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REVIEW

Right ventricular apex pacing: Is it obsolete?

La stimulation apicale ventriculaire droite : est-elle obsolète ?

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Summary Clinical trials in patients with pacemakers for sinus node dysfunction or atrioventricular block have highlighted the fact that desynchronization of ventricular contraction induced by right ventricular apical pacing is associated with long-term morbidity and mortality. These clinical data confirm pathophysiological results indicating that right ventricular apical pacing causes abnormal ventricular contraction, reduces pump function and leads to myocardial hypertrophy and ultrastructural abnormalities. In this manuscript, we discuss the clinical evidence for the adverse and beneficial effects of various right ventricular pacing sites, left ventricular pacing sites and biventricular pacing. We also propose a decisional algorithm for pacing modalities, based on atrioventricular conduction, left ventricular function and expected lifespan.

MOTS CLÉS
Stimulation cardiaque ;
Asynchronisme ventriculaire ;
Bloc auriculoventriculaire

Résumé Les essais cliniques réalisés chez les patients stimulés pour une dysfonction sinusale ou un bloc auriculoventriculaire ont mis en évidence une relation de causalité entre l'asynchronisme de contraction ventriculaire induite par la stimulation ventriculaire droite apicale et la morbimortalié à long terme de ces patients. Ces données viennent confirmer les résultats physiopathologiques qui montrent que la stimulation ventriculaire droite engendre des anomalies de la cinétique ventriculaire, réduit la fonction contractile et induit une hypertrophie et des anomalies ultrastructurales myocardiques. Dans cet article, les auteurs détaillent les avantages et les inconvénients des sites de stimulation ventriculaire droite, gauche ou biventriculaire et proposent un arbre décisionnel pour une stimulation cardiaque physiologique, basé sur la conduction auriculoventriculaire, la fraction d'éjection ventriculaire gauche et l'espérance de vie.

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Abbreviations

AAI/R	single-chamber rate-responsive atrial
DDD/R	dual-chamber rate-responsive
LVEF	left ventricular ejection fraction
NYHA	New York Heart Association
MVP	managed ventricular pacing
VVI/R	single-chamber rate-responsive ventricular

Cardiac pacing is still the only effective treatment for severe cardiac impulse formation or propagation disturbances. Despite nearly 50 years having elapsed since the first human implantations [1], the optimal pacing mode and ventricular pacing site have not been defined clearly.

Pathophysiological consequences of right ventricular apical pacing

The right ventricular apex is the pacing site that is used most frequently, because it can be reached easily and allows a chronically stable position and stimulation threshold. However, even if apical pacing results in haemodynamically efficient contraction, it remains antiphysiological, because the wave front propagates slowly through the common myocardium with no capture of the His-Purkinje system. The adverse consequences of right ventricular apical pacing were shown more than 80 years ago in mammals [2], but only recently in humans [3]. The deleterious effect is due to the asynchrony of ventricular activation; myocardial regions located close to the pacing lead contract first and stretch not-yet-activated remote regions. By virtue of the local Frank—Starling mechanism, this stretching increases the force of the local contraction of these remote regions and, in turn, stretches — paradoxically — regions activated earlier [4].

Using two models of pacing-induced cardiomyopathies, Spragg et al. studied the effects of asynchronous ventricular activation on the expression of proteins involved in myocyte contraction and arrhythmia vulnerability [5]. In cardiomyopathies induced by high-rate right ventricular apical pacing, they observed significant differences in the expression of these proteins, whereas such a gradient was not noted in high-rate atrial-pacing-induced cardiomyopathies in which ventricular activation was synchronous. The lateral left ventricular free wall (late-activated) shows the most pronounced cellular derangements, such as down-regulation of protein kinases, proteins involved in calcium homeostasis and intercellular connections. The heterogeneous expression of these proteins creates an intramyocardial gradient, which can lead to ventricular dysfunction and may favour arrhythmia genesis. Other authors have demonstrated that prolonged right ventricular apical pacing induces dystrophic fibro-fatty myocardial tissue development, mitochondrial disorganization [6], perfusion abnormalities and localized hypertrophy of the late-contracting myocardial regions [7].

Haemodynamically, asynchronous myocardial contraction decreases significantly the stroke volume and shifts rightward the left ventricular end-systolic pressure—volume relationship. Mismatch between the relaxation of early- and late-contracting regions leads to a decrease in left ventricular filling time and Doppler E-wave velocities [8].

Clinical consequences of right ventricular apical pacing

Two decades ago, the development of dual-chamber pacing represented a significant technological improvement; it allowed ventricular pacing to be synchronized with the atria and was hence adopted quickly as the 'physiological' pacing mode. However, large randomized clinical trials showed that despite the maintenance of auriculoventricular synchrony, DDD/R pacing did not reduce death compared with VVI/R pacing [9], and provided only modest benefits in progression of heart failure and atrial fibrillation [10,11], which became evident only after many years of follow-up [10].

The inability to show a clear superiority of 'physiological' dual-chamber pacing over 'non physiological' ventricular pacing might be explained by the right ventricular pacing that is performed in both modes. A retrospective analysis of the MOST [12] and MADIT [13] studies showed that the risks of atrial fibrillation and heart failure hospitalization are linked directly to the cumulative percentage of ventricular pacing, regardless of pacing mode. Furthermore, the DAVID trial [14] was terminated prematurely because of the high incidence of death and worsening of heart failure in the DDD/R (70 beats/min) pacing mode compared with the VVI/R (40 beats/min) mode. Conversely, single-chamber atrial pacing in patients with sinus node dysfunction preserves left ventricular function and reduces the incidence of atrial fibrillation significantly compared with dual-chamber pacing [15].

Alternatives to right ventricular apical pacing

Recognition of the adverse effects associated with right ventricular apical pacing fuelled research aimed at finding a means of abolishing or at least reducing these effects. Two strategies have been investigated: the first favours spontaneous atrioventricular conduction to minimize unnecessary ventricular pacing; the second involves pacing alternative ventricular sites to attenuate the deleterious effects of right ventricular apical pacing in patients in whom atrioventricular conduction is absent or unreliable.

Minimizing unnecessary ventricular pacing

In cases of sinus node dysfunction, AAI/R pacing prevents excessive bradycardia, provides chronotropic support if needed and hence corrects symptoms without any risk of adverse effects due to ventricular pacing. However, the risk of atrioventricular block in these patients, although low (annual incidence estimated at 1% [16]), leads in most cases to the implantation of a dual-chamber device without a significant increase in the cost-effectiveness of the procedure. Programming long atrioventricular delays with hysteresis (an additional increase in the atrioventricular delay) in the DDD/R pacing mode yields functional AAI/R behaviour, but a