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Non-classical Indications for Cardiac Resynchronization Therapy

Michael Glikson, MD[1], Eyal Nof, MD[2], Osnat Gurevitz, MD[3]

Sheba Medical Center and Tel Aviv University, Tel Hashomer, Israel

ABSTRACT

Based on randomized controlled studies, cardiac resynchronization therapy (CRT) is currently indicated in patients with systolic heart failure of New York Heart Association (NYHA) functional class III and IV, left ventricular ejection fraction < 35% and wide QRS (>120 ms). Most of the enrolled patients were in sinus rhythm, were not previously paced and had mainly LBBB. Thus, there are uncertainties regarding several other populations, not included or underrepresented in the main studies. These populations include patients with atrial fibrillation (AF), previous pacemakers considered for upgrade to CRT, RBBB, narrow QRS <120 ms, NYHA functional class <III, or right heart failure. These non-classical indications are herein reviewed. Although CRT seems to benefit patients with AF and patients with preexisting pacemakers, in patients with NYHA functional class II-III, or with narrow QRS, or with RBBB, or in those with predominant right heart failure, the role of CRT is not established yet and further relevant clinical trials are needed.

ABBREVIATIONS:
AF: atrial fibrillation
CHF: congestive heart failure
CRT: cardiac resynchronization therapy
CRT-D: cardiac resynchronization therapy-defibrillation
EF: (left ventricular) ejection fraction
LBBB: left bundle branch block
NYHA: New York Heart Association
RBBB, LBBB: right/left bundle branch block
TDI: tissue Doppler imaging

KEY WORDS: *cardiac resynchronization therapy; biventricular pacing; left bundle branch block; right bundle branch block; atrial fibrillation; cardiac pacemakers*

Address for correspondence:
Prof. Michael Glikson, MD
Director of Pacing and Electrophysiology
Heart Institute
Sheba Medical Center
Tel. Hashomer 52621, Israel
Tel./Fax: 972-3-5356605
E mail: mglikson@post.tau.ac.il

Cardiac resynchronization therapy (CRT) is currently indicated in patients with systolic heart failure of New York Heart Association (NYHA) functional class III and IV, left ventricular ejection fraction (EF) <35% and wide QRS (>120 ms) [1]. These indications are based on randomized controlled trials in which patients with these indications have been enrolled. Most of the patients enrolled into these studies were in sinus rhythm, were not previously paced and had left bundle branch block (LBBB) or another left intraventricular conduction delay [2-5].

There are still uncertainties regarding several other populations that were not included or underrepresented in the main studies. These populations include patients with atrial fibrillation, patients with previous pacemakers who are being considered for upgrade to CRT, patients with right bundle branch block (RBBB), patients with narrow QRS <120 ms, patients with NYHA functional class lower than III, patients with low EF who need pacemakers for other indications and do not have wide QRS yet, and patients with predominantly right heart failure. We will review here our experience and the available literature to try to determine the benefits of CRT in these populations.

PATIENTS WITH CHRONIC ATRIAL FIBRILLATION

Patients with permanent atrial fibrillation (AF) were not included in most of the ma-

jor studies, and therefore some guidelines that were recently published do not include them in the indications for CRT. [6] However, there are several studies that looked specifically at this population and demonstrated the benefits of CRT. Most of them demonstrated similar or somewhat decreased but significant benefit in AF patients when compared to patients paced in sinus rhythm [7-13]. It has been our experience as well that patients with atrial fibrillation improve with CRT as long as consistent pacing in the ventricles is achieved with appropriate rate control or atrioventricular (AV) nodal ablation. We have seen and are also aware of several reports of conversion of long-standing AF to sinus following establishment of CRT, which raises the possibility that an atrial lead may have to be placed in many patients with AF receiving CRT systems in anticipation of possible return to sinus rhythm. We therefore believe that CRT is indicated in patients with AF who otherwise have a CRT indication

PATIENTS WITH PREVIOUS PACEMAKERS

Patients with prior pacemakers with systolic heart failure were not included in the major CRT trials, but all series that looked specifically into this population demonstrated benefit that was similar or even greater than the benefit in the traditional CRT population [10,11,14]. We have also shown in 25 patients with prior pacing a somewhat better response to CRT than in patients with de novo CRT implantation [15]. Selection criteria for CRT among pacemaker patients are not established yet, but it is conceivable that paced QRS width is not an appropriate selection criterion, and measures of mechanical dyssynchrony may have to be taken into account [16].

PATIENTS WITH RBBB

Although patients with RBBB were included in several major trials [4,5,17], their results were not analyzed separately until recently, and they were not excluded from present indications in the current guidelines [1,6]. Nevertheless, a recent publication based on more than 60 cases demonstrated very little benefit of CRT in RBBB patients [17]. Garrigue et al [18] have demonstrated in the past a beneficial effect of CRT in patients with RBBB, but only in those having measures of mechanical dyssynchrony. It is conceivable that RBBB serves as a marker of left ventricular dyssynchrony in many but not all of CRT candidates, and it is therefore reasonable to decide on CRT implantation in patients with RBBB based on measures of mechanical dyssynchrony such as tissue Doppler imaging (TDI).

PATIENTS WITH NARROW QRS

Information is scarce about CRT in this population. As research in this area is expanding, it is becoming clearer that the traditional selection criteria of wide QRS are limited in their ability to predict success of CRT and that they are only markers of mechanical dyssynchrony, measures of which may provide better prediction of success [19]. It has been shown that there are quite a few patients with congestive heart failure (CHF) and narrow QRS (<120 ms) who have intraventricular dyssynchrony, and it has been shown in limited numbers of patients that CRT may benefit patients with narrow QRS if they have mechanical dyssynchrony [20,21]. This topic is the subject of intensive research in ongoing randomized controlled studies.

PATIENTS WITHOUT OVERT HEART FAILURE

Some of the major CRT-D trials included patients with NYHA class II heart failure [22,23]. These studies demonstrated an effect on echocardiographic measures of cardiac remodeling but very limited clinical effect on heart failure symptoms in this group. At this point, evidence is insufficient to recommend CRT in functional class class I or II patients. Ongoing randomized controlled trials are looking into this matter.

PATIENTS WITH CHF WHO NEED PACEMAKER IMPLANTATION

We often face patients with heart failure who need pacemaker implantation for bradycardic indication but do not have wide QRS yet. However, when paced they are likely to develop dyssynchrony and may deteriorate further, therefore the question of a priori CRT implantation is raised.

This issue was recently addressed by the PAVE trial which demonstrated beneficial effect to a priori CRT vs traditional pacing in patients undergoing AV nodal ablation especially in patients with EF <45% and with CHF symptoms (NYHA II-III) [24]. Whether this approach will apply to other patient populations undergoing pacemaker implantation will depend on the results of ongoing trials.

PATIENTS WITH RIGHT HEART FAILURE

This population is mixed within the populations of the large trials, and very few studies looked specifically at these

patients as candidates for CRT. A small series of congenital heart disease patients demonstrated the benefit of CRT, but this population is unlike the usual CRT candidate [25]. We have shown a beneficial effect of CRT on myocardial performance index of the right ventricle [26]. We also demonstrated the beneficial effect of CRT on functional capacity of seven patients with combined left and right heart failure [27]. Recently we have been able to show that among 20 patients with reduced right ventricular (RV) function (as expressed by RV fractional area shortening), 65 % improved their RV function after three months of CRT. This improvement was correlated with the degree of improvement in NYHA functional class (unpublished data).

CONCLUSIONS

Whereas the role of CRT is established in patients with the classical indications, its role is not established in several populations that are reviewed in this paper. Although CRT seems to benefit patients with AF and patients with preexisting pacemakers, its role in patients with NYHA functional class I – II, in patients with narrow QRS, in patients with RBBB, in patients who need pacing for other indications who do not have wide QRS and in patients with predominant right heart failure is not established yet. Many of these questions may be solved in the future by use of better predictors of success such as echo TDI, and will eventually be answered by ongoing clinical trials.

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