ASSESSING CARDIAC PERFORMANCE IN PATIENTS UNDERGOING CARDIAC RESYNCHRONIZATION THERAPY

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ASSESSING CARDIAC PERFORMANCE IN PATIENTS UNDERGOING CARDIAC RESYNCHRONIZATION THERAPY (Abstract). **Aim.** To analyze the effects (clinical, electrical and ultrasound) of cardiac resynchronization devices, with or without an implantable defibrillator (CRT-P or CRT-D) on the patients with heart failure in our clinic. **Material and Methods:** We retrospectively analyzed 56 patients with NYHA functional class II-IV heart failure who underwent CRT-P or CRT-D in our clinic in the interval January 1, 2010 – June 1, 2014. To evaluate the effects of cardiac resynchronization therapy (CRT) we focused on measuring the QRS complex duration on electrocardiogram, left ventricular ejection fraction (LVEF) and the NYHA functional class assessment. These parameters were assessed immediately before intervention and one month after device implantation. Patient characteristics were expressed as mean ± 1 standard deviation or as number and percentage. Variables were compared by paired t test. A p wave value less than 0.05 was considered statistically significant. **Results:** QRS complex duration decreased from an average of 155ms to 129ms, a statistically significant narrowing of 25.4ms (p < 0.0001). The LVEF increased from an average of 28% to 35% (p < 0.001). A statistically significant improvement (p < 0.0001) in NYHA functional class was recorded. **Conclusions:** CRT is an important therapeutic approach, in our study 82.56% of the patients being considered responders due to improvement in the NYHA functional class and at least a 5% increase in the LVEF. A narrowing of the QRS complex on electrocardiogram was obtained in all patients classified as responders, so this simple method for measuring QRS complex duration can be used to assess the response to biventricular stimulation. **Keywords:** HEART FAILURE, CARDIAC PACING, THERAPY, BIVENTRICULAR STIMULATION.

Cardiovascular diseases (CVD) in general and heart failure in particular are major health problems due to the large number of patients and the incurred implications, the socioeconomic ones included. For this reason, the diagnosis methods, treatment and prognosis were also of interest. Technical developments during the past decades had a tremendous impact in contemporary medicine leading to further improvement of the diagnostic and therapeutic approaches. Cardiology is one of the most privileged specialties in terms of technological advancements. Cardiac resynchronization therapy (CRT) plays an important role in the treatment of patients with NYHA functional class II-IV heart failure despite the optimal medical treatment. During the last decade, long-term clinical effects of CRT were evaluated by randomized multicentre trials, such
as MUSTIC-SR (Multisite Stimulation in Cardiomyopathy Study), MIRACLE (Multi-center InSync Randomized Clinical Evaluation Trial), COMPANION (Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure trial), CARE-HF (The Cardiac Resynchronization Heart Failure trial). These trials showed that CRT improves symptoms and exercise capacity and decreases morbidity and mortality from cardiovascular causes. Yet, despite the fact that the indications for CRT are well described, at present the parameters/criteria for patient selection are not well defined, so that studies revealed that up to 30% of the patients did not respond to CTR.

The response to CRT can be assessed by various methods, but there is no agreement on which method best predicts response to CRT. The most widely accepted method is the clinical criteria of the New York Heart Association (NYHA) functional classification. Echocardiographically, the most commonly used method remains the assessment of LVEF. Recently, much more confidence is granted to the comparatively simple method of measuring QRS complex duration.

The aim of our study was to analyze the effects (clinical, electrical and ultrasound) of CRT, with or without an implantable defibrillator (CRT-P or CRT-D) in patients with heart failure in our clinic.

**MATERIAL AND METHODS**

**Patient population.** This prospective observational study included 56 consecutive patients referred to the Cardiology Department of the “Prof. Dr. George I.M. Georgescu” Cardiovascular Disease Institute, Iasi, Romania for CRT between January 1, 2010 and June 1, 2014. All patients were in NYHA functional class III/IV on optimal pharmacological treatment and showed reduced left ventricular systolic function (ejection fraction [EF] ≤ 35%) and a QRS complex duration of > 120ms. Patients with permanent atrial fibrillation and recent myocardial infarction (< 3 month) were excluded.

All patients were on an optimal pharmacological treatment with the maximum tolerated doses of digitalis medication, beta blockers, diuretics and ACE inhibitors. Resting 12-lead EEGs (at a paper speed of 25 mm/s) were acquired immediately before and one month after CRT device implantation. Clinical evaluation included assessment of NYHA functional class before and one month after biventricular pacing.

Echocardiographic data were obtained using a conventional ACCUSON CV 70 System (Siemens, Germany). In all patients echocardiography was performed at rest, in the lateral decubitus position, at baseline and six months after implantation. A standard evaluation of left ventricular volumes was performed in the apical 4-chamber view according to Simpson’s rule method. To minimize the variability in measurements, all patients were evaluated by the same physician.

Classified as responders were those patients who presented at six month follow-up improvement by at least one NYHA functional class, an increase in LVEF of ≥5%, and decrease in left ventricular end-systolic volume (LVESV) and left ventricular end-diastolic volume (LVEDV) of ≥15%.

Patient characteristics were expressed as the mean ± 1 standard deviation or as a number and percentage. Variables were compared by paired t test. The value of p wave below 0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS statistical software (SPSS v.21.0, Mac OS X).
RESULTS

Baseline characteristics. The study population consisted of 40 men (71.42%) and 16 women (28.58%) with a mean age of 68.2 ± 10.4 years. 36.42% of the patients were in NYHA functional class IV and the mean QRS complex duration was 178.8 ± 18ms before cardiac stimulation (tab. I).

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Patients ( n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.8±10.4</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>71.42</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>28.58</td>
</tr>
<tr>
<td>QRS duration(ms)</td>
<td>178±14</td>
</tr>
<tr>
<td>NYHA III class (%)</td>
<td>62.8</td>
</tr>
<tr>
<td>Ischemic CMD (%)</td>
<td>28.32</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>20.3±6</td>
</tr>
<tr>
<td>DTDVS (ml)</td>
<td>224.8±68.5</td>
</tr>
<tr>
<td>DTGSVS (ml)</td>
<td>176.3±49</td>
</tr>
<tr>
<td>LAv (ml)</td>
<td>72.8±10.5</td>
</tr>
</tbody>
</table>

The evolution of heart failure expressed by NYHA functional class after biventricular stimulation After CRT functional capacity was improved, most patients presenting at one month follow up an improvement by at least one NYHA functional class. So, if the inclusion rate for NYHA class IV patients was of 37.2%, after one month it decreased to 21.4% (fig. 1).

The evolution of LVEF after CRT At baseline all patients had LVEF ≤35%. One month later, on echocardiographic assessment 82.26% of the patients showed an increase in LVEF of more than 5%, being classified as responders. 16.5% of them showed an LVEF improved by more than 15% - super-responders. 17.74% of the study patients showed no change in left ventricular systolic function - non-responders.

QRS duration on surface electrocardiogram decreased from an average of 178ms at baseline to 128ms, being a statistically significant correlation between QRS narrowing and the increase in LVEF. So, the patients with a narrowing of QRS complex of at least 30ms were classified as super-responders (16.5%), and those with a narrowing of 20 to 30ms as responders.

DISCUSSION

Heart failure is a syndrome characterized by cardiac remodeling; progressive left ventricular dilation, and consequently, reduced contractile function. Ventricular remodeling has been shown to be an independent negative prognostic factor. Atrial-ventricular and intraventricular delay further exacerbates left ventricular dysfunction and ventricular desynchronization favors mitral regurgitation and shortens left ventricular filling. Intraventricular delay is a pathophysiological process that directly depresses ventricular function, by causing ventricular remodeling and thus increasing morbidity and mortality. CRT has already been a major benefit in the treatment of heart failure. Numerous randomized trials have confirmed the important role of CRT on significant improvement in symptoms, increased exercise capacity, improved NYHA functional class (on average by 0.5-0.8 points) and increase by 20% in 6-minute walk distance. Quality of life was
significantly improved in all studies. Total mortality and hospitalization for heart failure were significantly reduced by CRT-P or CTR-D (COMPANION study).

The response to CRT can be assessed by various methods, but there is no agreement on which method best predicts response to CRT. The most widely accepted method is the clinical criteria of NYHA functional classification. Echocardiographically, the most commonly used method remains the assessment of LVEF. To these methods can be added the measuring of QRS duration on surface electrocardiogram as a simple but useful method of evaluation of clinical response to biventricular stimulation.

**CONCLUSIONS**
Cardiac resynchronization therapy is an important therapeutic option in patients with failure. In our study 82.56% of the patients were considered responders due to the improvement in NYHA functional class, increase in LVEF by at least 5% and narrowing of the QRS complex. The narrowing of the QRS complex on electrocardiogram was found in all patients classified as responders, so this simple method of measuring the duration of QRS complex can be used to assess the response to biventricular stimulation.

**ACKNOWLEDGEMENTS**
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Assessing cardiac performance in patients undergoing cardiac resynchronization therapy


**NEWS**

**ANTI-INFLAMMATORY EFFECT OF STAPHYLOCOCCUS AUREUS ON AIRWAY EPITHELIAL CELLS**

A study by Chekabab *et al* examined the way bacterial cells modulate inflammatory responses in the setting of polymicrobial infections. Two major respiratory pathogens, *Pseudomonas aeruginosa* and *Staphylococcus aureus* can simultaneously colonize the airways of patients with chronic obstructive diseases (e.g. cystic fibrosis). The mechanism by which airway epithelial cells integrate bacterial stimuli in the case of polymicrobial colonization or infection is unknown. Since epithelial cell signaling is crucial for the activation of innate immune responses, the study examined the inflammatory responses to *P. aeruginosa* and *S. aureus* co-stimulations. Immortalized airway epithelial cells exposed to bacteria-free filtrates from *P. aeruginosa* induced a high synthesis of IL-8, while bacteria-free filtrates from *S. aureus* showed a minimal effect. However, in the case of co-stimulation with bacteria-free filtrates from *P. aeruginosa* and *S. aureus*, *S. aureus* filtrates inhibited IL-8 production induced by *P. aeruginosa*, showing potent anti-inflammatory effects. It also decreased IL-8 production induced by the TLR1/TLR2 ligand Pam3CysSK4 and dampened TLR1/TLR2-mediated activation of the NF-κB pathway. These results demonstrate that *S. aureus* modulates inflammatory responses in the setting of polymicrobial infections (Chekabab SM, Silverman RJ, Lafayette SL, Luo Y, Rousseau S, Nguyen D. *Staphylococcus aureus* Inhibits IL-8 Responses Induced by *Pseudomonas aeruginosa* in Airway Epithelial Cells. PLoS One. 2015;10(9):e0137753. doi: 10.1371/journal.pone.0137753. eCollection 2015).

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