

The role of echocardiography in the indication and optimization of cardiac resynchronization therapy

Introduction

The prevalence of heart failure is about 2% among the adult population in developed countries. Most of the patients are over 70 years old and almost half of them has left ventricular ejection fraction under 50%, this pathology being responsible for about 5% of hospital admissions, despite the continuous progress in diagnostics and discoveries of new pharmacological treatments. The prognosis of this condition remains reserved, with a 30% mortality rate in one year following the first hospitalization for heart failure, with increased need for hospital readmissions (over half of the patients return for worsening of heart failure during the first six months after discharge) and over 50% of sudden deaths in this population.

Therefore, remains a challenge finding new therapies for this common pathology that may improve quality of life and prognosis of these patients. Recent decades have brought major advances in neurohormonal blocking therapy by the widespread use of sympathetic antagonists (beta-blockers) and inhibitors of the renin-angiotensin-aldosterone system (angiotensin converting enzyme receptor inhibitors, angiotensin II receptor blockers, spironolactone and eplerenone). However, despite the continuous research targeting other ways of neurohormonal response, negative results of several studies led to the conclusion that antagonizing completely the neurohormonal pathways cannot bring additional benefits. This limitation in the development of drug therapy conducted the search to new directions of non-pharmacological treatments, including interventional therapy with implantable devices. After the renin-angiotensin-aldosterone system inhibitors and beta blockers, cardiac resynchronization therapy (CRT) was the latest evolution and even revolution in the treatment of chronic heart failure, opening the era of electrical therapy of heart failure. CRT has become a widely accepted and highly effective treatment for patients with heart failure, left ventricular dysfunction and wide QRS complexes, with proven benefits on symptomatology and improvement of left ventricular function, increasing exercise capacity and quality of life, as well as long-term prognosis, reducing repeated hospitalizations and mortality rate. Still, about 30% of patients implanted with CRT do not respond to therapy, thus this high proportion of "non-responders" has remained the Achilles heel for CRT over the years, invoking considerable medical and financial resurces.

This paper attempts to make contributions to clarify the role of echocardiography in the management of patients with cardiac resynchronization therapy. Two prospective studies were carried out investigating the role of echocardiography in the assessment of cardiac dyssynchrony pre-implantation and the optimization of CRT devices after implantation.

Echocardiographic evaluation of mechanical dyssynchrony in heart failure patients with reduced ejection fraction

The aim of the first study was to analyse the differences between mechanical and electrical dyssynchrony in patients with impaired systolic left ventricular function and symptomatic heart failure and to highlight that mechanical dyssynchrony might be an important parameter to measure in addition to electrical dyssynchrony, actually the only criteria used in guidelines and in clinical practice. 81 patients with heart failure, NYHA functional class II-IV and ejection fraction under 35% were enrolled. Patients were divided in two groups, according to the duration of QRS complex (>120 ms and ≤ 120 ms respectively). Echocardiographic parameters of atrioventricular (LVDFTR/RR), interventricular

(interventricular mechanical delay – IMD) and intraventricular (SPWMD - septal-to-posterior wall motion delay) dyssynchrony were measured in both of the groups. Our results indicate that the duration of QRS complex (i.e. electrical dyssynchrony) is not a fully reliable indicator of ventricular dyssynchrony, therefore echocardiographic evaluation of mechanical dyssynchrony should be recommended to help better selection of candidates for cardiac resynchronization therapy (CRT). 21,05% of the group with wide QRS complex (with electrical dyssynchrony) had no mechanical dyssynchrony, a large proportion of non-responders to CRT could fit in this subgroup of patients. However, it is difficult to predict precisely the group of non-responders and may need to take into account other parameters (etiology of cardiomyopathy, morphology of the QRS complexes, etc.) in addition to echocardiography and ECG criteria. 25% of the group with narrow QRS complex (without electrical dyssynchrony) presented intra-ventricular mechanical dyssynchrony, these patients could have been represented a target group for CRT. But during the conduct of this study, two large trials (LESSER-EARTH and EchoCRT), published in 2013, demonstrated an increasing rate of mortality among these patients.

The group of non-responders to CRT might be consisting of those patients who have evidence of electrical dyssynchrony (large QRS), but not of mechanical dyssynchrony. The duration of QRS complex alone appear to be an insensitive indicator of ventricular dyssynchrony, hence ultrasound evaluation should also be recommended for a better selection of possible CRT candidates.

Evaluation of echocardiographic optimization of cardiac resynchronization therapy using VTI parameters

CRT can improve left ventricular function and symptoms of heart failure by restoring synchronous left ventricular contractions. Although this improvement is achieved in the majority of patients, some 30% of those who underwent CRT remain non-responders. A number of methods have been tested to improve the rate of responders and convert non-responders into responders, among which different echocardiographic methods. The aim of the second study was to establish whether echocardiographic parameters of mitral and aortic velocity time integral (VTI) can help optimize CRT settings. 27 patients with CRT have been included in the study; demographic, clinical (blood pressure, laboratory parameters, etiology of heart failure, comorbidities, ECG), therapeutic and echocardiographic (standard measurements, LVDF/RR, IMD, SPWMD, aortic and mitral VTI, LVEF, dp/dt, GMI) parameters were assessed. Patients underwent echocardiography to determine dyssynchrony parameters with actual CRT, without CRT and with optimized CRT settings, optimization which was carried out using aortic and mitral VTI. Our results indicate that echocardiographic optimization using VTI parameters did not improve mechanical dyssynchrony and acute left ventricular function parameters in patients with CRT and should be considered only in selected cases of CRT non-responders, possibly associated with other optimization methods.

Conclusions

Statistically significant correlation was found only between electrical (duration of QRS) and intra-ventricular dyssynchrony, measured with SPWMD. There was no statistically significant correlation between electrical and inter-ventricular (IMD) dyssynchrony, nor between electrical and atrio-ventricular (LVDF/RR) dyssynchrony.

A large proportion of non-responders' group can be made of those patients who present electrical dyssynchrony (wide QRS complex), but mechanical dyssynchrony cannot be revealed on echocardiographic examination.

There is a group of patients with narrow QRS complex (without electrical dyssynchrony) showing significant evidence of mechanical dyssynchrony on echocardiography. These patients might represent a target group for CRT. However, results of large randomized trials showed that CRT did not reduce, on the contrary, increased mortality in these patients.

The duration of QRS complex alone is an insensitive indicator of intra-ventricular dyssynchrony. Therefore echocardiographic evaluation of mechanical dyssynchrony might also be recommended for a better selection of candidates for cardiac resynchronization therapy.

Optimization of CRT settings using aortic and mitral VTI parameters, had no beneficial effect on mechanical dyssynchrony and acute left ventricular function parameters, in comparison with basal CRT settings established postimplantation, based on electrical criteria.

Echocardiographic optimization of AVD and VVD intervals with aortic and mitral VTI parameters is not suitable for routine use in all patients receiving CRT. Optimization through VTI should be considered only as a complementary tool in selected cases of non-responder patients and possibly in combination with other methods of optimization.

Keywords: heart failure, echocardiography, CRT, ventricular dyssynchrony, echocardiographic optimization, Mi-VTI, Ao-VTI, non-responders.