Cardiac Resynchronization Therapy Optimization Using Trans Esophageal Doppler in Patients with Dilated Cardiomyopathy

ABDALLAH YOUSSIF, M.Sc.*; AHMED ABDELAZIZ, M.D.*; HAMDY M. SABER, M.D.** and MOHAMED E. AFIFY, M.D.*
The Department of Critical Care, Faculty of Medicine, Cairo* & Beni Suef** Universities

Abstract

Introduction: Application of CRT remains a challenge, both from technical aspect and optimization. Transesophageal Doppler is a simple Hemodynamic monitoring technique, that my help in optimizing CRT devices.

Objectives: We investigated the utility of Trans esophageal Doppler to optimize cardiac resynchronization therapy (CRT) parameters.

Methods: Thirty patients underwent CRT implantation, baseline 2D echocardiogram (echo), 6min walk distance, and quality of life (QOL) questionnaire within 1 week of implant. Following implant, 15 patients (group A) had their CRT, CRTD device A-V delay and V-V delay optimized using trans esophageal Doppler. Optimal parameters were programmed. 15 patients (group B) were left with fixed AV delay 120ms and fixed VV delay 0ms. Echo, 6min walk, and QOL were repeated at 3-6 months post-implant.

Results: All parameters showed a significant improvement at follow-up when compared to baseline for whole study population, in comparison of the degree of improvement in both groups to each other, group A showed a statistically significant improvement at follow-up in LVED percentage of improvement compared to group B (11.9%±11% vs 1.5%±6.5% p-value 0.004). Also in the measurements of LVES & EF % (5.15cm±0.9cm & 38.5%±9% for group A versus 5.9cm±0.9cm & 31.4%±8.8% for group B, (p-value 0.03 & 0.04 respectively). Although comparing the degree of improvement in clinical parameters in both groups did not show any statistically significant difference in QOL (41.6±21.46 vs 50.67±20.19, respectively) or in six minute walk test (358.67±131.4 vs 265.87±126.2 respectively).

Conclusion: We can conclude that using the Transesophageal Doppler for optimization of CRT devices can only improve some of the Echo parameters with no impact on clinical parameters.

Key Words: CRT – Cardiac resynchronization – Transesophageal Doppler.

Correspondence to: Dr. Hamdy M. Saber, E-mail: hamdysaber@hotmail.com

Introduction

RECENTLY, cardiac resynchronization therapy has emerged as a novel therapy in treatment of patients with dilated cardiomyopathy, improving systolic function and initiating a process of reverse remodeling in patients with advanced HF and electromechanical delay.

Multiple clinical trials have demonstrated that CRT can improve symptoms, exercise tolerance, and left ventricular (LV) function in patients with depressed systolic function and intraventricular conduction delays [1-3]. Furthermore, other studies have demonstrated a mortality benefit from CRT [4].

At present, up to 40% of patients do not show improvement in left ventricular (LV) performance or clinical symptoms after cardiac resynchronization therapy (CRT) [5]. This suboptimal response may be the presence of suboptimal LV filling time (atrioventricular (AV) dyssynchrony) or remaining LV dyssynchrony [6]. Current CRT devices allow manipulation of the AV and interventricular (VV) timings in order to maximize LV filling and stroke volume. However, multiple single centre and few multicenter trials have provided controversial data on the beneficial effects of AV and VV intervals optimization on cardiac performance and clinical status [7]. In addition, multiple methodologies have been proposed to optimize AV and VV intervals but no consensus has been reached on which methodology should preferably be used [8].

Transesophageal Doppler is a simple technique, and most users acknowledge that it is fairly easy to achieve adequate probe positioning and obtain reproducible results [9]. The technique, initially introduced by Daigle and colleagues, measures...
blood flow velocity in the descending thoracic aorta, using a transducer that can be inserted easily in sedated patients. Stroke volume may then be derived using an algorithm based on: The beat-to-beat maximum velocity-time integral (or stroke distance); the cross-sectional area of the descending aorta; and a correcting factor which transforms descending aortic blood flow into global cardiac output [10]. Thus esophageal Doppler can be a potential method for cardiac resynchronization therapy.

Aim of the work:

This study aims to evaluate the role of transesophageal doppler as a method for cardiac resynchronization therapy optimization.

Patients and Methods

This is a prospective study conducted on thirty consecutive patients with advanced heart failure (NYHA class II or III) in the period from August 2011 to August 2012. All patients were indicated to cardiac resynchronization therapy and they were admitted to the Critical Care Unit, Cairo University for CRT-P or CRT-D implantation. The study was approved by the Ethical committee, and the Patients signed a written consent.

We included patients with advanced heart failure of any etiology on optimal drug therapy, NYHA class II or III, LVEF <35%, QRS duration >150ms in non LBBB and >120ms in LBBB, Stable condition within the last month. We excluded from the study patients with uncorrected valvular disease or dysfunctional prosthetic valve, recent ischemic episode (within 40 days) or correctable coronary heart disease, end stage renal or hepatic disease, frequent atrial and/or ventricular premature beats, atrial fibrillation.

The studied patients were subjected to baseline assessment including: Full history taking and clinical examination, ECHO heart, Quality of life questionnaire “Minnesota questionnaire” [11], Exercise test, i.e. 6-minute walk test [12]. All patients had the CRT or CRT-D device implanted at the cath lab of the Critical Care Department-Cairo University Hospital, One day after implantation patients were subjected to: Twelve lead ECG, Chest X-ray, Echocardiographic examination.

The patients were randomized into two groups:

Group A: 15 patients had their CRT, CRT-D device A-V delay and V-V delay optimized using Trans esophageal Doppler.

Group B: 15 patients were left un-optimized with fixed AV delay 120ms and fixed VV delay 0ms “simultaneous”.

Method of optimization:

Esophageal Doppler monitor: We used customized Deltex cardio Q system, the monitor was modified specifically to allow continuous acquisition of the Doppler velocity envelope signal slave directly into our analogue to digital conversion system (WIND-AQV 1.26, Dataq instruments Akron, Ohio, USA).

After the probe positioning the patients Atrioventricular (AV) delay was adjusted to (90,100, 110,120,130,140ms, biventricular simultaneous pacing) putting in consideration that AV delay should be shorter than the native PR interval of the patient to avoid patient’s own rhythm, pseudo-fusion or fusion rhythm. Then V-V delay was adjusted to (–40 to 40ms in 1 0ms increments) were varied every 60s the probe was used to monitor SV on a beat-to-beat basis optimal parameters were programmed.

The patients were followed-up after 3 to 6 months from implantation and the following was repeated: Quality of life questionnaire, Exercise test, (i.e. 6-minute walk test), Echocardiographic examination.

Six minute walk test (6 MWT):

Was done under standard conditions, in our study the 6 MWT was performed indoor “the Critical Care Unit”, on a long, flat, straight, enclosed corridor with a hard surface. The walking course was 30 meters in length from the starting line to the turnaround point. By the end of the test the total walked distance, the post walk dyspnea and fatigue levels and comparing it with pre test levels, the post walk heart rate and comparing it with pre test measures.

Results

A- General group demographics:

Table (1) shows no statistically significant difference regarding general characteristics of the study group.

B- Comparison for all study group at baseline and follow-up:

Baseline and follow-up parameters were compared for all patients in our study. All parameters showed significant improvement upon follow-up from baseline readings with p-value <0.001 (Table 2).
C- Comparing baseline echo parameters between TE Doppler optimized versus non-TE Doppler optimized patients:

Baseline parameters were compared for both TE Doppler and non-TE Doppler modified patients. There was no statistically significant difference between Baselines LVED (7.09cm±0.7cm vs 7.57±0.94), LVES (6.16cm±0.78cm vs 6.39cm±0.88cm) and EF % (26.67%±6.76% vs 30.13%±5.82%) in control patients versus cases (p-value 0.14,0.46,0.14 respectively), and also there was no statistically significant difference between Baseline 6MWT (209.6m±69.9 vs 263.4±82.08, p-value 0.06) and QOLQ (68.67±8.32 vs 65.4±9.42, p-value 0.32) respectively.

D- Comparing follow-up echo parameters between TE Doppler optimized versus non-TE Doppler optimized patients:

There was a statistically significant difference in the follow-up of percentage of change of LVED between cases and controls in the favor of optimized cases (11.9%±11 % vs 15%±6.5 % p-value 0.004) i.e. TE Doppler had significant contribution, (p-value 0.004) (Table 3).

There were also a statistically significant difference in the follow-up of LVES between cases and controls in the favor of optimized cases (5.87cm±0.87cm vs 5.15cm±0.9cm, p-value 0.03). Repeatedly comparing the EF % there were a statistically significant difference in the follow-up of EF % between cases and controls in the favor of optimized cases (31.4%±8.84% vs 38.47%±9.04%, p-value 0.04) TE Doppler had significant contribution.

There was no statistically significant difference in the follow-up of 6MWT between cases and controls (265.87m±126.2m vs 358.67m±131.4m, p-value 0.06) indicating that optimization by TE Doppler had no significant impact on 6MWT (Fig. 1).

Moreover there was no statistically significant effect in the follow-up QOLQ between cases and controls (50.67±20.19 vs 41.6±21.46, p-value 0.24) indicating that TE Doppler had no significant contribution (Fig. 2).

Table (1): General characteristics for cases and controls.

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.3±12.8</td>
<td>53.8±10.6</td>
<td>0.56</td>
</tr>
<tr>
<td>Gender</td>
<td>2 (13%)</td>
<td>2 (13%)</td>
<td>0.701</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (33.3%)</td>
<td>5 (33.3%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5 (33.3%)</td>
<td>9 (60%)</td>
<td>0.135</td>
</tr>
<tr>
<td>CAD</td>
<td>7 (46.7%)</td>
<td>9 (60%)</td>
<td>0.358</td>
</tr>
</tbody>
</table>

Table (2): Baseline and follow-up parameters for all patients.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Follow-up</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>LVED</td>
<td>7.33cm</td>
<td>0.9cm</td>
<td>6.79cm</td>
</tr>
<tr>
<td>LVES</td>
<td>6.273cm</td>
<td>0.8cm</td>
<td>5.51cm</td>
</tr>
<tr>
<td>EF %</td>
<td>28.40%</td>
<td>6.4%</td>
<td>34.93%</td>
</tr>
<tr>
<td>6MWT</td>
<td>236.50m</td>
<td>79.8m</td>
<td>312.27m</td>
</tr>
<tr>
<td>QOLQ</td>
<td>67.03</td>
<td>8.9</td>
<td>46.13</td>
</tr>
</tbody>
</table>

Table (3): Follow-up parameters for cases and controls.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Cases</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>LVED change %</td>
<td>11.9%</td>
<td>11%</td>
<td>1.5%</td>
</tr>
<tr>
<td>LVES</td>
<td>5.87cm</td>
<td>0.87cm</td>
<td>5.15cm</td>
</tr>
<tr>
<td>EF %</td>
<td>31.4%</td>
<td>8.84%</td>
<td>38.47%</td>
</tr>
<tr>
<td>6MWT</td>
<td>265.87m</td>
<td>126.2m</td>
<td>358.67m</td>
</tr>
<tr>
<td>QOLQ</td>
<td>50.67</td>
<td>20.19</td>
<td>41.6</td>
</tr>
</tbody>
</table>

Fig. (1): Baseline and follow-up parameters for 6MWT in both cases and controls.

Fig. (2): Baseline and follow-up parameters for QOLQ in both cases and controls.
Discussion

Despite recent advances in drug therapy, congestive heart failure (CHF) remains a major healthcare problem associated with a poor quality of life and a high mortality rate. Heart failure is a worldwide pandemic; it affects approximately 22 million individuals worldwide, with 2 million, new cases annually [13].

In the mid-1990s, investigators working largely in Europe began exploring the possibility that simultaneous electrical stimulation of both right and left ventricles could significantly improve cardiac function and clinical symptoms in patients with heart failure and discoordinate wall motion due to conduction delay [14].

The current study was done on 30 consecutive patients admitted to the Critical Care Department, Cairo University in Egypt from May 2011 to May 2012.

Our study did not differ from major studies discussing CRT and optimization regarding demographic criteria and indication for CRT implantation like most studies the inclusion criteria comprised of patients suffering from dilated cardiomyopathy with EF <35% and evidence of ventricular dyssynchrony defined by QRS duration >120ms in LBBB and >150ms in non LBBB.

The study of Stellbrink et al., 2001, investigated the impact of six months of cardiac resynchronization therapy (CRT) on echocardiographic variables of (LV) function. The study was conducted on twenty-five patients (12 women and 13 men; mean age 59.8±5.1 years) with advanced HF, echocardiographic measurements were compared before implantation and after six months of CRT, they found that Left ventricular end-diastolic and end-systolic diameters (LVEDD and LVESD, respectively) were significantly reduced after six months (LVEDD from 71±10 to 68±11mm, \( p=0.027 \); LVESD from 63±11 to 58±11mm, \( p=0.007 \)), as were LV end-diastolic and end-systolic volumes (LVEDV from 253±83 to 227±112ml, \( p=0.017 \); LVESV from 202±79 to 174±101ml, \( p=0.009 \)). Ejection fraction was significantly increased (from 22±7% to 26±9%, \( p=0.03 \)) [15].

This study comes in agreement with our results where we compared baseline and follow-up parameters for all the patients regarding Echo parameters, Quality of life questionnaire and 6 minutes walk test and found that CRT significantly improved all these parameters.

When the results of the optimized group of patients was compared to the previous studies we found that there was an improvement but not a statistically significant one and this might be attributed to the small number of the case group.

We compared the echocardiography parameters after CRT implantation in the two groups, the group that have been programmed with empirical settings (AV delay=120ms, VV delay=0) versus the group that have been optimized with esophageal Doppler probe and the optimized group showed significant improvement in LVES, LVED and EF %.

Most major studies evaluate only one optimization parameter AV or VV delay, very few studies compare both, we compared our results with studies evaluating one parameter at a time.

Our study comes in agreement with the InSync III study, this multicenter, prospective, nonrandomized six-month trial enrolled a total of 422 patients to determine the effectiveness of sequential CRT pacing. The study evaluated: Whether patients receiving sequential CRT for six months experienced improvement in 6-min hall walk (6MHW) distance, NYHA functional class, and quality of life (QoL) over control group patients obtained from the (Multicenter In Sync Randomized Clinical Evaluation “MIRACLE” trial) and whether sequential CRT increased stroke volume compared to simultaneous CRT; and whether an increase in stroke volume translated into greater clinical improvements compared to patients receiving simultaneous CRT. The InSync III patients experienced greater improvement in 6MHW, NYHA functional class, and QOLQ at six months compared to control (all \( p<0.0001 \)). Optimization of the sequential pacing increased (median 7.3%) stroke volume in 77% of patients. No additional improvement in NYHA functional class or QOLQ was seen compared to the simultaneous CRT group; however, InSync III patients demonstrated greater exercise capacity [16].

Our study comes in contrast to the Decrease-HF study [17] which is a multicenter trial in which 306 patients with New York Heart Association class III or IV heart failure, an LV ejection fraction <or=35%, and a QRS duration >or=150ms were randomized to simultaneous Biv, sequential Biv, or LV pacing. LV volumes and systolic and diastolic function were assessed with echocardiography at baseline, 3 months, and 6 months. All groups had a significant reduction in LV end-systolic and end-diastolic dimensions (\( p<0.001 \)). The simultaneous Biv pacing group had the greatest reduction in LV
end-systolic dimension ($p=0.007$) stroke volume ($p<0.001$) and LV ejection fraction ($p<0.001$) improved in all groups with no difference across groups.

Several data form single centre studies showed that the optimal AV settings further improved haemodynamic benefits of CRT. At present, only one single blind randomized trial investigated the impact of AV delay optimization based on aortic VTI on clinical status 3 months after CRT [18]. Sawhney et al., 2004 a randomized, prospective, single-blind clinical trial compared two methods of AV delay programming in 40 patients with severe heart failure referred for CRT. Patients were randomized to either an optimized AV delay determined by Doppler echocardiography (group 1, n=20) or an empiric AV delay of 120ms (group 2, n=20) with both groups programmed in the atrio-synchronous biventricular pacing (VDD) mode. Optimal AV delay was defined as the AV delay that yielded the largest aortic VTI at one of eight tested AV intervals (between 60 and 200ms). New York Heart Association (NYHA) functional classification improved by 1.0±0.5 vs 0.4±0.6 class points ($p<.02$), and QOL score improved by 23±13 versus 13±11 points ($p<.03$) for group 1 vs group 2, respectively. After 3 months, NYHA classification improved by 1.0±0.5 vs 0.4±0.6 class points ($p<.02$), and QOL score improved by 23±13 versus 13±11 points ($p<.03$) for group 1 vs group 2, respectively. They concluded that Echocardiography-guided AV delay optimization using the aortic Doppler VTI improves clinical outcomes at 3 months compared to an empiric AV delay program of 120ms. [18].

Conversely Malagoli et al., 2012 studied fifty one patients with refractory systolic HF and left bundle branch block before CRT implantation, their patients were 1: 1 randomized to either an optimized AV delay (AV Opt group) determined by continuous wave Doppler aortic velocity-time integral (VTI) or an empiric AVD of 1 10ms (AV Fixed group). Optimal AV delay was defined as the AV delay that yielded the largest aortic VTI at one of eight tested AV intervals (between 60 and 200ms). LA volumes and emptying fractions were assessed by two-dimensional echocardiography at baseline and 6months after CRT. At 6-month follow-up, CRT induced LA reverse remodeling in the whole population (maximal LA volume: 55.8±16.4ml/m² vs 50.3±18.9ml/m², $p=0.006$; pre-systolic LA volume: 47.0±15.2ml/m² vs 41.4±17.4ml/m², $p=0.003$; post-systolic LA volume: 36.4±15.0ml/m² vs 30.3±18.0ml/m², $p=0.001$); nevertheless, no substantial difference was observed about LA structural and functional remodeling between both AV Opt group and AV Fixed group [19].

We argue that Left atrial size and volume changes secondary to left ventricular size and volume, thus it is reasonable to assume that it takes much more time for atrial size or volume to be changed.

In light of this evidence, AV and VV interval optimization may be beneficial in some groups of heart failure patients treated with CRT, improving the clinical status and LV performance. Non-responder patients and ischaemic heart failure patients with extensive myocardial scar tissue may benefit most likely from VV interval optimization. Particularly, in ischaemic heart failure patients, the inter- and intra-ventricular conduction of the electrical pulse is very slow and may require larger LV pre-excitation [20].

Several echocardiographic and non-echocardiographic techniques have been used to perform optimization of CRT [21,22], and Trans esophageal Doppler can be comparable to other optimization techniques. In our study we proved that Trans esophageal Doppler as an optimization method significantly improved CRT responders regarding ECHO parameters only. The available multi-centre trials did show modest clinical benefits of AV and VV interval optimization. It remains to investigate whether AV and VV interval optimization may improve the long-term survival.

Conclusion:

We can conclude that Optimization of Cardiac resynchronization therapy with esophageal Doppler only improves some of the Echo parameters (LVES and EF %) in the optimized patients when compared to the non optimized patients. Optimization of Cardiac resynchronization therapy with esophageal Doppler had no statistically significant effect regarding (LVED, Quality of Life Questionnaire and Six Minute walk Test).

References


