

External Counter Pulsation (ECP) Therapy as an Effective Treatment among Patients with Heart Failure Undergoing Cardiac Rehabilitation

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2. Key words

External Counter Pulsation;
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mum Oxygen Consumption;
Maximum Oxygen Pulse; Heart
Failure; Cardiac Rehabilitation

1. Abstract

1.1. Background

External counter pulsation (ECP) is a noninvasive procedure using lower limbs pressure cuffs to improve coronary artery blood flow and offload the heart. There is currently no data on the effects of ECP among patients undergoing cardiac rehabilitation (CR). This pilot study aims to determine whether ECP improves exercise capacity among patients with heart failure or post acute myocardial infarction undergoing cardiac rehabilitation.

1.2. Methods

This is a prospective randomised-controlled pilot study of the effect of ECP in patients with mild to moderate heart failure or post-acute myocardial infarction undergoing CR. Eligible patients were randomised at ratio of 1:1 to either combination of CR and ECP or CR only. All subjects received up to 16 sessions of conventional CR. For the combination arm, subjects received up to 16 one-hour sessions of one-hour ECP therapy following each CR session. All underwent baseline cardiopulmonary testing (CPET) and NT-Pro BNP determination and after completion of study.

1.3. Results

A total of 4 patients were enrolled in the study from June 2016 to Jan 2017. Two were randomised to combination arm and two into CR arm. Post treatment VO₂MAX improved 12 % in the combination arm (23.3±5.6 ml/min/kg from 20.8±5.3 ml/min/kg at baseline) compared to 5% in the CR arm (23.0±6.2 ml/min/kg from 21.9±2.3 ml/min/kg at baseline). There were no significant difference in the post treatment VO₂MAX between groups, p=0.97. There was a 16% increase in post treatment maximum oxygen pulse in the combination group (14.4±1.0 ml/beat from 12.4±0.5 ml/beat at baseline) compared to a 7.8% increase in the CR group (12.4±2.2 ml/beat from 11.5±1.4 ml/beat at baseline). Interestingly, NT proBNP level worsened post treatment in the combination group (447.5±563.6 pre treatment to 472.7±560.5 post treatment), whereas improved in the CR only group (950.5±522.9 pre treatment to 327.5±202.6 post treatment).

1.4. Conclusion

Cardiac Rehabilitation is known to improve exercise capacity among heart failure patients. ECP can further enhance maximum oxygen consumption and maximum oxygen pulse in patients with mild to moderate degree of heart failure or post myocardial infarction undergoing cardiac rehabilitation. More studies with larger numbers are needed to prove this benefit of ECP.

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2. Background

External counter pulsation (ECP) is a noninvasive procedure using lower limbs pressure cuffs to improve coronary artery blood flow and offload the heart. It imitates the hemodynamic outcome of an intra-aortic balloon pump which is an invasive method. ECP is inflated sequentially during diastolic phase of the cardiac cycle. This can effectively increase diastolic and coronary pressures and leads to improved coronary flow. Furthermore, rapid deflation of the cuffs can reduce systolic pressure in the aorta thus reducing the workload of the heart.

ECP has been shown to reduce angina symptoms and prolong time to exercise induced ischemia [1]. Moreover, ECP enhanced exercise capacity, NYHA classification and quality of life, in patients with mild to moderate heart failure [2].

There is currently no data on the effects of ECP among patients undergoing cardiac rehabilitation (CR). This pilot study aims to determine whether ECP improves exercise capacity among patients with mild to moderate heart failure or post myocardial infarction undergoing cardiac rehabilitation.

3. Methods

3.1. Study Design

This is a prospective randomised-controlled pilot study conducted at the CR department at the National Heart Center of Singapore. After providing informed consent, eligible patients were randomised at ratio of 1:1 to either combination of CR and ECP or CR only. For the combination arm, subjects received up to 16 one-hour sessions of CR together with one-hour ECP therapy following each CR session. For the CR arm, subjects received up to 16 one-hour sessions of CR only. All eligible patients underwent baseline cardiopulmonary testing (CPET) and NT-Pro BNP determination within two-weeks prior to initiation of ECP and within one-week after completion of study.

3.2. Aims

This study primarily aims to assess the benefits of ECP in the treatment of patients with mild to moderate heart failure or post myocardial infarction undergoing CR in terms of improvement in exercise capacity measured as peak VO₂ max and maximum oxygen pulse.

Apart from the primary aim, the study also intends to assess response of heart failure biomarker, NTproBNP in subjects undergoing ECP and CR as compare to the routine CR only.

3.3. Ecp

A standard ECP treatment course comprises 35 one-hour sessions over a seven-week period.¹ In our study, a shorter treatment course of ECP was chosen to enhance patient compliance and

minimize drop outs. The ECP sessions also take placed during the subjects scheduled CR session.

3.4. Study population

The study intend to enroll a total of 16 patients, with symptoms of mild to moderate heart failure and LVEF <40%, or patients with post-acute myocardial infarction in last 3 month, undergoing phase II cardiac rehab at the National Heart Centre of Singapore. These patients were randomised in the ratio of 1: 1 to either combination of CR and ECP therapy or the routine CR only. As pregnancy is a contraindication to ECP.

All patients undergoing phase II cardiac rehab were screened for possible enrolment in the study. Patients were approached by the study coordinator, investigators or staff to discuss trial participation. A copy of patient information sheet was provided to the patient to read and understand the study. Patients signed an informed consent if he/she keen to participate in the study. Patient case sheets were reviewed during the screening for verification of ejection fraction. Once a subject meets inclusion and exclusion criteria, he would be enrolled into the study.

4. Inclusion Criteria

The subject must meet all of the inclusion criteria to participate in this study:

- a) Age between 21- 80 years old
- b) Enrolment in phase II cardiac rehab
- c) Left ventricular systolic dysfunction (LVEF<40% by 2 Decho or Myocardial perfusion Imaging), or post-acute myocardial infarction within the last 3 months.
- d) Symptoms of heart failure NYHA Class I – II from ischemic and non-ischemic causes
- e) Able to provide informed consent

5. Exclusion Criteria

Subjects meeting any of the exclusion criteria were excluded from participation:

- a) acute decompensated heart failure, unstable angina pectoris, STsegment elevation. and non-ST elevation MI at the time of enrolment.
- b) Heart Failure NYHA Class III - IV
- c) active plan on revascularization or open heart surgery at the time of enrolment.
- d) Patients who have undergone any surgical procedure within 6 weeks from start of treatment
- e) Cardiac catheterization procedure within 6 weeks from

start of treatment

f) Patients in atrial fibrillation or any arrhythmia that could interfere with ECP inflation and deflation triggering

g) Deep vein thrombosis

h) Bleeding disorders

i) Uncorrected symptomatic moderate to severe mitral and aortic stenosis

j) Moderate to severe AR

k) Patients on dual chamber pacemaker/AICD

l) Severe hypertension

m) Presence of local infection or vasculitis of the extremities

n) Women of childbearing potential

For subject who randomised to combination arm (Cardiac Rehab follow by ECP therapy)

Patients received up to 16 one-hour sessions of ECP, following their routine rehab session. This was at least twice a week. Make up session was arranged for the subject in the event that he/she has missed the session but minimum required session of at least once a week in order to be continued in the study.

6. ECP Therapy

6.1. The ECP therapies were conducted using Renew TM NCP-4 Device

Three pressure cuffs similar to blood pressure cuffs were placed at the calves, thighs and hips. The cuffs inflate sequentially upward at the onset of diastole, and deflate rapidly and concurrently before the start of systole (**Figure 1**). The permissible level of pressure applied to the cuffs for each subject range between 150 mm Hg/ 3 PSI and 300/6 PSI mm Hg.

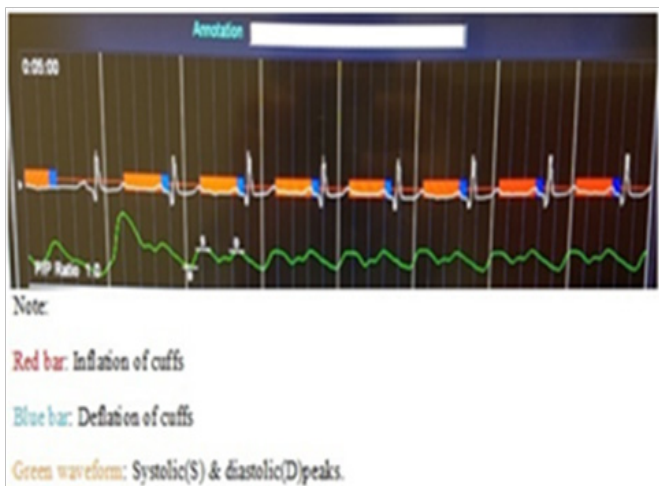


Figure 1: Three pressure cuffs similar to blood pressure cuffs were placed at the calves, thighs and hips. The cuffs inflate sequentially upward at the onset of diastole, and deflate rapidly and concurrently before the start of systole.

At the start, the skilled operator set a pressure level of 50mmHg/1 PSI on the participant. After 2 minutes, the operator raised the pressure level by 50mmHg/1 PSI to 100/2 PSI mmHg. The participant was asked if the pressure level is comfortable. In a similar manner, 2 minutes later, the operator checked on the participant before increasing the pressure level by an additional 50mmHg/1 PSI. This was continue up to the level which the participant feels uncomfortable, after which the operator lowered the pressure level by 50mmHg/1 PSI. The pressure level is then recorded and used for subsequent ECP sessions.

6.2. For subject randomised to CR arm only

Subjects attended the CR sessions. All underwent baseline cardiopulmonary testing (CPET) and NT-Pro BNP determination within two-weeks prior to initiation of ECP and within one -week after completion of study.

Make up session was arranged for the subject in the event that he/she has missed the session but minimum required session of at least once a week in order to be continued in the study.

7. Discontinuation Criteria

Participants who experience an event (MI, stroke, decompensated heart failure, hospitalization from any cause) and those who cannot tolerate with the session or expresses a desire to discontinue participation were withdrawn from the study.

If duration between two sessions was more than 7 calendar days, patient was considered to have dropped out from the study.

8. Ethics

The study has obtained approval from the ethics board, the Centralised institutional review board.

9. Statistical Analysis

Statistical analysis was performed using SPSS version21. The control and intervention arm were compared using independent T test and p value was reported.

10. Results

A total of 4 patients were enrolled in the study from June 2016 to Jan 2017. The study was only able to recruit 4 patients out of the intended 16. Two patients were randomised to the combination arm and two into the CR arm.

Mean age was 54.5±6.4 years and 47.0±5.7 years respectively between the combination and CR arm. All participants were male, mainly of Chinese race. Baseline characteristic BMI, NYHA class and baseline LVEF were comparable. All of them had history of ischemic heart disease and hyperlipidemia (Table 1).

Improvement in post treatment maximum oxygen consump-

tion (VO₂MAX) was observed in both the combination arm (23.3±5.6 ml/min/kg from 20.8±5.3 ml/min/kg at baseline) and CR arm (23.0±6.2 ml/min/kg from 21.9±2.3 ml/min/kg at baseline). The combination arm VO₂MAX improved 12% from baseline, whereas the CR arm improved 5%.

Similarly, post treatment maximum oxygen pulse were much increased compare to baseline in both the combination arm (14.4±1.0ml/beat from 12.4±0.5ml/beat at baseline) and CR arm (12.4±2.2ml/beat from 11.5±1.4ml/beat at baseline). There was a 16% increased from baseline in the combination group compare to 7.8% increased in the CR group.

NT proBNP increased 5.6% from 447.5±563.6 pre treatment to 472.7±560.5 post treatment in the combination group. In contrary to this, the CR group demonstrated a marked decrease, around 65% in NT-pro BNP level from 950.5±522.9 to 327.5±202.6.

11. Discussion

This pilot study demonstrated that ECP further improves exercise capacity among patients with heart failure or post acute myocardial infarction undergoing cardiac rehabilitation.

Post treatment maximum oxygen consumption (VO₂MAX) showed much improvement in both the combination arm and CR arm with the combination arm improving 12% from baseline, and CR arm 5%. Maximal oxygen consumption reflects the cardio respiratory fitness and is a key factor determining a person cardiovascular stamina during extended exercise. VO₂MAX can be applied as a robust predictor of cardiac events, much better than the prediction by the usual recognized risk factors.³ CR alone is known to improve VO₂MAX, the addition of ECP into CR combination confers a greater VO₂max in our study. However, in another trial which randomized subjects with mild-to-moderate symptoms of HF to either ECP or without ECP, no disparity found between the intervention and control groups change in peak VO₂ [2].

Post treatment maximum oxygen pulse were also much increased compare to baseline in both the combination arm and CR arm. There was a 16% increased from baseline in the combination group compare to 7.8% increased in the CR group. Maximal oxygen pulse depicts the stroke volume response to exercise [3]. Oxygen pulse rises nearly linearly till the point it reaches the greatest value in normal circumstances, conversely in those with impaired left ventricular ejection fraction, oxygen pulse only rises to a small degree with progressive workloads [4]. Studies demonstrated the possible utility of maximum oxygen pulse in forecasting prognosis for individuals with heart failure with reduced ejection fraction [5]. As far as we know, no studies have reported the increase in maximum oxygen pulse with the use of

ECP in individuals undergoing CR.

NT pro BNP increased 5.6% after treatment in the combination group. In contrary to this, the CR group demonstrated a marked decrease, around 65% in NT-pro BNP level post treatment. A slight increased in NT-pro BNP level could possibly be due to increase venous return as a result of ECP lower limb compressions in patients with reduced left ventricular ejection fraction. This had led to higher number of decompensated heart failure as a consequence of rise in preload. This was previously reported in earlier studies.⁶ However, in another prospective ECP study performed on ischemic heart disease and chronic Heart failure patients, remarkable improvement in post-intervention BNP levels, NYHA class, left ventricular ejection fraction have been noted [7].

12. Limitations

Small numbers of participants in this pilot study posed a limitation. With larger numbers, results are likely to reach significance in view of the large treatment effect.

13. Conclusion

Cardiac Rehabilitation is known to improve exercise capacity among mild to moderate degree heart failure and ischemic heart disease patients. ECP can further enhanced maximum oxygen consumption and maximum oxygen pulse in these patients. More studies with larger numbers are needed to prove this benefit of ECP.

14. Acknowledgement

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