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Is Traditional Resynchronization Therapy Obsolete? Is Para-Hisian Pacingthe New Paradigm?

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At the beginning of cardiac pacing, the main concern was the maintenance of an adequate heart rate, regardless of some aspects of cardiac function, given the absence of deleterious effects demonstrated during the acute period. The classic pacing site in the right ventricle (RV) was the apical region. In the 1980s, some harmful effects of pacing in RV apex began to be described, such as asymmetric ventricular hypertrophy, ventricular dilation, abnormal disposition of myocardial fibers, increased myocardial catecholamine concentration and myocardial perfusion abnormalities.

More recently, some studies, such as DAVID,[1] showed that in patients with implantable defibrillator indication and decreased ejection fraction (EF: 40%), and in the absence of an indication of bradyarrhythmia pacing, patients randomized to DDD-R pacing with a minimum rate of 70 beats per minute (bpm) had worse clinical evolution (combined objective of death and/or hospitalization due to heart failure) than those assigned to VVI pacing with a minimum rate of 40 bpm.

In a post hoc sub-study of the MOST study, which compared DDD-R pacing with VVI-R pacing in patients with sinus dysfunction, the relationship between the proportion of beats with ventricular pacing and hospitalization due to heart failure or appearance of atrial fibrillation was analyzed. This study revealed a significant and direct relationship between the proportion of paced beats and the deterioration of ventricular function and/or the risk of developing ventricular fibrillation, regardless of whether the form of pacing was DDDR or VVIR. Therefore, in this sub-study a high proportion of stimulated beats were a predictor of deterioration of ventricular function and/or atrial fibrillation. In the search for alternative pacing sites in order to avoid the deleterious effects of pacing at RV apex, alternative pacing sites, such as the RV outflow tract, were started with the help of new active fixation catheters. However, the results have been neither very concordant nor very encouraging.

We studied the instantaneous electrical and mechanical effect of pacing at different sites of the RV and showed that the site of pacing with less delay of the free wall of the left ventricle (VI), in patients without intraventricular conduction disorder is, without a doubt , the interventricular septum, at para-Hisian level[2]. Pacing at that level a QRS complex with similar characteristics to the basal is attempted.

Thus demonstrated which is the best site of RV pacing, common sense indicates that para-Hisianpacing is the closest to the natural pathway of the electrical impulse. However, there are still technical difficulties that make this pacing less easy to achieve than that of the apex of the RV

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There are reports of usually higher chronic thresholds and lower R-wave amplitudes. The stability of the catheters in that area would not be a big problem, and while locating the area requires more care and time, the potential benefit of the ventricular function of the patient justifies it.

In any case, and in the absence of large series of long-term follow-up with para-Hisbianpacing, it is preferable to indicate this area of pacing cautiously, trying to ensure that patients are not dependent (due to the possible pathological threshold increase or possible catheter displacement). There is a controversy between the Hisian and para-Hisian pacing, being the Hisian less reliable although more elegant, mimicking the normal QRS, the para-Hisian is ventricular and safer, although they share the same electrical synchrony and that is why the method should be of choice.

Some groups systematically use a three-chamber pacemaker, (two catheters in the RV, one in the apex and one in the para-Hisian region) in order to have a safety catheter in the RV apex. In our series in pacemaker-dependent patients we have used it regularly without complications, but we accept that a more meticulous study would be important to analyze in which patients this type of pacing should be indicated, attentive to the aforementioned drawbacks. However, in our series of more than 300 patients, para-Hisianpacing would not require additional safety pacing at the RV apex.

Another interesting aspect observed in our series is the use of conventional active fixation catheters, which did not show any disadvantages with respect to those designed for this purpose.

The catheter implanted in the septal or para-Hisian area, guided by an electrical synchrony assessment method that ensures that the stimulation of the chosen area does not produce dyssynchronies or "electrical decoupling" between RV and LV, is highly reliable with conventional active fixation catheters .

High Septal Penetration Stimulation - Electric Bypass: An Approach to Permanent Physiological Stimulation

Various ways have been developed to stimulate the His bundle trunk by septal stimulation. However, there are numerous difficulties in its implementation and special training is required for catheter placement, with varying results. It has been shown that if the penetration of the wavefront to the trunk is obtained by septal stimulation, the result is a narrow QRS complex, similar to that of normal conduction and exhibiting a similar hemodynamic performance.[3]

We have developed a new technique of right septal stimulation, which allows generating a wavefront with simultaneous ventricular depolarization and a narrow QRS complex, both in patients with normal basic QRS and in those with conduction disorders such as left bundle branch block

(LBBB).

To achieve pacing as physiological as possible through the Node-Hisian conduction system without directly stimulating the His fascicle, the concept of "virtual electrode" has been postulated. The virtual electrode is achieved with a stimulation wave in each electrode, one in the distal and one in the proximal, each unipolar referred to a common mass, which allows to achieve a significantly greater stimulation field than that of a conventional electrode, generating a larger current field, thus allowing to compromise areas more distant from the stimulation site, with which it is possible to circumvent existing conduction disorders, so it is called electrical bypass (EB). The use of this "virtual electrode" ensures energy savings with respect to the high output required and facilitates placement in the interventricular septum avoiding complicated electrophysiological mapping.[3]

Electrical synchrony assessment is achieved by the method of analysis of the spatial depolarization variance as a cardiac descriptor(EXO-SINCHROMAX® METHOD). Interestingly, when the "virtual electrode" stimulation was performed, achieving the electrical bypass, changes in the axis and voltage were observed in relation to the basal electrocardiographic records. This was observed both in patients with conduction disorders and with normal QRS complexes. And we saw that there were changes in all of them, even in patients in whom the QRS complex was not so narrow. Initially these findings were interpreted as a greater "recruitment" of fibers of the specific conduction system.

These changes were then quantified under an index that allowed the use of averaging signals to compare these electrical changes with the echocardiographic findings. This analysis was also correlated with an electrophysiological study[4-5]. The analysis of spatial depolarization variance then allowed the creation of an index called the "Synchrony Index" which ranges between 0 and 1. Indexes between 0 and 0.4 mean ormal synchrony; between 0.4 and 0.6, moderate dyssynchrony and when the value is close to 1, the dyssynchrony is maximum. The curves of normal patients are positive and aligned to each other, without offset (RV-LV decoupling) with low Index. The most abnormal are curves of opposite polarity between each other (Figure 1).

Patients with resynchronizers (CRT) were also studied with this method to obtain the best synchronization rate during this stimulation.

An interesting group is the patients with conventional pacemakers with apex pacing and those who are not pacemaker-dependent or have an acceptable rate of their own. In those patients ventricular pacing can be compared with basal rhythm. In basal rhythm, the different conduction disorders have some degree of dyssynchrony but apex pacing is frankly different. Some patients with apex pacing are dysynchronous and others are not. A different spatial activation of both ventricles can be observed among the group of dysynchronic patients, while RV is activated from apex to base, LVdoes it from base to apex, generating an evident electrical and mechanical dyssynchrony between both cavities. Those with an acceptable Synchrony Index, on the other hand, exhibit an activation of both ventricular chambers simultaneously and in the same direction, and even if it is an apex-based activation, the dyssynchrony is moderate, and in patients with LBBB there are not too many changes in the ECG, neither in QRS width or its electrical axis.

But the most notable thing is that apex stimulation always shows negative curves (unnatural, caudo-cephalic stimulation), although the Indexes are almost normal or low. Simultaneity and perfect spatial coupling of both cameras seems to be fundamental in cardiac synchrony Clinical practice shows that if apex pacing is synchronous with low Synchrony Indexes, in spite of caudo-cephalic activation, the clinical or hemodynamic impact is minimal or clinically unobjectionable.

With traditional resynchronizers, the curves are also negative, but when septalpacing is chosen and activation is more physiological from base to tip, synchronization curves are positive and very similar to normal, then septal stimulation is more physiological than conventional apex pacing, being more ectopic than septal pacing. On the other hand, the LV is frequently stimulated from a coronary vein that ensures the activation of the LV in the caudo-apical direction while the apex catheter generates an exactly reverse, apico-caudal activation, which is a real obstacle to achieving biventricular synchrony. It is interesting to ask then if septalpacing of the RV that generates almost normal synchrony indexesand base to apex stimulation, being synchronous at the time of contraction of both ventricles really requires the implantation of a third catheter through the coronary sinus; this lead would be necessary only at failure of septal or para-Hisian stimulation to achieve biventricular synchrony and the only way to correct the decoupling between RV and LV activation is the VI lateral wall pacing through the coronary sinus .

Are we facing a new pacing paradigm?

We have currently found an area near the apex of the RV that does not cause dyssynchrony in patients with conventional pacing. At present, and in our experience with more than 300 implants we can assert that in most cases we achieve similar results to CRT.

Currently, with the development of Synchromax ®, electrical dysynchrony can be easily identified, with the aforementioned indexes, which always correlate with echocardiographic findings and the electrophysiological study. Normal curves are positive and synchronous same as those of septal stimulation Pacemakers with apical stimulation do not always produce dyssynchrony, and we have observed that in half of them, the curves show an acceptable synchrony. In fact, apex pacemakers without dysynchrony present negative curves with low, synchronous rates indexes, similar to those observed in patients with optimized resynchronizer.

In some patients with resynchronizers it is impossible to obtain synchronous curves, either due to the position of the catheter or due to the myocardium. These are the cases called "electric non-responders" and represent less than 10%.

In some patients with resynchronizers it is better to stimulate the LV first and in others the VD first, to optimize the curves.

Several authors are already working on these issues and give birth to new perspectives on electrical dyssynchrony[6]

Anyway the para-Hisian pacing is generating new adherents and some editorials already speculateswhether para-Hisian pacing is making resynchronyzation therapy obsolete.[7] Are we going that way?

To answer this, it must be taken into account that conventional resynchronization is not physiological and there are already studies showing that para-Hisian pacing is equal to

or better than resynchronizing, but simpler[8-9]

How would these principles change?

Left bundle branch block in patients with and without heart failure: there is debate on this issue.When we started practicing para-Hisian pacing, it was only an idea because there were not active fixation leads at that time[10]. Today, standard catheters and some emerging from recent designs make it possible to fix them in an area that normalizes the QRS, or electrically synchronizes both ventricles.

If we add an XStim wave to this mode of stimulation, the task of resynchronizing would be much easier but the latter is not currently available.

It is known that trunk blocks are not similar to branch blocks in patients with heart failure and the response in the latter is encouraging.

In patients with AV conduction disorders, in whom there is a need to implant a definitive pacing device, the choice is a DDD pacemaker with septal or para-Hisianpacing site which guarantees stability and long-term synchrony and safety without the need for back-up catheter.[11] The same happens with those patients with narrow QRS, our first choice is, without a doubt, para-Hisianpacing.

This behavior is being imposed in many places in South America guided by the non-invasive QRS variance analysis method (Synchromax), and various publications are stating that this type of stimulation is becoming more frequent.

In patients with left deviation the electric axis which happens in the left anterior fascicular block it is common that they have dyssynchrony because RV activation is mostly in the caudo-cephalic direction due to the absence of septal activation forces of the left hemi-branch, while that the LV is just the opposite. Para-Hisianpacing normalizes this deviation, and QRS normalization in patients with right bundle branch block is almost certain.

Brugada Syndrome is an atypical RBBB;para-Hisianpacing could become an alternative therapy in this anomaly. In 2016, the case of a patient admitted by electrical storm was presented, with the history of Brugada Syndrome, who hada VVI defibrillator implanted. She was refractory to multiple antiarrhythmic medical treatments, including endocardial ablation of ventricular tachycardia of the right ventricle outflow tract due to numerous syncopal episodes secondary to this arrhythmia. The patient was admitted by electrical storm with five appropriate electrical shocks by ventricular fibrillation in one day. An upgrade of the device was performed by implanting a defibrillator with cardiac resynchronization therapy (TRC-D) in order, among others, to restore AV synchrony. A septal catheter was implanted in the para-Hisian area to eliminate the Brugada patent during sinus rhythm. By means of para-Hisiana pacing it was possible not only to eliminate the Brugada patent but also to maintain the electrical synchrony measured with the Synchromax method[12]. At present, the patient continues with a DDD pacemaker and permanent ventricular pacing, without repeating arrhythmias with a follow-up of more than 3 years, probably linked to the fact that she no longer presents the Brugada patent.

From that moment, and according to our experience, we could speculate all the CDI implants in Brugada syndrome patients should follow the para-Hisian pacing technique to normalize the QRS. Something similar happens with those defibrillators implanted for other causes to avoid the adverse effects stated in the DAVID study.

In the special case of Brugada syndrome it is not necessary to pace the ventricle in all cases permanently since in many of them the pattern is intermittent. In that sense we have developed a special algorithm so that the ventricle is stimulated only when they have the Brugadapattern, in other words, when the QRS duration increases. We believe that this can substantially change the evolution of patients with Brugada Syndrome, if the future CDI devices include considers this programming possibility.

Final comment

Conventional pacing is a matter of controversy worldwide, in relation to its long-term deleterious effects[13]. Conventional resynchronization therapy is already being questioned in light of the findings obtained with para-Hisian pacing. The future and new studies will give light to this new path that for many South American working groups is the new path.

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