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Ventricular pacing – Electromechanical consequences and valvular function

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ABSTRACT

Although great strides have been made in the areas of ventricular pacing, it is still appreciated that dyssynchrony can be malignant, and that appropriately placed pacing leads may ameliorate mechanical dyssynchrony. However, the unknowns at present include:

1. The mechanisms by which ventricular pacing itself can induce dyssynchrony;
2. Whether or not various pacing locations can decrease the deleterious effects caused by ventricular pacing;
3. The impact of novel methods of pacing, such as atrioventricular septal, lead-less, and far-field surface stimulation;
4. The utility of ECG and echocardiography in predicting response to therapy and/or development of dyssynchrony in the setting of cardiac resynchronization therapy (CRT) lead placement;
5. The impact of ventricular pacing-induced dyssynchrony on valvular function, and how lead position correlates to potential improvement.

This review examines the existing literature to put these issues into context, to provide a basis for understanding how electrical, mechanical, and functional aspects of the heart can be distorted with ventricular pacing. We highlight the central role of the mitral valve and its function as it relates to pacing strategies, especially in the setting of CRT. We also provide future directions for improved pacing modalities via alternative pacing sites and speculate over mechanisms on how lead position may affect the critical function of the mitral valve and thus overall efficacy of CRT.

Abbreviations: CRT, cardiac resynchronization therapy; ECG, electrocardiogram; LBBB, left bundle branch block; LV, left ventricle; MR, mitral regurgitation; RBB, right bundle branch; RV, right ventricle; TR, tricuspid regurgitation.

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Contents

Introduction

Cardiac pacing is an established and effective treatment for sinus node disease and atrioventricular block [1,2]. The right ventricular (RV) apex has been the standard pacing site since the development of implantable pacemaker technology because of the relative ease of access, lead stability, and the presumed safety of the right-sided circulation compared to the left (fewer fatal thromboembolic sequelae) [3]. However, several studies have shown that RV apical pacing creates electrical dyssynchrony and has detrimental effects on cardiac structure, function, and can lead to development of atrial fibrillation, valvular regurgitation and severe congestive heart failure [4–12].

Cardiac resynchronization device therapy (CRT) has shown to improve morbidity and mortality in patients with congestive heart failure [13–16], and recent trial data has expanded the indications for its use [17–24]. CRT is thought to improve atrioventricular, intraventricular and interventricular dyssynchrony through the simultaneous activation of the RV and the left ventricle (LV) [1]. The Achilles heel of CRT is the substantial number (up to 1/3) of patients that do not benefit, termed "non-responders" [25].

The utility of baseline electrocardiogram (ECG) in detecting dyssynchrony, together with multiple imaging and device based studies have attempted to identify criteria for improved patient selection, but no single validated and reliable marker has been identified [26–28]. Alternative pacing locations and the impact of novel pacing methods such as atrioventricular, leadless and far-field stimulation from the surface of the heart seem to decrease the deleterious dyssynchronous effects of pacing [29–31].

Finally, pacing-induced dyssynchrony affects valvular function as well. Tricuspid and mitral regurgitation occur or worsen if abnormal ventricular mechanic is present [32–34], and appropriately placed pacing leads can actually improve valvular function through various mechanisms [35–37].

We review the current knowledge on RV pacing and CRT, provide an overview on pacing modalities and mechanisms of dyssynchrony-induced ventricular dysfunction and valvular regurgitation, ways to improve CRT through innovation, and how this can be translated to tangible therapeutic options that are safe, effective, and mechanistically sound.

Ventricular pacing effects on the electrical, mechanical, and structural functions of the heart

Part 1. Electrical activation of the heart, pathophysiology of pacing and why mechanical dysfunction occurs from ventricular pacing

During normal sinus rhythm, electrical activation occurs through the cardiac conduction system. The depolarization wave front spreads sequentially from the atria, to the atrioventricular node, through the His-Purkinje system, resulting in almost simultaneous activation of both ventricles. The result of this is manifesting on ECG as a narrow QRS complex. In contrast, RV apical pacing causes the earliest depolarization to occur at the segment of the RV apex, followed by slow, cell-to-cell spread of the activation wavefront, with latest depolarization at the inferoposterior base of the LV [38]. This produces a wide QRS and a left superior axis on ECG.

RV pacing produces an iatrogenic form of left bundle branch block (LBBB). Native LBBB can cause hemodynamic deterioration due to ventricular dyssynchrony, mainly in patients with heart failure. However, LBBB induced by RV apical pacing seems to lead to worse outcomes when compared to native LBBB, increasing ventricular dyssynchrony [39–41]. The latest LV mechanical activation during RV apical pacing, indeed, is different from that during native LBBB, being more delayed at the baso-lateral LV wall [42].

The abnormal electrical and mechanical activation caused by RV apical pacing reduces stroke volume and causes a right-shift of the left ventricular end-systolic pressure–volume relationship. In addition to hemodynamic consequences, RV apical pacing can worsen coronary blood flow, regional myocardial fiber shortening, and any pre-existing mechanical dyssynchrony [12,43,44]. Moreover, regional patterns of ventricular activation are also altered in a complex manner [45]. Early activation of the RV apex results in vigorous RV apical shortening. Early apical shortening leads to stretching of remote ventricular regions, such as the LV free wall, and subsequent stronger contraction of these regions is needed compared to the local RV apical regions. Another important mechanical effect of RV apical pacing is abrupt posterior motion of the interventricular