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CARDIAC PACING & ICD UPDATE

Right Ventricular Pacing in Bradycardia Patients With Preserved Systolic Function: Results of the PACE Trial

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ABBREVIATIONS
AV = atrioventricular
CRT = cardiac resynchronization
EF = ejection fraction
LBBB = left bundle branch block
LV = left ventricular
LVEF = left ventricular ejection fraction
RV = right ventricular

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In medicine, it is encouraging when research yields results consistent with our understanding of the operative mechanisms, especially when there is a direct potential impact on clinical practice. Adverse left ventricular (LV) remodeling is a complex maladaptive process involving structural, hemodynamic, histopathological, and genetics changes.[1] The process may be multifactorial and is frequently encountered in patients after loss of myocardium (myocardial infarction), volume overload (valvular insufficiency), or pressure overload (hypertension). It involves both LV hypertrophy and dilation, and is initially an adaptive response that serves to maintain stroke volume. If persistent and progressive, the process becomes maladaptive and leads to further deterioration of LV function, LV dilation, and eventually the typical symptoms of heart failure.

It is evident that substantial prolongation of the QRS complex, especially with a left bundle branch block (LBBB) pattern, results in a delayed and dyssynchronous LV contraction.[2] This dyssynchrony may be a major contributor that can both initiate and aggravate the process of adverse remodeling. In patients with symptomatic heart failure, systolic dysfunction, and QRS prolongation, cardiac resynchronization therapy (CRT) has been shown to be highly efficacious in reducing morbidity and prolonging survival.[3] There is concordance between the reductions in LV volumes, the best indices of LV remodeling, and improvement in clinical outcomes.[4]

Acute and chronic right ventricular (RV) pacing results in substantial widening of the QRS complex and induces both inter- and intra-ventricular dyssynchrony (iatrogenic LBBB).[5] Improvements in measures of dyssynchrony following CRT in patients with heart failure and previous RV pacing have been demonstrated.[6]

The PACE trial, a prospective double-blind, multicenter study, was designed to compare apical RV pacing with CRT in patients with bradycardia and a preserved LV ejection fraction (EF). A total of 177 patients with a conventional indication for a pacemaker and preserved LV function (EF >45%), were following successful implantation of a CRT device, randomized and programmed to either RV pacing or CRT pacing. The trial evaluated LV function and measurements of remodeling over 12 months at a blinded core laboratory using three-dimensional echocardiography. The results published in the New England Journal of Medicine in 2010 demonstrated significant and substantial reductions in LVEF and increases in end-systolic LV volumes in the RV pacing group during the 1- year follow up. Evidence of deterioration in LV function was not observed in the group with CRT pacing. Adverse changes in patients paced only in the RV included: A significant increase of 6.3 milliliter on average in the size of the LV at the end contraction and a decrease of 6.8 percent in

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the EF, or the amount of available blood pumped from the LV. These results show bi-ventricular pacing may be superior to pacing only in the RV to preserve the heart´s normal LV size and pumping ability for these pacemaker patients.[7] The reported findings are consistent with previous reports, apart from the PREVENT-HF trial which did not demonstrate LV function differences over 1 year in a similar population with preserved EF.[8]

The PACE trial provides trial evidence that should be taken into consideration by physicians responsible for the management of patients with conventional pacing indication. However, there remain several important unanswered questions.

Right ventricular pacing in patients with sinus node dysfunction without atrioventricular block is not required and may have resulted in avoidable reverse remodeling in these patients. This is perhaps the most important methodological and ethical criticism of this trial. The lack of between-group difference on 6-minute walk distance or the quality of life tool may appear surprising at first. However, these were not patients with heart failure or reduced EF. As we know, CRT is associated with improvements in symptoms, functional capacity, and clinical outcomes in symptomatic patients with systolic dysfunction.

The PACE trial was underpowered for analysis of clinical events. The sample was small and the follow up was short, especially for asymptomatic patients with preserved EF.

There is of course some non-trivial, added morbidity associated with CRT implantation as compared with RV pacing, especially with inexperienced operators. What amount of benefit would justify the modest increased risk at implantation as well as the increase cost of a device with shorter longevity.

Obviously, much depends on the pacing indication. Patients with infrequent episodes of bradycardia requiring a back up pacemaker would not be candidates. However, if there is AV block and expectation of pacemaker dependency, a device that results in chronic RV pacing will be likely to put the patient at risk for adverse remodeling and it may begin soon after the implantation and progress. However, isolated sinus node dysfunction without AV block may not required an RV lead, and the PACE trial results do not support implantation of a CRT in this population. As with all therapies, the patient's biological age, functional status, and extent of co-morbidity will enter into the management decision.

Future clinical research must address the major unanswered questions. How should we identify the target population at greatest risk for adverse remodeling following RV pacing and therefore likely to benefit from a CRT device. Will CRT in patients with bradycardia and preserved systolic function translate into prevention of meaningful adverse endpoints such as hospitalization for heart failure. If so, it becomes a good investment. Benjamin Franklin put it well: An ounce of prevention is worth a pound of cure. In this case, it is about 2 ounces.

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