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PERCUTANEOUS INTERVENTIONS FOR THE TREATMENT OF CARDIAC ARRHYTHMIAS: TRANSLATIONAL APPROACH

INTERVENÇÕES PERCUTÂNEAS PARA O TRATAMENTO DAS ARRITMIAS CARDÍACAS: ABORDAGEM TRANSLACIONAL

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ABSTRACT

In the last fifty years, elegant clinical and experimental models have prompted new translational concepts on cellular and tissue substrate of cardiac arrhythmias, favoring the development of non-pharmacological interventions, with important therapeutic achievements when compared to conventional treatment with antiarrhythmic drugs. Besides the gradually increasing knowledge of the anatomical and electrophysiological complexity, sophisticated mapping methods, special catheters, and controlled clinical trials have favored the progression of ablation of tachyarrythmias, particularly of ventricular tachyarrythmias and atrial fibrillation.

Keywords: Cardiac arrhythmias; Catheter ablation; Translational medicine.

RESUMO

Nos últimos 50 anos, elegantes modelos clínicos e experimentais impulsionaram a investigação translacional do substrato celular e tissular das arritmias cardíacas, favorecendo o desenvolvimento de intervenções não farmacológicas, com grandes conquistas terapêuticas quando comparadas ao tratamento convencional com drogas antiarrítmicas. Além do progressivo conhecimento da complexidade anatômica e eletrofisiológica, os métodos de mapeamento sofisticados, os cateteres especiais e os estudos clínicos controlados favoreceram o progresso da ablação das taquiarritmias, principalmente das taquicardias ventriculares e da fibrilação atrial.

Descritores: *Arritmias cardíacas; Ablação por cateter; Medicina translacional.*

In the last 50 years, there have been important advances in the understanding of the anatomical and electrophysiological concepts of the heart, which have largely contributed to rational approaches in the diagnosis and therapy of cardiac arrhythmias.

In the 1960s, after Lown's introduction of direct current defibrillators, there were other excellent contributions that, in a translational manner, provided support for the continued development of techniques for the percutaneous treatment of arrhythmias, including recording of the His bundle activity by Scherlag et al.,[2] electrical stimulation of the heart by Wellens,[3] anatomical surgical ablation of the accessory tracts by Cobb et al.[4], and, finally, catheter-induced ablation with initial direct current by Scheinman et al.,[5] which were later consolidated with the use of radiofrequency as a source of energy.

During this same period, the Cardiac Arrhythmia Suppression Trial[6] demonstrated the inability of antiarrhythmic drugs in reducing mortality in patients with ventricular arrhythmias. Moreover, no effective drugs for atrial arrhythmias, which act on specific channels such as the potassium channel, were available. Thus, the introduction of radiofrequency-induced ablation techniques in the United States and Europe at the end of 1980[7] and in Brazil at the beginning of the 1990s[8] was a necessary strategy to enable the control of many arrhythmias, which will be addressed herein, following their physiopathological and translational concepts.

BIOPHYSICAL CONCEPTS

Catheter interventions to destroy arrhythmogenic tissues have mostly used heating with direct current, microwave, ultrasound, laser, and radiofrequency. The most commonly used form of energy was radiofrequency, a form of alternating electrical activation of 500–1000 kHz, which, when applied unipolarly between the distal pole of a catheter and a surface, affects the cell membrane, cytoskeleton, nucleus, and cellular metabolism, including the microvascular inflammatory response. After reaching a temperature of 50°C, well-defined and irreversible heating lesions develop because of the sarcolemma lesion and intracellular calcium overload. Temperature monitoring prevents excessive heating at the catheter tip (which can also be avoided with the use of irrigated catheters), formation of blood clots, and increase in impedance.

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Another thermal mechanism is cryoablation, in which pressurized liquid nitrogen is used to freeze and crystallize the structures in contact with a balloon catheter, reversibly (up to -40°C) or irreversibly (<-40°C) compromising the cardiac structures that are in direct contact with the freezing source.

ANATOMICAL AND ELECTROPHYSIOLOGICAL CONCEPTS

Automatism

The myocyte depolarization ability is dependent on an intra- and extracellular ionic gradient, mediated mainly by the influx/efflux of sodium and potassium. This ionic movement is controlled by multiple channels (Figure 1A), which, normally, can be automatically depolarized. These automatic cells ensure the cardiac frequency and its variations, from structures hierarchically arranged preferably in the sinus node, atrioventricular (AV) junction, and in the His-Purkinje (HP) system.

Through automation or triggered activity (early or late depolarizations), there is an increased depolarization of cells with faster rhythms located topically (sinus node, AV node [AVN], and HP system) or atopically in the right heart (junction with the superior vena cava, terminal ridge, and right ventricular outflow tract [RVOT]) or the left heart (pulmonary veins, left atrial appendage, left ventricular outflow tract [LVOT], and papillary muscles) (Figure 1B) (junction with the superior vena cava, left atrial appendage, left ventricular outflow tract [LVOT], and papillary muscles) (Figure 1B).

The ionic basis of late post-depolarization is related to the overload of calcium in the myoplasma and sarcoplasmic reticulum and to the secondary release of the calcium ion after repolarization, especially in the presence of catecholamines or cyclic AMP. Generally, these are focal rhythms, and their early activity in one place allows establishing the source focus and mapping for the ablation of this arrhythmia, if percutaneously accessible.

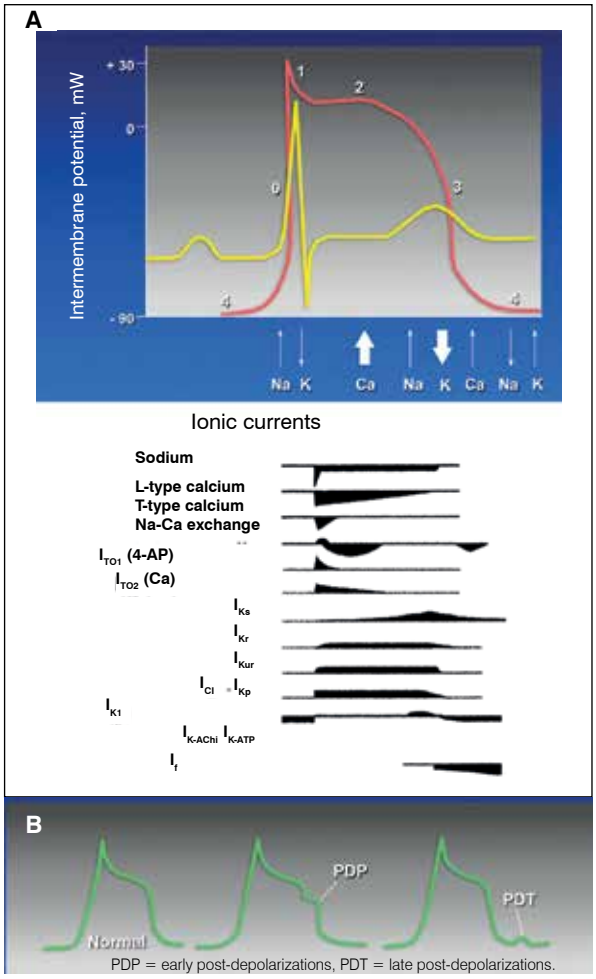


Figure 1. (A) Ionic currents that determine the action potential: those with lower orientation are directed from outside to inside the cell; those with superior orientation come from within the cell and are directed to the extracellular environment. (B) Automatic cells, with oscillations in their action potential by early and late ionic fluxes.[9]

Reentry

In the presence of conduction changes, the activated electric current navigates through tissues with different conduction and refractory properties. Thus, it is possible that a stimulus will have its conduction perpetuated by finding, before being extinguished, an adjacent tissue functioning as a conduction circuit and heterogeneous refractory periods, unlike in normal tissue. This phenomenon (Figure 2) of reentry can reproduce in the laboratory the nodal, AV, and ventricular monomorphic tachyarrhythmias, which may be related to normal or pathological tissues, the latter being represented by scars in the atria and ventricles, due to ischemia or degenerative processes.

The most frequent sustained arrhythmias with reentrance mechanisms were the first to be treated with catheter ablation, notably nodal, AV, and ventricular reentrant tachycardias, which will be described below. Subsequently, automaticity arrhythmias were also managed using this technique.

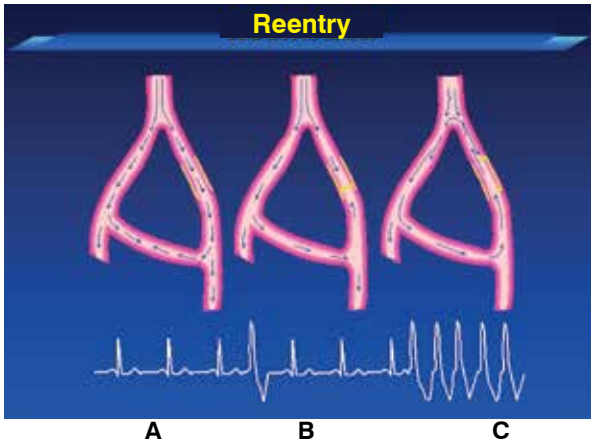


Figure 2. (A) Tissue with structural or functional change in conduction without impairing passage in the stimulus under normal conditions. (B) In the presence of an ectopia, there is a bidirectional block. (C) During a precocious ectopia, there is a unidirectional anterograde block and, due to the delayed conduction, there is time to enable retrograde activation and triggering of arrhythmia.

Natrioventricular nodal reentrant tachycardias (AVNRT)

The NAV is the natural filter for the slower conduction of the action potentials of the atria to the ventricles, ensuring, by the slowing of the impulse in the NAV, the AV contractile

physiological sequence and the protection of the conduction to the ventricle of fast atrial rhythms such as atrial fibrillation (AF). This slower conduction velocity is determined by the small diameters of the nodal myocytes, interposition of connective tissue, and, mostly, by the failure of continuity determined by the connexins. Thus, optical, histological mapping, and immunological assays with marker proteins demonstrated, along with action potential recording, the coexistence of rapid (transitional tissue) and slow (lower nodal extensions) nodal tracts, characterized by large and small expression of the connexins Cx40 and Cx43, respectively.[10] In 20% of individuals, slower routes (Figure 3) with a short refractory period are found in the vicinity of the NAV and may, in special circumstances, trigger NRT.

The positioning of the catheters and the ablation of the slow pathway of patients with NRT is generally simple, with a success rate of 95%; it consists of the radioscopic topographic localization (Figure 3D) and electrophysiological evaluation of the potential of the slow pathway for the application of radiofrequency (30-50 W, 1 min, temperature 40-50°C). Complications that occur are related to vascular access (1% of deep venous thrombosis) and proximity of the NAV (1% of the total AV block) with a 1-year recurrence of 5%.

AV reentrant tachycardias

The accessory tracts are anomalous bundles consisting of myocardial cells inserted freely along the mitral annulus (60%), tricuspid (15%), or the right or left septal side of these valves (25%). Rarely, the accessory tracts emerge directly from the atriofascicular atria, the NAV (nodofascicular, nodoventricular), or the bundle of His (His-fascicular). They may be multiple 13% of the time and, in the presence of Ebstein's disease, are 4-fold more frequent (52%). They may also present decremental conduction such as in Mahaim's right lateral fibers with anterograde conduction only, behaving functionally as a duplicated His bundle in the lateral region of the tricuspid ring and inserted distally in the right HP system, near the apex of the right ventricle. Finally, there are posteroseptal fibers with exclusively retrograde decremental conduction, generating Coumel-type tachycardia that, because of its incessantness, can lead to the development of tachycardia.

Radiological and electrophysiological techniques seek to define the insertion of tracts along the AV ring, with the success and clinical outcome of ablation of accessory tracts being similar to those of NRTs. There is a greater technical difficulty in the epicardial ablation of tracts, multiple tracts, or when the accessory tracts are associated with complex heart diseases.

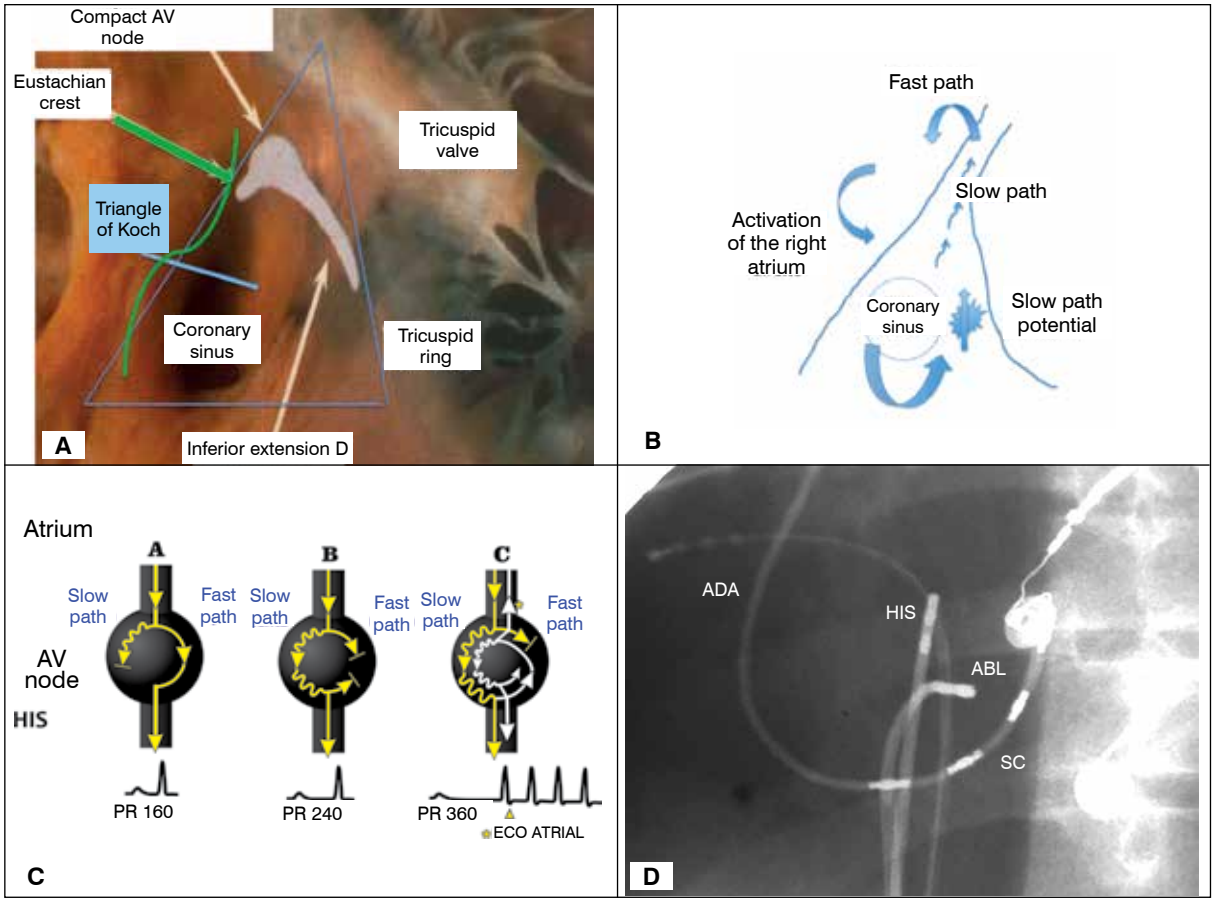


Figure 3. (A and B) Anatomy of structures related to tachycardia by nodal reentry, which follows the same principles of reentry of the electrocardiographic (C) identification of leap in the conduction through the atrioventricular node that precedes the tachycardia. (D) Radiographic image of catheters used in the left anterior oblique projection and their positions. AV = atrioventricular, HRA = high right atrium, H = His, CS = coronary sinus, ABL = ablation catheter.

Some muscle fibers that involve the coronary sinus and its tributary veins can function as a connecting muscle bridge between the atria and ventricles. When there is a need for ablation in this location of limited blood flow, irrigation at the catheter tip is performed; in this way, the lesion will be formed without limiting the increase of impedance and temperature. The proximity of the arteries (mainly the posterior descending artery) with the branches of the venous sinus requires anatomical definition and special care during ablation.

Depending on the anatomical peculiarities of anomalous bundles, sheaths can be used to stabilize the mapping of larger rings such as the tricuspid, for the transeptal access in left routes and pericardial access for epicardial routes.

Ventricular reentrant tachycardias

The scar substrate of sustained ventricular tachycardias (VTs) after myocardial infarction provided a reproducible reentry model, intensely studied by contemporary electrophysiology. The scar region is composed not only of a dense scar but also of surrounding tissues with myocardial fibrils inserted into the scar, characterized by alterations in CX43, decreased intercellular coupling, slow conduction, and predisposition to reentrant VT. Adaptive changes in the sympathetic and parasympathetic nervous system with increased efferences and decreased neuronal afference of the infarcted area result in greater heterogeneity and multiplicity of the arrhythmogenic substrate circuits, identified by fractional potentials, late potentials, and abnormal localized ventricular activity (Figure 4).

Structural remodeling of the myocardium is associated with the appearance of myofibroblasts, fundamental cells, and the translational biological basis of the VT substrate. Recent animal studies showed that after 6 weeks of experimental infarction, the isthmus of the VT has a very high density of myofibroblasts (increase of 5 times) and increased vascularity (increase of 1.7 times) in the borders of the scars, due to the increase in cellular recruitment or by pro-angiogenic factors of these same myofibroblastic cells. There are also cell bridges between the myofibroblasts and the remaining cardiomyocytes, with organized heterogeneity at the edges of the scar and isolated by collagen septa, with altered tissue heterogeneity and resistance due to the non-uniform heterocellular coupling between the cardiomyocytes.[11] These experimental findings were based on the relationship between electrical heterogeneity and conduction abnormalities and the inducibility of ventricular arrhythmias.

The presence of a stable substrate, characterized by a scar with viable myocardial tissue in its interior, establishes the conditions for the reentry mechanism and, with it, the reproduction of human monomorphic VT in the laboratory.

The possibility of mapping of sustained VTs (SVTs) by using electrophysiological techniques has defined locations that display a good correlation with the surface electrocardiogram, offering the possibility of non-invasive diagnosis of their origin (Figure 5).

The substrate of SVTs consists of regions of abnormal myocardium where the ventricular muscle is replaced by

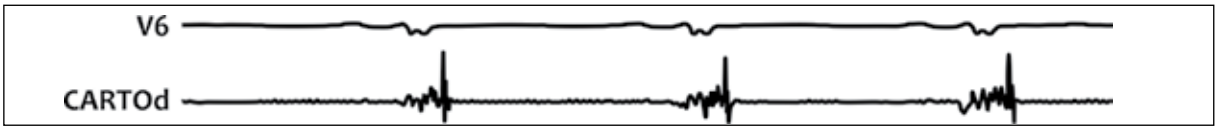
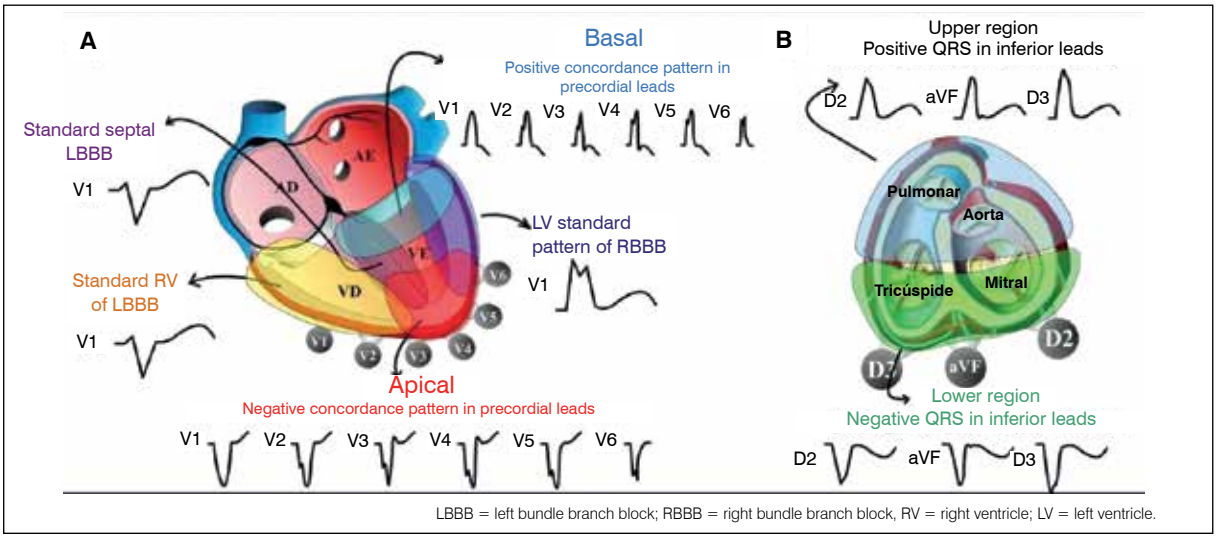


Figure 4. Surface lead (V6) and the ablation catheter electrogram (Cartod). Fragmented and late potentials observed in sinus rhythm on the target of the arrhythmogenic substrate of patients with sustained ventricular tachycardia, who underwent radiofrequency ablation.



LBBB = left bundle branch block; RBBB = right bundle branch block, RV = right ventricle; LV = left ventricle.

Figure 5. (A) Sagittal and (B) transverse section of the heart. (A) The presentation of complete left bundle-branch block ventricular tachycardia (VT) in V1 suggests the origin to be the right ventricle, comprising idiopathic VSVD VT, branch reentrant VT, and scar-related VT, whose most frequent examples are arrhythmogenic right ventricular dysplasias, cardiomyopathies, and sarcoidosis. The BCRD morphology almost always defines the origin in the left ventricle, being exceptionally found in severe right ventricular dysplasias or in complex scars resulting from tetralogy of Fallot repair surgeries. The derivations V3 and V4 are able to characterize the basal and apical left ventricular regions and, by the vectorial result in the electrocardiogram, differentiate the basal (predominant R waves) from the apical (predominant S waves) origins.

fibrous tissue, creating regions of slow conduction and the occurrence of reentry, characterized regionally by low local electrical activity and segmental contraction deficit. The response of these regions to programmed electrical stimulation, allowing the laboratory reproduction of clinical SVT in patients with previous myocardial infarction, was one of the most important translational milestones for the understanding of the arrhythmogenic mechanisms of modern electrophysiology. Subsequently, the advent of radiofrequency as an energy source enhanced the accuracy of cardiac electrophysiological mapping techniques, increasing the knowledge of important pathophysiologic bases of arrhythmogenesis.

In these patients with heart disease and monomorphic SVTs, the most frequent presence of reentrant macrocircuits facilitates the investigation of critical locations for maintenance of these arrhythmias, located in the endocardium, epicardium, or intramural region of the ventricles. These circuits are usually made of scars that have residual surviving myocytes, constituting true conducting channels (Figure 6). These channels, called isthmuses, are myocardial corridors surrounded by inextricable anatomical (scar, valve annulus) or functional (blockage of conduction during tachycardia) barriers, which allow, by the slow conduction of the electric impulse, the wavefront to perpetuate the SVTs.

In addition to characterization of the circuits, electrophysiological techniques have enabled the localization and non-pharmacological treatment of SVTs, which evolved with the electroanatomic mapping techniques, for the most accurate localization of the arrhythmogenic circuits (Figure 7)

The propagation of the electrical impulse to the ventricles in the endocardium has a high velocity, owing to the participation of the Purkinje system. When the tachycardia originates from the epicardium, there is a longer duration of the QRS complex and the absence of the initial R waves in the derivations related to the origin of the VT, including the presence of pseudo-delta waves with greater intrinsicoid deflection resulting from the slower conduction by the epicardium, owing to the lack of a specific conduction system (Figure 8).

It has been emphasized that epicardial tachycardias are more frequent in cardiomyopathies, mainly in chagasic cardiopathy, which is responsible for >50% of the cases.

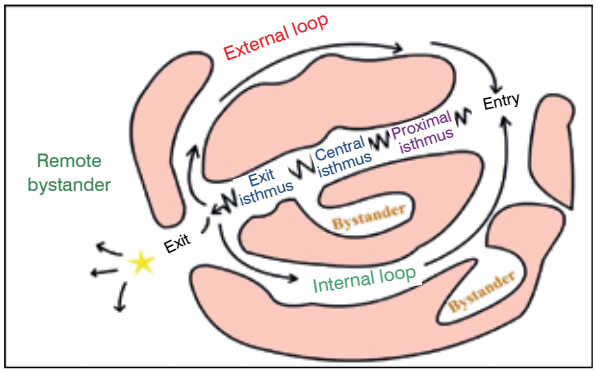


Figure 6. Reentry models in a scheme represented by pink areas of non-conducting fibrosis, surrounded by viable muscle that allows the passage of the stimulus in the form of "figure 8." "Bystander" areas do not actively participate in the circuit but can communicate with the external stimulus loops that will enter a central channel called the isthmus, a true corridor of viable tissue, surrounded by barriers of unexcitable tissue, which aids in the stability and perpetuation of arrhythmia. This mechanism defines reentry, a continuous, repetitive, and circular propagation of the wavefront, which returns and reactivates its place of origin.

Ventricular arrhythmias and the HP system

The HP system consists of specialized fibers insulated from their origin to their peripheral afforestation. In the right ventricle, they present with a single branch and in the left ventricle with two interconnected fascicles, coordinating the electrical conduction of the NAV to the cardiac cells. It has different cellular, ionic, and electrophysiological structures from the rest of the conduction system, and may lead to ectopias or VTs that can be treated using conventional ablation techniques.

Knowledge of HP system arrhythmias helped break an important paradigm in electrophysiology, explaining sudden death and electrical storms in the normal heart. The fact that some patients with idiopathic ventricular fibrillation (VF) have, as a triggering factor, ectopy localized in the HP system has given rise to the demand for techniques and strategies for the elimination of these foci. Opportunistic ablations[12] in cases

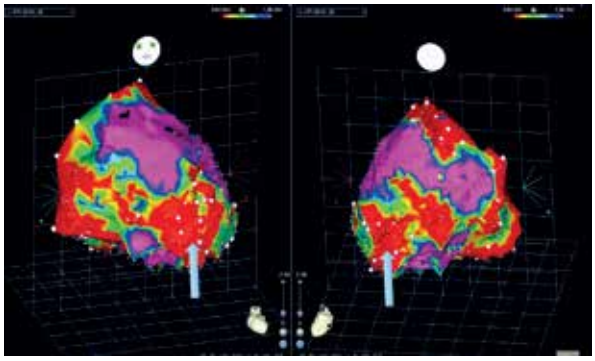


Figure 7. Electroanatomic mapping in anterior and posterior projections showing regions of low voltage in red, which, combined with conventional electrophysiology techniques, identify the location of the ablation in the epicardium of the left ventricle (arrow = inferoapical region).

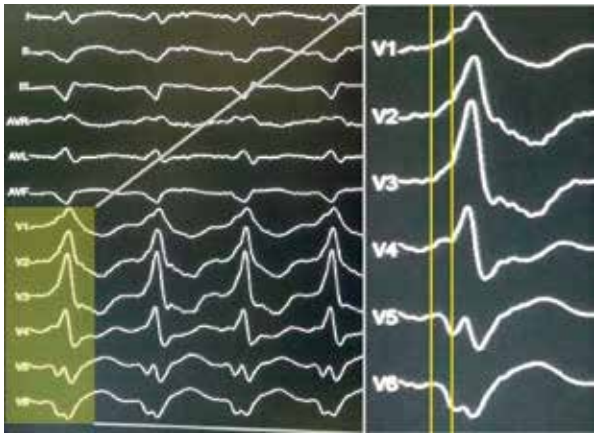


Figure 8. Tracing of a patient with sustained ventricular tachycardia with an epicardial focus, showing the pseudo delta wave (between yellow lines in precordial leads V1 to V6) originated by the slow conduction of the epicardial activation.

with ectopia facilitate the mapping, ablation, and control of this delicate and catastrophic clinical situation (Figure 9).

Situations very similar to an HP system ectopia were also recognized in cases of VF associated with the presence of moderating bandwidth of the right ventricle, long QT syndrome, and early repolarization syndrome.

Focal VTs

The mechanism of focal idiopathic monomorphic VTs may be secondary to the automaticity, microreentry, or triggered activity related to the activity of cyclic AMP.[4] Thus, the stimulation of beta-adrenergic receptors by catecholamines result in the release of calcium from the sarcoplasmic reticulum and, subsequently, an increase of intracellular calcium, after late depolarization and triggering of the VTs. These VTs are more often located in the RVOT and LVOT.

VTs in the RVOT are the most commonly found VTs, and located more frequently in the septum than the free wall of the right ventricle. In the LVOT, the most frequent location is the cusps, followed by the region below the left coronary cusp, also called aortic mitral continuity.

The RVOT is positioned to the left and anteriorly in relation to the LVOT, whereas the pulmonary valve is positioned superiorly in relation to the aortic valve. The careful placement of electrodes on the anterior region of the thorax allows the electrocardiographic recording of precordial derivations to allow a differential diagnosis between RVOT VT and LVOT VT (Figure 10). The typical morphology of the QRS complex is complete left bundle-branch block, with lower shaft. The transition from the appearance of the R wave in the precordial derivations suggests the left ventricular outflow when it occurs in V2, and occasionally in V3. The definition of the anatomical details assists in the success of the procedure, which has reached around 90% in published series.[13]

IMAGING DURING VT ABLATION

The imaging modalities for the investigation of patients with VT has expanded. Transthoracic Doppler echocardiography,

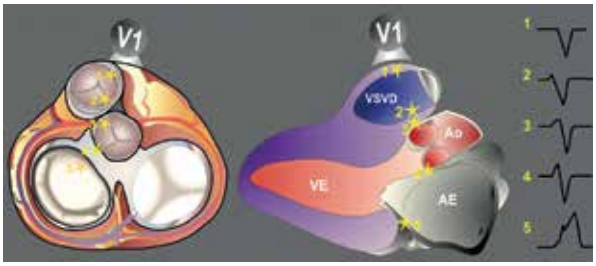


Figure 10. Sagittal section of the heart showing relations between the right ventricular outflow tract, aorta, left atrium, and left ventricle and the morphology of the QRS complex in lead V1, in 5 possibilities of the source of ventricular tachycardia. Note the growth of R-wave to the extent that the origin of the ventricular tachycardia or ventricular extrasystoles is more posterior. Modified from Asirvatham.[14]

a simple and routinely performed method, can analyze the thickening of the wall and infer the presence of scarring, although it presents limitations in the definition of the image in 10–15% of the cases.[15]

Most VT ablation techniques are related to electro-anatomical systems (Carto, Biosense Webster Inc.; NAVX, St Jude Medical; Rhythmia Mapping, Boston Scientific Inc.). Although the large technological leap has allowed the reconstruction of a virtual organ by catheter contact, details of scars and myocardial thickness may be incorrectly estimated. The use of cardiac magnetic resonance (CMR) imaging allows the endocardial, epicardial, or even intramural delineation of the scar, with a better planning of the ablation strategy. Similarly, the integration of CMR imaging with electro-anatomical mapping (EAM) allows the identification of heterogeneous regions where transmurality and scar borders frequently correspond to the isthmus of the reentrant circuits, which are potential targets of ablation.[16-18]

These advances in echocardiography, cardiac computed tomography with multiple detectors, CMR imaging, and EAM can provide integrated hybrid images, far beyond the simple ejection fraction, to provide further details of the innervation, cardiac metabolism, architecture of the scar, and electrical activation. The use of imaging methods of the patient

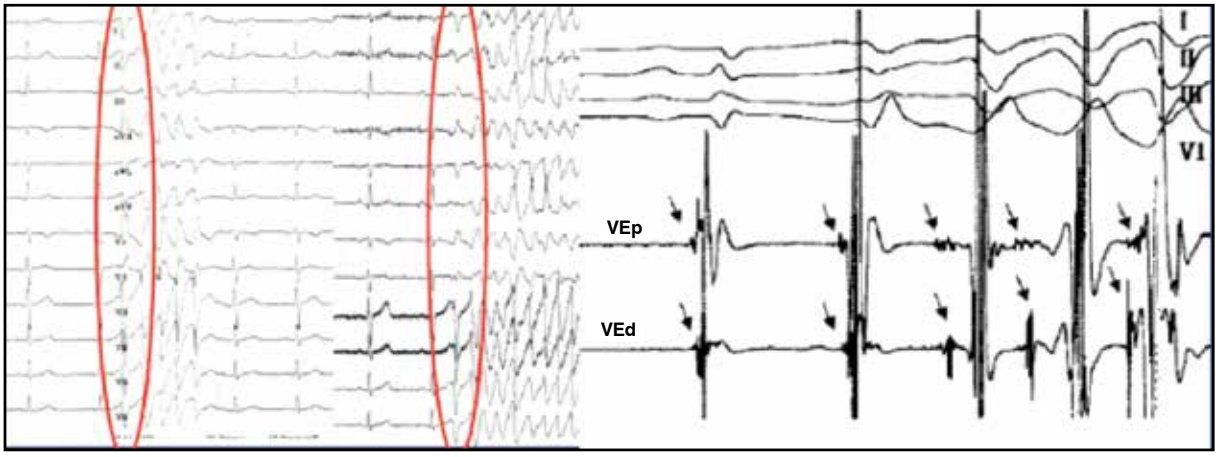


Figure 9. Patient with idiopathic ventricular fibrillation related to the His-Purkinje system. (A) Electrocardiographic tracing demonstrating that the ventricular extrasystole that triggers the polymorphic ventricular tachycardia (VT) has a morphology compatible with its origin in the His-Purkinje system of the left ventricular posterior-inferior region. (B) Register of the ablation catheter signals positioned in this region (VEd and VEp) demonstrating the potential and the probable region of slow conduction that gives rise to polymorphic VT.

himself has enabled models for proof-of-concept studies to predict not only the arrhythmogenic substrate and the characteristics of their circuits, but also the ability to predict future arrhythmic events.[19,20]

TRANSLATIONAL ASPECTS OF AF ABLATION

The increase in the prevalence of AF is associated with greater longevity of the worldwide population and the high incidence of cardiovascular diseases. It is estimated that 1–2% of the population have AF and, in selected cases, mainly after the failure of pharmacological treatment, ablation may be indicated.[21] The perception of AF symptoms is very variable, being more frequently asymptomatic in men, the elderly, and in those with persistent AF. After the ablation, many patients with AF show altered clinical expression and become asymptomatic, hindering the effectiveness of the procedure.

AF substrate

In addition to the cardiomyocytes, vascular cells, nerve cells, and fibrous tissue are present in the atria. A few days after the occurrence of AF, atrial electrical remodeling, shortening of the action potential, and refractoriness with lower speed and heterogeneity of conduction occur, which favor the reentry mechanism. After several months, interstitial fibrosis occurs with induction of persistent AF, alteration of expression of ion channels, and suppressive activity of calcium and sodium currents (ICaL and INa and increment of IK1).

For decades, the conceptual mechanistic hypotheses of AF were (a) multiple reentrant waves, (b) automatic foci, and (c) single reentry with fibrillatory conduction. Recently, a series of sophisticated studies involving computer simulations (*in vitro* and *in vivo*), surface mapping, and the use of spherical catheters (basket) also indicate other possibilities, such as automatic activities generating multiple wavefronts with the presence of rotors or spiral waves, which result in the peripheral fragmentation of the electric activity fronts. Thus, current knowledge indicates that ectopic activities and reentrant phenomena, anchored in complex anatomical structures or atrial fibrotic regions, can generate and maintain AF. Over time, AF, initially related to triggers, becomes more dependent on substrate changes and structural remodeling occurring in its natural history.[22]

The autonomic nervous system with its extrinsic sympathetic and parasympathetic (brain neurons and medulla) and intrinsic (epicardial ganglion plexuses, predominantly parasympathetic) components present higher density in the epicardial region of the antrum, in the proximal 5 mm of atrial junction E with the pulmonary veins. This proximity between nerve structures and myocytes greatly favors local ectopic activity, sympathetic or parasympathetic stimulation with proarrhythmic action in the atrium, and, consequently, shortening of the refractory period and increased repolarization heterogeneity. Although parasympathetic activity is more related to the genesis of AF in patients without heart disease and the sympathetic activity in patients with heart disease, sympatho-vagal discharge is strongly pro-arrhythmogenic and pro-fibrillatory, often triggering paroxysms of atrial tachycardia and AF. The results of autonomic modulation as an adjunct therapeutic strategy in AF ablation are controversial; there have been favorable[23,24] and unfavorable results,[25,26] besides experimental evidence of increased induction of AF with partial vagal denervation. The possibility of other locations of nerve responses and the capacity for reinnervation suggests that the interactions between the autonomic nervous system and AF are much more complex than current knowledge indicates, with different individual variations and responses.

Translational anatomical basis for AF ablation

One of the seminal observations of Haissaguerre et al.[27] was the behavior of cardiomyocytes, which, when embedded in the pulmonary veins, favor the emergence of automatic foci and microreentry activities. The anatomical lessons of the past[28] have shown that the muscle transition between the atria and the veins is geometrically favorable for electrical disturbances and is an important target for AF catheter ablation and mapping (Figure 11).

Thus, the elimination of triggers and the arrhythmogenic substrate must be part of the therapeutic strategy for AF, by using catheter ablation that basically involves the confection of circumferential lesions around the right pulmonary veins and arteries, addressing the veno-atrial junctions, which are critical locations for the genesis and maintenance of AF by its automatic capacity, microreentrant sites, and rich in ganglionic plexus.

Proof-of-concept studies have been consolidated in recent decades; thus, the fundamental role of the pulmonary veins in the genesis of AF has been confirmed clinically and experimentally. The selective monitoring of veins (Figure 12) determining the culprit vein, venous tachycardia triggering AF, and the ability of the antral ablation supported by sophisticated imaging systems, enabled the development of techniques that allow the elimination of clinically important AF in approximately 70–80% of patients.[29]

Triggering factors not related to the pulmonary veins

Supraventricular tachycardias (AVNRT or AVRT) may be present in 4% of cases. High doses of isoproterenol (20–30 μg/min)

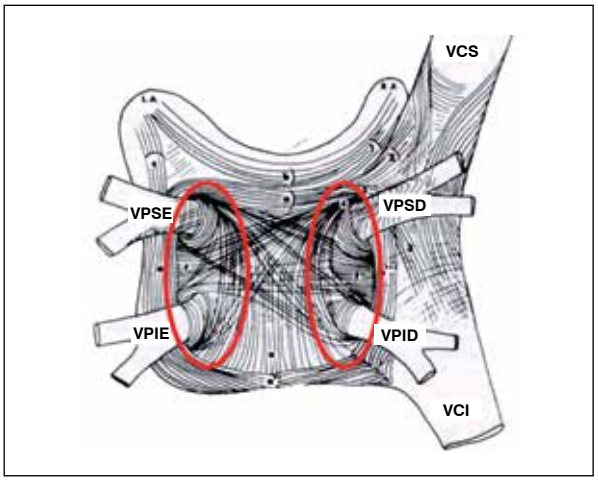


Figure 11. Posterior view of the left atrium (red circle) showing that the complex mesh of muscle fibers is more entrapped in the pulmonary vein ostium, allowing anisotropic conduction and arrhythmogenic phenomena. Modified from Nathan et al.[28]

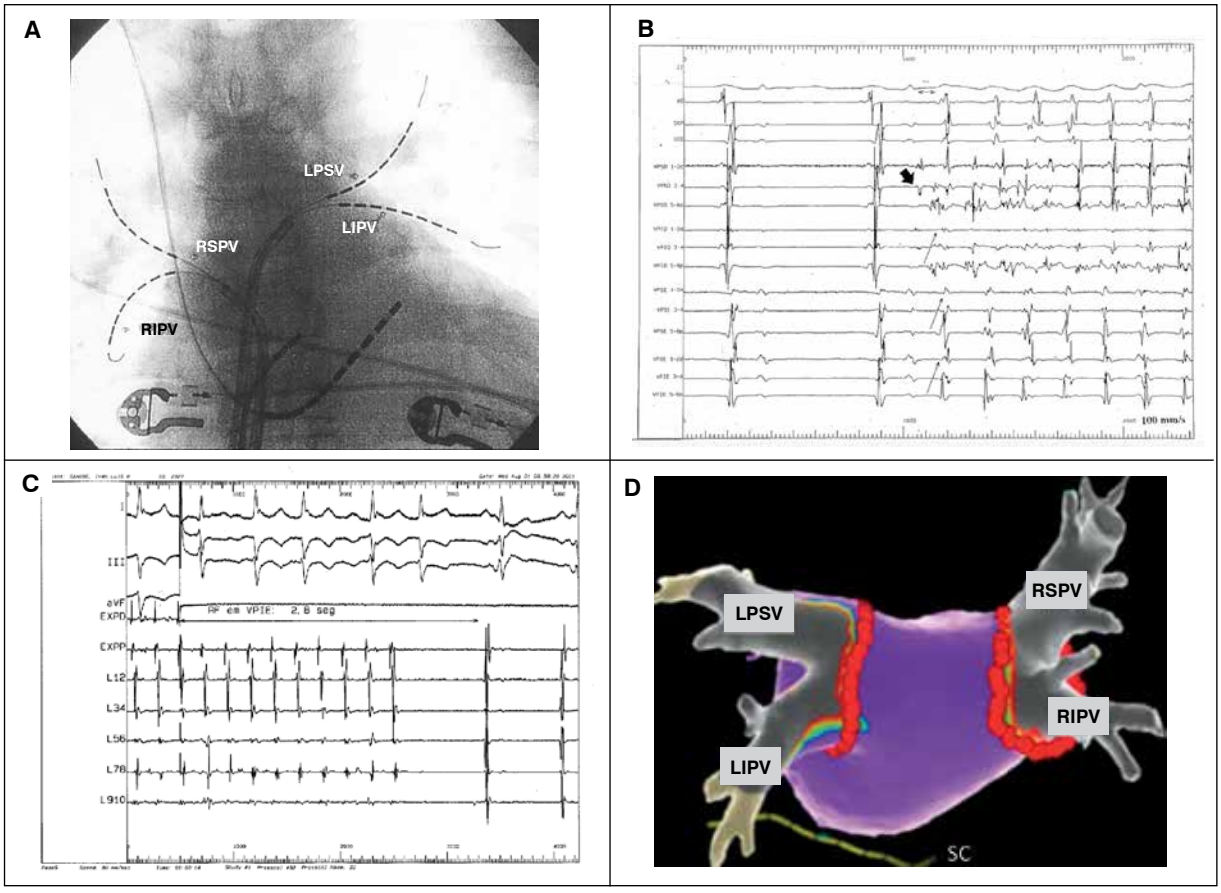


Figure 12. Images related to the ablation of atrial fibrillation (AF) directed to the pulmonary veins. (A) Radiograph in postero-anterior projection demonstrating the insertion of microcatheters into pulmonary veins to detect the culprit vein. (B) During the induction of AF. (C) Termination of venous tachycardia and AF control after the application of radiofrequency LPSV in another patient. (D) Electroanatomic mapping coupled to computed tomography of the left atrium in posteroanterior projection, with a 3-dimensional image demonstrating the area of antral ablation and isolation of the pulmonary veins (red dots).

may reveal other trigger sites to be addressed during AF ablation, including the left atrial posterior wall, SVC, crista terminalis, fossa ovalis, Eustachian valve, Marshall ligament, valvular angles, and left atrial appendage.

Approach of complex fractionated Electrograms, fibrosis, rotors, and left atrial appendage

The success rate of ablation in patients with paroxysmal AF (up to 80%) when multiple procedures are considered was not achieved in patients with persistent AF (>1 week) or persistent AF of a long duration (>1 year), probably because of the involvement of other mechanisms.

The need for new percutaneous strategies to address more chronic cases sought to reproduce the maze (labyrinthine) surgery by creating lines in the atrial cap E and in the mitral isthmus, addressing slower conduction regions with ablation of complex fractional electrograms, and finally, directing the strategies for the complex pathophysiology of AF using phase map analysis for the detection and ablation of rotors described in the CONFIRM (Conventional Ablation for Atrial Fibrillation with or without Focal Impulse and Rotor Modulation) study.[30]

Despite the physiopathological foundations involved in the ablation of cases of persistent AF, the initial encouraging results[31,32] were not reproducible and were not superior to the conventional techniques of an isolated approach of the pulmonary veins. Clinical and laboratory observations now suggest that some signals, such as fractional electrograms (0.06–0.25 mV or <120 ms cycle), probably represent passive electrical signals resulting from wavefront collision, do not mean local intrinsic activity, and have no benefit demonstrated in the STAR AF II (Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial Part II)[33] and CHASE-AF (Randomized Catheter Ablation of Persist End Atrial Fibrillation Study) trial.[34]

The clinical impact of the approach of fibrosis as a substrate is not yet defined. The delayed enhancement obtained by CMR to classify the structural changes of the atrium in progressive degrees of fibrosis (stages I–IV of Utah) are difficult to reproduce and, in the same way, the electrophysiological approach of sites of fibrosis (<0.5 mV [dense fibrosis] or 0.5–1.5 mV [moderate fibrosis]) did not bring consistent clinical results. Finally, ablation guided by the identification of atrial areas with rotational and fibrillatory activity and promoters of AF (rotors with >50 sustained rotations) in the CONFIRM[30] study, by electrocardiographic imaging,[34] or by dominant frequency analysis were not reproducible[35] or did not demonstrate superiority to the isolation of the pulmonary veins.[36,37]

Models of ablation with balloon and other energy sources

The need to approach the atrial tissue in the adjacent areas (antrum) of the pulmonary veins encouraged the development of simple models to optimize the access and contact of these regions. Circumferential catheters with multiple electrodes and balloons specially developed to occlude the ostium of the pulmonary veins and to perform proximal ablations are being tested with different energy modalities. Examples are PVAC and nMARQ catheters for circular radiofrequency, laser balloon systems (deuterium oxide), ultrasound, radiofrequency ("hot balloon"), and, finally, cryoablation with clinical results similar to those of radiofrequency.[38]

Perioperative image in AF ablation

The most common thrombogenic risk score is CHA2DS-2-VASc (C = heart failure, H = arterial hypertension, A = age >65 years, A2 = age >75 years, S = previous vascular accident, V = vascular disease, S = women). Thrombogenesis of non-valvular AF, mediated mainly by the left atrial appendage, presents a risk of <0.3% when CHA2DS2-VASc is 0 and> 5% when CHA2DS2-VASc is ≥2. Patients with a score of ≥2 receive oral anticoagulation that is normally maintained uninterrupted during ablation. In these patients, preoperative transesophageal echocardiography is always performed to rule out thrombus in the preoperative period. In addition to the ability to detect thrombi, computed tomographic angiography and intracardiac ultrasound provide important images that may be useful during the procedure, either for image coupling or for intracardiac echocardiographic monitoring online of atrial structures and catheters, providing higher safety to the procedure.

Although the ablation of AF does not dispense chronic anticoagulation in patients with CHA2DS2-VASc ≥2, some studies suggest that such an approach may be possible in patients with successful ablation, when the meticulous monitoring demonstrates the absence of these arrhythmias.[39] Studies in progress such as the EAST (Early Treatment of Atrial Fibrillation for Stroke Prevention Trial, ClinicalTrials.gov identifier NCT01288352), CABANA (Catheter Ablation vs Anti-arrhythmic Drug Therapy for Atrial Fibrillation Trial, NCT00911508), and OCEAN (Optimal Anticoagulation for Higher Risk Patients Post-catheter Ablation for Atrial Fibrillation, NCT02168829) may provide more consistent data for such an approach.

The presence of silent cerebral microembolism in patients with AF ablation can be detected very accurately by using diffusion magnetic resonance imaging (with or without fluid-attenuated inversion recovery) 30 min after ablation and, depending on the ablation systems used, can be present in up to 50% of procedures. These worrying findings that require more meticulous and prolonged observation may also be present in other invasive procedures such as coronary angiography, stenting in the carotid arteries, and insertion of valve prostheses. Fortunately, most studies demonstrate regression without glial sequelae, with complete normalization of imaging examinations at 3 months,[40] with no solid data on declining neurocognitive functions[41] in the populations studied.

CONCLUSION

The translational research of cardiac arrhythmias has ensured the development of techniques of percutaneous ablation with definitively superior results, including the cure of some supraventricular tachyarrhythmias, such as VTs without structural cardiopathy and selected cases of paroxysmal AF. Some frontiers of knowledge, such as cases of VT with structural cardiopathy and persistent AF of long durations, are important medical challenges with a need for extensive clinical and experimental research.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest in conducting this study.

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