Exercise training after cardiac resynchronization in chronic heart failure. Results of a pilot study.

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ABSTRACT
Background: Exercise training improves exercise tolerance in chronic heart failure (CHF) patients. Recently, cardiac resynchronization has been shown also to increase functional capacity in CHF patients with intraventricular conduction delay. The aim of this pilot study was to assess complementary effects of these two non-pharmacological approaches to optimize both hemodynamic and symptomatic improvements.

Methods: We studied 8 CHF pts (mean age: 67±7 years, 7 men, mean LVEF: 0.18±0.08 ) who underwent 18±8 sessions of exercise training after bi-ventricular pacing implantation. Exercise tolerance were evaluated before and after pace-maker implantation, and at the end of the rehabilitation.

Results:

<table>
<thead>
<tr>
<th></th>
<th>Before PM</th>
<th>After PM</th>
<th>After Ex training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise duration (sec)</td>
<td>112±37</td>
<td>218±22</td>
<td>243±45*</td>
</tr>
<tr>
<td>Workload (watts)</td>
<td>44±5</td>
<td>58±0</td>
<td>61±8*</td>
</tr>
<tr>
<td>Peak VO2 (ml/kg/min)</td>
<td>9.5±1.0</td>
<td>13.2±1.28</td>
<td>14.6±2.8*</td>
</tr>
<tr>
<td>% theor VO2</td>
<td>0.39±0.09</td>
<td>0.53±0.07</td>
<td>0.62±0.2*</td>
</tr>
</tbody>
</table>

= p<0.05 before-PM, *= p<0.05 before PM-after training, #= p<0.05 after PM-after training

Conclusion: Exercise training after cardiac resynchronization provides additional improvement in effort tolerance in CHF patients. These preliminary results encourage to perform a randomized study to evaluate benefits of combined strategy (resynchronization and exercise training) compared to resynchronization therapy alone in CHF patients.

INTRODUCTION
Benefits of exercise training in heart failure patients include an improvement of exercise tolerance, which seems to be mainly related to peripheral adaptations [1-3].

Recently, cardiac resynchronization therapy (CRT) was proposed as a treatment for heart failure patients with intra ventricular conduction delays [4-6]. This technique has shown also an improvement in functional capacity [7-8].

So, complementary effects (cardiac by pace-maker and peripheral by training may be effective to optimize symptomatic improvements.

AIM OF THE STUDY
The aim of our pilot study was to detect additional improvement in exercise capacity after training in patients who underwent bi-ventricular pacing for symptomatic heart failure despite optimised drug treatment.

METHODS
For this purpose, we evaluated exercise tolerance using a cardiopulmonary exercise test, before implantation, just after pacing and after a relatively short training program.

Selection of patients for CRT included not only electrical conduction abnormalities (with a QRS duration greater than 140 milliseconds), but also echo Doppler inter and intra ventricular mechanical asynchrony.
We included 8 patients (all men) referred to our cardiac rehabilitation centre. The mean age was sixty seven years. In six cases, aetiology of heart failure was ischemic and in two it was dilated cardiomyopathy. Patients were symptomatic before pace maker implantation, most of them in NYHA class four. The mean left ventricular ejection fraction was eighteen percent. All the patients were in sinus rhythm, patients with permanent atrial fibrillation were excluded.

All the patients were treated by ACE inhibitors and diuretics. Only fifty percent by beta blockers, Amiodarone and Spironolactone. Three patients were treated by anticoagulants and two by Digoxin.

Patients were implanted with a bi-ventricular pace maker, with a left ventricular lead placed in a left lateral vein across the coronary sinus. After implantation, the pace maker was programmed with an optimized AV delay according to left ventricular filling analysis by echocardiography (Figure 1).

Exercise test were performed in the same lab, on cyclo-ergometer using an initial workload of 30 watts and followed by a classical ramp protocol of ten watts per minute. Study parameters included: rest and maximal heart rate, rest and maximal systolic blood pressure, exercise duration, VO\textsubscript{2} and VE/VCO\textsubscript{2} at maximal exercise and at anaerobic threshold, and calculated values derived from those parameters (oxygen pulse and circulatory power). Circulatory power is defined as the product of systolic arterial pressure and VO\textsubscript{2}, and is a prognostic factor in heart failure patients [9].

All the training sessions were performed under telemetry monitoring. Exercise training program included resistance and endurance training; resistance training included work on separate muscles groups, using small free weights, 1 hour per day; endurance training included, after a ten min warm-up, rectangular cycling during 20 minutes a day, 5 times per week. The intensity of training was determined by the anaerobic threshold if possible or at 60% of peak VO\textsubscript{2}.

RESULTS
No adverse event was observed in those patients. Patients of this study underwent 18 sessions during 4 weeks by mean. The compliance evaluated as a ratio of number of sessions performed and proposed was relatively good: 90%. The results in exercise test before and after pacing and after training program are displayed in Figure 2.
Rest and maximal heart rate and systolic blood pressure values: we observed a non significant reduction in rest heart rate just after PM implantation, and after training. The chronotropic response to exercise was improved after pacing and after training, but the differences are not statistically significant. Rest systolic blood pressure increased after pacing and after training. Maximal systolic blood pressure increased significantly at the end of exercise program as compared to baseline.

After CRT and after exercise training patients improve their exercise duration and their maximal workload (Figure 3).

Changes in peak VO₂ expressed in ml/kg/min and in percentage of theoretical VO₂ (Figure 4): peak VO₂ increased from 9.5 to 13.2 ml/kg/min after pacing and to 14.6 ml/kg/min after training. This represents a 49 % increase, 38 % due to pacing and 11% due to training. Figure 5 shows an example of cardiopulmonary exercise tests in a 78 years old man. In this patient beta blockers were contra indicated, he was symptomatic and frequent acute heart failure episodes required hospitalizations. At baseline, peak VO₂ was 9.5 ml/kg/min. Ten days after pace maker implantation, the peak VO₂ increased to 11.5 ml/kg/min, and the patient reported...
symptomatic improvement. After 25 sessions of endurance training, peak VO$_2$ reached 80 % of normal range according age and weight.

Calculated values derived from a cardiopulmonary exercise test at the peak exercise demonstrated also an improvement after pacing and after exercise training (Figure 6).
VE/VCO₂ ratio at anaerobic threshold or its slope determine metabolic response to sub maximal exercise.

In this small population VE/VCO₂ at anaerobic threshold decreased from 50 at baseline to 45 after pacing and 37 after training (Figure 7). Decrease in VE/VCO₂ induced by training was statistically significant (p<0.05).

**DISCUSSION**

Our preliminary results confirm improvement of exercise tolerance after CRT in chronic heart failure. We showed an additional improvement after exercise training in this group of patients. This is may due to peripheral modifications (muscular, endothelial) [10-12] which enhanced cardiac effects of CRT (beneficial remodeling, cardiac output) [13,14]. Improvement in exercise duration and in workload are statistically significant only after combined therapy (CRT and exercise training). Cardiopulmonary response (VO₂), a more
The most important part of improvement in peak VO\textsubscript{2} seems to be due to CRT. However, exercise training adds a substantial improvement, specially for the most severe patients. The kinetics of the recovery in exercise tolerance after bi-ventricular pacing is unknown, and a similar recovery may be obtained without training. But, even in this case, exercise may shortened the time to recovery, and be beneficial for patients. Furthermore, exercise training is generally included in a cardiac rehabilitation program in which medical adaptations, counselling, education and secondary prevention may optimise the management of heart failure [15,16]. However, these preliminary results should be confirmed in a large randomized study designed to assess the effects of combined strategies. This study will compare results after CRT alone and after CRT followed by exercise training, and analyze specific effects of the two strategies.

**CONCLUSION**

In conclusion, Exercise training after cardiac resynchronization seems to provide additional improvement in effort tolerance in heart failure patients. This may be obtained by combined central and peripheral effects of the two non-pharmacological treatments.

**REFERENCES**

1. European Heart Failure Training Group: Experience from controlled trials of physical training training in chronic heart failure. Eur Heart J 1998;19:466-75