THE ASSESSMENT OF THE CARDIAC FUNCTION IN A GROUP OF PATIENTS BEFORE AND AFTER CARDIAC RESYNCHRONIZATION THERAPY

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ABSTRACT

A. GENERAL PART

1. THE ANATOMY AND PHYSIOLOGY OF THE CARDIAC CONDUCTION SYSTEM

We presented the general concepts of the anatomy and physiology of the conduction system of the heart.

2. NONINVASIVE EVALUATION OF THE HEART

The purpose of this chapter was to present some investigations useful in the assessment of the cardiac function, related to the present study and it was not intended to be a description in detail of all methods. References were made especially to electrocardiogram and echocardiography.

3. THE ECHOCARDIOGRAPHIC ASSESSMENT OF THE CARDIAC FUNCTION

Echocardiography is the imaging technique used to assess the LV function due to the accuracy, noninvasive nature, and the repetitive manner without risk parameters and calculated indexes. Information obtained by echocardiography is useful for the diagnosis, prognosis, treatment and follow-up of the therapeutic effect. We presented in separate chapters the assessment of the LV systolic and diastolic function and also the Doppler evaluation of cardiac asynchronies.

4. CARDIAC RESYNCHRONIZATION THERAPY

Heart failure (HF) is a syndrome characterized by cardiac remodeling, ie the progressive LV dilatation and consequent reduction of contractile function. Ventricular remodeling proved to be a negative prognostic factor by itself, and for this reason drugs with the greatest benefit are those that prevent or reduce left ventricular dilation. Intraventricular delay AV conduction and further aggravate LV
dysfunction in patients with preexisting cardiomyopathy. Intraventricular desynchronization favors shortening mitral regurgitation and left ventricular filling. Inter- and intraventricular asynchronies are both pathophysiological processes that directly depress the ventricular function, cause LV remodeling, heart failure and as a consequence, they induce an increased risk of morbidity and mortality.

Clinical application of the cardiac pacing techniques known nowadays as cardiac resynchronization therapy (CRT) began in 1994, when the authors described the first cases of atrio-biventricular stimulation in patients with severe heart failure and without conventional indications of stimulation (Cazeau S. et al, 1994 P. Bakker et al, 2000). Subsequently, all randomized trials have confirmed significant improvement in symptoms and increased exercise capacity from biventricular pacing. Cumulative improvements were observed when CRT was added to standard heart failure therapy (J.G. Cleland et al, 2005). In the COMPANION trial, resynchronization therapy with or without defibrillation, reduced the total mortality and hospitalization for heart failure by 35-40% and reduced the total number of hospitalizations by 76% (Bristow MR et al, 2004).

The biventricular pacing is currently approved for patients with moderate and severe heart failure, NYHA functional classes from II to IV, with sinus rhythm and QRS duration increased ( >120 ms). The left bundle branch block morphology of the QRS complex and an ejection fraction below 35% are additional criteria for the selection of these patients to implant a triple chamber pacemaker. The latest heart failure guidelines from the European Society of Cardiology have endorsed that subjects presenting with an EF below 35% and a QRS complex over 150 ms, regardless of its morphology can benefit from resynchronization therapy. In this paper, it was stressed very straight from the first time in the literature a clear recommendation that favours CRT-D devices implantation versus CRT-P devices, in patients with heart failure, ejection fraction less than 30% and left bundle branch block with QRS duration more than 130 ms.
B. PERSONAL CONTRIBUTION

The aim of this research was to evaluate resynchronization therapy in a group of patients, monitoring their cardiac function before and after cardiac resynchronization therapy was delivered.

The study objectives were:

• The assessment of cardiac performance in patients with heart failure NYHA class III-IV with CRT by conventional echocardiographic parameters: ejection fraction, velocity time integral (VTI), dp/dt, systolic and diastolic diameters of the left ventricle, left atrial size and parameters for assessing ventricular relaxation: the E/A ratio and deceleration time (DT), izovolumic relaxation time (IVRT).

• The assessment of cardiac resynchronization therapy effects in patients with heart failure by monitoring the cardiac peptide NT pro BNP and 6 minutes test walk every 3 months after the implant.

METHODS

The study population consisted of 86 patients admitted for biventricular pacemaker implantation between 2010 and 2011. All were in normal sinus rhythm.

Patient inclusion criteria were: patients with heart failure who are in NYHA functional class III-IV who remained symptomatic despite optimal pharmacological treatment with LV ejection fraction (EF%) ≤ 35%, increased LV end diastolic diameter of 55-60 mm, increased LV end systolic diameter more than 45 mm, left atrial size more than 40 mm and wide QRS ≥ 120 ms.

Cardiac resynchronization therapy (CRT) is a relatively new therapy for patients with symptomatic heart failure resulting from systolic dysfunction. CRT is achieved by simultaneously pacing both the left and right ventricles. Biventricular pacing resynchronizes the timing of global left ventricular depolarization and improves mechanical contractility and mitral regurgitation.

Echocardiography is a useful tool for quantitative measurement of the severity of dyssynchrony in these patients before and after CRT. Various echocardiographic techniques in the assessment of systolic dyssynchrony include M mode measurement
of septal-to-posterior wall delay, tissue Doppler imaging for septal-to-lateral wall delay, the measurement of standard deviation of peak contraction time over 12 left ventricular segments, delayed longitudinal contraction, and potentially three dimensional echocardiography. In particular, tissue Doppler imaging may allow further identification of potential responders to CRT, based on assessment of inter-and intraventricular dyssynchrony. Tissue Doppler imaging was also used to demonstrate interventricular resynchronization. A large mechanical delay between the free right ventricular wall and the lateral wall of the LV, which was completely reversed after CRT.

An optimized atrioventricular (AV) interval can maximize the benefits of cardiac resynchronization therapy (CRT). There are many echocardiographic techniques for AV optimization but there is no universally accepted gold standard. The optimal AV delay varies with time, necessitating periodic re-evaluation.

Systolic and diastolic parameters can also be obtained with conventional Doppler echocardiography and include: aortic velocity-time-integral, diastolic filling time, myocardial performance index (Tei), E/A ratio, E-deceleration time, isovolumetric relaxation, and pulmonary vein flow. Some of these parameters showed improvement after CRT, although interpretation is hampered by AV delay optimization as frequently performed with CRT.

Color Doppler imaging have shown a reduction in mitral regurgitation after CRT and have demonstrated that the effective regurgitant orifice area decreased immediately after biventricular pacing. Additional have demonstrated significant reverse remodeling after CRT by reduction in LV end-diastolic volume and end-systolic volume after six months of CRT. Restoration of an optimal AV timing may improve systolic performance by optimizing LV preload after resynchronization.

The acute hemodynamic benefits have been monitored noninvasively by Doppler echocardiography. We have assessed the aortic velocity time integral and a prolongation of the diastolic filling time at the mitral valve and also the interventricular dyssynchrony, as measured by IVMD.
**RESULTS**

After the implant, the functional capacity of the heart was improved, most of the patients had a clinical benefit from the reduction of at least one NYHA class. A percentage of 38.38% of patients showed improvement of cardiac function, passing in NYHA functional class II immediately after the resynchronization therapy was delivered. After 12 months of follow up the percentage of the patients with class III NYHA was 47.67%.

The best results were obtained in the subgroup of hypertensive heart failure etiology, where 83.34% of patients in this group after 12 months were in functional class NYHA II, while the subgroup with ischemic etiology of heart failure only a percentage of 68.57% of patients at the end of 12 months pass in functional class NYHA II.

After resynchronization, the levels of NT proBNP decreased, so that after 6 months 72.09% of patients had levels < 400 (ng/L) and after 12 months of follow up, high levels of NT proBNP over 2000 (ng / L) were encountered only in 10.46% of patients.

We found a statistically significant correlation between NYHA functional class and the NT proBNP levels. 11.63% procent of the patients that remained in the NYHA class IV after 12 months of follow up still showed elevated levels of NT proBNP more than 2000 ng/L.

Three months after the procedure, assessing exercise tolerance by 6 minutes walk test showed a significant improvement. After 6 months, 50% of patients could walk between 250 and 450 meters and 19.77% patients over 450 meters.

At the end of the study, the percentage of patients with ejection fraction between 30 and 35% was 37.20% of those with an EF over 35% ejection fraction was 29.08%, demonstrating the clear benefit of the resynchronization therapy.

The improving of the systolic function after biventricular pacing depends on the etiology of heart failure. The results were weaker in the subgroup with ischemic heart disease. In the subgroup of patients with idiopathic dilated cardiomyopathy and
heart failure, it was observed that the percentage of patients with ejection fraction >10 units is 42.31%, that was almost double that of those with ischemic etiology.

The intraventricular asynchrony evaluation by the maximum intraventricular septum interventricular and posterior wall motion delay (SPWMD) before the procedure showed elevated values of 212 ± 21 ms, with a significant decrease immediately after the implant to 26 ± 16 ms (p = 0.001). This decrease was maintained after 3 months of follow up to 21 ± 14 ms (p = 0.001) and also after 6, 9 and 12 months after the procedure.

The interventricular asynchrony assessment calculated by the time difference between the 2 ventricles shortened from 72 ± 24 ms before resynchronization to 36 ± 14 after 3 months (p = 0.001) and this trend was maintained all the period of follow up.

At the end of the study, 76 of the 86 (88.37%) patients included responded positively after resynchronisation therapy and they were considered responders.

**CONCLUSIONS**

Cardiac resynchronization therapy (CRT) is a revolutionary interventional technique for patients with heart failure refractory to maximal medical treatment. Evidence is accumulating that echocardiography may be the ideal technique to identify responders to CRT and also can guide the LV lead positioning and to optimize the AV and V-V delays.
REFERENCES


