

Echocardiography and Cardiac Resynchronization Therapy. Room for Hope?

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The characterization of heart failure as one of the major problems of society today is now a classical maxim. In fact, the prevalence of symptomatic heart failure in Europe is between 0.4% and 2%.¹ Despite the fact that our understanding of the disease and its pathophysiological mechanisms has improved, and the continuous advances in its treatment, the rate of mortality due to this cause continues to be high.¹

Approximately 30% to 50% of the patients with heart failure also have some type of electrical changes on surface electrocardiogram, most of which result from left bundle branch block.² This change in conduction, which involves a change in ventricular mechanics, ultimately leads to the development of both ventricular and interventricular dyssynchronous contraction and, finally, remodeling and deterioration of the contraction-relaxation dynamics.² Reduced cardiac output and ventricular filling time and an increase in wall stress and ventricular end-systolic volume have been reported in patients of this type.²

The original idea that biventricular stimulation could synchronize the contraction between the 2 ventricles and between the different ventricular segments has undoubtedly generated great expectations in the treatment of these patients.³⁻⁵ Different randomized clinical trials have demonstrated that not all the patients benefited from resynchronization therapy. In fact, there are patients that not only do not improve following resynchronization, but can even become worse.³⁻⁵ The MUSTIC study⁵ and the MIRACLE study included patients with severe heart failure, in sinus rhythm and with a QRS longer than 150 milliseconds in the first and of over 130 milliseconds in the second. In most of the patients in the 2 studies,

improvements in quality of life parameters, ventricular remodeling, and oxygen consumption were observed.

More recently, the COMPANION study revealed a decrease in mortality in patients who underwent resynchronization therapy.³⁻⁷ As in the previous studies, the indication for the implantation of a device for resynchronization therapy was based, above all, on clinical criteria and the QRS duration, and echocardiographic criteria for dyssynchrony were not taken into account.

The QRS width is the principal criterion for the selection of patients who are candidates for resynchronization. However, according to the major clinical trials carried out, 30% of those selected do not respond to the therapy.⁴ On the other hand, it should also be pointed out that ventricular mechanical dyssynchrony has been reported in patients with narrow QRS, in whom resynchronization has also been found to have a favorable effect.^{8,9} Thus, echocardiography has acquired a great theoretical relevance in the selection of patients as candidates for resynchronization. Theoretically, dyssynchrony in the echocardiography should be a main criterion for patient selection, since it could reduce the number of nonresponders. A number of echocardiographic techniques have been tested for the detection of interventricular or ventricular dyssynchrony: M mode, Doppler, tissue Doppler, flow and flow rate, tissue tracking and real-time 3-dimensional echocardiography are those that have been analyzed in depth.⁸⁻¹⁰

In their work, Pitzalis et al¹⁰ analyzed 60 patients with ventricular dysfunction and left bundle branch block, and demonstrated that a delay in the peak septal-to-posterior wall motion less than or equal to 130 milliseconds in M mode prospectively identified those patients who would improve after resynchronization. The studies with tissue Doppler have also pointed out that intraventricular dyssynchrony, defined as a difference greater than 40 milliseconds between the peak systolic contraction in contralateral walls detected by tissue Doppler, is also predictive of an improvement following resynchronization in patients with heart failure.¹¹ Other studies with tissue Doppler have provided other time spans between the peaks of systolic contraction to better predict the response to resynchronization therapy. In this respect, it has been indicated that a maximum delay greater than or equal to 65 milliseconds between the anterior, inferior, septal, and basal lateral walls is

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associated with a better prognosis in the patients who undergo this therapy.⁸⁻¹⁰ While all these studies demonstrated that the different methods could predict which patients would benefit from the therapy, the major problem arose when it was confirmed that the degree of agreement among them is very low, with a kappa value ranging between 0.1 and 0.34. This fact is also apparent in the article published by Delgado et al in this issue of *Revista Española de Cardiología*,¹² in which variations in the information provided by each technique can be observed. This immediately raises the question as to which of the different methods studied can predict a better response, a question for which we still have no answer. Secondly, recent clinical trials (CARE-HF and PROSPECT) have utilized echocardiographic techniques for patient selection, but have offered no advantage over the classical clinical and electrical criteria.

In the CARE-HF study,⁸ resynchronization tended to produce greater benefits in patients with a higher degree of interventricular dyssynchrony. However, on the basis of this trial, it can not be concluded that echocardiography should be a main criterion for the selection of the patients. On the other hand, the PROSPECT study presents once again the wide variety of echocardiographic techniques employed in patient selection.

Three-dimensional echocardiography is a novel technique that has also been evaluated in the selection of patients for resynchronization therapy. The pioneering study of Kapetanakis et al¹³ defined the *Systolic Dyssynchrony Index* (DI), which is the same method used by the authors of the article being discussed here¹² to evaluate dyssynchrony. The authors clearly show that the DI is altered in patients with dyssynchrony and changes following resynchronization. Three-dimensional echocardiography provides us with a more “overall and real” view of ventricular hemodynamics. Thus, initially, there was a great deal of expectation as to its contribution to a better selection of candidates for resynchronization. We see with optimism that, as was previously reported, it can predict changes in ventricular hemodynamics, but it leaves us once again with a bittersweet taste when we see that the degree of agreement in the assessment of dyssynchrony with other echocardiographic techniques is far from adequate. Moreover, like the others, it provides no information on predictors of mortality or major events and, thus, its clinical impact also leaves us with doubts.

In conclusion, we know that resynchronization therapy improves ventricular hemodynamics in the majority of the patients who undergo the procedure. Moreover, it prolongs survival and reduces hospital admissions. However, we still have not solved the problem of that 30% of the patients who do not respond to the technique.¹⁴⁻¹⁶ For some, it will seem a high percentage and for others, that which would be expected for any therapy for patients with serious diseases. Each one should address this question when he plans the treatment of his patients. When analyzing the reasons for the lack

of response, we obviously should consider defects in candidate selection, but we should not disregard the errors that occur in the implantation of the electrodes or in the optimization of the device once implanted. Undoubtedly, echocardiography is of great help in selection and optimization of the device, but it is too early for us to be able to decide which of the echocardiographic techniques described is the ideal one. Three-dimensional echocardiography is a promising technique, but it has yet to be shown to be the technique of choice. We should still wait for more conclusive data.

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