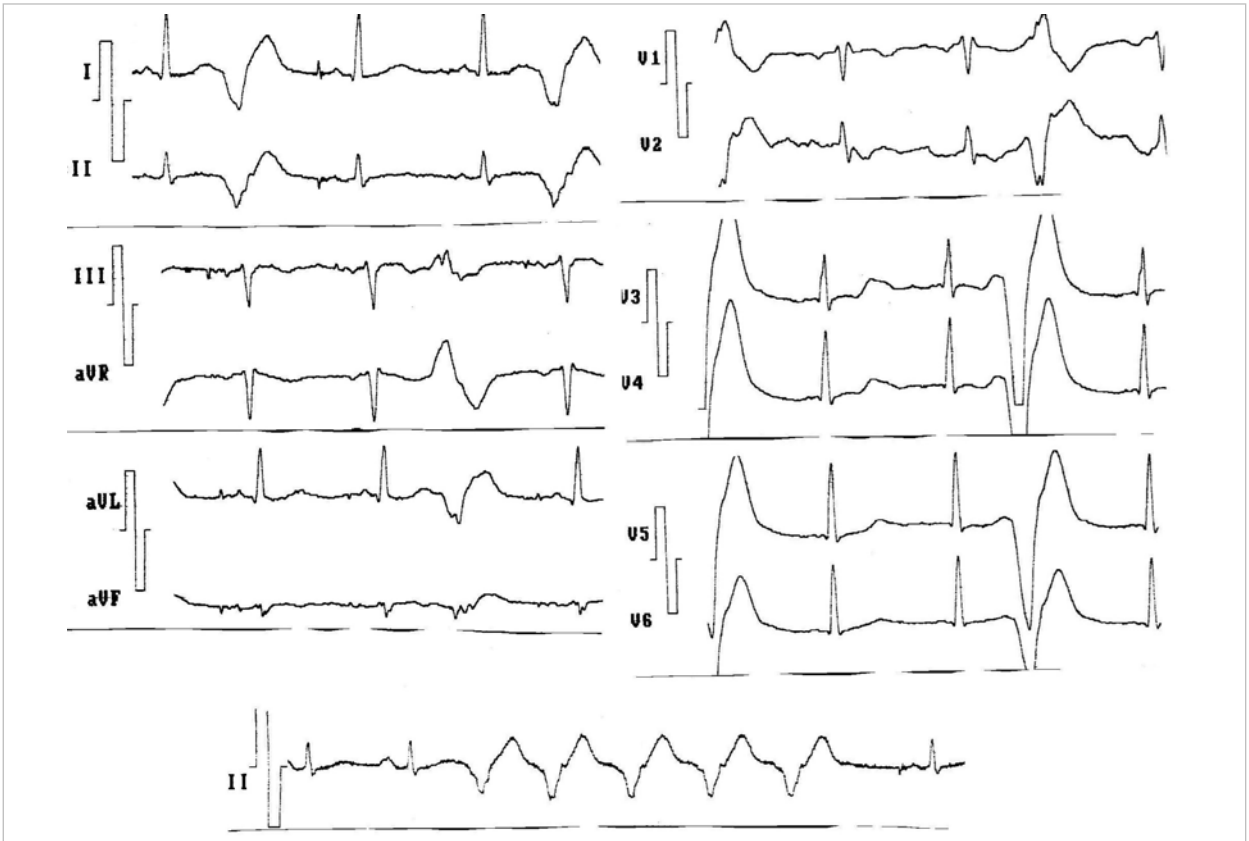

Figure 1. Patient with myocardial infarction and heart failure, reanimated from a sudden death event due to ventricular fibrillation. Premature ventricular contractions with short coupling interval are observed. In the inferior tracing, repetitive ventricular responses. The patient also made streaks of ventricular tachycardia and electrical storm. A cardioverter-defibrillator was implanted.

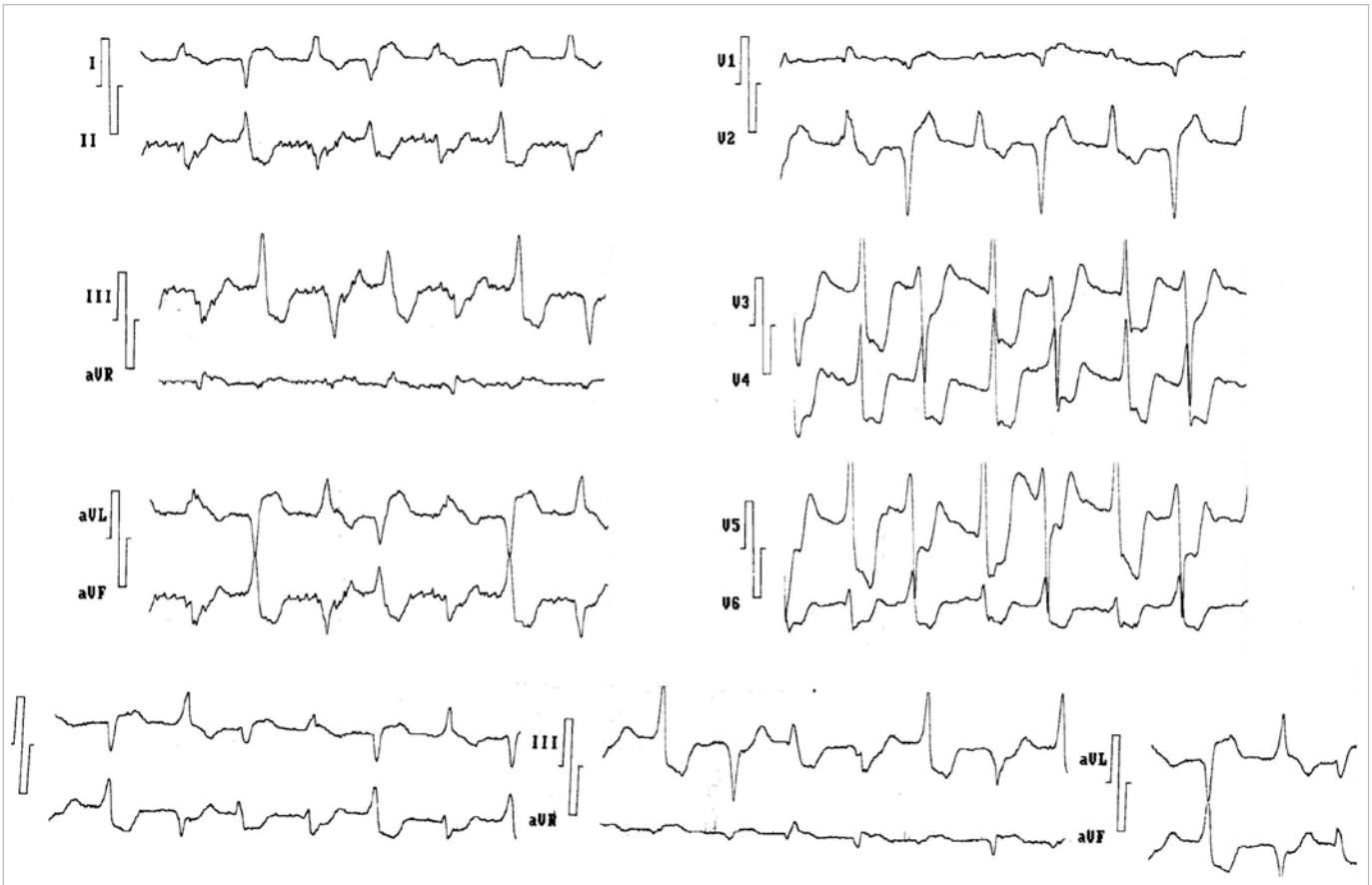

Figure 2. Cardiomyopathy and heart failure. Bidirectional ventricular tachycardia, alternating positive and negative polarity of the QRS complex is observed.

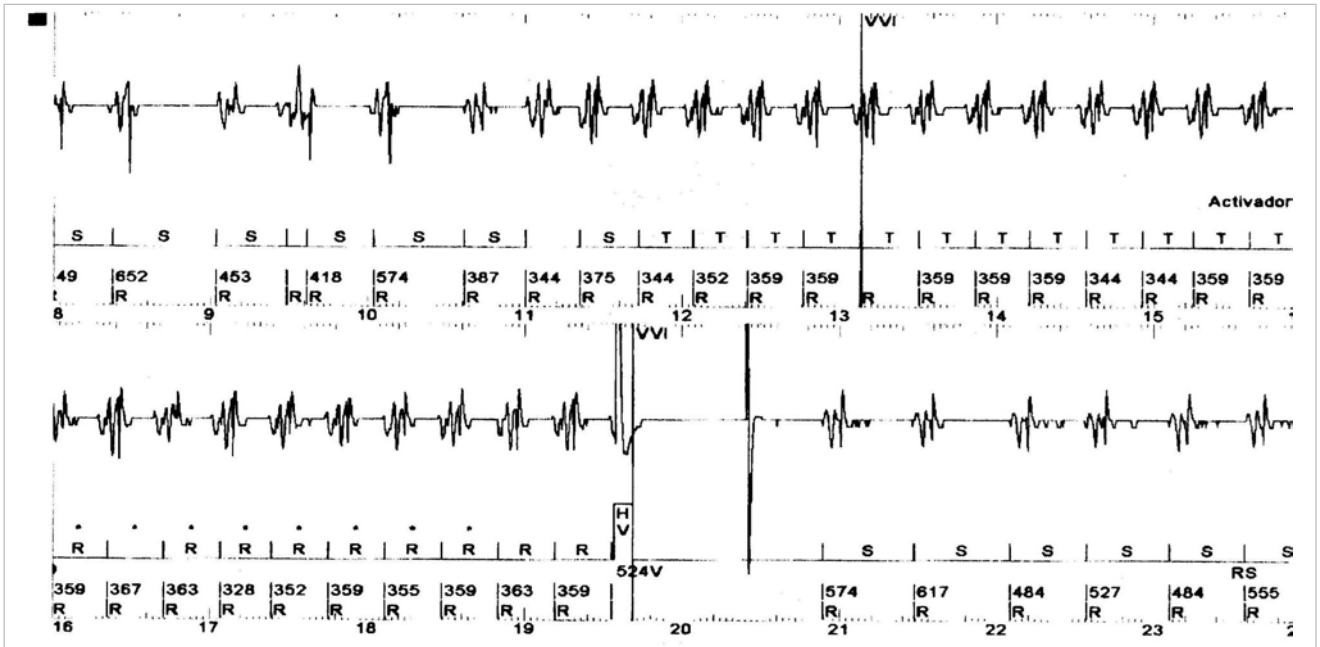

Figure 3. Patient with ischemic dilated cardiomyopathy, left ventricular aneurysm, ventricular tachycardia, electrical storm and electric shock of the implantable cardioverter-defibrillator that reverses the arrhythmia to sinus rhythm.

rillator would be implanted (**Figure 3**). The sudden death (SD) takes place in HF, because monomorphic ventricular tachycardia can degenerate into ventricular fibrillation and cause most arrhythmic SD. The various MVA (ventricular fibrillation, sustained and non-sustained ventricular tachycardia, and premature ventricular contractions [PVC], these transcendent not only by their density but by their irregularity) are facilitated by factors such as ventricular hypertrophy, myocardial infarction, sympathetic activation, electrolyte alterations, bradyarrhythmias, electromechanical dissociation, antiarrhythmic drugs (pro-arrhythmia) and atrial fibrillation[2-4].

The mechanisms of the arrhythmic SD in HF can be multiple: triggered activity, stretch receptors, abnormal automatism, reentries and early post-depolarizations[2-4].

Premonitory electrical signs

The HF and arrhythmias coexist, aggravate or one originates the other. In the **box** below are enumerated some of the premonitory electrical signs stratifying the MVA (both, debut and recurrences) and SD risk, all are of low sensitivity and specificity; some of them can go from normal to pathological[5].

Nothing should be considered isolated, nothing should be neither forgotten nor granted absolute value; an integral vision is required to put everything in its place and approach as closely as possible to the reality of each patient, which has not yet been achieved in spite of the numerous scientific works and publications on these subjects. More than 70 electrical signs that may represent a poor prognosis have been described, but they are elusive, none is negligible but not absolute, others were forgotten and have been resumed later. A resuscitated individual from a MVA or SD episode can have a normal electrocardiogram and electrical sequences, or present the electrical alterations characteristic of his/her basal disease (ischemia, CMP, valvulopathy, congenital disease). If the patient has had MVA or has been reanimated from an episode of SD, it is easy to go back and specify the premonitory electrical signs, as well as to observe those that appear in the follow-up. But the really difficult or impossible thing is to anticipate the events in those who have not had the fatal episode and predict who will present it. High risk patients only represent 10% and in them, it is easy to stratify prognosis and take the appropriate behavior. What is truly conflictive is, among low-risk (90%, unprotected), to specify those that are at high risk[5]

Box. Some premonitory electrical signs for stratifying the risk of malignant ventricular arrhythmias and sudden death[5].

- Premature ventricular contractions
- Non-sustained ventricular tachycardia
- Bidirectional ventricular tachycardia
- Depression of the vagus and the ventricular frequency curve
- T wave alteration (in polarity, magnitude, morphology, duration of its base)
- Hyperconductor node
- Bradycardia and sinus tachycardia
- Prolonged PR interval
- Branch block
- Atrioventricular and sinoatrial blocks
- Sinus arrest
- Voltage greater or lesser of the QRS complex
- Alterations of the ST segment and the T wave
- Left ventricular hypertrophy
- Paradoxical and stunned QT interval
- T1-T2, T-U, epsilon waves
- Late potentials
- Atrial fibrillation
- Electrical memory
- T_{PEAK} T_{END} (Tp-Te expressing dispersion of ventricular repolarization)
- Discordance between the T and U waves
- Terminal distortion and QRS complex fragmentation
- Zig-zag conduction with spikes of the QRS complex without branch block
- Atrioventricular and intraventricular dyssynchrony
- Giant T-U
- Prominent R in aVR
- Ventricular rate turbulence
- Delayed transition in precordial leads
- Prolonged intrinsicoid deflection
- Wilson's space gradient
- Post-extrasystolic T
- Prolonged interval of the PVC that is considered a predictor of structural disease
- Union rhythm
- Varied alternations
- QRS mortises
- High and narrow QRS (manifestation of accelerated conduction)
- R/T total cosine: vectocardiographic marker that reflects the spatial difference between depolarization and repolarization, average angle of QRS vectors by reconstruction of the electrocardiogram and it predicts SD in myocardial infarction, ventricular fibrillation and ventricular tachycardia

Torsades de pointes

In the *torsades de pointes*, Kirchhof *et al*[6] point out some indexes to predict risk of presenting: onset of arrhythmia with giant T-U wave, abnormal T-U, early postdespolarization as trigger, slow rise of QRS of the PVC, short-long-short cycles, pauses, long duration of the QRS in the first beat of the *torsade*, low QRS angle, prominent U wave, alternating QT interval and T wave (in duration, configuration, polarity, amplitude), QRS fragmentation, increase of QT and T_{PEAK}-T_{END} intervals.

In the left ventricular dysfunction, some predictors of MVA are highlighted: the duration of the QRS complex, the QT interval dispersion, alterations in the Holter monitoring and electrogram averaged signals, the abnormal heart rate variability, the alternation of the T wave, the programmed electrical stimulation (if this is positive it indicates high risk, if it is negative it is not always conclusive). Kentta *et al*[7] studied spatial heterogeneity of the depolarization and repolarization (waves R, J and T) in the 12-lead electrocardiogram with automatic methods, in individuals with healthy heart and reanimated SD. This heterogeneity can lead to a lethal arrhythmia[7].

Wellens wrote in 2008: *"Despite extensive efforts to better identify people dying an arrhythmic death out of hospital, we are able to recognize only ≈10% of those victims as being at high risk before the event"*[8].

Then, we reach to the big conclusion that we would not want to arrive: the premonitory electrical signs of MVA and SD are good to identify large risk groups but not so much for, within the large group of low risk (the majority), identifying high risk individuals.

His-Purkinje System

The His-Purkinje system is important in the genesis of MVA. In general, it is narrow PVC and short coupling interval, involved in mechanisms of reentry, ectopia and triggered activity and whose ablation is performed in some laboratories[9].

Ventricular fibrillation

Ideker *et al*[10] deal with the amount of types of ventricular fibrillation, several, many, 300000, referring to the annual number of SD in the United States; this variability is explained because one body is not exact to another, each one has its type of instability, the same organ can have different types of ventricular fibrillation at different times, and even the same body can have different types in different regions at the same time. In general, there are two mechanisms in ventricular fibrillation: type I, fast reentrant waves, short-lived, changing and with little repetition; and type II, mother rotor with slower daughter waves, long fronts and similar ways with repeatability. Or both types, because they are not excluded, can interact and are influenced by the underlying disease, the use of antiarrhythmic drugs and the duration of the arrhythmia itself[10,11].

Premature ventricular contractions

The PVC can be predictors or triggers of MVA, consequence or cause of a CMP induced by PVC. The PVC can trigger MVA and cause arrhythmic death but also lead to a reversible CMP, left ventricular dysfunction and function as modifiable risk factor (with and without structural cardiac disease, to induce or aggravate a preexisting one). The behavior may vary: abstention, the use of antiarrhythmic drugs or ablation, always with the aim of achieving improvement in ventricular function[12-16].

As for the CMP induced by PVC, there are several factors to consider: the basic disease, left ventricular function, ionic disorders, comorbidity, degree of dyssynchrony, tachycardia, bradycardia, ventricular remodeling and their dimensions. On the other hand, there are factors dependent on PVC: density, pleomorphism, width, origin, long coupling, interpolated character, increase in dispersion and duration of action potential, number of foci, ionic alterations, heterogeneity, models and duration time.

It is necessary to determine in each case, what is first: the PVC that leads to severe or subtle dysfunction and the CMP, or the dysfunction is the one that originates the PVC, in all of which there can be overlaps and changes. The PVC density is a risk factor, not the only one, for predicting an adverse end in patients with disease or without structural cardiac disease; if there is any preexisting alteration, frequent PVC potentiate left ventricular dysfunction (which would be reversible). Even when the CMP induced by PVC is a real entity, some doubts arise: the presence of numerous PVC without CI; first evidence of CMP (structural cardiac disease marker underlying preclinical), even if the PVC are suppressed; hidden substrates (identifiable by nuclear magnetic resonance or by mappings), inflammation, myocarditis, fibrosis; epiphenomena; varied causes and mechanisms; required density ("dose") to take place; use of antiarrhythmic drugs and their conflicts (CAST study); effective ablation of low risk PVC (the ejection fraction is normalized and there is no HF);

similar density of PVC in cases with and without left ventricular dysfunction; several sites of origin (right ventricular outflow tract, sinus of Valsalva, free wall of right left ventricle, epicardium and intramural); when the PVC is a predictor of HF and mortality; what is the duration of the QRS that arises risk of CMP induced by PVC and how much for the suppression of the PVC to improve the left ventricle function. In some cases, the PVC is an independent predictor of left ventricular dysfunc-tion[12-17].

The dyssynchrony is a transcendental factor in the CMP for pacing of the right ventricle, by left bundle branch block and by preexcitation (it induces papillary muscle dysfunction, mitral regurgitation, left ventricular volume overload and modified autonomic response by ventricular-auricular conduction). The PVC of the right ventricle are more adverse than those of the left ventricle and, those of the free wall of the right or left ventricle more than those of the outflow tract of the right ventricle. The treatment should be done if the symptoms related to PVC worsen (this is not always the case), cranial function is impaired or ventricular tachyarrhythmias take place[12-16].

The CMP induced by extrasystoles has to do with the electrophysiological remodeling in the context of the cardiac chambers' remodeling. Early and frequent contractions can be associated with a structural cardiac disease with increased SD and total mortality[12-16].

Regarding whether or not to treat PVC, there are opinions in favor, against and quite the opposite... because how aggressive should we be? The PVC are modest, humble, but if deleted the cardiac function to the CMP induced by PVC improves, then it should be first-line treatment? Others think that we would be fools again when treating post-infarction PVC as when their suppression was proposed with antiarrhythmic drugs in the 80s, and a harsh lesson was taught when interpreting that post-myocardial PVC increased the risk of MVA by triggering them, and by suppressing them, the risk would decrease but ... it was found that there was danger even if improvement of the ejection fraction was achieved. The CAST study revolutionized these concepts, it could decrease the number of PVC but increase mortality and the Electrophysiology Study vs. Electrocardiographic Monitoring, the density of the PVC and their successful treatment with the use of antiarrhythmics was independent of the risk of sustained MVA. The same idea was reborn some time later with ablative procedures that could revert the CMP and change the potential high risk population. There is not always a relationship between the frequency of PVC and the ejection fraction; There may be an underreporting of the PVC in one or two ways, with a damaged fraction, and a greater benefit can be obtained with its suppression. Another factor to be taken into account is postextrasystolic potentiation that can also improve the ejection fraction, at least in the short term[18-21].

In this field, there are many more questions than answers: How many PVC are too many? Is ablation of PVC effective and reduces the need for an implantable cardioverter-defibrillator? What myocardial postinfarction patients require ablation? Why can patients with PVC have less eschar? What is the explanation for the CMP induced by PVC? Which patients with ventricular dysfunction need the implantable automatic cardioverter-defibrillator? The ablation of the PVC in selected post-infarction patients can improve the ejection fraction, but is this good enough and improves the end? The survival increases, but can there be recurrences months and years after the CMP induced by PVC?[18-21]

Atrial fibrillation

The association of HF with atrial fibrillation is common and transcendental, increasing the risk of stroke, hospitalization time and mortality. The CMP may also be induced by the arrhythmia. It has been discussed whether rhythm control with antiarrhythmic drugs is superior or not to the control of heart rate in patients with HF and atrial fibrillation, but morbidity and mortality are higher than in isolated failure. In recent times, the treatment of atrial fibrillation by means of ablation has been discussed in relation to its drug therapy and it is argued that the former decreases in-hospital mortality, improves ejection fraction and episodes of arrhythmia (CASTLE-AF study, Catheter Ablation vs. Standard conventional Therapy in patients with Left Ventricular dysfunction and atrial fibrillation). These are two emerging epidemics and two linked epidemic emergencies. Atrial fibrillation and ventricular dysfunction represent an electromechanical vicious circle: the fibrillation as a cause or consequence of ventricular systolic dysfunction, with reduction of the ejection fraction and presentation of HF, is considered an independent predictor of cardiovascular death at all ages, in men and women. There is fibrillation without pre-existing structural cardiac disease with severe reversible left ventricular dysfunction (uncommon, but not rare), arrhythmia leading to

light or moderate, more common dysfunction, and preexisting dysfunction that leads to fibrillation with reduced left ventricular function not clinically recognized[22,23].

Electric storm

The electrical storm is an independent marker of higher mortality in patients with ventricular dysfunction and implantable cardioverter-defibrillator, caused by worsening of HF and it occurs twice more if the ejection fraction is less than 35%. However, it is difficult to identify the precipitating factor of the electrical storm, which is only achieved in 26% of cases. In our experience, it was possible to identify the precipitating factor of the storm in 26.7% patients with cardioverter and in half of them, the HF was the trigger[24].

FINAL WORDS

There are close links between HF, MVA, atrial fibrillation, other arrhythmias and SD. Like the historical phrase and the song: who threw the first stone? Given the complexity of arrhythmias, their varied pathophysiology, the many factors involved, their own variability and the numerous electrical predictors described, can the doctor approach the electrical risk stratification by groups?: Yes! And for individuals?: Very difficult or impossible! And what is the role of PVC ablation and atrial fibrillation in patients with HF?

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