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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/20637
DOI URL: <http://dx.doi.org/10.21474/IJAR01/20637>



RESEARCH ARTICLE

A PILOT STUDY ON CORRELATION BETWEEN SIX-MINUTE WALK TEST AND BREATH HOLDING TIME TEST BETWEEN NORMOTENSIVE AND HYPERTENSIVE INDIVIDUALS

More Himani Hanumant¹ and Dileep Verma²

1. Assistant Professor, Department of Physiology, Autonomous State Medical College, Amethi, India.
2. Professor, Department of Physiology, King George's Medical University, Lucknow, India.

Manuscript Info

Manuscript History

Received: 18 January 2025

Final Accepted: 21 February 2025

Published: March 2025

Key words:-

Six-Minute Walk Test, Functional Exercise Capacity, Normotensive, Hypertensive, Breath Holding Time

Abstract

This study wants to check efficiency of breath holding time in comparison with six-minute walk test as a parameter of physical fitness in normotensive and hypersensitive individuals. Six-minute walk test is widely used sub-maximal intensity exercise test. This test is easy to perform, inexpensive, easily repeated. It is widely popular for cardiorespiratory assessment. Measurement of functional exercise capacity is required in many conditions like chronic obstructive diseases, cardiac failure etc. six-minute walk test is a validated tool for measurement of functional exercise capacity. It is good for determining prognosis in major pulmonary surgeries, COPD, cardiac failure, pulmonary hypertension etc. Six-minute walk test needs more space and time to be performed. Also, it is quite ineffective for patients with walking disabilities. Use of breath holding time test instead of six-minute walk test will fasten the process of cardio-respiratory evaluation since it is even more easy to perform and requires lesser time as well as space. Here we compared the two tests among the population of 151 in which 73 were normotensive individuals while 78 were found to be hypertensive. The comparison between the two tests among these two populations was done to see whether the two tests are linearly correlated to each other in spite of variations in the status of blood pressure. It was found that the two tests are linearly correlated in the normotensive group but hypertensive population did not show any such correlation. Overall population showed moderated correlation between the two tests.

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Introduction:-

Measurement of functional exercise capacity is required in many conditions like chronic obstructive diseases, cardiac failure etc. The six-minute walk test (6MWT) is widely used to measure functional exercise performance, response to treatment and disease progression across a wide range of respiratory and neuromuscular diseases in clinical settings.⁽¹⁾ It is quiet simple to perform with minimum risk to patients and an inexpensive tool which makes the process more affordable so any patient can be advised this test regardless of the socioeconomic strata he/she belongs. A self paced walk for 6 minutes is exercise of sub-maximal intensity. Sub-maximal intensity of this kind of exercise makes it more important for practical scenarios, as most of our daily activities are of sub-maximal intensity.

Corresponding Author:-More Himani Hanumant

Address:-Assistant Professor, Department of Physiology, Autonomous State Medical College, Amethi, India.

That is why six minute walk test gives a better reflection of functional exercise level.⁽²⁾ The 6-minute walk test (6MWT) is a key study providing a functional, therapeutic response, and prognostic data that is valuable in the care of patients with respiratory as well as cardiac diseases. It is used widely due to its simplicity and reproducibility, delivering a consolidated image of the cardiopulmonary and musculoskeletal response to exercise.⁽³⁾ This test is reliable, less expensive and easily repeated.⁽⁴⁾ Also, this test integrates many bodily systems while performing this particular test. Co-ordination of cardio respiratory system, circulatory system, neuromuscular system is required to perform the test successfully.⁽⁵⁾ This test holds importance in comparing pretreatment and post-treatment results in major pulmonary surgeries like lung transplant, lung resection, lung volume reduction surgery etc.⁽⁶⁾ It is used to evaluate the progress in pulmonary rehabilitation program. This test holds great importance in assessing the response to treatment in COPD case, heart failure patients and patients of pulmonary hypertension. It is used to measure aerobic capacity in the exercise programs like cardiac rehabilitation. This test is good morbidity and mortality predictor in cases of heart failure patients, COPD patients and patients of primary pulmonary hypertension. It is safe, simple, inexpensive nature and requirement of minimum training to the technician makes it a very popular test.^(7,8,9)

As per the official statement of the American Thoracic Society by the ATS Board of Directors in March 2002 the minimum required space to perform 6-minute walk test is 30 m corridor which is long, straight and flat. The basic requirement to perform this test is 'space for walking' either indoor or outdoor. It is preferred to perform the test indoors as external environment factors like temperature, humidity, sunlight exposure can be controlled and maintained similar for every subject since these factors do affect the performance of subject.⁽¹⁰⁾ Therefore, it is necessary to keep the external environmental factors comfortable to obtain the performance as per their best capability. It can be performed outdoors, if the environmental conditions are comfortable for subjects. Although, 6-minute walk distance is simple, reliable & inexpensive test, it has its own limitations. It is not possible to have at least 30-meter-long, straight corridor in every OPD or ward scenario. Also rush of patients and relatives keep disturbing the walk of subject in case of availability of corridor space. So, it is little cumbersome for the doctor to perform the particular test. Also, minimum time required to complete the test is 6 minutes. Patient is required to be wearing comfortable shoes and comfortable loose clothes. It is not possible in case of every patient. Some of the patients who are advised to perform the test might not be wearing required clothing and footwear which results in affecting their performance. In case of outdoor performance of test like weather is limiting factor. It is not constant and suitable the whole year. Also, intensity of sunlight is not constant throughout the day causing a bias in the performance of the patient. The shortcomings of the test make us to seek for alternatives which is equally effective but has even lesser requirements.

Breath Holding Time Test is simple, non-invasive, inexpensive and recently validated test. Breath holding time is used as a tool in respiratory fitness testing. It can determine respiratory capacity of an individual.⁽¹¹⁾ Breath Holding Time is the maximum amount of time for which a subject can hold his/her breath voluntarily. Breath holding time can show variation in the same individual depending on the phase of respiration which is followed by holding the breath. For an instance, BHT will be less if followed after expiration than inspiration and Vice Versa.⁽⁸⁾ One can hold the process of inhalation & exhalation as per his/her desire for a limited time, but it is not a completely voluntary process.^(8,28) After a particular point, the voluntary control is lost. The point is called as the breaking point when breathing cannot be held voluntarily.⁽¹²⁾ What happens at this point is the arterial PCO₂ keep on arising and Po₂ in the arteries keep of falling? Even if the subject holds her/his breath, the body tissues keep on utilizing the oxygen and producing carbon dioxide. This results in rise of arterial PCO₂ and fall of arterial Po₂. This stimulates arterial and peripheral chemoreceptors. Thus, results in inhibition of holding of breath and initiation of respiration. Proprioceptive impulses from the respiratory muscles and joints may have involvement in the causation of the breaking point^(13,14). Breath Holding Time can vary in the same individual. If the person breaths 100% oxygen before holding his/her breath, it will result in increment of duration of breath holding time for that particular individual. If room is well ventilated that will also help in improvement of breath holding time. Verbal encouragement can have positive influence on the test.⁽¹⁵⁾ If we keep all these influencing parameters constant. We can have reproducibility of results for the same test in the same individual keeping these parameters constant is much easier task compared to the required constant factors for 6-minute walk test.

Breath holding time test also correlates and work in integrated fashion with multiple systems of human body. It not only involves cardiorespiratory system but also hemodynamic perturbation occurs during our self-induced breath holding time. There is vagal nerve stimulation and changes in sympathetic as well as parasympathetic system. Simply, autonomic nervous system is involved in this test.⁽¹⁶⁾

Information about reflex regulation of cardiorespiratory system is provided by post-inhalation breath holding time. The hypoxia produced due to voluntary breath holding results in elevation of angiotensin II along with increased expression of AT2 receptor in carotid bodies and impaired NO production. K⁺ channels are responsible for hypoxic stimulus in glomus channel. Sensitivity the changes like NO dysregulation and up-regulation of angiotensin receptors results in K⁺ ion channel changes in glomus cells. Sensitivity of peripheral chemoreflexes is increased in cases of arterial hypertension. In these cases of arterial hypertension morphological changes in carotid glomus are seen. Also decrement in baroreflex sensitivity is observed in subjects of arterial hypertension.^(9,17,18) In patients of chronic obstructive Pulmonary Disorders, the sensitivity of peripheral chemoreflex due to hypoxic stimulus is seen causing decrease in Breath Holding Time. Breath Holding Time can be used as predictor of severity in developing cardiorespiratory disorders.^(17,19) It can be sensitive towards morbidity and mortality. Also, it can be useful to evaluate effectiveness of treatment in case of Chronic Obstructive Pulmonary Disorders patients.⁽²⁰⁾

Breath Holding Time has even lesser requirements than 6-minute walk test. This test can be performed comfortably in indoors where it is easy to provide similar external environment to every subject and every attempt of test of each subject. The requirement of space is no extraordinary. It is inexpensive, simple, and easy to perform. It takes lesser time than 6-minute walk test.

If linear correlation is found in the two tests viz, 6-minute walk test and Breath Holding Time Test we can replace six-minute walk by breath holding time test. This will result in fastening the process of cardiorespiratory evaluation. So here in this study we are checking whether the relationship exists between the above mentioned two test and whether that relationship is constant in spite of variations in blood pressure status of subjects.

Aim:-

To check efficiency of breath holding test in comparison to six-minute walk test as a parameter of physical fitness in normotensive and hypertensive individuals.

Objective:-

To study the correlation between breath holding time and six-minute walk test in normotensive and hypertensive individuals.

Hypothesis:-

Breath holding test is as good as six-minute walk test for determining physical fitness in normotensive and hypertensive individuals.

Materials & Methods:-

The study took place in Department of physiology, King George's Medical University, Lucknow after obtaining ethical clearance. We have taken 151 apparently healthy individuals i.e. subjects with no complains of any weakness or disease and demonstrating high working ability. Subjects were instructed not to have tea, coffee or any stimulant before test as it can affect blood pressure for that person.⁽²¹⁾ Known cases of hypertension who are taking their antihypertensive medications were excluded. On the arrival of subjects they were told to sit comfortably on a chair and rest till subject feels ready to perform expected tests. Participants were observed for 2 minutes under their resting voluntary conditions.⁽²¹⁾ Blood pressure of every individual was noted down. Individuals with resting blood pressure more than 130/80 were labelled as hypertensive. Apparently healthy individuals having blood pressure less than 130/80 were labelled as normotensive.⁽²²⁾

As per Viechtbauer et al., 2015 sample size for a pilot study is dependent on confidence interval and probability. At 95% confidence and 10% probability required sample size 45. For linear correlation minimum sample size requirement for a mild to moderate positive correlation ($r=+0.4$) is 45 which again is close to sample size determined for 10% probability at 95% confidence interval.⁽⁴⁾ However, we were able to attain a sample size of 151.⁽²³⁾

The effort was to find correlation between six-minute walk test and breath holding time test in different subjects having variations in the resting blood pressure. Blood pressure measuring device for blood pressure measurement and pulse measurement by Omron blood pressure monitor HEM-1724. 30 meters long, straight, area was measured on a plain ground with marking at every 1 meter for measurement of distance walked during 6-minute walk test.

Subjects were told to take a deep inspiration and stop breathing at inspiratory reserve volume. When subject started inhaling, he / she was told to point a finger.⁽²⁴⁾ Nose clips were put on their nose. Subjects were instructed to close their mouth and avoid deglutition. One hand of the observer was put on diaphragmatic area of the subject so that any of the slightest expiration can be noted by the observer.⁽²⁴⁾ Subjects were verbally motivated to get their optimum performance. When subjects could not hold their breath voluntarily any longer, he was instructed to point finger and remove nose clip. The time from start of inhalation till the start of expiration which was shown by pointing finger by subject was noted by a stop watch. The time for which breath was held was recorded. Immediately after this once again oxygen saturation, blood pressure and pulse rate was measured. The same process of recording breath holding time was repeated for 3 times by giving a gap of 10 minutes between two continuous efforts. The average of the three attempts was taken as a recorded data.⁽²⁴⁾

Once breath holding time was noted subject was told to take his / her own time to get relaxed. He was told to walk for 6 minutes on the measured ground with his maximum walking speed. Each subject was verbally motivated to get his best performance. After completion of the six-minute walk, walking distance of that person was measured and noted down. Blood pressure and pulse after 6-minute walk was noted down.

Inclusion criteria:

Apparently healthy adults between 20 to 40 years

Exclusion criteria:

1. Subjects taking any medication
2. Subjects above and below mentioned age group
3. Smokers

Statistical Analysis:-

The collected data was analyzed using IBM statistical package for Social Science (SPSS) software version 24. Data was expressed in numbers, percentage or mean +/-, standard deviation, students t test were used. A p- value of 0.001 was considered as cut off for statistically significant Association

Result:-

Table 1:-Group wise Distribution of Study Population (N=151)

SN	Group	No.	%
1-	Normal BP	73	48.3
2-	High BP	78	51.7
		151	100.0

48.3% population was normotensive and 51.7% of population was found to be hypertensive

Table 2:- Between Group Comparison of Age and Anthropometric Parameters.

SN	Parameter	Normal BP (n=73)		High BP (n=78)		Student 't' test	
		Mean	SD	Mean	SD	't'	'p'
1-	Age (yrs)	33.85	9.48	41.37	9.40	-4.895	<0.001
2-	Weight (kg)	75.82	6.64	77.87	8.00	-1.708	0.090
3-	Height (cms)	172.18	3.21	173.88	4.82	-2.543	0.012
4-	BMI (kg/m ²)	25.57	2.04	25.74	2.30	-0.499	0.619

Population of high blood pressure found to be slightly older than normotensive population. No significant variations were observed in both the groups for weight, height and body mass index

Table 3:- Between Group Comparison of Hemodynamic Parameters (Before and After 6m Walk test).

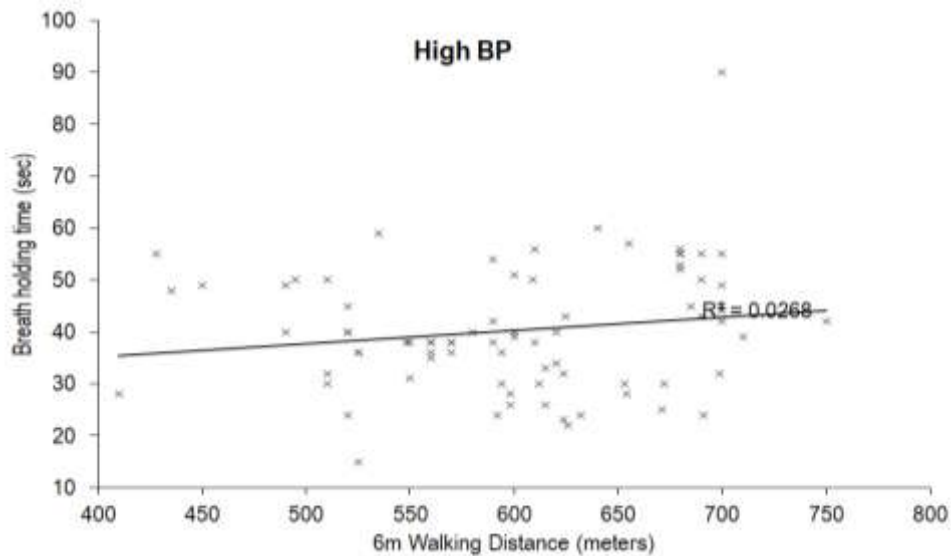
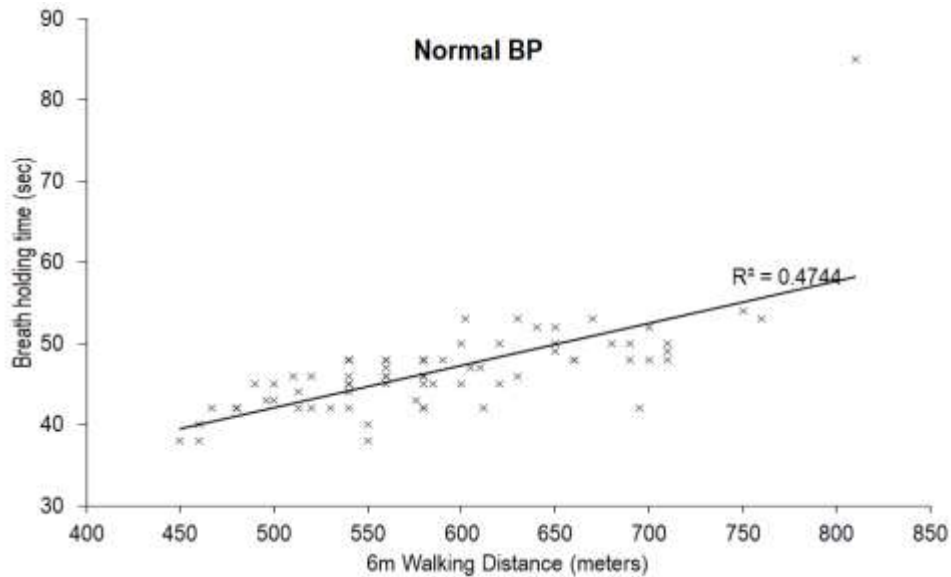
SN	Parameter	Normal BP (n=73)		High BP (n=78)		Student 't' test	
		Mean	SD	Mean	SD	't'	'p'
Before 6m Walk Test							
1-	Systolic BP	125.92	5.16	150.72	11.82	-16.509	<0.001
2-	Diastolic BP	82.93	5.50	89.56	9.86	-5.060	<0.001

3-	Pulse	80.18	2.77	85.13	10.12	-4.039	<0.001
4-	SpO2	98.22	0.45	97.37	2.01	3.514	0.001
After 6m Walk Test							
1-	Systolic BP	131.68	5.35	153.76	24.57	-7.510	<0.001
2-	Diastolic BP	87.77	5.09	92.42	12.21	-3.021	0.003
3-	Pulse	82.03	2.52	90.22	8.66	-7.774	<0.001
4-	SpO2	97.68	2.31	98.15	1.28	-1.557	0.122

Increment was observed in systolic blood pressure, diastolic blood pressure pulse and oxygen saturation in both groups after completion of sex-minute walk.

Table 4:- Correlation of Breath holding time and 6m Walk test.

Group	'r'	Level of correlation	'p'	Level of significance
Normal BP	0.689	Moderate	<0.001	Highly significant
High BP	0.164	Weak/No correlation	0.718	Non-significant
Overall	0.271	Weak/No correlation	0.001	Significant



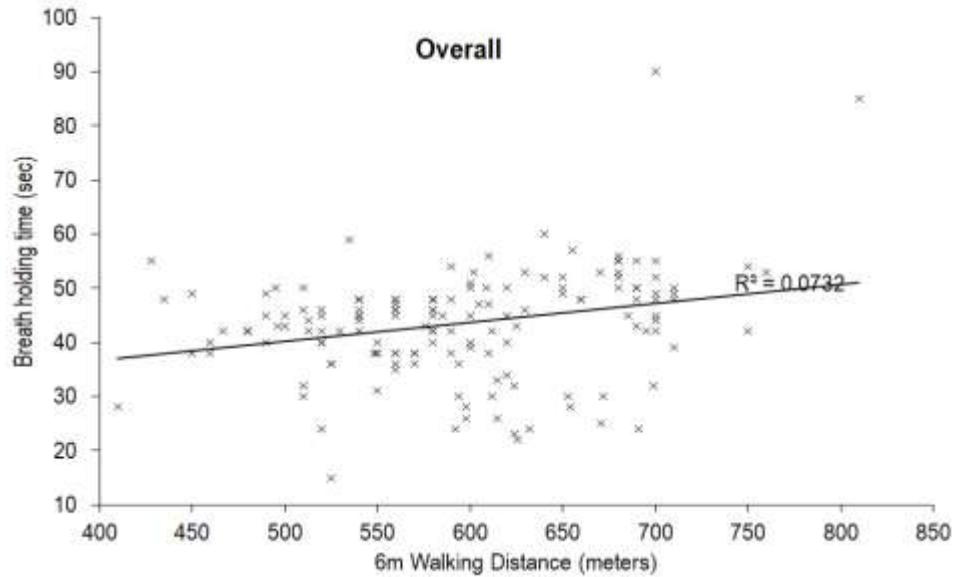


Table 5:- Group Comparison between Breath holding time and 6m Walk test.

SN	Parameter	Normal BP (n=73)		High BP (n=78)		Student 't' test	
		Mean	SD	Mean	SD	't'	'p'
1-	Breath holding time (sec)	46.66	5.93	40.35	11.92	4.076	<0.001
2-	6m Walk distance (meters)	587.04	78.69	600.44	75.70	-1.066	0.288

Significant linear correlation is seen between breath holding time and six-minute walk test in case of normotensive subjects. Breath holding time and six-minute walk test does not show linear correlation in case of hypertensive individuals. Moderate correlation was observed in overall population between the two tests.

Discussion:-

The data of 151 apparently healthy individual was collected. The participants were divided in two groups as normotensive and hypertensive individuals. Intergroup comparison were done for the purpose of analysis as per the status of bloodpressure of that subject. This showed that breath holding time and six-minute walk distance are correlated to each other even though subjects might have variation in their range of blood pressure.

Also, breath holding test has been used to evaluate the sensation of experimentally induced dyspnea. This test is a useful guide to evaluate fatal asthma in case of diagnosed asthma patients. Inoue et al. have reported that BHT has revealed an early stage of lung function abnormalities. Voluntary breath holding after maximum inspiration serves as a useful index to the severity of COPD and its impact.⁽¹²⁾ Smoking can affect the performance of subject for BHT. So, all the 151-subject chosen were nonsmokers to eliminate the cofounding factor of smoking.

The duration of breath holding after deep inspiration depends on several factors e.g.- chemoreception, mechanoreception, the impact of descending cortical respiratory drive. Chemoreception are involuntary but plays a significant role also, the air which person is breathing effects breed holding time. Voluntary Apnea can have double duration if the breath holding is after inhalation of hyperoxic air mixture.^(24,25) On the contrary, duration of voluntary apnea can be seen reduced under hypoxemic and hypercapnic.⁽²⁶⁾ Keeping this condition in mind, all the participants performed the test under similar circumstances at the same place.

Breath holding time was measured in the same position for all the participants i.e. sitting position in the chair. Even the chair was kept constant for all the participants. The study published by Indu Taneja et al. states that postural change alters the autonomic responses to breath holding time. Supine position has much shorter breath holding time as compared to upright posture. Also, bradycardia is associated with breath holding in supine as compared to same

test in upright position.⁽²⁵⁾ Keeping this in mind, we kept constant position for all our study participant to avoid any kind of bias in our readings.

Also, timing of day can have influence on duration of breath holding time. Whether the test was performed in morning or evening can have influence the duration of breath holding.⁽²⁶⁾ By taking this in account all the subjects performed a breath holding test in the evenings. Clothing also was similar of all the recruited subjects to avoid any kind of bias.

Six-minute walk test is been used to assess the morbidity of COPD patients. The test is simple and easy to perform. Weather conditions can have great influence on the walking distance of subject.^(27,32) The test was performed outdoor on flat ground where 30 meter distance was measured. Entire data was collected in winters just to keep the weather condition constant for the whole study population. Subject did wear comfortable cloths and comfortable footwear. Verbal motivation was given to each and every subject for optimum performance.

Limitations of Study:-

In spite of our motivation, it is up to the person's own mindset how much he or she pushes himself /herself. This might lead to difference in the optimum performance of the subject. Some of the subjects might be anxious and that is why he might not have performed to the best of his ability. Keeping rest of the possible factors constant except blood pressure status, we tried to compare the two tests of interest i.e. 6 minute walk test and breath holding time test. Parameters like systolic blood pressure, diastolic blood pressure, pulse, percentage of oxygen saturation should have been taken just before and after breath holding time test also. This could have given us the impact of breath holding on above mentioned vital parameters.

Future Perspective:-

Linear correlation between the two tests can help to fasten the process of evaluation of prognosis in cardio-respiratory conditions. Also, this study can be further expanded to check impact of breath holding on the vital parameters of the body. This impact of breath holding on vital parameters can be compared to six-minute walk test.

Conclusion:-

A significant correlation was found between six-minute walk test and breath holding time test in case of normotensive subjects. Hypertensive subjects did not show significant correlation between six-minute walk test and breath holding time. The variation in blood pressure range of subjects did affect the linear relationship between the two tests. Individuals who covered more distance in self-paced walk during six-minute time were able to hold the breath more efficiently than those who covered lesser distance during six-minute walk test in case of normotensive subjects. However, such correlation was not shown by hypertensive individuals. Overall population did show moderate linear correlation between the two tests. In conclusion, breath holding time can be used instead of six-minute walk test in subjects with normal blood pressure.

Declaration by Authors:-

Ethical Approval: Approved

Acknowledgement: None

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

References:-

1. Nguyen DT, Penta M, Questienne C, Garbusinski J, Nguyen CV, Sauvage C. Normative values in healthy adults for the 6-minute and 2-minute walk tests in Belgium and Vietnam: implications for clinical practice. *J Rehabil Med.* 2024 Mar 19;56:jrm18628. doi: 10.2340/jrm.v56.18628. PMID: 38501732; PMCID: PMC10964022.
2. Eaton T, Young P, Milne D, Wells AU. Six-minute walk, maximal exercise tests: reproducibility in fibrotic interstitial pneumonia. *Am J Respir Crit Care Med.* 2005 May 15;171(10):1150-7. doi: 10.1164/rccm.200405-578OC. Epub 2005 Jan 7. PMID: 15640367.
3. Matos Casano HA, Anjum F. Six-Minute Walk Test. 2023 Aug 14. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. PMID: 35015445.

4. Halliday SJ, Wang L, Yu C, Vickers BP, Newman JH, Fremont RD, Huerta LE, Brittain EL, Hemnes AR. Six-minute walk distance in healthy young adults. *Respir Med.* 2020 Apr-May;165:105933. doi: 10.1016/j.rmed.2020.105933. Epub 2020 Mar 19. PMID: 32308201; PMCID: PMC7174378.
5. McDonald CM, Henricson EK, Abresch RT, Florence J, Eagle M, Gappmaier E, Glanzman AM; PTC124-GD-007-DMD Study Group; Spiegel R, Barth J, Elfring G, Reha A, Peltz SW. The 6-minute walk test and other clinical endpoints in duchenne muscular dystrophy: reliability, concurrent validity, and minimal clinically important differences from a multicenter study. *Muscle Nerve.* 2013 Sep;48(3):357-68. doi: 10.1002/mus.23905. Epub 2013 Jul 17. PMID: 23674289; PMCID: PMC3826053.
6. Wesolowski S, Orłowski TM, Kram M. The 6-min walk test in the functional evaluation of patients with lung cancer qualified for lobectomy. *Interact Cardiovasc Thorac Surg.* 2020 Apr 1;30(4):559-564. doi: 10.1093/icvts/ivz313. PMID: 32068846.
7. du Bois RM, Albera C, Bradford WZ, Costabel U, Leff JA, Noble PW, Sahn SA, Valeyre D, Weycker D, King TE Jr. 6-Minute walk distance is an independent predictor of mortality in patients with idiopathic pulmonary fibrosis. *Eur Respir J.* 2014 May;43(5):1421-9. doi: 10.1183/09031936.00131813. Epub 2013 Dec 5. PMID: 24311766.
8. Nathan SD, du Bois RM, Albera C, Bradford WZ, Costabel U, Kartashov A, Noble PW, Sahn SA, Valeyre D, Weycker D, King TE Jr. Validation of test performance characteristics and minimal clinically important difference of the 6-minute walk test in patients with idiopathic pulmonary fibrosis. *Respir Med.* 2015 Jul;109(7):914-22. doi: 10.1016/j.rmed.2015.04.008. Epub 2015 Apr 24. PMID: 25956020.
9. Swigris JJ, Swick J, Wamboldt FS, Sprunger D, du Bois R, Fischer A, Cosgrove GP, Frankel SK, Fernandez-Perez ER, Kervitsky D, Brown KK. Heart rate recovery after 6-min walk test predicts survival in patients with idiopathic pulmonary fibrosis. *Chest.* 2009 Sep;136(3):841-848. doi: 10.1378/chest.09-0211. Epub 2009 Apr 24. PMID: 19395579; PMCID: PMC2775995.
10. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med.* 2002 Jul 1;166(1):111-7. doi: 10.1164/ajrccm.166.1.at1102. Erratum in: *Am J Respir Crit Care Med.* 2016 May 15;193(10):1185. doi: 10.1164/rccm.19310erratum. PMID: 12091180.
11. Ideguchi H, Ichiyasu H, Fukushima K, Okabayashi H, Akaike K, Hamada S, Nakamura K, Hirotsako S, Kohrogi H, Sakagami T, Fujii K. Validation of a breath-holding test as a screening test for exercise-induced hypoxemia in chronic respiratory diseases. *Chron Respir Dis.* 2021 Jan-Dec;18:14799731211012965. doi: 10.1177/14799731211012965. PMID: 33906454; PMCID: PMC8718165.
12. Hedhli A, Slim A, Ouahchi Y, Mjid M, Koumenji J, CheikhRouhou S, Toujani S, Dhahri B. Maximal Voluntary Breath-Holding Tele-Inspiratory Test in Patients with Chronic Obstructive Pulmonary Disease. *Am J Mens Health.* 2021 May-Jun;15(3):15579883211015857. doi: 10.1177/15579883211015857. PMID: 33993797; PMCID: PMC8127757.
13. Ganong, W.F., 2020. *Ganong's review of medical physiology.* 26th ed. McGraw-Hill Education(India) Reprint 2019. p.655-656.
14. Pal GK. *Textbook of Practical Physiology.* 4th ed. New Delhi: Jaypee Brothers Medical Publishers; 2018. p.140.
15. Hideharu Ideguchi,1 Hidenori Ichiyasu,1 Kazuaki Fukushima, et. al. Validation of a breath-holding test as a screening test for exercise-induced hypoxemia in chronic respiratory diseases *Chron Respir Dis.* 2021 Jan-Dec; 18: 14799731211012965. Published online 2021 Apr 28. doi: 10.1177/14799731211012965 PMCID: PMC8718165 PMID: 3390645
16. DiMario FJ Jr, Burleson JA. Autonomic nervous system function in severe breath-holding spells. *Pediatr Neurol.* 1993 Jul-Aug;9(4):268-74. doi: 10.1016/0887-8994(93)90062-h. PMID: 8216538.
17. Guyton AC, Hall JE. *Guyton and Hall Textbook of Medical Physiology.* 14th ed. Philadelphia: Elsevier; 2020. p.535-536.
18. Agarwala P, Salzman SH. Six-Minute Walk Test: Clinical Role, Technique, Coding, and Reimbursement. *Chest.* 2020 Mar;157(3):603-611. doi: 10.1016/j.chest.2019.10.014. Epub 2019 Nov 2. PMID: 31689414; PMCID: PMC7609960.
19. Lama VN, Flaherty KR, Toews GB, Colby TV, Travis WD, Long Q, Murray S, Kazerooni EA, Gross BH, Lynch JP 3rd, Martinez FJ. Prognostic value of desaturation during a 6-minute walk test in idiopathic interstitial pneumonia. *Am J Respir Crit Care Med.* 2003 Nov 1;168(9):1084-90. doi: 10.1164/rccm.200302-219OC. Epub 2003 Aug 13. PMID: 12917227.

20. Trembach N, Zabolotskikh I. Breath-holding test in evaluation of peripheral chemoreflex sensitivity in healthy subjects. *Respir Physiol Neurobiol*. 2017 Jan;235:79-82. doi: 10.1016/j.resp.2016.10.005. Epub 2016 Oct 15. PMID: 27756650.
21. Daxiang Li, Ruru Wang, Jinbao Huang, Qingshuang Cai, Chung S. Yang, Xiaochun Wan, Zhongwen Xie, Effects and Mechanisms of Tea Regulating Blood Pressure: Evidences and Promises Nutrients. 2019 May; 11(5): 1115. Published online 2019 May 18. doi: 10.3390/nu11051115 PMID: PMC6567086
22. Coll-de-Tuero G, Saez M, Rodriguez-Poncelas A, Bayó-Llibre J, Beltran-Vilella M, Reyes-Negre C, Dalfó-Baqué A, Barceló M. What is the optimal cut-off threshold in self-home blood pressure measurement?: A cohort study according to STROBE statement. *Medicine (Baltimore)*. 2019 Mar;98(10):e14817. doi: 10.1097/MD.00000000000014817. PMID: 30855506; PMID: PMC6417491.
23. Viechtbauer W, Smits L, Kotz D, Budé L, Spigt M, Serroyen J, Crutzen R. A simple formula for the calculation of sample size in pilot studies. *J Clin Epidemiol*. 2015 Nov;68(11):1375-9. doi: 10.1016/j.jclinepi.2015.04.014. Epub 2015 Jun 6. PMID: 26146089.
24. Ideguchi H, Ichiyasu H, Fukushima K, Okabayashi H, Akaike K, Hamada S, Nakamura K, Hirosako S, Kohroggi H, Sakagami T, Fujii K. Validation of a breath-holding test as a screening test for exercise-induced hypoxemia in chronic respiratory diseases. *Chron Respir Dis*. 2021 Jan-Dec;18:14799731211012965. doi: 10.1177/14799731211012965. PMID: 33906454; PMID: PMC8718165.
25. Taneja I, Medow MS, Clarke DA, Ocon AJ, Stewart JM. Postural change alters autonomic responses to breath-holding. *Clin Auton Res*. 2010 Apr;20(2):65-72. doi: 10.1007/s10286-009-0046-x. Epub 2009 Dec 11. PMID: 20012144; PMID: PMC3378244.
26. Bosco G, Ionadi A, Data PG, Mortola JP. Voluntary breath-holding in the morning and in the evening. *Clin Sci (Lond)*. 2004 Apr;106(4):347-52. doi: 10.1042/CS20030260. PMID: 14613480.
27. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, Barnes PJ, Fabbri LM, Martinez FJ, Nishimura M, Stockley RA, Sin DD, Rodriguez-Roisin R. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med*. 2013 Feb 15;187(4):347-65. doi: 10.1164/rccm.201204-0596PP. Epub 2012 Aug 9. PMID: 22878278.
28. Casanova C, Cote C, Marin JM, Pinto-Plata V, de Torres JP, Aguirre-Jaime A, Vassaux C, Celli BR. Distance and oxygen desaturation during the 6-min walk test as predictors of long-term mortality in patients with COPD. *Chest*. 2008 Oct;134(4):746-752. doi: 10.1378/chest.08-0520. Epub 2008 Jul 14. PMID: 18625667.
29. Trembach N, Zabolotskikh I. The Influence of Age on Interaction between Breath-Holding Test and Single-Breath Carbon Dioxide Test. *Biomed Res Int*. 2017;2017:1010289. doi: 10.1155/2017/1010289. Epub 2017 Jan 31. PMID: 28251147; PMID: PMC5306978.
30. Hedhli A, Slim A, Ouahchi Y, Mjid M, Koumenji J, CheikhRouhou S, Toujani S, Dhahri B. Maximal Voluntary Breath-Holding Tele-Inspiratory Test in Patients with Chronic Obstructive Pulmonary Disease. *Am J Mens Health*. 2021 May-Jun;15(3):15579883211015857. doi: 10.1177/15579883211015857. PMID: 33993797; PMID: PMC8127757.