

# Endurance training improves oxygen uptake and endurance capacity in patients with...

[Health & Medicine](#)



**ASSIGN  
BUSTER**

## Introduction

The clinical value of cardiopulmonary exercise test (CPET) offers diagnostic and prognostic information in patients with cardiovascular disease, especially concerning the peak oxygen uptake (peakVO<sub>2</sub>) ( [1](#) - [4](#) ). A higher peakVO<sub>2</sub> is associated with lower cardiac mortality and morbidity in patients with cardiovascular disease ( [4](#) , [5](#) ). PeakVO<sub>2</sub> measured during CPET was found to objectively assess functional capacity in patients with valve disease ( [6](#) - [8](#) ).

Endurance training improves exercise capacity and quality of life in patients after myocardial infarction, coronary artery bypass graft surgery, and with heart failure ( [9](#) - [11](#) ) as well as after heart valve surgery ( [12](#) - [14](#) ). While exercise training is recommended in patients with moderate valve disease ( [15](#) - [18](#) ), the implication of training in patients with severe disease remains unclear.

The aim of this study was to investigate the effects of a 12 weeks supervised aerobic endurance training in patients with moderate to severe valve disease on the primary outcome peakVO<sub>2</sub> and secondary outcomes maximum working capacity and endurance capacity.

## Methods

### Study Design and Population

A total of 37 patients with asymptomatic moderate to severe aortic valve or moderate to severe mitral valve disease attended a cardiac referral center at Medical University of Vienna over a study period of 2.5 years. Of these 6 patients declined and 1 patient was unable to exercise. Major exclusion <https://assignbuster.com/endurance-training-improves-oxygen-uptake-and-endurance-capacity-in-patients-with-moderate-to-severe-valvular-disease/>

criteria included a history of exercise-induced syncope or ventricular arrhythmias, history of hypotensive response with exercise testing ( $> 20$  mm Hg decrease of systolic blood pressure from baseline blood pressure or an initial increase in systolic blood pressure followed by a decrease of systolic blood pressure  $> 20$  mmHg), clinical decompensation in the previous 3 months, acute exacerbation, uncontrolled hypertension, pregnancy, inability to exercise to non-cardiovascular limitations, unwillingness to refrain from competitive sports or endurance or strength training for the duration of the study.

Thirty patients were randomly allocated to either a training group receiving 12 weeks of moderate-intensity endurance training in addition to standard care (training group, TG) or to a non-exercising control group (standard care, SC). Random allocation was performed by blocking randomization using a web-based sequence generator (<http://www.randomization.com>). Before randomization and after the study period of 12 weeks all patients underwent an echocardiography, a symptom limited cardiopulmonary exercise test, an endurance exercise test at 80% intensity of peak  $\text{VO}_2$  and a blood test. The study received approval from the local research ethics committee (EC 311/2009) and all subjects gave written informed consent.

### **Echocardiographic Data**

All patients underwent an echocardiographic examination by an experienced echo cardiographer. Apical 4- and 2- chamber views were used for calculation of ventricular volumes and ejections fraction using Simpson's biplane formula. Quantification of mitral regurgitation severity was based on an integrative approach including valve morphology, color Doppler jet, cavity

<https://assignbuster.com/endurance-training-improves-oxygen-uptake-and-endurance-capacity-in-patients-with-moderate-to-severe-valvular-disease/>

sizes and left ventricular function. Mitral valve prolapse was defined as displacement of 1 or both leaflets by at least 2 mm below the mitral annulus level into the left atrium during systole. Flail mitral leaflet was defined as freely moving leaflet edge located in the left atrium. Systolic pulmonary artery pressure was derived from tricuspid regurgitation velocity. Aortic jet velocities were measured by continuous-wave Doppler using multiple imaging windows including the apical three and five chamber, right parasternal and suprasternal windows and taking care to record the highest velocity signal. Pressure gradients were estimated by the use of Bernoulli's equation, and aortic valve area was calculated with the continuity equation.

### **Cardiopulmonary Exercise Test (CPET)**

All patients underwent a symptom limited CPET on an Ergoline 800 bicycle (Sensormedics, United States) with respiratory gas-exchange analysis, using a step protocol with progressive increase in workload every minute according to a total exercise time between 8 and 12 min. The increment was adapted to the expected maximum working capacity. The CPET was performed within 3 weeks following echocardiographic examination. All patients took their medication as usual. Patients were encouraged to exercise until exhaustion. Blood pressure was measured every 2 min and continuous 12-lead electrocardiogram and oxygen saturation ( $SpO_2$ ) were recorded. Breath-by-breath minute ventilation, carbon dioxide production ( $VCO_2$ ) and oxygen uptake ( $VO_2$ ) were measured using Sensormedics 2900 Metabolic Measurement Cart. The respiratory exchange ratio (RER) was defined as  $VCO_2/VO_2$ , the oxygen pulse was calculated by  $VO_2/\text{heart rate}$  and the ventilatory equivalents of  $VO_2$  and  $VCO_2$  were measured.

### **Endurance Exercise Test at 80% Intensity of PeakVO<sub>2</sub>**

An endurance exercise test was performed at an intensity of 80% of peakVO<sub>2</sub>. After a resting period of 3 min and a warm up period of 1 min in order to achieve the exercise workload (80% of the individual peakVO<sub>2</sub>), the patients were pedaling between a pedaling rate of 60 and 80/min at the given workload. The time to exhaustion, which was determined as the inability to keep a pedaling rate over 60/min, was reported. During the test every 2 min the blood pressure was measured, and continuous 12-lead electrocardiogram and oxygen saturation (SpO<sub>2</sub>) were recorded during the test.

### **Endurance Training**

The training consisted of a 3 times per week endurance training at an intensity of 60% of peakVO<sub>2</sub>. The training intensity was controlled by heart rate monitor (Polar Watch M420) during each training session. One training per week was performed under supervision of a physician at an outpatient clinic on an ergometer, and the other 2 training sessions per week were home-based. Oxygen saturation, blood pressure and heart rate at rest were measured before every training session and noticed by the patient and controlled every week by the physician. The training duration was between 20 and 30 min per session depending on the maximum exercise capacity tested at baseline. Every 4 weeks the training duration was increased by 15 min per week, the training intensity was unchanged during the study period of 12 weeks.

### **Statistical Analysis**

Calculation of sample size was based on the primary efficacy endpoint, which was defined as the change in peakVO<sub>2</sub>/kg between baseline and 12 weeks

<https://assignbuster.com/endurance-training-improves-oxygen-uptake-and-endurance-capacity-in-patients-with-moderate-to-severe-valvular-disease/>

of exercise training. The null hypothesis to be assessed states that there is no difference in the changes of the peak  $\text{VO}_2$  /kg value between training group and usual care group. To detect a difference in peak  $\text{VO}_2$  /kg of 5 ml/min/kg with a standard deviation of 2 ml/kg, with a power of 80%, and a two-sided significance level of 5%, it was calculated a total sample size of 26 patients. A two-sided level of significance of  $\alpha = 0.05$  was used. Data were analyzed using the SPSS statistical package version 26 (IBM, New York, USA).

Normally distributed interval scaled data are presented as mean  $\pm$  standard deviation (SD), ordinal scaled data as median and quartiles (25th and 75th percentile). For categorical data number of cases (n) and valid percent were (%) are shown. Between group differences between training group and standard care in baseline characteristics are estimated by *t*-test for independent samples for homogenous variances (if homogeneity is given), *t*-tests for independent samples for heterogeneous variances (if homogeneity is not given), Mann-Whitney-U-tests for ordinal data and  $\chi^2$ -tests for categorical/dichotomous data. Effects of intervention (TG vs. SC) and time (baseline vs. 12 weeks) were analyzed simultaneous by General linear Models for Repeated Measurements (Analysis of Variances), while Box's-M-Test and Levene's Tests were used for proofing requirements of homogeneity of variances and covariances. Effects of time and independency between time and study group were examined via Wilk's  $\lambda$ . For additional examining changes within study groups, Student's *t*-test for dependent samples (for interval scaled data) and Mann-Whitney-U-test (for ordinal scaled data) were applied.

## Results

### Patients Characteristics

Patients characteristics are presented in [Table 1](#). Thirty patients with moderate to severe asymptomatic valvular disease were included in the study, 17 patients with moderate to severe asymptomatic aortic stenosis (15 patients with severe and 2 patients with moderate-to severe aortic stenosis). Thirteen patients with moderate to severe mitral regurgitation and preserved left ventricular function (5 patients with moderate and 8 patients with severe mitral regurgitation), defined as an ejection fraction of  $\geq 55$  and normal sinus rhythm. The mean age of the patients was  $44 \pm 13$  years, 17 (56.7%) were men. The baseline peak  $\text{VO}_2/\text{kg}$  was  $25.9 \pm 5.3$  ml/min/kg and maximum working capacity was  $152 \pm 37.8$  Watt. The mean endurance time at baseline was  $14 \pm 8$  min at 80% intensity of maximum workload. Medication remained unchanged during the study period. Eleven patients were on ACE (angiotensin converting enzyme) inhibitor or angiotensin II inhibitor therapy, 7 patients on betablocker therapy, 7 patients on statin, 4 patients on acetylsalicylic acid and 2 patients on metformin therapy. None of the patients had significant coronary heart disease.

#### TABLE 1

Baseline characteristics of study population.

After baseline assessment 16 patients were randomized to the training group, 9 patients with aortic stenosis, and 7 patients with mitral regurgitation. One of the patients with aortic stenosis had severe aortic

stenosis and aortic regurgitation. Fourteen patients were randomized to the standard care group, eight patients with severe aortic stenosis, 6 patients with mitral regurgitation. One of the patients with aortic stenosis had moderate aortic stenosis and aortic regurgitation. There were no significant differences for the baseline characteristics between both groups.

## Outcomes

### Primary Endpoint: Peak Oxygen Uptake (PeakVO<sub>2</sub>)

Primary endpoint was the change in peakVO<sub>2</sub> ml/min/kg. A significant effect of intervention and time (baseline vs. 12 weeks) for peakVO<sub>2</sub> ml/min/kg could be shown ( [Table 2](#) ). The peakVO<sub>2</sub> ml/min/kg was significantly higher in the TG after the study period of 12 weeks (peakVO<sub>2</sub> ml/min/kg 30. 4±6. 3 ml/min/kg) compared to the SC (peakVO<sub>2</sub> ml/min/kg 24. 7±3. 8 ml/min/kg  $p < 0. 007$ ). PeakVO<sub>2</sub> ml/min/kg increased in the TG from 27. 2±5. 9 to 30. 4±6. 3 ml/min/kg, mean increase relative to baseline +16. 5%,  $p < 0. 001$ , no significant changes between the peakVO<sub>2</sub> ml/min/kg could be seen in the SC (peakVO<sub>2</sub> ml/min/kg from 24. 6±4. 4 to 24. 7±3. 8 ml/min/kg,  $p = 0. 916$ ) after the 12-weeks study period ( [Table 2](#) ).

## TABLE 2

Parameters at baseline and after training period.

### Secondary Outcomes: Maximum Working Capacity, Endurance Capacity

Significant effects of intervention and time could be shown for maximum working capacity, Watt<sub>max</sub>/kg and endurance time ( [Table 2](#) ). Watt<sub>max</sub>



significantly improved in the training group after the 12 weeks ( $\text{Watt}_{\max} = 151.8 \pm 41.0$  Watt to  $171.2 \pm 49.7$  Watt,  $p < 0.001$ ) compared to the control group ( $\text{Watt}_{\max} = 152.9 \pm 35.6$  Watt to  $149.2 \pm 28.4$  Watt,  $p < 0.410$ ). In the training group the endurance capacity increased significantly from  $17.0 \pm 9.4$  s to  $32.8 \pm 16.8$  s ( $p < 0.004$ ) after the 12 weeks study period. No significant changes could be observed in the control group ( $10.8 \pm 6$  s to  $11.2 \pm 7.6$  s,  $p = 0.850$ ). The submaximal heart rate at 80% intensity of maximum capacity decreased after the 12 weeks in the training group from  $154.3366 \pm 14$  to  $141.8 \pm 20$  ( $p = 0.014$ ), no changes could be seen in the control group ( $158.8 \pm 20$  to  $159.3 \pm 24$ ,  $p = 0.442$ , [Table 2](#)). No significant changes could be seen concerning the NT-proBNP levels between both groups.

## Discussion

In this randomized controlled trial, we investigated the effect of a 12 week endurance training compared to standard care in patients with moderate to severe heart disease. Thereby we could show that the exercise training can increase the peak $\text{VO}_2$  and the endurance capacity significantly in these patients without adverse events over a training period of 12 weeks. Moreover, no significant worsening in echocardiography could be observed after the training period with no adverse events during the training sessions or significant changes of NT-proBNP levels. Our findings are in accordance with previous studies demonstrating that physical exercise training can improve peak $\text{VO}_2$  in patients with valvular heart disease after heart valve surgery ([11](#) - [14](#)). Whereas, there are strong recommendations concerning exercise training in mild to moderate valvular disease, there are no clear

<https://assignbuster.com/endurance-training-improves-oxygen-uptake-and-endurance-capacity-in-patients-with-moderate-to-severe-valvular-disease/>

recommendations regarding exercise training in asymptomatic moderate to severe valvular disease ( [15](#) - [19](#) ). In previous studies a relationship between peakVO<sub>2</sub> and the prognosis and mortality of patients with valvular heart disease has been reported ( [4](#) - [6](#) ). Defining the optimal timing of surgery in severe valvular heart disease is often difficult, but abnormal exercise response, such as symptoms during exercise, is one of the parameters which is taken into account for the surgery time point ( [7](#), [8](#) ). Improvement of peakVO<sub>2</sub> may therefore be strongly related to the prognosis of these patients and the course of the disease. While peakVO<sub>2</sub> describes the net limitation in exercise capacity, submaximal tests such as endurance tests at 80% of maximum capacity often correlated more with activities of daily livings.

To our knowledge, no previous trials have investigated the effects of an endurance training in patients with moderate to severe valvular heart disease concerning the peak VO<sub>2</sub> and submaximal endurance performance in patients with moderate to severe valvular disease.

Several limitations have to be noted, the most important was the low sample size. However, the trial was designed to be more explorative rather than confirmative. The study may result in further investigational studies with larger sample sizes. Further there might be selection bias as only highly selected individuals accept participation, which is common in training studies. Another possible limitation is the missing evaluation of quality of life, which could support the efficacy of endurance training, even though all the

patients were asymptomatic at baseline, during the stress test and the study period.

In summary, in this study it could be shown, that a home-based exercise training combined with a part-time supervision is safe and effective in these patients and can improve the peak  $\text{VO}_2$  and the endurance capacity significantly in patients with moderate to severe valvular disease.

### **Data Availability Statement**

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

### **Ethics Statement**

The studies involving human participants were reviewed and approved by Ethics committee Medical University of Vienna. The patients/participants provided their written informed consent to participate in this study.

### **Author's Note**

Peak oxygen uptake (peak $\text{VO}_2$ ) is one of the strongest predictors of survival in patients with valvular heart disease. In patients with mild to moderate disease endurance training is strongly recommended for prognosis and the course of the disease. Whereas, symptom limited cardiopulmonary exercise test is usually performed in patients with severe valvular heart disease there are still concerns how to exercise these patients. Symptoms like dyspnea on exertion are parameters taken into account for the surgery time point, but they may be non-specific and due to inactivity. Endurance training and

improvement of peakVO<sub>2</sub> in patients with severe valvular heart disease could not only improve the exercise capacity of these patients but can also provide more information about the functional status and prognosis.

## **Author Contributions**

KV designed the study, performed study examination, acquired data, analyzed data, and wrote the manuscript draft. DH performed study examination, acquired, and analyzed the data. RR, MS, SA, and HG performed study examination and acquired data. RR and HG designed the study. All listed authors read, revised, and finally approved the manuscript.

## **Funding**

This study received grant support from the Austrian Heart Research Fund/Austria.

## **Conflict of Interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## **References**

1. Arena R, Myers J, Williams MA, Gulati M, Kligfield P, Balady GJ, et al. Assessment of functional capacity in clinical and research settings: a scientific statement from the American Heart Association committee on exercise, rehabilitation and prevention of the council on clinical cardiology and the council on cardiovascular. *Circulation*. (2007) 116: 329–43. doi: 10.1161/CIRCULATIONAHA.106.184461

<https://assignbuster.com/endurance-training-improves-oxygen-uptake-and-endurance-capacity-in-patients-with-moderate-to-severe-valvular-disease/>

2. Balady GJ, Arena R, Sietsema K, Myers J, Coke L, Fletcher GF. Clinician' s guide to cardiopulmonary exercise testing in adults: a scientific statement from the American heart association. *Circulation*. (2010) 122: 191–225. doi: 10. 1161/CIR. 0b013e3181e52e69
3. Corra U, Agostoni PG, Anker SD, Coats AJS, Crespo Leiro MG, de Boer RA, et al. Role of CPET in clinical stratification in heart failure. A position paper from the committee on exercise physiology and training of the heart failure association of the European Society of Cardiology. *Eur J Heart Fail*. (2018) 20: 3–15. doi: 10. 1002/ejhf. 979
4. Snoek JA, Eijsvogels TMH, Van't Hof AWJ, Prescott E, Hopman MT, Kolkman E, et al. Impact of graded exercise program on VO<sub>2</sub> peak and survival in heart failure patients. *Med Sci Sports Exerc*. (2018) 50: 2185–91. doi: 10. 1249/MSS. 0000000000001688
5. Kraus WE, Powell KE, Haskell WL, Janz KF, Campbell WW, Jakicic JM, et al. Physical activity, all-cause and cardiovascular mortality and cardiovascular disease. *Med Sci Sports Exerc*. (2019) 51: 1270–81. doi: 10. 1249/MSS. 0000000000001939
6. Domanski O, Richardson M, Coisne A, Polge AS, Mouton S, Godart F, et al. Cardiopulmonary exercise testing is a better outcome predictor than exercise echocardiography in asymptomatic aortic stenosis. *Int J Cardiol*. (2017) 227: 908–14. doi: 10. 1016/j. ijcard. 2016. 10. 070
7. Dhoble A, Enriquez-Sarano M, Kopecky SI, Abdelmoneim SS, Cruz P, Thomas RJ, et al. Cardiopulmonary responses to exercise and its utility in <https://assignbuster.com/endurance-training-improves-oxygen-uptake-and-endurance-capacity-in-patients-with-moderate-to-severe-valvular-disease/>

patients with aortic stenosis. *Am J Cardiol.* (2014) 113: 1711–6. doi: 10.1016/j.amjcard.2014.02.027

8. Messika-Zeitoun D, Johnson BD, Nkomo V, Avierinos JF, Allison TG, Scott C, et al. Cardiopulmonary exercise testing determination of functional capacity in mitral regurgitation: physiologic and outcome implications. *J Am Coll Cardiol.* (2006) 47: 2521–7. doi: 10.1016/j.jacc.2006.02.043

9. Anderson L, Taylor RS. Cardiac rehabilitation for people with heart disease: an overview of Cochrane systematic reviews. *Int J Cardiol.* (2014) 177: 348–61. doi: 10.1016/j.ijcard.2014.10.011

10. Berg SK, Pedersen PU, Zwisler AD, Winkel P, Gluud C, Pedersen BD, et al. Comprehensive cardiac rehabilitation improves outcome for patients with implantable cardioverter defibrillator. Findings from the COPE-ICD randomized clinical trial. *Eur J Cardiol Nurs.* (2015) 14: 34–44. doi: 10.1177/1474515114521920

11. Prescott E, Eser P, Mikkelsen N, Eser P, Marcin T, Wilhelm M, et al. Cardiac rehabilitation in the elderly patients in eight rehabilitation units in western Europe: outcome data from the EU-CaRE multi-centre observational study. *Eur J Prev Cardiol.* (2020) 26: 1052–63. doi: 10.1177/2047487320903869

12. Ribeiro GS, Melo RD, Deresz LF, Dal Lago P, Pontes MR, Karsten M. Cardiac rehabilitation programme after transcatheter aortic valve implantation versus surgical aortic valve replacement: systemic review and

meta-analysis. *Eur J Prev Cardiol.* (2017) 24: 688–97. doi: 10.

1177/2047487316686442

13. Sibilitz KL, Berg SK, Tang LH, Risom SS, Gluud C, Lindschou J, et al.

Exercise-based cardiac rehabilitation for adults after heart valve surgery.

*Cochrane Database Syst Rev.* (2016) 3: CD010876. doi: 10. 1002/14651858.

CD010876. pub2

14. Pressler A, Förchner L, Hummel J, Haller B, Christle JW, Halle Ml. Long-

term effect of exercise training in patients after transcatheter aortic valve

replacement: follow-up of the SPORT: TAVI randomized pilot study. *Eur J Prev*

*Cardiol.* (2018) 25: 794–801. doi: 10. 1177/2047487318765233

15. Bonow RO, Nishimura RA, Thompson PD, Udelson JE. Eligibility and

disqualification recommendations for competitive athletes with

cardiovascular abnormalities: task force 5: valvular heart disease: a scientific

statement from the American Heart Association and American College of

Cardiology. *Circulation.* (2015) 132: 292–7. doi: 10. 1161/CIR.

0000000000000241

16. Pelliccia A, Fagard R, Bjornstad HH, Anastassakis A, Arbustini E, Assanelli

D, et al. Recommendation for competitive sports participation in athletes

with cardiovascular disease: a consensus document from the study group of

sports cardiology of the working group of cardiac rehabilitation and exercise

physiology and the working group of myocardial and pericardial diseases of

the European Society of Cardiology. *Eur Heart J.* (2005) 26: 1422–45. doi: 10.

1093/eurheartj/ehi325

<https://assignbuster.com/endurance-training-improves-oxygen-uptake-and-endurance-capacity-in-patients-with-moderate-to-severe-valvular-disease/>

17. Cheitlin MD, Douglas PS, Parmley WW. 26th Bethesda Conference: recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities. Task force 2: acquired valvular heart disease. *Med Sci Sports Exerc* . (1994) 26: 254-0.
18. Pellicia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, et al. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Eur Heart J* . (2020) 42: ehaa605. doi: 10.1093/eurheartj/ehaa605
19. Sibilitz KL, Berg SK, Rasmussen TB, Risom SS, Thygesen LC, Tang L, et al. Cardiac rehabilitation increases physical capacity but not mental health after heart valve surgery: a randomized clinical trial. *Heart*. (2016) 102: 1995–2003. doi: 10.1136/heartjnl-2016-309414