



## EDITORIAL COMMENT

# Response to cardiac resynchronization therapy: Dichotomous or continuous variable?☆



## Resposta à terapêutica de ressincronização cardíaca: uma variável dicotômica ou contínua?

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Cardiac resynchronization therapy (CRT), with or without defibrillation, has revolutionized the treatment of heart failure, leading to reverse remodeling (the main prognostic factor in heart failure) and improvements in quality of life, functional class, hospitalizations for heart failure and mortality.<sup>1</sup> However, since CRT was introduced, the proportion of patients who do not respond to the therapy has remained high (30–40% depending on the series).

Analysis of non-response to CRT is difficult for a variety of reasons. The most important are to do with the reasons for failure to respond,<sup>2</sup> which are multifactorial and differ among patients. Patients with ischemic heart disease are less likely to respond, as are those with atrial fibrillation (AF), without left bundle branch block, or with pulmonary hypertension, biventricular dysfunction or other comorbidities such as respiratory or renal failure. There are also factors related to the implantation procedure itself – ineffective biventricular pacing due to lead malpositioning (in the anterior branch of the coronary sinus or in too apical a location), or failure of the QRS interval to shorten even when the lead is correctly placed – and post-procedural factors, particularly low biventricular pacing rates, such as in patients with persistent AF, in whom atrioventricular (AV)

node ablation is recommended, and in those with many ventricular extrasystoles, for whom ablation may be required. Other comorbidities, significant mitral regurgitation after implantation, and inadequate medical therapy may also play a part.<sup>3</sup>

The study by Rio et al. in this issue of the *Journal*<sup>4</sup> sets out to assess the prognostic impact of response to CRT using echocardiographic criteria. The follow-up period used to define response was rather short, given that there may be a late echocardiographic response in patients who do not respond initially, as acknowledged by the authors in the limitations section. The authors do not mention whether echocardiography was repeated over the course of the study, but it is possible that some patients considered non-responders may have had a late response, which could obviously affect the results.

The study population is of a reasonable size (178 patients), and in terms of selection, is typical of patients found outside the context of clinical trials: all had prolonged QRS (defined as >120 ms), most had complete left bundle branch block, and 35% had ischemic heart disease. The retrospective nature of the registry implies some limitations, including the fact that it only includes patients in whom

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implantation was successful. It is also stated that the lead was implanted in a lateral or posterolateral position in all cases. This is the optimal location for the left lead, but it is not clear whether patients with leads in less favorable positions (who are always to be found among patients receiving CRT devices) were excluded.

The description of the methodology is somewhat vague on some points. For example, it is stated that the devices were programmed in DDD mode; however, 40% of the initial population had AF. It is also not clear how many of these patients had intermittent AF and how many had persistent or permanent AF, nor how such a high percentage of biventricular pacing was achieved in AF patients (by AV node ablation? by drug therapy?).

Over the eight-year study period there were significant advances in CRT systems, which may have affected the results. For example, quadripolar left ventricular leads were introduced in 2012 and are now standard.

Nevertheless, real-world studies such as this have the advantage of reflecting the types of patients seen in clinical practice, rather than the study populations of clinical trials.

The study by Rio et al. shows a high rate of echocardiographic response (61%) and an even higher rate of clinical response. Mortality and hospitalization rates were higher in patients without echocardiographic response, while clinical response was better in those with a good echocardiographic response. The study's results appear to indicate that in this population, clinical but not echocardiographic responders have a better prognosis than those without an echocardiographic response who do not improve clinically. This finding, while not wholly new, having been published in other series,<sup>5</sup>

is a reminder that response to CRT, as well as being multifactorial as pointed out above, is also not dichotomous; it represents a spectrum of possibilities. Patients respond to a greater or lesser extent, ranging from those whose ejection fraction normalizes to the other extreme of those who, though not presenting improvement in echocardiographic parameters, show improvement in functional class and in other parameters related to heart failure.

## Conflicts of interest

The author has no conflicts of interest to declare.

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