# A COMPARATIVE STUDY ON HIGH INTENSITY INTERVAL TRAINING (HIIT) VERSUS ANAEROBIC TRAINING FOR INSPIRATORY MUSCLES TO IMPROVE QUALITY OF LIFE INNON SPECIFIED PULMONARY DISEASE PATIENTS

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# **ABSTRACT**

**BACKGROUND**: A type Pulmonary disease that affects the lungs and other parts of respiratory system. Pulmonary disease may be caused by infection, by smoking tobacco, or by breathing in secondhand tobacco smoke, radon, asbestos, or other forms of air pollution. Pulmonary diseases include asthma, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, pneumonia, and lung cancer. Also called lung disorder and respiratory disease. The present investigation was planned to find out to compare the effect of high intensity interval training and anaerobic training on improving the inspiratory muscle and quality of life in non specified pulmonary disease patient.

**<u>AIMS AND OBJECTIVES</u>**: To compare the effectiveness of high intensity interval training versus anaerobic training for inspiratory muscle to improve quality of life in non specified pulmonary disease patient.

**METHODOLOGY:** 30 patients are non-specified pulmonary disease according to inclusion and exclusion criteria and divide into two groups. Group A. treadmill exercise in High intensity interval training program. Group B. chest mobility exercise in anaerobic training.

**RESULT:** The data showed that with the use of 12 weeks protocol there was a significance difference (p < 0.001) between pre and post test values of 6MWT AND GHQ both group in Male and female patient subjects. The study shows that there was no significance difference between post treatment value of chest mobility exercise.

<u>**CONCLUSION</u>**: The findings of the study conclude that adding a Anaerobic training like chest mobility exercises did not show any significant difference in inspiratory muscle to improve quality of life when compared with High intensity interval training.</u>

Keywords: Non Specified Pulmonary disease, Chest mobility, Treadmill, Anaerobic training.

#### INTRODUCTION

Adult respiratory diseases are caused by many factors, including genetic-environmental interaction. Genetic abnormalities can impact early fetal lung development, postnatal lung maturation, as well as adult lung injury and repair. A type of disease that affects the lungs and other parts of respiratory system. Pulmonary disease may be caused by infection, by smoking tobacco, or by breathing in secondhand tobacco smoke, radon, asbestos, or other forms of air pollution. Pulmonary diseases include asthma, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, pneumonia, and lung cancer. Also called lung disorder and respiratory diseases. In world prevalence of pulmonary disease 65 million people have moderate to severe chronic obstructive pulmonary disease (COPD), from which about 3 million die each year, making it the third leading cause of death worldwide – and the numbers are increasing[2][3]. About 334 million people suffer from asthma [4], which is the most common chronic disease of childhood, affecting 14% of children globally. The prevalence of asthma in children is rising [5]. Both lungs have oblique fissure and the right is further divided by a transverse fissure. The oblique fissure in the left lung separates the superior and the inferior lobe. The oblique and horizontal fissure divides the lungs into superior, middle and inferior lobes. Thus the right lung has three lobes while the left has two. Each lobe is supplied by a lobar bronchus. The lobes are subdivided by bronchopulmonary segments which are supplied by the segmental bronchi. All the respiratory passages from the trachea to the respiratory bronchiole are called the tracheobronchial tree [1][2][3]. The right main bronchus is larger in diameter and more vertical making it directly in line with the trachea than the left main bronchus [2]. Thus swallowed objects that accidentally enter the lower respiratory tract are most likely to become lodged in the right main bronchus [4]. Functionally, the lung is divided into a series of bronchopulmonary segments. The bronchopulmonary segments are the largest subdivision of a lobe. They are separated from adjacent segments by connective tissue septa and are also surgically respectable. They are 10 bronchopulmonary segments in the left lung and 8-10 in the left lung [5].

The muscles of respiration are also called the 'breathing pump muscles'; they form a complex arrangement in the form of semi-rigid bellows around the lungs. All muscles that are attached to the human rib cage have the inherent potential to cause a breathing action.

Muscles that helpful in expanding the thoracic cavity are called the inspiratory muscles because they help in inhalation, while those that compress the thoracic cavity are called expiratory muscles and they induce exhalation. These muscles possess exactly the same basic structure as all other skeletal muscles, and they work in concert to expand or compress the thoracic cavity[1][2].Primary Muscles The primary inspiratory muscles are the diaphragm and external intercostals. Relaxed normal expiration is a passive process, happens because of the elastic recoil of the lungs and surface tension. However there are a few muscles that help in forceful expiration and include the internal intercostals, intercostalisintimi, subcostals and the abdominal muscles[3].The muscles of inspiration elevate the ribs

and sternum, and the muscles of expiration depress them [4]. Accessory Muscles The accessory inspiratory muscles are the sternocleidomastoid, the scalenus anterior, medius, and posterior, the pectoralis major and minor, the inferior fibres of serratus anterior and latissimus dorsi, the serratus posterior superior may help in inspiration also the iliocostaliscervicis[4][5]. Intercostalmuscles they are three types: External intercostal muscles (the most superficial muscle of intercostal muscles), internal intercostal muscles, and innermost intercostal muscles.External intercostal muscles: Origin: inferior border of rib above and Insertion: superior border of rib below. Nerve supply: all the intercostal muscles are supplied by their respective intercostal nerves.[7]Blood supply: all three muscles receive blood supply from anterior and posterior intercostal arteries, in addition to internal thoracic and musculophrenic arteries; costocervical trunk for internal and innermost intercostal muscles[9]

Anaerobic exercise has been defined by the ACSM as intense physical activity of very short duration, fueled by the energy sources within the contracting muscles and independent of the use of inhaled oxygen as an energy source [14]. Without the use of oxygen, our cells revert to the formation of ATP via glycolysis and fermentation. This process produces significantly less ATP than its aerobic counterpart and leads to the build-up of lactic acid. Exercises typically thought of as anaerobic consist of fast twitch muscles and include sprinting, high-intensity interval training (HIIT), power-lifting, etc. Sustained anaerobic metabolism, in other words, anaerobic exercise, causes a sustained increase in lactate and metabolic acidosis and this transition point is referred to anaerobic threshold (AT)[26]. AT can be directly measured via frequent blood samples

High-intensity exercise can be realistically tolerated by people with sedentary lifestyle, obesity, old age, or cardiac disease only in the form of interval training.

Therefore main purpose of this study to compare on high intensity interval training (hiit) versus anaerobic training for inspiratory muscles to improve quality of life in non-specified pulmonary disease patients.

## METHODOLOGY

Comparative study in which with the help of random sampling we have selected 30 patients with diagnosis nonspecific pulmonary disease were selected according to inclusion and exclusion criteria and divide into two groups – Group A: High intensity interval training, Group B: Anaerobic training. Study was conducted in the Opd of Chitrini College of physiotherapy where study duration was12 weeks, 4 Days in week, 25 minute per day.

#### OUTCOME MEASURES

- 1. 6-Minute Walk Test
- 2. General health questionnaire

#### INCLUSION CRITERIA

a) Age of 35 -50 years.

- b) Both Male and female patients.
- c) Diagnosed Non specific pulmonary disease.

## EXCLUSION CRITERIA

- a) Age below 35 and above 50
- b) Neurological problems
- c) Resent any surgery
- d) Ribs fracture
- e) Present of lung ulcer
- f) Spine fracture
- g) Diabetic
- h) Any cancer patient
- i) Psychiatric disorder
- j) Hypertension

## PROCEDURE

30 Patients with Non specific subjects were randomly selected based on inclusion and exclusion criteria. Then divided into 2 groups Group A & Group B (15 subjects each group). Group – A was treated with High intensity interval training

- 1 Warm up 5 minutes (General warm up exercise )
- 2 HIIT( On Treadmill) 4 mph for 45 seconds
- 3 Repetition- 5 times
- 4 Intervals between two repetation-90 seconds
- 5 Cool down 5 minutes (diaphragmatic breathing )

# Treadmill test



#### GROUP B- was treated with Anaerobic training.

- 1 Warm up 5 minutes (General warm up exercise )
- 2 Anaerobic exercise( chest mobility exercise) 2 minutes
- 3 Repetition- 5 times
- 4 Intervals between two repetition -30 seconds
- 5 Cool down 5 minutes (diaphragmatic breathing )

Chest mobility exercise

Chest mobility exercises are designed to maintain or improve mobility of the chest wall, trunk and shoulders girdles when it effects ventilation or postural alignment. Chest mobilization exercises are also used to reinforce or emphasize the depth of inspiration or controlled expiration. Mobilization of lateral Side of the Chest

Position of the patient; sitting The patient is asked to bend away from the tight side to lengthen hypomobile structures and expand the chest during inspiration. Then have the patient push the fisted hand into the lateral aspect of the chest, as he bends toward the tight side and breathes out.





Mobilize Lateral Side of the Ches

hest Expansion

Measure the chest with a tape at three levels (axilla, xiphoid, lower costal). Document change in girth after a maximum inspiration and a maximum expiration.

Place both hands on the patient's chest or back as previously described. Note the distance between your thumbs after a maximum inspiration





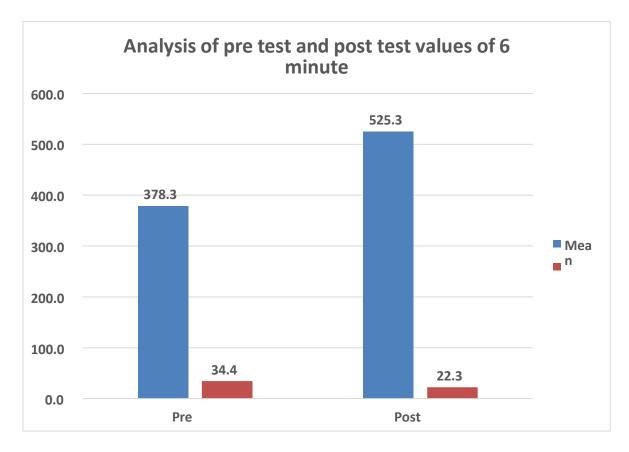
Inch Tape Measurement of Chest Expansion

Mean, Standard deviation, paired 't'test and unpaired't' test would be performed for analysis of pre and post data evaluation within and between groups.

## TABLE -I

Group A

Group A	Mean	N	SD	Std Error Mean	R	Mean Difference	Т	Р
Pre Test	378.33	15	34.42	8.89		147.00	13.818	<0.001
Post Test	525.33	15	22.32	5.76	0.074573			



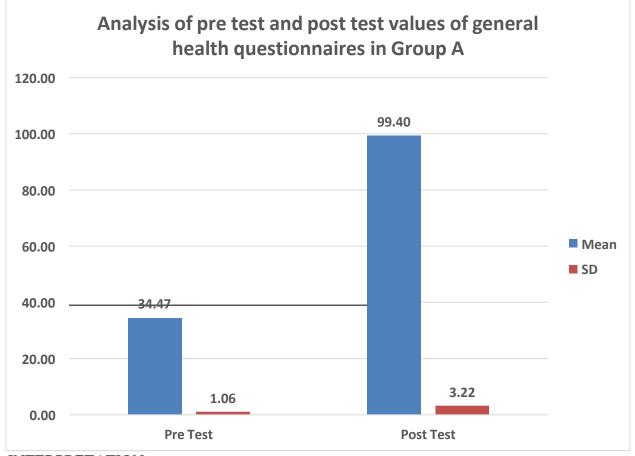
# INTERPRETATION:

The above table and graph shows the Analysis of pre and post test values of 6 minute walk test in Group A.

## **TABLE-II**

Group A

	Mean	N	SD	Std Error Mean	R	Mean Difference	Т	Р
Pre Test	34.47	15	1.06	0.27		64.93	74.181	<0.001
Post Test	99.40	15	3.22	0.83	0.07324			

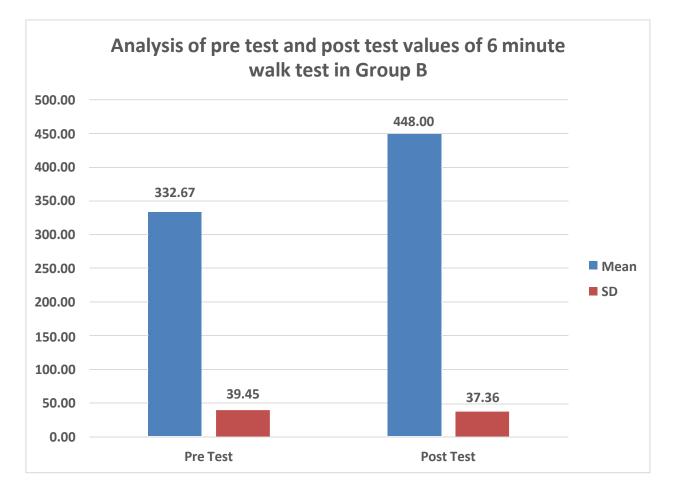


# $\operatorname{INTERPRETATION}$ :

The above table and graph shows the Analysis of pre test and post test values of general health questionnaires in Group A.

Group B

	Mean	Ν	SD	Std Error Mean	R	Mean Difference	Т	Р
Pre Test	332.67	15	39.45	10.19		115.33	8.221	<0.001
Post Test	448.00	15	37.36	9.65	0.192276			



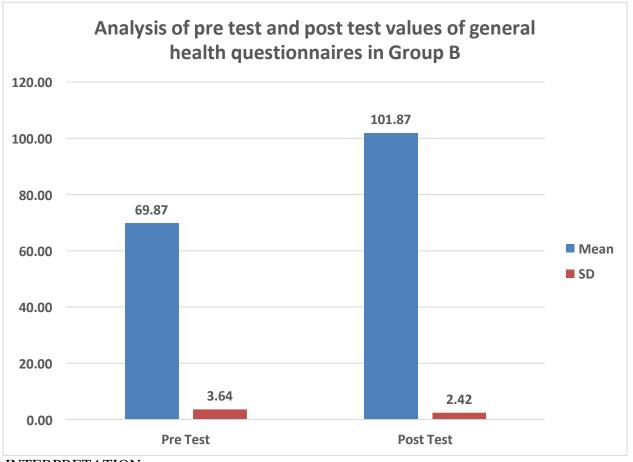
### INTERPRETATION:

The above table and graph shows the Analysis of pre and post test values of 6 minute walk test in Group B.

## TABLE - IV

## Group B

	Mean	Ν	SD	Std Error Mean	R	Mean Difference	т	Р
Pre Test	69.87	15	3.64	0.94		32.00	28.354	<0.001
Post Test	101.87	15	2.42	0.62	0.167005			



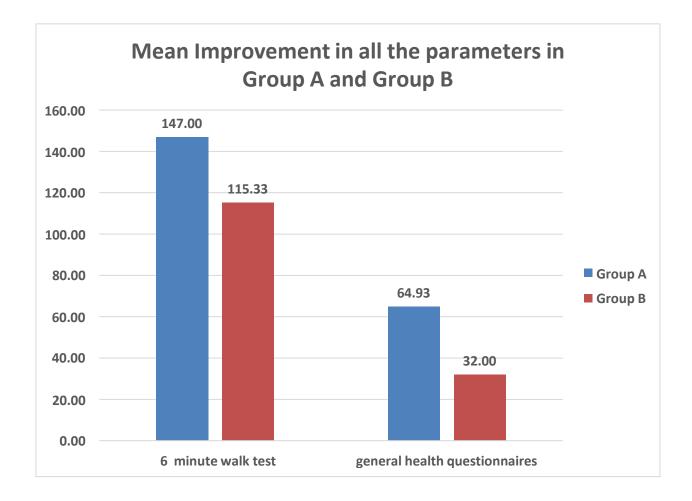
## INTERPRETATION :

The above table and graph shows the Analysis of pre test and post test values of general health questionnaires in Group B.

### TABLE - V

Mean Improvement in all the parameters in Group A and Group B

	Group	Ν	Mean		Group	Ν	Mean
Carriente	A	15	147.00	gonoral boalth	А	15	64.93
6 minute walk test	В	15	115.33	general health questionnaires	В	15	32.00



# **RESULTS& DISCUSSION**

**Result:** The data showed that with the use of 12 weeks protocol there was a significance difference (p < 0.001) between pre and post test values of 6MWT AND GHQ both group in Male and female patient subjects. The study shows that there was no significance difference between post treatment value of chest mobility exercise.

The purpose of the study was to find out the comparative on High intensity interval training and Anaerobic training. The subjects showed improvement in both the groups after the treatment. Analysis of 6MWT and GHQ scores of before and after treatment in group B patients reveal that there was no significant improvement of inspiratory muscle to quality of life when compared to the group A. The patients were assessed after 12 weeks of treatment.

In a study conducted by Ester AlferNorsteboc, Karen Marie Thomas, et.al in the study "Highintensity interval training and pulmonary hemodynamic in COPD with hypoxemia" conclude that High-intensity interval training significantly improved exercise capacity while pulmonary hemodynamic remained unchanged. The improvement may therefore be due to mechanisms other than altered pulmonary artery pressure.

In another study conducted by Chidozie E. Mbad,OladayoJideAdeagbo,Jibril Mohammed, et.al. in the study "Comparative Effects of Six-minute Treadmill Walk and Six-minute Treadmill Walk-talk Test on the Cardiopulmonary Parameters of Healthy Individuals". Concluded that 6MTWT and 6MTWTT, similarly evoke cardiopulmonary changes among apparently healthy young individuals. However, 6MTWTT led to less oxygen consumption and myocardial oxygen demand compared with 6MTWT. This finding may be potentially beneficial for future cardiopulmonary exercise testing using 6MWT.Journal of rehabilitation sciences and research.

2007 Tanaffos showed that the treadmill exercise improve inspiratory muscle strength, dyspnea and health-related quality of life.

2014 Helena Turnip showed that the treadmill exercise improve functional capacity, quality of life in copd patients.

In our study both the group showed statistical significant but while comparing the group A treated treadmill exercise showed significant effect on reducing the scores of our both the outcome measures (6MWT & GHQ) than the group B treated with Chest mobility exercise.

# Conclusion

The findings of the study conclude that adding a Anaerobic training like chest mobility exercises did not show significant difference in inspiratory muscle to improve quality of life when compared with High intensity interval training.

# Limitations of The Study

- 1. The study was limited due to shorter duration of treatment.
- 2. The study was limited due to less number of patients.
- 3. The study was limited age group.
- 4. Psychological status was not evaluated.
- 5. The study was limited due to non-specified pulmonary disease.

## Recommendations

It may recommended that treatment Course Could be more than 12 weeks, So that more results would be evaluated.

It may recommended that Study Could be done on different age group.

It may be recommended that different interventions may be chosen in Non Specific Pulmonary Disease patients.

It may recommended that evaluation of patient's condition may be taken in mid of the study duration to evaluate better results.

Different type of professionals may be use in further study

### REFERENCES

- Kim MJ, Larson JL, Covey MK, Vitalo CA, Alex CG, Patel M. Inspiratory muscle training in patients with chronic obstructive pulmonary disease. Nurs Res 1993; 42: 356–362.
- 2. Preusser BA, Winningham ML, Clanton TL. High- versus low-intensity inspiratory muscle interval training in patients with COPD. Chest 1994; 106: 110–117.
- Lisboa C, Villafranca C, Levia A, Cruz E, Pertuze J, Borzone G. Inspiratory muscle training in chronic airflow limitation: effect on exercise performance. Eur Respir J 1997; 10: 537–542.
- Villafranca C, Borzone G, Levia A, Lisboa C. Effect of inspiratory muscle training with an intermediate load on inspiratory power output in COPD. Eur Respir J 1998; 11: 28– 33.
- Larson JL, Covey MK, Wirtz SE, et al. Cycle ergometer and inspiratory muscle training in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1999; 160: 500–507.
- Covey MK, Larson JL, Wirtz SE, et al. High intensity inspiratory muscle training in patients with chronic obstructive pulmonary disease and severely reduced function. J Cardiopulm Rehabil 2001; 21: 231–240.
- Lotters F, van Tol B, Kwakkel G, Gosselink R. Effects of controlled inspiratory muscle training in patients with COPD: a meta-analysis. Eur Respir J 2002; 20: 570– 578.

- Selvadurai, H.C.; Blimkie, C.J.; Meyers, N.; Mellis, C.M.; Cooper, P.J.; Van Asperen, P.P. Randomized controlled study of in-hospital exercise training programs in children with cystic fibrosis. Pediatr. Pulmonol. 2002, 33, 194–200.[PubMed]
- Gulmans VA, de Meer K, Brackel HJ, et al. Outpatient exercise training in children with cystic fibrosis: physiological effects, perceived competence, and acceptability. Pediatr Pulmonol 1999; 28:39–46
- 10. 12.Orenstein DM, Franklin BA, Doershuk CF, et al. Exercise conditioning and cardiopulmonary fitness in cystic fibrosis: the effect of a three-month supervised running program. Chest 1981; 80:392–398
- Stanghelle JK, Skyberg D, Haanæs OC. Eight-year follow-up of pulmonary function and oxygen uptake during exercise in 16-year-old males with cystic fibrosis. Acta Paediatr 1992; 81:527–531.
- Vanhees L, Fagard R, Thijs L, Staessen J, Amery A. Prognostic significance of peak exercise capacity in patients with coronary artery disease. J Am Coll Cardiol 1994;23:358–63.
- Hammill BG, Curtis LH, Schulman KA, Whellan DJ. Relationship between cardiac rehabilitation and long-term risks of death and myocardial infarction among elderly Medicare beneficiaries. Circulation 2010;121:63–70.
- Kavanagh T, Mertens DJ, Hamm LF, Beyene J, Kennedy J, Corey P, et al. Prediction of long-term prognosis in 12,169 men referred for cardiac rehabilitation. Circulation 2002;106:666–71.
- 15. Moholdt T, Aamot IL, Granoien I, Gjerde L, Myklebust G, Walderhaug L, et al. Aerobic interval training increases peak oxygen uptake more than usual care exercise training in myocardial infarction patients: a randomized controlled study. Clin Rehabil 2012;26:33–44.
- Munk PS, Breland UM, Aukrust P, Ueland T, Kvaloy JT, Larsen AI. High intensity interval training reduces systemic inflammation in post-PCI patients. Eur J Cardiovasc Prev Rehabil 2011;18:850–7.

- 17. Chest. 2007 Aug;132(2):651-6. doi: 10.1378/chest.06-2663.PMID: 17699136.
- American Academy of Physical Medicine and Rehabilitation. Published by Elsevier Inc.
- 19. Chartered Society of Physiotherapy. Published by Elsevier Ltd.
- 20. International Journal of Health Sciences and Research.
- 21. Scanlon, VC, anders, T. Essentials of anatomy and physiology. 6<sup>th</sup> eds. F.A. Davis. Philadelphia, 2011.
- 22. Drake, RL, Vogl, W, Mitchell, AW, Gray, H. Gray's anatomy for Students 2nd ed. Philadelphia : Churchill Livingstone/Elsevier, 2010.
- Paulin E, Brunetto AF, Carvalho CRF. Effects of a physical exercises program designed to increase thoracic mobility in patients with chronic obstructive pulmonary disease. J Pneumol. 2003;29(5):287–295.
- 24. Montaldo BC, Gleeson K, Zwillich CW. The control of breathing in clinical practice. Chest. 2000;117(1):205–225.
- 25. Smodlaka VN. Use of the interval work capacity test in the evaluation of severely disabled patients. J Chronic Dis 1972;25:345–52.
- 26. Hickson RC, Bomze HA, Holloszy JO. Linear increase in aerobic power induced by a strenuous program of endurance exercise. J Appl Physiol 1977;42:372–76.
- 27. Paterson DH, Shephard RJ, Cunningham D, et al. Effects of physical training on cardiovascular function following myocardial infarction. J Appl Physiol 1979;47:482–9.

- 28. Ehsani AA, Heath GW, Hagberg JM, et al. Effects of 12 months of intense exercise training on ischemic ST-segment depression in patients with coronary artery disease. Circulation 1981;64:1116–24.
- 29. Blumenthal JA, Rejeski WJ, Walsh-Riddle M, et al. Comparison of high- and lowintensity exercise training early after acute myocardial infarction. Am J Cardiol 1988;61:26–30.
- Levine SA, Lown B. 'Armchair' treatment of acute coronary thrombosis. JAMA 1952; 148:1365–9.
- Hellerstein HK, Ford AB. Rehabilitation of the cardiac patient. JAMA 1957;164:225– 31.
- 32. Smodlaka VN. Use of the interval work capacity test in the evaluation of severely disabled patients. J Chronic Dis 1972;25:345–52.
- Hickson RC, Bomze HA, Holloszy JO. Linear increase in aerobic power induced by a strenuous program of endurance exercise. J Appl Physiol 1977;42:372–76.
- 34. Paterson DH, Shephard RJ, Cunningham D, et al. Effects of physical training on cardiovascular function following myocardial infarction. J Appl Physiol 1979;47:482–9.
- 35. Ehsani AA, Heath GW, Hagberg JM, et al. Effects of 12 months of intense exercise training on ischemic ST-segment depression in patients with coronary artery disease. Circulation 1981;64:1116–24.
- 36. Blumenthal JA, Rejeski WJ, Walsh-Riddle M, et al. Comparison of high- and lowintensity exercise training early after acute myocardial infarction. Am J Cardiol 1988;61:26–30.

- 37. Ekblom B, Lovgren O, Alderin M, Fridstrom M, Satterstrom G. Effect of short-term physical training on patients with rheumatoid arthritis I. Scand J Rheumatol 1975;4:80–6.
- 38. Ekdahl C, Andersson SI, Moritz U, Svensson B. Dynamic versus static training in patients with rheumatoid arthritis. Scand J Rheumatol 1990;19:17–26.
- 39. Van den Ende CHM, Hazes JMW, le Cessie S, Mulder WJ, Belfor DG, Breedveld FC, et al. Comparison of high and low intensity training in well controlled rheumatoid arthritis: results of a randomised clinical trial. Ann Rheum Dis 1996;55:798–805.
- 40. Ha kkinen A, Sokka T, Kotaniemi A, Hannonen P. A randomized two-year study of the effects of dynamic strength training on muscle strength, disease activity, functional capacity, and bone mineral density in early rheumatoid arthritis. Arthritis Rheum 2001;44:515–22.
- 41. Manson JE, Greenland P, LaCroix AZ, Stefanick ML, Mouton CP, Oberman A, et al. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. N Engl J Med 2002;347:716–25.
- 42. Wells AU, Hirani N. Interstitial lung disease guideline. Thorax. 2008;63(Suppl 5):v1–v58.
- 43. Spruit MA, Singh S, Garvey C, ZuWallack R, Nici L, Rochester C, Hill K, Holland AE, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med. 2013;188(8):13–64.
- 44. Dowman L, Cox N, Morris N, Nakazawa A, Bondarenko J, Parker L, Prasad J, Glaspole I, Holland AE. Acute physiological responses to interval and continuous

training in ILD. Thoracic Society of Austrlia and New Zealand Annual Scientific Meeting. Gold Coast: Wiley; 2019.

- 45. Jones LW, Eves ND, Peterson BL, Garst J, Crawford J, West MJ, Mabe S, Harpole D, Kraus WE, Douglas PS. Safety and feasibility of aerobic training on cardiopulmonary function and quality of life in postsurgical nonsmall cell lung cancer patients. Cancer. 2008;113(12):3430–9.
- 46. Hackett ML, Anderson CS, House A, Halteh C. Interventions for preventing depression after stroke. Cochrane Database Syst Rev. 2008;3:CD003689. https://doi.org/10.1002/14651858.CD003689.pub3.
- 47. Hawkins RJ, Jowett A, Godfrey M, Mellish K, Young J, Farrin A, et al. Poststroke trajectories: the process of recovery over the longer term following stroke. Glob Qual Nurs Res. 2017;4:233393617730209. https://doi.org/10.1177/2333393617730209.
- 48. van Mierlo M, van Heugten C, Post MWM, Hoekstra T, Visser-Meily A. Trajectories of health-related quality of life after stroke: results from a oneyear prospective cohort study. Disabil Rehabil. 2017:1–10. https://doi.org/10. 1080/09638288.2017.1292320.
- Goldberg D, Williams P. A user's guide to the general health questionnaire. London: Nfer-Nelson; 1991. 6. Goldberg DP, Hillier VF. A scaled version of the general health questionnaire. Psychol Med. 1979;9(1):139–45.
- Arcasoy SM, Christie JD, Ferrari VA, et al. Echocardiographic assessment of pulmonary hypertension in patients with advanced lung disease. Am J Respir Crit Care Med. 2003 Mar 1;167(5):735–740.
- 51. Sala E, Roca J, Marrades RM, et al. Effects of endurance training on skeletal muscle bioenergetics in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 1999 Jun;159(6):1726–1734.

- 52. Maltais F, LeBlanc P, Simard C, et al. Skeletal muscle adaptation to endurance training in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 1996 Aug;154(2 Pt 1):442–447.
- 53. Whittom F, Jobin J, Simard PM, et al. Histochemical and morphological characteristics of the vastus lateralis muscle in patients with chronic obstructive pulmonary disease. Med Sci Sports Exerc. 1998 Oct;30 (10):1467–1474.
- Bowen TS, Aakerøy L, Eisenkolb S, et al. Exercise Training Reverses Extrapulmonary Impairments in Smoke-exposed Mice. Med Sci Sports Exerc. 2017 May;49(5):879– 887. [
- 55. Polverino F, Laucho-Contreras ME, Petersen H, et al. A pilot study linking endothelial injury in lungs and kidneys in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2017 Jun 1;195 (11):1464–1476.
- 56. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al: An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med 2013;188:e13–e64.
- Ries AL, Bauldoff GS, Carlin BW, Casaburi R, Emery CF, Mahler DA, et al: Pulmonary rehabilitation: joint ACCP/AACVPR evidencebased clinical practice guidelines. Chest 2007; 131(suppl):4S–42S.
- 58. Radlinger L, Bachmann W, Homburg J, Leuenberger U, Thaddey G: Rehabilitatives Krafttraining. Stuttgart/New York, Thieme, 1998. 16 Jenkins SC: 6-minute walk test in patients with COPD: clinical applications in pulmonary rehabilitation. Physiotherapy 2007;93: 175–182.

- 59. Jones PW, Quirk FH, Baveystock CM, Littlejohns P: A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. Am Rev Respir Dis 1992;145:1321–1327.
- 60. Seymour JM, Ward K, Sidhu PS, Puthucheary Z, Steier J, Jolley CJ, et al: Ultrasound measurement of rectus femoris cross-sectional area and the relationship with quadriceps strength in COPD. Thorax 2009;64:418–423.
- 61. Spruit MA, Polkey MI, Celli B, Edwards LD, Watkins ML, Pinto-Plata V, et al: Predicting outcomes from 6-minute walk distance in chronic obstructive pulmonary disease. J Am Med Dir Assoc 2012;13:291–297.
- Pinto-Plata VM, Cote C, Cabral H, Taylor J, Celli BR: The 6-min walk distance: change over time and value as a predictor of survival in severe COPD. Eur Respir J 2004;23:28–33.
- **63.** Hui KP, Hewitt AB: A simple pulmonary rehabilitation program improves health outcomes and reduces hospital utilization in patients with COPD. Chest 2003;124:94–