

## OBESITY IN CHRONIC HEART FAILURE IS ASSOCIATED WITH REDUCED EXERCISE HYPERPNEIC RESPONSE

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### Contribution

All the authors contributed significantly to the research that resulted in the submitted manuscript.

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### ABSTRACT

**Objective:** Patients with chronic heart failure manifest an inappropriate elevation in their ventilatory response to treadmill exercise. Increased body mass index may restrict the ventilatory response to exercise, but the relationship between obesity and ventilatory response in chronic heart failure (CHF) has not been well characterised.

**Methodology:** We analysed data from 246 consecutive patients with chronic heart failure, who underwent cardiopulmonary exercise testing.

Exercise testing was performed on a treadmill according to the modified Bruce protocol, with continuous on-line respiratory gas. The slope of the relationship between ventilation (VE) and CO<sub>2</sub> production (VCO<sub>2</sub>) was determined by computerised graphical analysis (VE/VCO<sub>2</sub> slope).

**Results:** Patients were aged 60±10.7 years (mean±SD), and had mean left ventricular ejection fraction 27.7±13.9%, peak oxygen uptake 17.2±6.2 ml/min/kg. The subjects had mean body mass index (BMI) of 26.6±4.3 kg/m<sup>2</sup> (mean±SD), and VE/VCO<sub>2</sub> slope values of 37.3±10.2. The correlation between BMI and VE/VCO<sub>2</sub> slope was highly significant and inverse -0.455 (p<0.0001). When the patients were divided into categories according to BMI (<22, 22-30, >30), there were differences between the mean VE/VCO<sub>2</sub> slopes of each group, which was significant for each pair of comparisons.

**Conclusion:** This study suggests that patients with normal or mildly increased BMI show a relatively greater hyperpneic response to exercise. In contrast, patients with marked obesity (BMI>30) demonstrate a much milder hyperpneic response to exercise.

**Keywords:** Obesity, Heart failure, Exercise

## INTRODUCTION:

Chronic heart failure (CHF) is associated with a high mortality and morbidity. Obesity is a risk factor for cardiovascular mortality and is frequently associated with coronary artery disease and CHF.<sup>1-3</sup> In the Framingham Heart Study, obesity was found to be an independent predictor of coronary heart disease, congestive heart failure, stroke, and cardiovascular death.<sup>4</sup> The precise role of increased body mass index as an independent cardiac risk factor and its effect on cardiac function remains unclear. It is appreciated that obesity is associated with a marked increase in blood volume and cardiac output as a result of a physiological adaptation to increased blood flow to adipose tissue associated with elevated oxygen consumption. Numerous reports have described patients with obesity, somnolence, CHF and acute respiratory failure.<sup>5,6</sup> Another study on obesity described a series of patients with obesity, hypoventilation and reduced ventilatory responses to hypoxia as well as to CO<sub>2</sub>.<sup>7</sup> Exercising different body muscle groups generate different exercise responses. This may in part be due to the different size and bulk of the muscle groups. A difference in peak oxygen consumption was found between the genders in patients with chronic heart failure after adjustment for age, peak heart rate, peak respiratory exchange ratio, left ventricular ejection fraction, and etiology of heart failure. The difference in body composition i.e.; percent body fat, was the only major factor for the difference in peak oxygen consumption and body composition depends on the age and fitness level of the patient.<sup>8,9</sup> Despite a considerable volume of work in obesity and chronic heart failure and different physiological and clinical parameters in this condition little has been reported estimating the effect of body mass index on the cardiopulmonary exercise testing in CHF patients. Patients with chronic heart failure demonstrate an inappropriate ventilatory response to exercise.<sup>10,11</sup> This manifests as increase in the slope of VE/VCO<sub>2</sub> and an increase in the work of breathing during exercise. Individuals with increased body mass index may show a different ventilatory response.

We therefore designed the present study to investigate the influence of BMI on ventilatory responses to cardiopulmonary exercise in patients with stable chronic heart failure.

## METHODOLOGY

Two hundred and forty-six consecutive patients with CHF who performed a cardiopulmonary exercise test in a tertiary referral centre were studied retrospectively. We excluded subjects with diabetes, lipid abnormalities, valvular heart disease and hypertension, and who were smokers. Patients were stable at the time of investigations. All these patients underwent cardiopulmonary exercise

testing on a treadmill. Maximal symptom limited cardiopulmonary exercise testing was performed on the treadmill using modified Bruce protocol.<sup>12,13</sup> During exercise, subjects breathed through a mouth piece and a 1-way valve attached to a mass spectrometer and calibrated pneumotachographs (AMIS 2000 system, Innovision, Odense, Denmark) every 10 seconds using the inert gas dilution technique.<sup>14</sup> This allowed on-line measurement of metabolic gas exchange and ventilation. The slope of the relationship between ventilation (VE) and CO<sub>2</sub> production (VCO<sub>2</sub>) was determined by computerised graphical analysis (VE/VCO<sub>2</sub> slope). Patients were grouped into three according to their BMI, group 1 consisted of patients with BMI of less than 22, group 2 consisted of patients with BMI ranging between 22-30, and group 3 consisted of patients with BMI of greater than 30.

The data are presented as mean standard deviation. Fisher's exact test was used to compare the three groups of the study population and significance was determined by ANOVA post hoc test. P values of less than 0.05 are considered to be statistically significant. Correlation between variables was determined by simple linear regression. Statview 5.0 (Abacus Concepts Inc. USA) for windows, a computer statistical package, was used to analyse the data.

## RESULTS

Base line characteristics are given in table 1. The total number of patients was 246. The mean age of the patients was 60±10.7 years. Patients having NYHA class I were 6% while 36% in NYHA class II, 46% in NYHA class III and 12% in NYHA IV. Table 2 shows the overall results obtained during exercise. Mean peak oxygen consumption was 17.2±6.1 ml/min/kg in all subjects. The mean VE/VCO<sub>2</sub> slope was 37.3±10.2. Mean left ventricular ejection fraction was 27.7±13.9%.

Figure 1 shows the relationship between body mass index and ventilatory response. VE/VCO<sub>2</sub> slope declines with the increasing BMI. There was an inverse relation between BMI and ventilatory response as shown by the regression line in the fig. 1 ( $r = -0.455$ ;  $p < 0.0001$ ) in chronic heart failure patients. When the patients were divided into categories according to BMI (<22, 22-30, >30), there were differences between the mean VE/VCO<sub>2</sub> slopes of each group as shown in fig.2. There is a graded decrease in the ventilatory response as there is increase in the BMI from group 1 to 2 and 3 (VE/VCO<sub>2</sub> slope from 48.5±12.9 to 37.6±9.6 and 31.9±5.2) respectively. When all the patients were divided into three groups and data were analysed according to the groups, there was no significant difference in total exercise time between the groups (Group 1; 7.0±3.6 min, group 2; 7.4±2.8 min, group 3; 6.6±2.2

**Table 1: Baseline characteristics**

Total number of patients	246
Mean Age	60±10.7 year
NYHA I	6%
NYHA II	36%
NYHA III	46%
NYHA IV	12%
Mean left ventricular ejection fraction	27.7±13.9%

NYAH- New York Heart Association

**Table 2: Results obtained during exercise**

Peak Oxygen consumption	246
Mean VE/VCO <sub>2</sub> slope of all patients	60±10.7 year
Correlation between BMI & VE/VCO <sub>2</sub> slope	r = -0.455 P= <0.0001
Mean VE/VCO <sub>2</sub> slope of individual groups	
Group 1	48.5±12.9
Group 2	37.6±9.6
Group 3	31.9±5.2

Figure 1: Relation between body mass index and degree of exercise hyperpnea

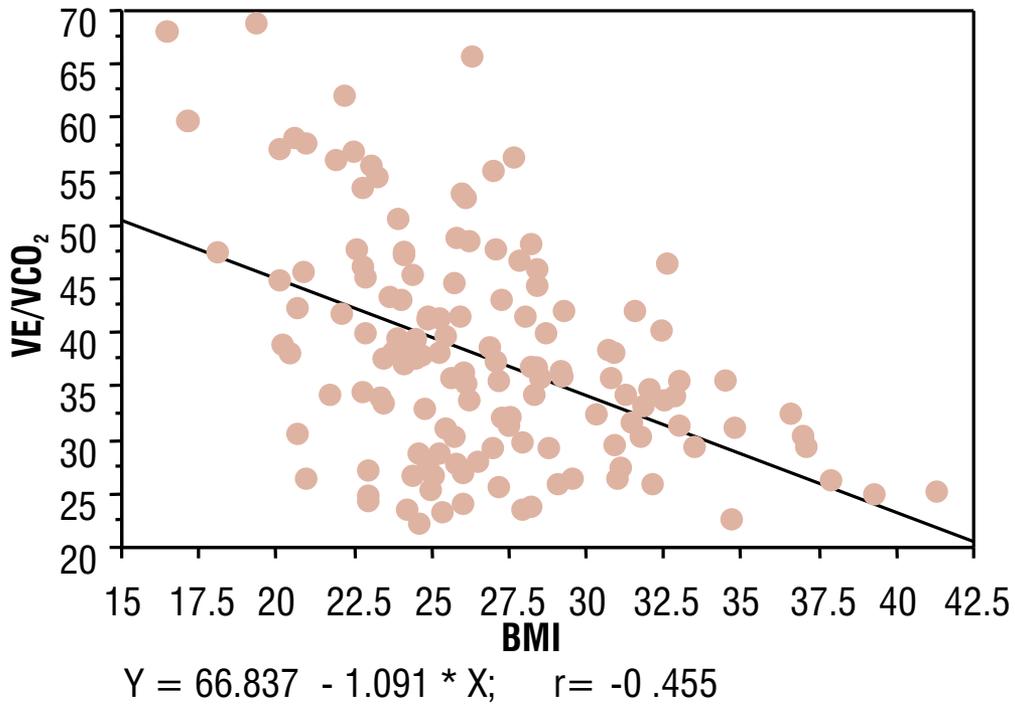
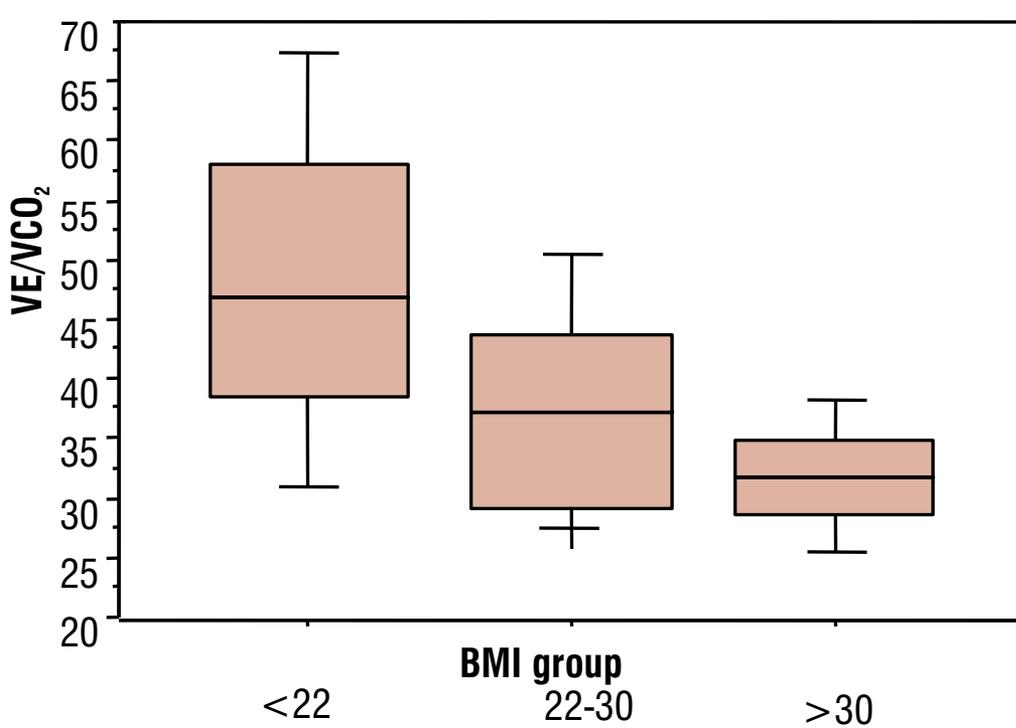


Figure 2: Relationship of VE/VO<sub>2</sub> slope and patients according to BMI groups



**Table 3: Results according to BMI Groups.**

Variables	Group1	Group2	Group3	p-values 1 & 2	p-values 2 & 3	p-values 1 & 3
LVEF %	25.9±13.1	26.5±12.9	31.9±12.9	0.89	0.17	0.07
VE / VCO <sub>2</sub> slope	48.5±12.9	37.6±9.6	31.9±5.2	<0.0001	>0.0001	0.0047
MVO <sub>2</sub>	14.4±5.0	17.5±6.3	15.7±4.6	0.053	0.4	0.14
AT	8.6±2.7	10.2±2.8	9.8±1.8	0.09	0.28	0.49
Exercise time	7.0±3.6	7.4±2.8	6.6±2.2	0.6	0.6	0.18

min with the p-values as shown in table 3). Difference between the groups in LVEF%, and AT was also not statistically significant. Peak oxygen consumption was lower in group 1 and higher in group 2 than group 3 but this difference is not significant statistically as shown in table 3. Subgroup analysis shows that there is significant difference in VE/VCO<sub>2</sub> slope in three groups.

## DISCUSSION

The present study shows that BMI of CHF patients is significantly related to their exercise hyperpneic response. There is an increase in the hyperpneic response as BMI decreases (an inverse correlation between VE/VCO<sub>2</sub> slope and BMI in CHF patients). Our results also show that patients with marked had demonstrated only a mildly hyperpneic response to exercise.

The clinical syndrome of heart failure is associated with a markedly impaired prognosis inspite of increasing number of new diagnostic techniques and therapeutic agents. Identification of patients with higher risk is important in selecting them for further specific management. Different parameters are now being used to identify moderate to high-risk patients, requiring different medications and/or other management procedures.

Among cardiopulmonary exercise test parameters, peak oxygen consumption, anaerobic threshold, exercise time and ventilatory response have all been recognised as important prognostic factors.

Peak oxygen consumption and its relation to weight and height of the patient have already been studied and now it is in use in cardiopulmonary exercise laboratories. Depending

on the age and level of physical fitness gender differences in peak oxygen consumption have been shown in a study.<sup>16</sup> Several mechanisms have been reported to explain the differences in the exercise tolerance. Women are usually less physically active than men and have lower fat-free mass, lower oxygen carrying capacity, and a smaller skeletal muscle fibre area.<sup>17</sup> Similar may be the case in BMI and VE/VCO<sub>2</sub> in chronic heart failure. Ventilatory response to exercise is also impaired in chronic heart failure. The relationship of VE/VCO<sub>2</sub> slope with body weight and height has not been studied before.

As the results of this study show, that ventilator response to exercise in chronic heart failure has important relationship with body mass index. Patients with increased BMI have reduced hyperpneic response to exercise and these patients may need more exercise training or may need a different management approach for their heart failures compared to patients with reduced BMI but higher hyperpneic response to exercise. The exact mechanism of this cannot be explained at this stage. Cardiac performance is reduced in obese patients despite increase in cardiac output. Increase in cardiac out put depends on oxygen consumption, which is also elevated and correlated with body mass index.<sup>15</sup> Also the pulmonary vascular resistance has been found to be higher in the obese patients with CHF.<sup>16</sup>

This is a retrospective study that requires prospective confirmation. It assessed a large group of patients with CHF and included all that fulfilled relatively broad criteria.

## CONCLUSION

In the conclusion, this study suggests that patients with

normal or mildly increased BMI show relatively more hyperpneic response to exercise. In contrast, patients with marked obesity (BMI>30) demonstrate a much milder hyperpneic response to exercise.

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