بسم الله الرحمن الرحيم

ANTIREMODLING AND PROGNOSTIC VALUES OF INSPIRATORY MUSCLE TRAINING IN CHRONIC HEART FAILURE PATIENTS

اعاده الهيكله والقيم التنبؤيه لتدريب عضلات الشهيق في مرضي فشل القلب المزمن


Acknowledgment

First of all, I would like to kneel thanking for ALLAH, the most beneficial that enable me to conduct this work.

I would like to thank **Prof. Dr. Zeinab Mohammed Helmy** chairman of Physical Therapy departement for Cardiovascular/ Respiratory Disorder and Geriatrics, Faculty of Physical Therapy, Cairo University, for her great support and advice that gave me the confidence and encouragement to start and complete this study as the best as I could do.

I would like to thank **Prof. Dr. Sherin Hassan Mohammed**, Vice Dean for education and students affairs, Faculty of Physical Therapy Beni Suef University for her expertise, assistance and encouragement. I appreciated the time and thoughtful consideration she provided in guiding and reviewing this work.

I would like to thank the other member of my committee **Prof. Dr. Bassem Sobhy Ibrahim** Consultant of Cardiology Director of heart failure unit National heart institute for his assistance, feedback and clinical suggestion that helping me to complete the thesis.

Warmest and deep thanks to **Prof. Dr. Randa Abd El Aziz Mohammed** Consultant of Clinical Pathology National Heart Institute, for providing support to complete the practice parts of this thesis.

My deepest thanks and prayers for the late Prof. **Dr. Mostafa H. Gad** my mentor and whose priceless efforts helped me to bring this work to life.

Finally I cannot forget to thank physical therapists at National Heart Institute, patients and subjects who gave me their support, time and effort voluntarily.


To my family,
my husband
and my sons.

Introduction

The most common complaints are exercise intolerance, dyspnea, and fatigue in patients with heart failure (HF) . Mechanisms are multifactorial and interacting each other in patients with HF . Dominant catabolic process caused by left ventricular impairment, leads to respiratory and skeletal muscle myopathy. Increased ergoreflex activation caused by myopathy results in exercise intolerance. (**Bosnak-Guclu et al .,2011).**

The progression of HF is associated with left ventricular remodeling. Cardiac remodeling involves molecular, cellular, and interstitial changes that manifest clinically as changes in size, shape, and function of the heart after injury or stress stimulation.. This process is usually associated with a continuous decline in ejection fraction (EF). .(**Kerkhof .,2015).**

(Haykowsky et al., 2007) and **(Zwisler et al ., 2008)** concluded that aerobic exercise training reverses ventricular remodeling in clinically stable individuals with HF. Long-term moderate exercise training has been shown to induce reverse remodeling in patients with stable CHF , and this was associated with significant increases in work capacity and peak oxygen uptake.

Selective IMT is effective in patients with CHF. Mechanisms underlying these beneficial effects of IMT included attenuated metaboreflex and improved ventilatory efficiency during incremental exercise. It is proposed that the metabolic products accumulated from fatiguing respiratory muscle contraction could increase sympathetic vasoconstriction activity (the inspiratory muscle metaboreflex), and the attenuation of the metaboreflex could then improve blood flow redistribution to skeletal muscles in the body, thereby delaying the time to fatigue and decreasing workload on the heart . IMT may decrease work of breathing, metabolic costs of breathing and perception of nervous system's perception of inspiratory output, so that dyspnea and exercise capacity would be improved. **(Wong et al .,2011).**

Purpose of the study

The purpose of this study was to investigate the effect of inspiratory muscle training (IMT) on left ventricular remodeling , improving functional capacity (CPX parameters), MIP , prognostic biomarkers (High sensitive C-reactive protein (Hs-CRP)) and Quality of Life (Minnesota Living With Heart Failure Questionnaire) in chronic heart failure patients

Significance of the study:

Now it is estimated that 5 million people in the USA live with HF, and the cost of HF is now estimated at US$56 billion a year, 70% of which is due to hospitalization. **(Chen et al ., 2010).**

.

Whole-body aerobic exercise training is currently indicated for patients with HF for improvement in functional capacity and possibly for reduction in mortality, it is not known whether the beneficial effects of IMT would further improve the functional capacity of patients with HF who perform aerobic exercise regularly. the two programs may result in complementary effects because IMT improves exercise capacity in HF by mechanisms that are probably different from those of aerobic exercise ,it is conceivable that IMT could have additional effects to aerobic exercise .


Research
Methodology

Subjects

Forty eligible male patients with chronic heart failure secondary to ischemic heart disease and ten patients had dropped out from the study for reasons due to time constraints , work commitments and could not be contact. Because of this, the study included only thirty patients. They were diagnosed by echocardiography and coronary angiography. They were selected from National Heart Institute, heart failure outpatient Clinic and their ages ranged from 50-60 years old. This study was started from March 2013 till July 2014 .The patients had been clinically and medically stable for more than three months prior to the onset of study period

Patients were assigned into two main groups

(study group):

Fifteen patients participated in a supervised comprehensive CR rehabilitation program

A).Aerobic training: in form of interval aerobic training.
B) Strengthening exercise: Resistance training.
C) Inspiratory muscle trainer

(control group):

Fifteen patients participated in comprehensive training

sham unloadd IMT, interval aerobic and resistance training

Patients were selected according to the following criteria:

- The diagnosis of ischemic cardiomyopathy

They were on optimal medical therapy with no major changes in treatment regimen during the study.

Left ventricular end-diastolic dimension > 5.5cm and end-systolic diameter > 4.5cm.

Fractional shortening < 25% and ejection fraction < 40%.

Sinus rhythm.
New York Heart Association (NYHA) class II-III.
Blood pressure and diabetes should be controlled

Exclusion Criteria:

- Chronic heart failure due to other causes
- Severe functional mitral regurgitation (MR).
- History of pulmonary disease (chronic obstructive lung disease, moderate to severe pulmonary hypertension).
- recent acute coronary syndrome or revascularization (3 months).
- logistic problems to attend regular exercise training sessions;
- exercise limited by angina or peripheral arterial occlusive disease;
- Cerebrovascular or musculoskeletal disease preventing exercise testing or training.
- Poorly controlled or exercise-induced cardiac arrhythmias.

INSTRUMENTATION

A- Evaluation Instrumentation

- **Pulsed Doppler echocardiography :**

-Oxycon pro (ER-900, Ergoline, Jaeger, Würzburg, Germany) cardiopulmonary exercise test unit with 12 channel ECG, gas analyzer to measure maximal heart rate and resting heart rate and $EqCO_2$ at anaerobic threshold,

-Mercurial sphygmomanometer :

Free weights:

Maximum Inspiratory Pressure meter:

Minnesota Living With Heart Failure Questionnaire(MLWHF):

B- Exercise training Instrumentation:

- Electronic Bicycle ergometer:
- ElectronicTreadmaill
- ECG telemetry:
- Inspiratory muscle trainer:
-Free weights as sand bags

B- Exercise training Instrumentation:

Procedures

Evaluation procedures

Cardiopulmonary exercise testing (CPET):

After a period of rest to allow the patient to become familiar with the equipment and the bicycle, the resting HR, blood Pressure (BP), , ECG and gas exchange values were recorded. Then work rate was increased by 10 to 20 W. min-1 by the computer, increasing the resistance of the pedals (bicycle) while the patient maintaineds a constant pedaling rate (bicycle). .All patients were subjected to a submaximal symptom limited exercise testing on stationary ergometry of the cardiopulmonary exercise test before and after training programs according to Ramp protocol. **Chatterjee et al., 2013).**

Evaluation procedures

-Echocardiographic evaluation :
M -mode measurements included LVIDs (left ventricular internal dimensions during systole) , and Ejection fraction (EF%) was calculated using two dimension view (2D). - Echocardiography data were collected, before and after the period of six months for both groups.

-One repetition maximum test:
to assess Maximum voluntary contraction (MVC) which used to determine the intensity of resisted exercise training for both groups. Each patient was asked to contract his muscles groups for right and left sides.

-Maximum inspiratory pressure test:
Was performed for both patients groups for assessing inspiratory muscle strength pre and post the training programme and to identify the training load of the inspiratory muscle trainer.

-Minnesota Living With Heart Failure Questionnaire:

-laboratory investigation:
In both groups, blood samples were drawn before and after completion of the study for measurement of HS- CRP. Serums was kept frozen at –20ºC.

Treatment procedures

Both groups of patients performed a supervised individual training program based on the result of cardiopulmonary exercise testing, they were trained using heart rate range or reserve method (**Karvonen's method**); training heart rate ($THR=HR_{rest} + (HR_{max} – HR_{res})$ 55-85% (**Kennedy et al .,2012).**

The session began with warming up exercise in form of active stretching exercise and quite walking for 5 minutes. The study group patients performed the breathing exercise with the IMT for 7 sets every set 3 minutes with enough resting period in between sets (1 min) . Total time of training 28 minutes, three times per week for six months. inspiratory load at 30% of PImax , Training loads were adjusted to maintain 30% of the PImax**(Winkelmann et al, 2009).**

Treatment procedures

Patients in control group perform combined exercise training (aerobic and resistive training) plus sham IMT unloaded to allow motivation to this group of patients . **(Adamopoulos et al ., 2014)**

Both groups of patients conducted to the conditioning phase of each session contained circuit training including a combination of cycle ergometer, treadmill walking and resistive weight training**).** Each session started with measuring blood pressure and telemetry ECG to observe and monitor ECG trace consequently during the session .an exercise circuit consisted of eight resistive exercises for different eight large muscle groups (shoulder flexors and extensors, elbow flexors and extensors, hip flexors and extensors and knee flexors and extensors) every alternated with seven aerobic exercise (cycling and treadmill) stations in-between resistive exercise. Each resisted exercise was performed for 45 s, with 15-s intervals, signaled by a timer when apply in the beginning 1 set of 15 repetations (every repletion was taken 3 sec) total time of resisted exercise 8 minutes. (**Mandic et al, 2009).**

Exercise procedures

Resistive training intensity commenced at 40-50% of pre-training MVC for the upper limb, as determined from initial 1RM strength tests (the average weights clinically were 2 kg for the muscles groups of the upper limb and 3 kg for the muscles groups of the lower limbs), and50-60% for the lower limb. **(Diab ., 2013)**

Cycle ergometer and treadmill walking commenced at 55-65% of the maximum HR observed during the initial cardiopulmonary exercise test and increased to 80-85% by end of the programme. Every aerobic exercise (cycling and treadmill) stations in-between resistive exercise completed in 7 minutes so the total time of aerobic training lasts for 49 minutes .(**Mandic et al, 2009)**

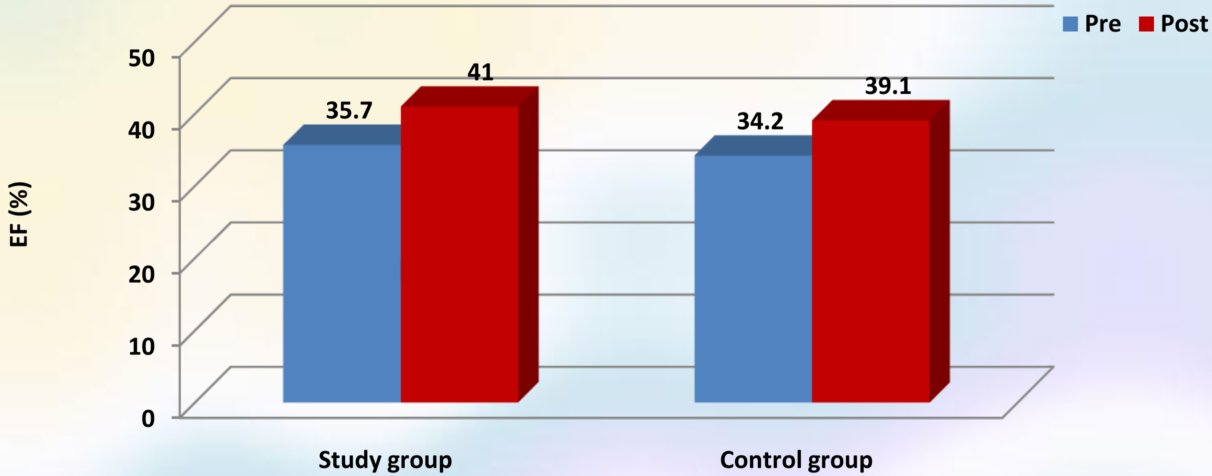
Cooling down was applied for all patients after finishing the rehabilitation session for 5 minutes.

Exercise procedures

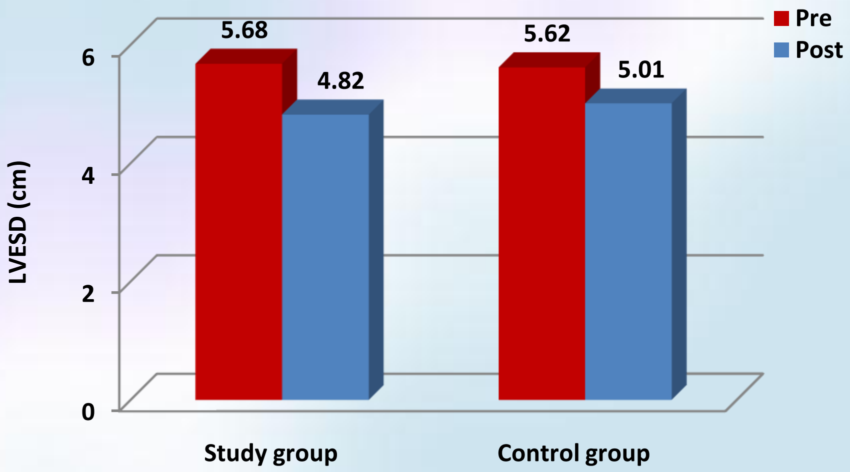

RESULTS
Straight Ahead

Effect of training on antiremodling :

a) Effect of training on EF%:

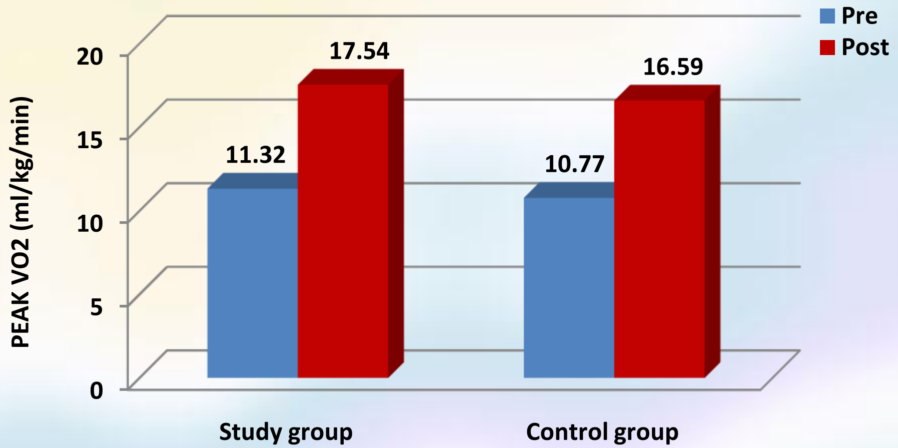


b) Effect of training on LVESD:

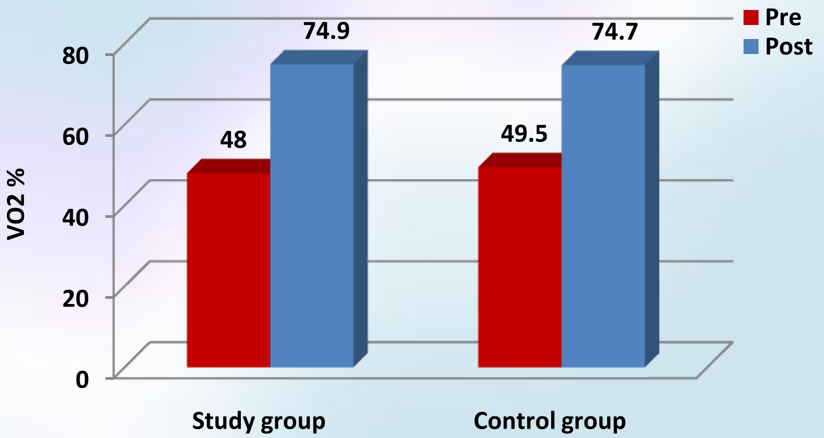


2-**Effect of training on functional capacity :**

a) Effect of training on peak VO2:

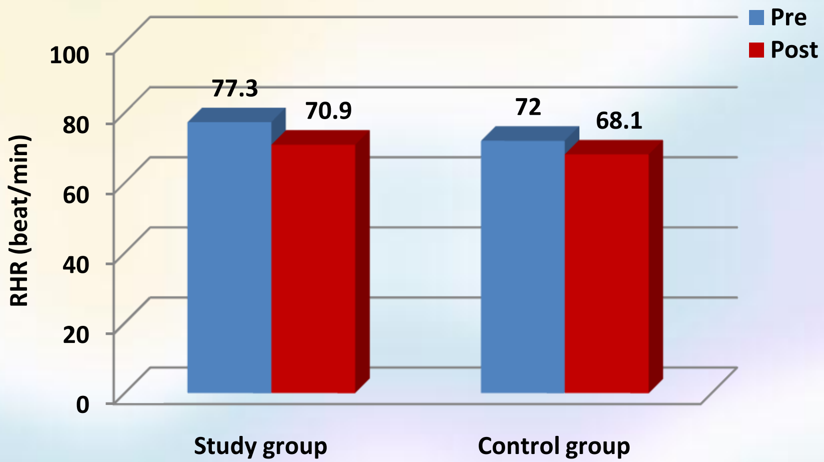


b) Effect of training on VO2%:

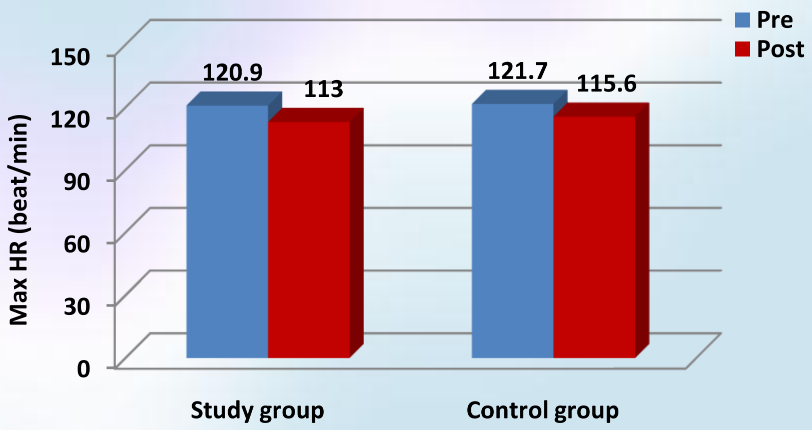


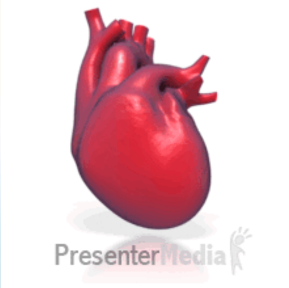
2-**Effect of training on functional capacity :**

c) Effect of training on RHR:



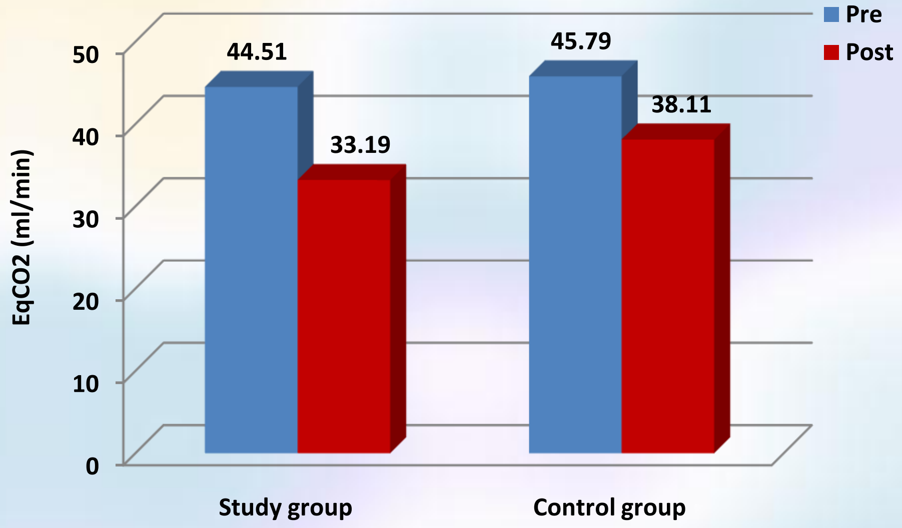
d- Effect of training on Max HR:



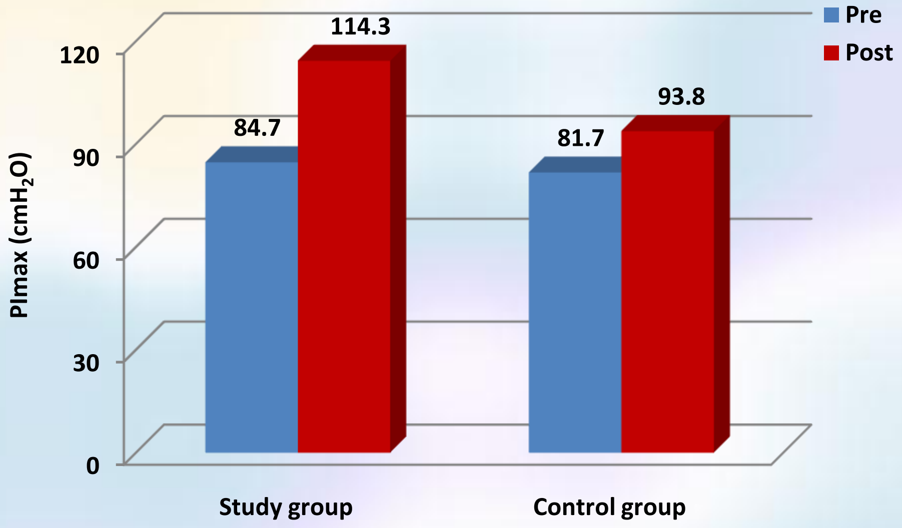


2-**Effect of training on functional capacity :**

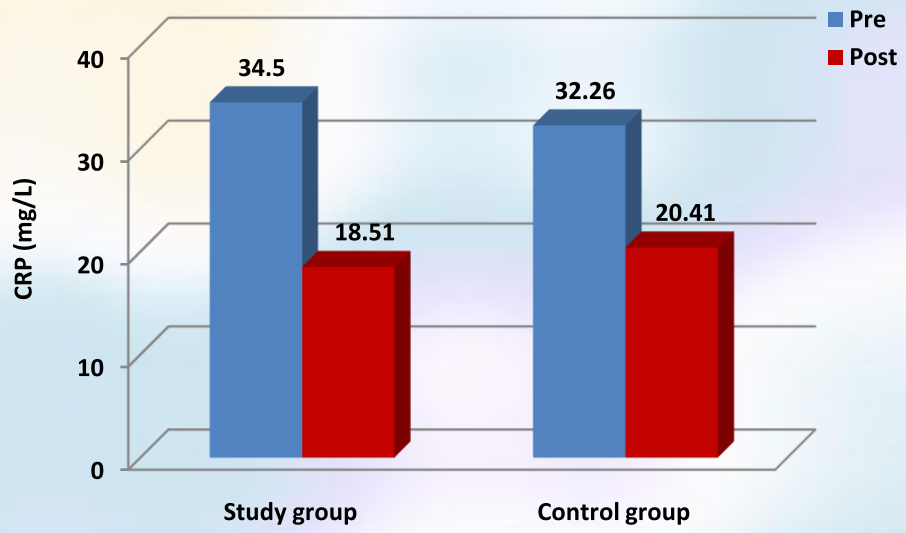
e)- Effect of training on EqCO2:



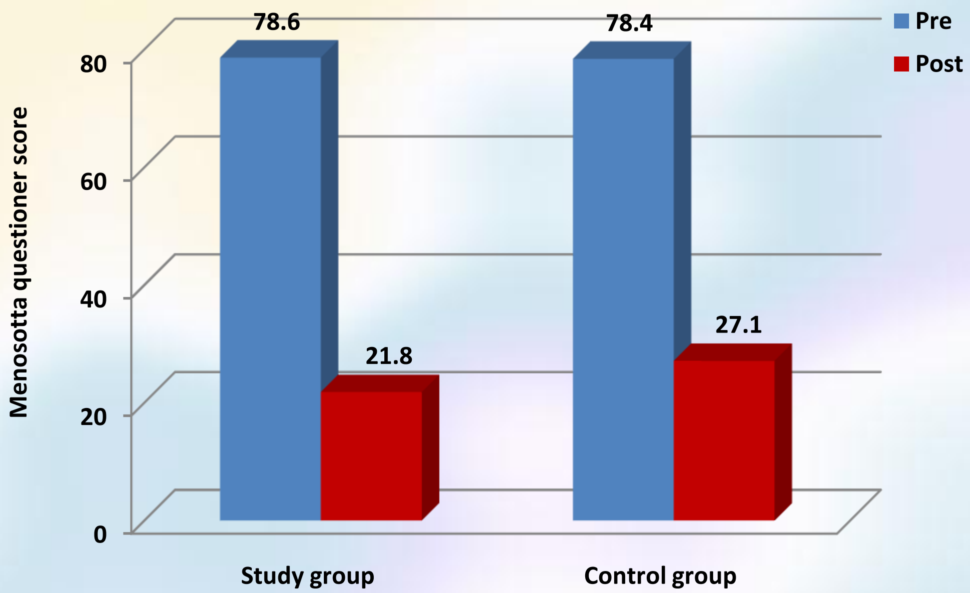
3- Effect of training onPImax:



4- Effect of training on CRP:



5- Effect of training on Minnesota living with heart failure :-



.

DISCUSSION

DISCUSSION

With regard to the comparison between the two groups this study showed that both groups were similar in improving cardiopulmonary parameters as peak oxygen consumption (vo2max), peak VO_2 as a percentage of the predicted $VO_{2\ max}$ (vo2%) , resting heart rate (RHR)) and maximal heart rate (MHR) , prognostic biomarker (HS CRP) and Quality of life (QoL) , and so that there was no significant difference between both groups in this variables.

DISCUSSION

While in ventilatory parameters of exercise tolerance indice and PI max there was signifant difference in ventilatory equivalent of CO_2 at anaerobic threshold (EqCO_2 at AT, ml/min) and PI max in favor to study group

For Echocardiogrphic, there was significant improvement of resting systolic functions through reduction of LVISD and , increase in EF% in study group and control group and there was no statistical difference between both groups.

DISCUSSION

The significant increase of peak VO_2 seen in both groups may be attributed to improved central adaptations (improved FS%, EF% and reduction of LVIDs, there was a significant proportional correlation between relative changes in EF% and peak VO_2) along with peripheral adaptations (improved cardiac output redistribution, improved endothelial function, increased capacity of the muscles to extract oxygen owing to an increase in capillary density, providing enough time for oxygen diffusion which is facilitated by the increase in the number of mitochondria). It may also be partially due to improvement of autonomic balance. (Haykowsky *et al.* 2012).

DISCUSSION

Exercise training by improving diastolic and systolic dysfunction can contribute to an increase in cardiac output and oxygen supply to the skeletal muscles. The greater peripheral oxygen availability results in an increased oxidative capacity of exercised skeletal muscles, which both delays the onset of anaerobic threshold and improves exercise capacity. Even patients with severe depression of left ventricular performance, who are otherwise confined to physical inactivity, may benefit from a training-induced increase in aerobic capacity of peripheral muscle. Therefore, it appears prudent to offer a carefully and individually tailored program of physical activity to patients with compromised cardiac performance to maintain peripheral muscle function and prevent the deleterious effects of deconditioning **(Mehani .,2007)**.

DISCUSSION

ET intervenes in the various stages of the inflammatory process in patients with CHF and exerts a favorable control of remodeling by reducing the major circulating proinflammatory cytokines and their soluble receptors (**Adamopoulos et al .,2002)**

Mechanisms underlying these beneficial effects of IMT included attenuated metaboreflex, improved ventilatory efficiency, and lower ventilatory oscillations during incremental exercise. It is proposed that the metabolic products accumulated from fatiguing respiratory muscle contraction could increase sympathetic vasoconstriction activity (the inspiratory muscle metaboreflex), and the attenuation of the metaboreflex could then improve blood flow redistribution to skeletal muscles in the body, thereby delaying the time to fatigue and decreasing workload on the heart. The effect of IMT on respiratory muscle strength in patients with stable heart failure is evident**. .(Lin et al .,2012).**

DISCUSSION

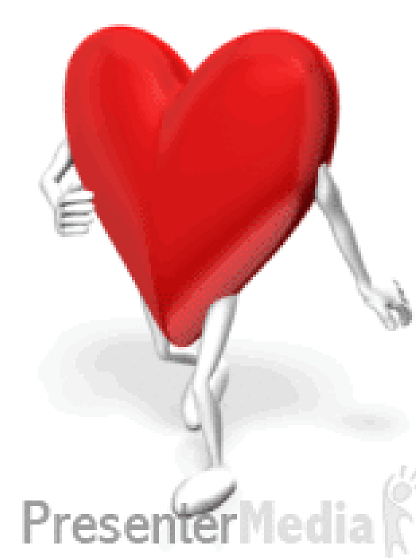
The improved ventilatory efficiency seen in the training group may be attributed to improvement of EF% and cardiac output as there was significant inverse correlation between relative changes % in EF% and $EqCO_2$ at AT in the training group. (**Adamopoulos et al .,2014).**

Increased exercise performance after IMT could be due to a higher consumption of oxygen by the respiratory muscles. There was a trend for an increase in VO2 at AT, thus a systemic aerobic effect on both respiratory and/or other muscles cannot be excluded. (**Laoutaris et al .,2012**)

DISCUSSION

The results obtained in the present study suggested that cardiac rehabilitation programme consisted of inspiratory muscle traininer , resisted training and aerobic exercise improves maximum inspiratory pressure and inspiratory muscle strength that improve one of the most worse symptoms of chronic heart failure which is dyspnea and sense of breathlessness. These results suggested that aerobic and resisted exercises and inspiratory muscle training should be part in cardiac rehabilitation program for patients with chronic heart failure for successful cardiac rehabilitation in CHF.


Conclusion


PresenterMedia

Conclusions

The results of this study confirmed the following conclusion;

- The additional of inspiratory muscle training to cardiac rehabilitation programme is very effective physical therapy modalities for improving ventilatory parameters of cardiopulmonary exercise test and maximal inspiratory pressure which lead to improvement in dyspnea and breathlessness sensation in chronic heart failure patients.
- So inspiratory muscle training should be involved in the physiotherapy program for chronic heart failure patients.


Recommendation

Recommendations

- The results of this study consider the following recommendation:
- Inspiratory muscle training device should be a part of a cardiac rehabilitation program in all sections of physiotherapy hospitals and institutes who work in the rehabilitation of heart patients.
- Increasing the size of the sample to help get the most accurate results of the study.
- Further researches are needed to compare the high and low resistance of inspiratory muscle training device.
- Further studies are needed to differentiate between the use of inspiratory muscle training device on chronic heart failure males and females.
- Recommended evaluation of the effect of home use inspiratory muscle training in chronic heart faliure.
- Further studies are needed to investigate effect of combined exercise training and IMT on diastolic dysfunction .


Thank You!


Thank You!