Effect of rapid exercise test on mild COVID-19 pneumonia patients and its significance on the detection of COVID-19 disease at an early stage

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Thesis Supervisor's Signature: ____

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AUGUST, 2020

Declaration

I certify that this research work titled "*Effect of rapid exercise test on mild COVID-19 pneumonia patients and its significance in detection of COVID-19 at an early stage*" is my own work. The work has not been presented elsewhere for assessment. The material that has been used from other sources it has been properly acknowledged / referred.

Signature of Student

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Registration Number

0000273647

Signature of Supervisor

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Mr. and Mrs. Arif Mehmood Sheikh

Abstract

The world is currently facing a dramatic disruption of everyday life owing to rapid progression of COVI-19 pandemic. As the pandemic evolves there is an urgent need to understand its epidemiology and its impact on the society to advert its mortality rate. Silent hypoxia has shown to be one of the major reasons of high death rates of people suffering from COVID-19 especially in third world countries. Measurement of oxygen saturation has been proposed to assess hypoxia in suspected COVID-19 infected patients. Clinicians have noted that patients with suspected COVID-19 and relatively normal oxygen saturation may desaturate after exertion, but the clinical importance of this finding is uncertain. In this research we aim to determine the-clinical importance of oxygen desaturation in the patients suffering from COVID-19 and the effect of rapid exercise test on COVID-19 patients in order to identify the disease before actual symptoms appear using an oximeter especially in third world countries where people cannot afford advance technologies and had suffered highest death rates due to COVID-19.This study aims to provide a reliable methodological guidance and evidence of silent hypoxia present in COVID-19 patiennts and method to detect the disesase at an early stage. Due to extreme load on hospitals ,there is an urgent need to detect the disease at an early stage using oximeter in order to reduce the load on hospitals.One minute sit-stand test has been used to assess the effect of rapid exercise on oxygen saturation of three sets of individuals(COVID-19 patients,healthy individuals and individuals with comorbidities), one-way ANOVA test was conducted to assess the difference in oxygen saturation of the subjects before and after exercise and it has been observed that COVID-19 patients showed significant decrease in their oxygen saturation levels before and after exercise with p value ($p \leq 0.05$) where as the results of healthy individual and people with comorbidities showed no significance($p=0.312$, $p=0.36$). Results confirmed that oxygen saturation levels of COVID-19 patients have decreased after one-minute exercise test. Therefore,These findings may help to detect the disease at an early stage without the use of costly diagnostic tests and can prevent the disease from getting worse which will ultimately save many lives.

Keywords: Rapid exercise test, arterial desaturation, COVID-19, silent hypoxia

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CHAPTER 1: INTRODUCTION

Corona virus commonly known as COVID-19 is an infectious disease that was first identified in December 2019 in the city of Wuhan, China. It started spreading to other parts of China and it spread around the whole world. WHO soon declared COVID-19 as a pandemic and an international public health emergency which became a threat to society and affected human health, the economy as well as the lifestyle of people all around the globe[1,2]. Till 2nd January 2021, 85,027,813 cases of COVID-19 have been reported with 1,844,685 deaths worldwide [3]. Third world countries were severely affected by the disease and Pakistan being a third world country has also been severely affected by the pandemic resulting in 486,634 cases till 2nd January 2021 [4].Initial symptoms include fever, dry cough, fatigue, pharyngeal pain, muscle soreness, nasal congestion and runny nose specifically.Most of the symptoms remained unnoticed for the first few days and started appearing after the disease has gotten worse. All these symptoms worsen with the passage of time and eventually lead to shortness of breath and pneumonia in both lungs which is the main cause of hypoxia(reduced level of tissue oxygenation which can be fatal for life) and requires intensive care treatment between 7-12 days [5,6] . The initial clinical symptoms are somehow similar to influenza and the patient doesn’t show any symptoms of respiratory distress syndrome.However most people with COVID-19 experience mild to moderate illness and the percentage of people suffering from mild disease is 81%, but around 15% progress to severe pneumonia and almost about 5% of patients progress to acute respiratory distress syndrome (breathing disorder due to which fluid starts accumulating in the alveoli)[7]. Mostly elderly people ranging between the age of 30-60 were affected severely by the virus severely and the reason is that they have weak immune system. COVID-19 can cause some serious lasting symptoms in people leading to reduction in their daily

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activities which mainly includes breathlessness and fatigue. These symptoms can continue for a number of months and hence can affect your life immensely[8]. It has been found out thet the symptoms of COVID-19 lasts for ≥3 months and can cause breathlessness ,fatigue, muscle pain for a longer period of time. If the symptoms are not treated properly than there are chances that the patient may suffer from some serious disorders[9].According to some new reports in Italy inpatients, 53% patirents experienced fatigue, 43% patients experienced dyspnoea and 22% were experiencing chest pain even after COVID-19 has subsided these symptopms continue to effect the life of individuals [10].

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1.1: PROBLEM STATEMENT

Hypoxia is silently killing COVID-19 patients. Most of the patients didn't show any symptoms of breathlessness but their lungs have diffused pneumonia which eventually leads to hypoxia and acute respiratory distress syndrome. Therefore, it is extremely necessary to detect the disease at an early stage in order to save lives. In third world countries most of the patients cannot afford the test and ultimately became prey to COVID-19 virus. The goal of this study is to present a test which can be used in order to detect COVID-19 at an early stage. In third World countries where the people are unaware of the advance technologies or they didn't have enough resources to get a proper treatment this test can help them to identify the disease at an early stage and can reduce the load on the hospitals too. The study aims to assess the possible impacts of rapid exercise testing on arterial oxygen desaturation in early mild COVID-19 pneumonia to detect early COVID complications. As rapid exercise tests are cost-effective and reliable means for identifying patients that are at high risk requiring hospital care and treatment to improve the disease outcome.

1.2: Core Objectives

The core objectives of this study are,

- To evaluate the effect of rapid exercise on oxygen saturation levels of mild COVID-19 patients.
- To estimate the difference in oxygen saturation of different groups performing the same exercise course.
- To determine the significance of rapid exercise test in detection of COVID-19 at an early stage.

1.3: Areas of Application

This technique can be used in the following areas in order to find out the oxygen saturation levels .

- Laboratories
- Hospitals
- Domestic Use

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1.4: Thesis Overview

Chapter 1 contains the introduction along with the possible suggested solution and description of the problem statement. In Chapter 2 , the work that has been done in the related area is included. In Chapter 3 the detailed information about the experimental protocol and the techniques being used is provided. Chapter 4 contains the results obtained from this study. Chapter 5 contains the discussions of the results and conclusion of the whole work. In chapter 6 provides references for all the citations. Annexure is also provided.

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CHAPTER: 2 LITERATURE REVIEW

A research that was carried out at The Center For Evidence Based Medicine and according to Trisha Greenhalgh et.al, COVID-19 virus can cause an unusual lung disease which is usually characterized by tendency of lungs to desaturate after little exertion or exercise. In order to prove this they performed two diagnostic tests which showed low oxygen level on oximeter reading [11].

Levitan et.al,suggested that silent hypoxia is silently killing COVID-19 patients. He observed that the patients without respiratory complaints also had Covid pneumonia. Most of the patients didn't have any sensation of breathing problems even though their chest showed diffused pneumonia and their oxygen was below normal. He observed that the patients who reported at hospital were very severe and needed ventilation. Almost all the patients have severe lung injury when they arrive in emergency rooms. According to him silent hypoxia causes respiratory failure in Covid patients and can cause sudden death even without shortness of breath[12].

Hypoxemia that may go unnoticed by the patients initially is usually termed as silent hypoxemia which is a known factor associated with poor prognosis but very little documented data exists to time in this regard. International Journal on Infectious Diseases reported on January 2021, that asymptomatic hypoxia can cause severe breathing issues in COVID-19 patients leading to complete lungs damage. The journal suggested that the poor prognosis of asymptomatic hypoxia, highlight the severity of this mild clinical presentation. According to this research, pulse oximetry is an important mean to predict the outcome along with news score and LDCT scanner [13].

Martin J. Tubin et.al, found out that COVID-19 virus has silent action on receptors involved in chemo sensitivity to oxygen causing hypoxemia in patients which causes left shift in oxygen dissociation curve and happy hypoxia in COVID-19 patients. He suggested the mechanism underlying silent hypoxia can only be understood if we know the exact physiology of how the respiratory receptors react to the low levels of oxygen in blood otherwise it is not possible to

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indicate the proper cause of hypoxia [14].

Rehman et.al, provided evidences that suggested that the virus is affecting the brain of COVID-19 patients due to which these patients suffer from low hypoxic pulmonary vasoconstriction and leads to hypoxia. Low hypoxic pulmonary vasoconstriction is a physiological term in which there is constriction of small pulmonary arteries leading to alveolar hypoxia. [15].

Jounieaux et.al, found out that hypoxia and hypocapnia are interrelated and hypocapnia has a powerful braking effect on respiratory system of COVID-19 patients and intrapulmonary shunts are the key factors in patients with COVID-19 that accounts for both the presence of hypoxia and absence of dyspnea in these patients [16].

Most of the recent reports suggested that prevalence of silent hypoxia in COVID-19 patients ranges from 20-40%. This sughgests that almost 40%of the people suffering from COVID-19 experience hypoxia and need proper care . Some of these patients also faces severe hypoxi and needs to be administered in intensive care units for proper ventilation [17].

Mathias Ochs et.al, suggested that COVID-19 virus primarily attacks alveolar epithelial cells which causes hypoxia and breathing issues in the patients and leads to severe lung diseases.Lungs of the patients are severely affected and can be letal for their life. The scientist says that the walls of alveoli gets blocked severely and causes breathlessness and hypoxia ultimately [18].

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CHAPTER:3 METHODOLOGY

In this analytical study, we have recorded the data from three sets of people in order to compare the effect of rapid exercise test on the oxygen saturation level of these three groups of people. First set includes COVID-19 patients who didn’t show any symptoms of breathlessness ,second set includes healthy subjects without any comorbidity , the last set includes subjects who are COVID-19 negative but have other co morbidities(blood pressure, mild cardiovascular issues,diabetes and other mild diseases).All the participants included in the study have average age between 20-55 years.In this study we will not include pregnant women, postoperative infections, psychopaths, patients with severe pneumonia or other diseases due to which the patient cannot do exercise are not included in the study. Furthermore, patients with severe cardiovascular, liver and kidney diseases are also not a part of this study. All the patients suffering from any orthopedic disease are also not included in this study. There were 150 COVID-19 patients , 50 patients with comorbidities and 50 healthy individuals.

3.1. Study Protocol

First of all the patients were properly guided about the test that was going to be performed on them. A written consent was signed from the patients after proper guidance regarding the test. The test was performed under proper supervision of the clinicians and if any subject felt discomfort while performing the test then the test was immediately stopped.

3.2. Data Collection

The survey was conducted in CMH hospital that is situated in Rawalpindi from April 2020 till September 2020. The procedure of the test was explained to the participants prior to data collection. All the subjects were asked to do the same exercise for one minute and then the data was recorded. It has to be mentioned here that there was a set protocol according to which the individuals were characterized as healthy individuals. According to this all the individuals having weight according to set BMI rules and have all the vitals within range and are physically active are considered to be healthy .

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3.3. One-minute sit-to-stand exercise test

First of all the subjects were made comfortable and the consent forms were signed. All of them were guided about the exercise that they were going to perform properly. All the subjects were told to perform repetitive sit and stand as possible as they can in one minute on an armless chair of a standard height with the arms folded on the chest. Pre-exercise and post-exercise oxygen saturation level of each individual was recorded using a pulse oximeter. The test was performed under the supervision of the hospital ethical committee.The same test was performed by all the individuals included in the study(COVID-19 patients, healthy individuals, individuals with comorbidities).

The data was first entered into excel for proper and safe documentation and after that SPSS was further applied for the analysis of the data .One-way ANOVA test was applied to compare the results of pre and post exercise oxygen saturation levels of individuals.

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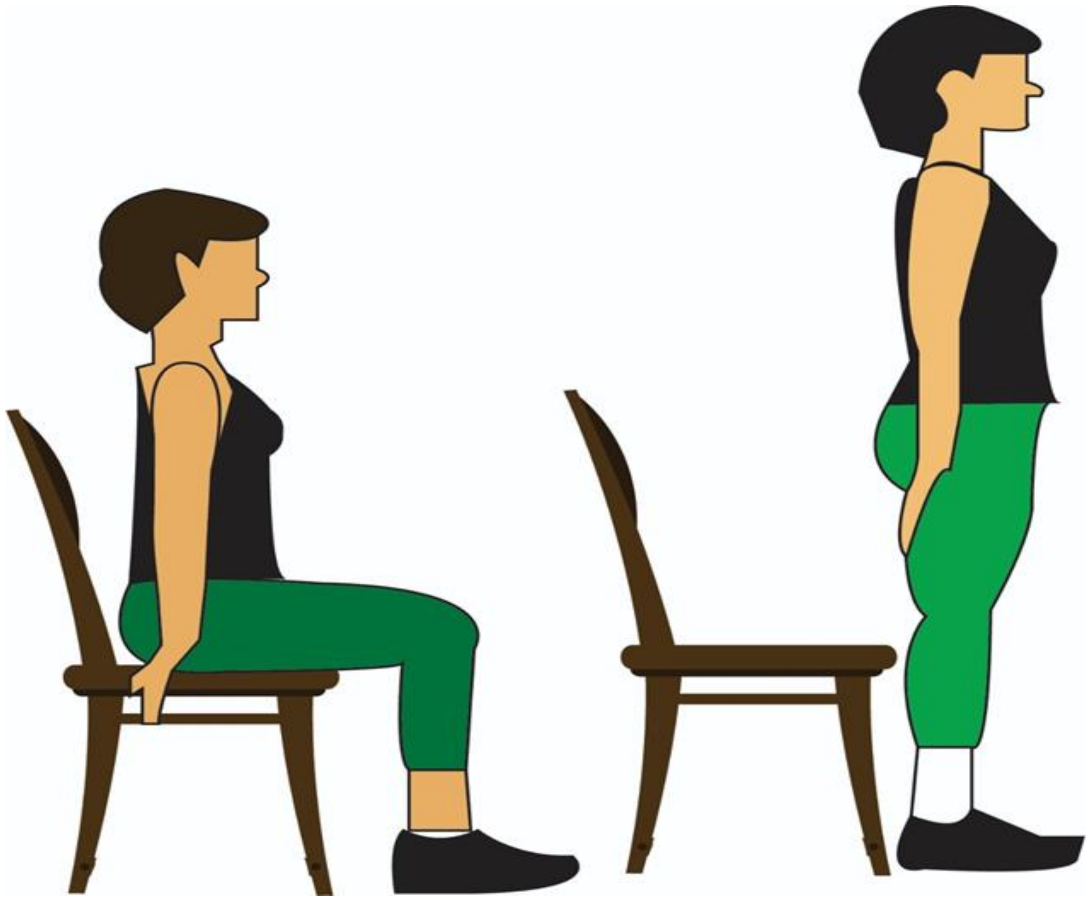

Figure 1: Visual representation of Sit to stand test

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3.4 : Demographic Representation of the Subjects

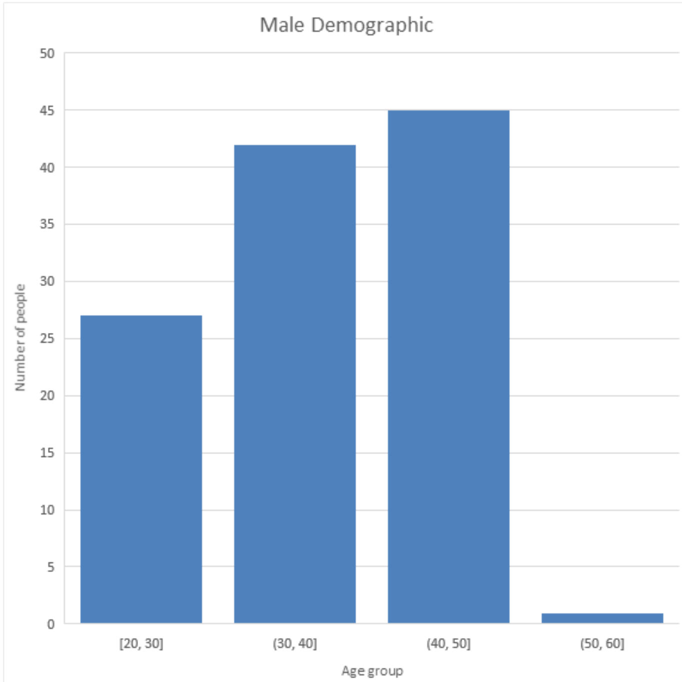

Fig 2: Demographic representation of male COVID-19 patients

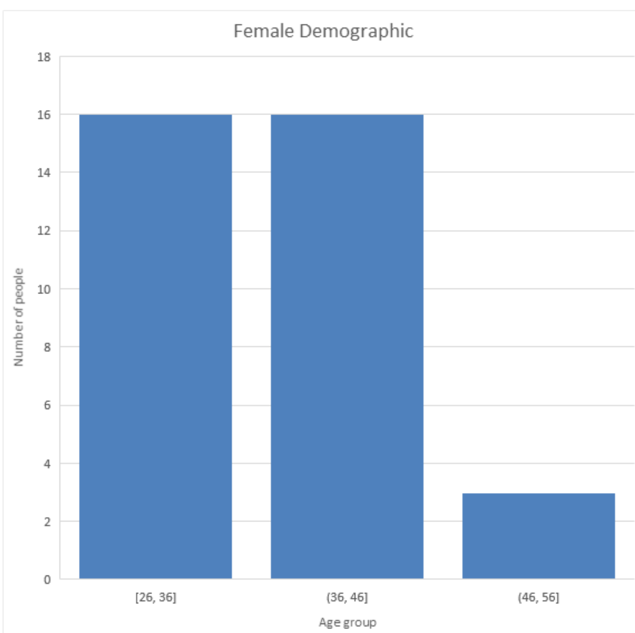

Fig 3: Demographic representation of female COVID-19 patients

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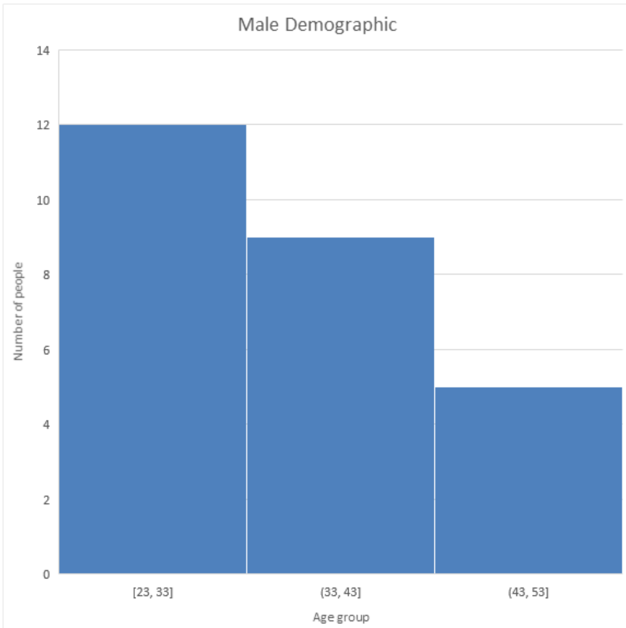

Fig 4: Demographic representation of Healthy male

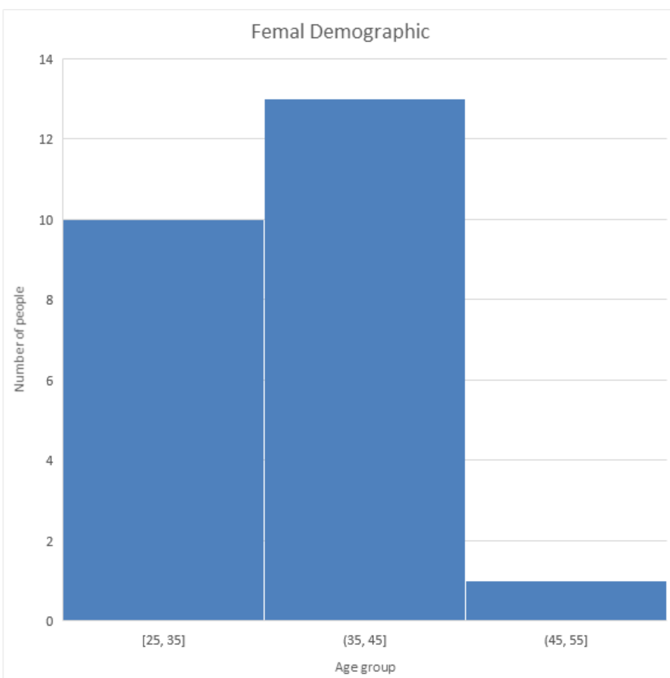

Fig 4: Demographic representation of Healthy female

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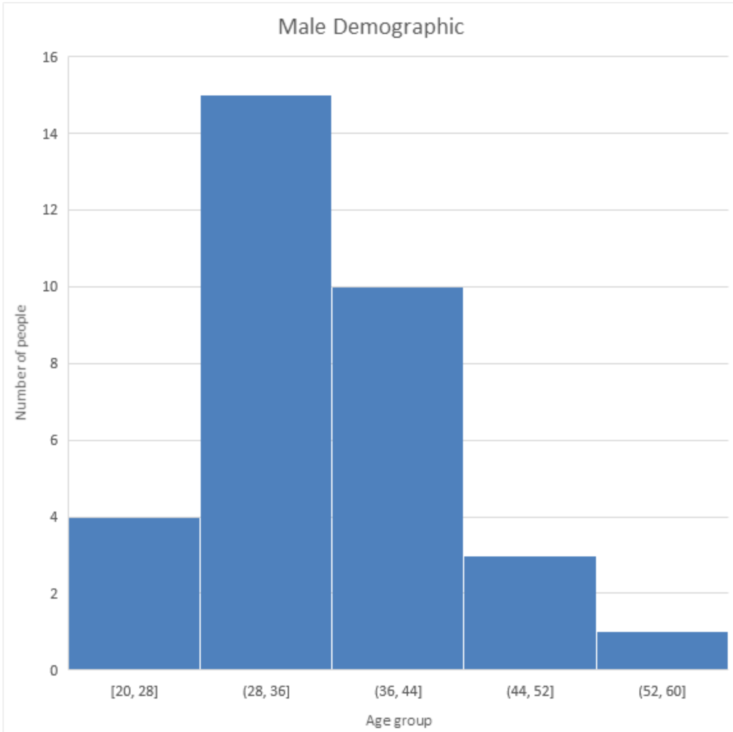

Fig 6: Demographic Representation of male patients with comorbidities

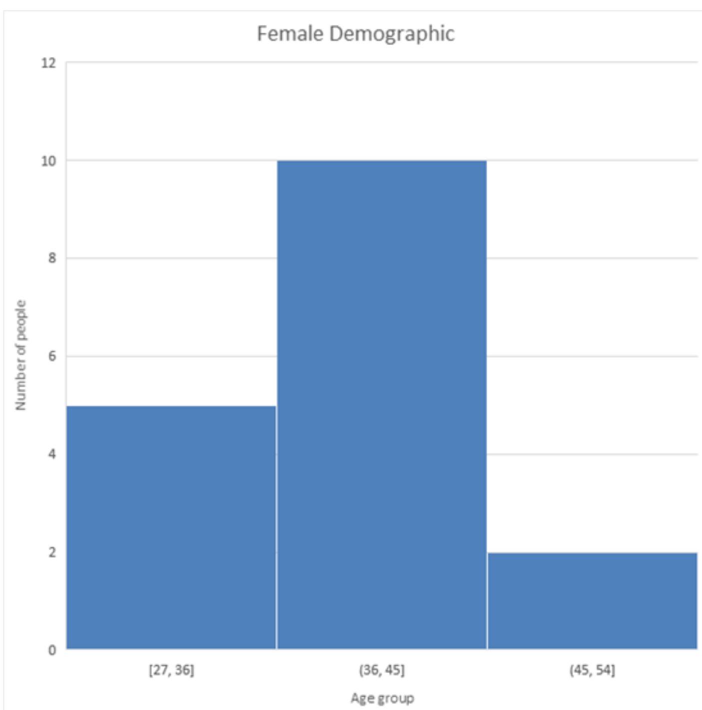

Fig 7: Demographic representation of female patients with comorbidities

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CHAPTER: 4 RESULTS

A one way ANOVA was conducted to compare the effect of rapid exercise test on mild COVID-19 patients before and after one minute exercise test. An analysis of variance showed that the effect of rapid exercise test on COVID-19 patients is significant $F(1,298) = 26.524$, $p \leq 0.005$ .Fig 2, represents the graphical analysis of average difference between the oxygen saturation levels of COVID-19 before and after exercise which clearly shows almost 2% drop in oxygen saturation level after exercise.

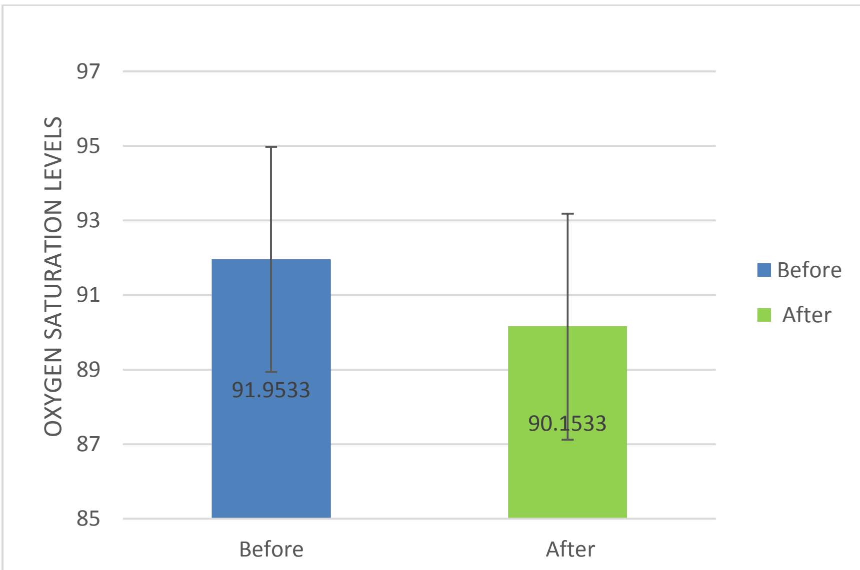

Figure 8: Result of oxygen saturation level of 150 COVID-19 patients before and after exercise.

Compared to COVID patients when one way ANOVA was conducted to find the effect of rapid exercise test on healthy individuals the analysis of variance showed no significance $F(1,98)=1.031, p=0.312$. Fig 3, represents the graphical analysis of average difference between the oxygen saturation level of healthy individuals before and after exercise which is 0.3 near to negligible

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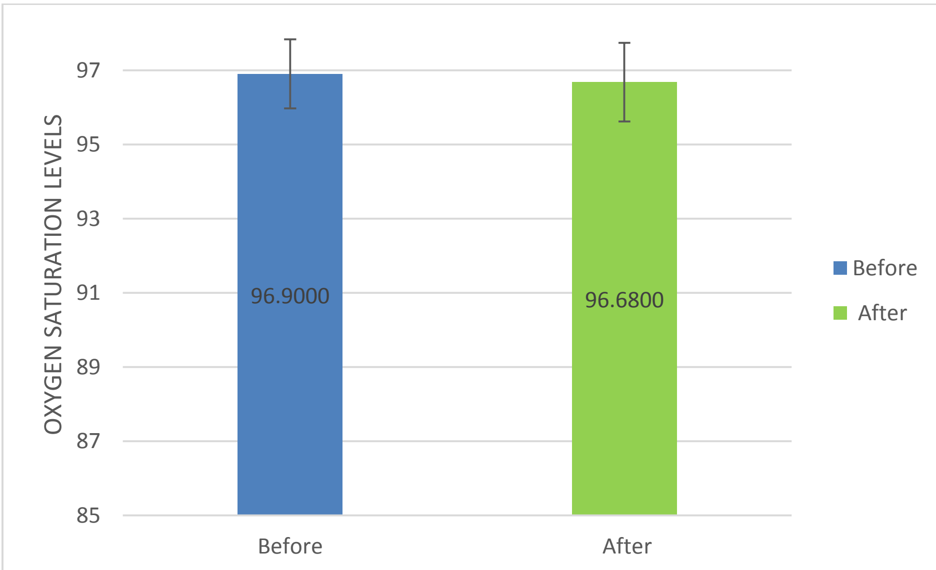

Figure 9: Result of the oxygen saturation level of Healthy Individuals before and after exercise

Now when one-way ANOVA was conducted to find the effect of rapid exercise test on individuals with comorbidities except COVID-19 the analysis of variance again showed no significance $F(1,98)=0.843, p=0.361$. Fig 4, represents the graphical analysis of average difference between the oxygen saturation level of individuals with comorbidities before and after exercise which is 0.3 near to negligible.

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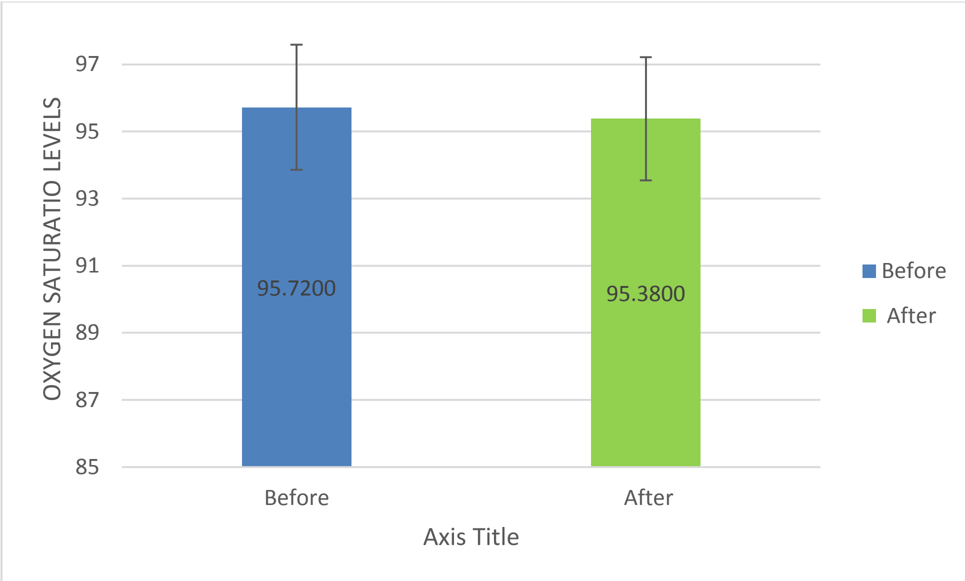

Figure 10: Result of oxygen saturation levels of patients with comorbidities before and after exercise

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CHAPTER

Many patients with COVID-19 experience arterial desaturation without any obvious clinical symptoms or any signs of hypoxemia. This type of hypoxemia is called silent hypoxemia. Some of the studies also show the presence of dyspnea in hospitalized patients with COVID-19[19].

There are various mechanisms that contribute to profound hypoxemia with lack of clinical signs of dyspnea in COVID-19 patients. Left ward shift of oxyheamoglobin curve due to the underlying hypocapnea and increased ferritin due to the viral interactions with heme results in normal arterial saturation inspite of the low oxygen saturation in early COVID patients[20].

The main mechanism suggested for hypoxemia in COVID-19 mismatch due to intrapulmonary shunting due to persistent blood flow to poorly ventilated lung resulting from interstitial edema, intravascular micro thrombi in lungs, impaired diffusion capacity of lungs all leading to increased volume of inspired air[13].

Presence of hypoxemia in COVID-19 Patients predicts a complicated in hospital course and indicates the need for timely admission and observation in intense care setting[18]. One of the recent studies shows 25% of the people infected from COVID-19 have oxygen saturation less than or equal to 92% and almost 10% of the patients are later admitted to intensive care units[21].

Patients who are suffering from COVID-19 having normal oximeter reading can desaturate easily with mild exertional exercise therefore hypoxemia test should be used in order to find out the clinical dyspnea which can be treated promptly in order to prevent the disease progression. The pneumonia in COVID-19 behaves similarly to pneumocystis pneumonia.

Many different exercise test protocols are being used for the assessment of arterial desaturation in multiple lungs disorders. None of these tests have been used in studying COVID-19 patients. Little data is available to the implications of exercise included in hypoxemia in COVID-19. The exercises include 30 minute walk, a stair climb test,Chester step test and modified chester test andminute sit to stand test[22,23].

One minute sit to stand test is a test in which patients sits and stands fully as many times as he can be in one minute and desaturation of lungs is measured properly. This test is used to identify the interstitial lung disease and obstructive airway disease[24,25,26].

We examined three groups of people and found out the results of before and after exercise oxygen saturation. The group that contained only healthy patients showed no such difference in before and after

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exercise oxygen saturation levels. The group that contained people with few comorbidities showed a slight difference in their oxygen saturation levels. One thing has to mentioned here that the people with heart diseases showed increase in their oxygen saturation before and after exercise. The group that contained only COVID-19 patients showed a remarkable difference in their oxygen saturation levels almost more than 3 percent increase or decrease in their oxygen saturation levels before and after exercise was observed in COVID-19 patients which predicts adverse outcomes and calls for admission in hospital in early disease course.

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5.1 :Limitations

Despite the adequate methodology and the findings , the present study has certain limitations.As the individuals included in this study were between 25-45 years of age therefore, individuals of older age might show alered responses to the same exercise test.

5.2Conclusion

Rapid exercise tests are quick tests that can be used in early mild cases of COVID-19 in order to predict in hospital course of disease and identifying high risk patients who will need admission in hospital as the disease progresses. In this way we can identify the silent hypoxia and can reduce in hospital complications.Therefore, we can conclude that in third world countries where advance tecnologies are not easily available for all the people or the people who can't afford multiple tests

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Gender	Before	After	change	Age
male	91	90	1	20
male	92	89	3	21
male	92	91	1	24
male	86	86	0	24
male	86	84	2	25
male	95	94	1	25
male	89	89	0	26
female	91	90	1	26
male	91	91	0	26
male	89	88	1	26
male	96	94	2	26
male	93	92	1	27
male	94	91	3	27
male	94	91	3	27
female	93	92	1	27
female	85	84	1	27
male	95	93	2	27
male	89	86	3	27
male	90	90	0	28
female	89	89	0	28
male	90	88	2	28
male	83	82	1	28
male	91	89	2	28
male	94	92	2	29
male	92	91	1	29
male	89	85	4	29
male	96	94	2	29
male	90	88	2	30
female	91	88	3	30
male	94	92	2	30
male	98	88	2	30
male	89	87	2	30
female	91	89	2	31
female	95	93	2	31
male	93	91	2	31
female	90	89	1	31
male	92	90	2	31
male	93	91	2	31
female	94	93	1	31
female	96	94	2	31
male	93	91	2	31
female	90	85	5	32
male	95	93	2	32
male	89	89	1	32
male	91	89	2	32
male	96	95	1	32
male	93	92	1	32
male	91	89	2	32
male	94	92	3	32
male	94	92	2	33
male	95	91	4	33
male	97	95	2	33
male	89	88	1	33
male	91	89	2	33
male	93	91	2	33
male	92	90	2	34
male	95	93	2	34
male	93	93	0	34
female	96	94	2	34
male	90	89	1	34
male	93	91	2	34
male	92	91	1	34
female	90	88	2	34
male	94	93	1	35
female	90	88	2	35
male	96	93	3	35
male	91	90	1	36
female	83	82	1	36
male	94	92	2	36
female	88	88	0	36
male	87	86	1	36
male	86	84	2	37
male	96	93	3	37
male	95	94	1	37
male	92	90	2	38
female	95	92	3	38
female	89	88	1	38
male	92	90	2	38
male	95	93	2	38

Table 1 :Data of COVID-19 Individuals

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male	92	89	3	38
male	94	92	2	38
male	84	84	0	38
male	94	92	2	39
male	93	90	3	39
female	95	93	2	39
male	93	91	2	39
female	97	96	1	39
male	90	87	3	40
female	89	86	3	40
female	92	90	2	40
female	90	88	2	40
male	92	91	1	40
male	96	95	1	41
male	94	92	2	41
male	93	91	2	41
male	84	82	2	41
male	90	89	1	41
male	88	86	2	41
female	94	91	3	41
female	92	91	1	41
female	94	93	1	41
male	93	92	1	42
male	91	89	2	42
male	91	90	1	42
male	90	88	2	42
male	95	94	1	42
male	90	87	3	42
female	98	95	3	42
female	83	85	2	42
male	92	91	1	42
male	93	90	3	42
male	93	92	1	43
male	94	93	1	43
male	94	93	1	43
male	88	85	3	43
male	93	91	2	43
male	93	93	0	43
female	92	90	2	43
male	87	86	1	43

male	94	93	1	43
male	92	91	1	44
male	92	90	2	44
female	93	91	2	44
male	89	87	2	44
male	96	95	1	44
male	93	92	1	44
male	95	93	2	44
female	93	91	2	45
male	89	88	1	45
male	90	79	1	45
male	91	91	0	45
male	90	88	2	45
male	91	89	2	45
male	95	93	2	45
male	96	94	2	45
female	93	91	2	46
male	88	86	2	47
male	96	95	1	47
male	93	92	1	47
female	91	90	1	48
female	95	92	2	48
male	95	93	2	48
male	92	90	2	48
male	92	90	2	48
male	90	88	2	48
male	92	92	0	49
female	93	91	2	49
male	93	90	3	49
male	94	93	1	49
male	91	88	3	56

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Gender	BEFORE	AFTER	Change	Age
male	97	97	0	28
male	99	99	0	35
female	98	98	0	44
male	97	96	1	43
male	97	96	1	36
female	98	98	0	25
male	96	96	0	28
male	96	95	1	33
female	97	95	2	45
female	96	96	0	41
female	98	98	0	40
female	98	98	0	37
female	98	97	1	41
male	97	97	0	43
male	96	96	0	29
female	97	96	1	30
female	97	97	0	45
male	96	95	1	46
male	97	97	0	45
female	96	96	0	41
female	97	97	0	40
female	98	97	1	31
male	98	98	0	33
female	96	96	0	32
female	95	95	0	38
female	96	96	0	39
male	98	98	0	32
male	96	96	0	36
female	98	98	0	29
male	96	96	0	44
female	95	95	0	47
female	98	98	0	45
male	98	98	0	23
female	97	97	0	29
female	97	97	0	27
male	96	96	0	26
female	96	95	1	28
female	98	98	0	34
male	96	96	0	41
male	96	96	0	27
male	98	98	0	29
male	97	97	0	34
male	97	97	0	33
male	96	96	0	40
male	97	97	0	46
male	98	98	0	48
female	97	97	0	26
female	97	97	0	37
male	96	95	1	27
male	96	96	0	34

Table 2: Data of Healthy Individuals

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Gender	Before	After	Change	Age
male	88	91	3	56
male	92	94	2	47
male	92	90	2	38
female	96	95	1	27
male	95	94	1	36
male	92	91	1	34
male	93	92	1	33
female	96	95	1	32
male	96	95	1	31
male	95	94	1	30
male	95	94	1	26
male	93	91	2	45
female	95	95	0	43
female	96	95	1	43
female	97	96	1	42
female	96	96	0	41
female	97	97	0	44
female	96	96	0	45
female	95	95	0	36
male	97	96	1	38
male	98	97	1	39
male	97	97	0	32
male	97	97	0	31
male	96	95	1	45
male	98	97	1	43
male	98	98	0	44
male	95	95	0	41
female	97	97	0	40
female	96	96	0	48
female	95	95	0	49
male	97	96	1	32
male	96	96	0	42
male	96	96	0	27
female	95	94	1	28
male	97	96	1	29
male	97	97	0	20
male	95	95	0	25
female	96	95	1	38
male	96	96	0	38
male	97	97	0	39
male	95	95	0	33
male	97	97	0	32
male	96	96	0	31
female	98	99	1	32
female	97	97	0	45
female	96	96	0	39
male	95	95	0	40
male	97	97	0	31
male	96	96	0	32
male	98	97	1	34

Fig 3: Data of patients with Comorbidities

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REFERENCES

1: Woods, J., Hutchinson, N.T., Powers, S.K., Roberts, W.O., Gomez-Cabrera, M.C., Radak, Z., Berkes, I., Boros, A., Boldogh, I., Leeuwenburgh, C. and Coelho-Júnior, H.J., 2020. The COVID-19 pandemic and physical activity.

2: Jin, Y.H., Cai, L., Cheng, Z.S., Cheng, H., Deng, T., Fan, Y.P., Fang, C., Huang, D., Huang, L.Q., Huang, Q. and Han, Y., 2020. Management ftZHoWUNC, Research Team E-BMCoCIE, Promotive Association for M, Health C. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Military Medical Research*, *7*.

3:. Jiang, S., Xia, S., Ying, T. and Lu, L., 2020. A novel coronavirus (2019-nCoV) causing pneumonia-associated respiratory syndrome. *Cellular & molecular immunology*, *17*(5), pp.554-554

4: Yousaf, M., Zahir, S., Riaz, M., Hussain, S.M. and Shah, K., 2020. Statistical analysis of forecasting COVID-19 for upcoming month in Pakistan. *Chaos, Solitons & Fractals*, *138*, p.109926.

5. : Bernacki, E.J., 2020. COVID-19 Information for Texas Mutual Policyholders A Population Health Perspective of Covid-19 and the Workplace

6: Hui, D.S., Azhar, E.I., Madani, T.A., Ntoumi, F., Kock, R., Dar, O., Ippolito, G., Mchugh, T.D., Memish, Z.A., Drosten, C. and Zumla, A., 2020. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health—The latest 2019 novel coronavirus outbreak in Wuhan, China. *International journal of infectious diseases*, *91*, pp.264-266.

7: Zheng, P., Bao, L., Yang, W. and Wang, J.J., 2020. Clinical symptoms between severe and non-severe COVID-19 pneumonia: A protocol for systematic review and meta-analysis. *Medicine*, *99*(33).

8:Spruit, M.A., Holland, A.E., Singh, S.J., Tonia, T., Wilson, K.C. and Troosters, T., 2020. COVID-19: interim guidance on rehabilitation in the hospital and post-hospital phase from a European Respiratory Society-and American Thoracic Society-coordinated international task force. *European respiratory journal*, *56*(6).

Footnote may be given with Font size 10 of Times New Roman.

9: Daynes, E., Gerlis, C., Briggs-Price, S., Jones, P. and Singh, S.J., 2021. COPD assessment test for the evaluation of COVID-19 symptoms. *Thorax*, *76*(2), pp.185-187.

10: Chan, A.T., Drew, D.A., Nguyen, L.H., Joshi, A.D., Ma, W., Guo, C.G., Lo, C.H., Mehta, R.S., Kwon, S., Sikavi, D.R. and Magicheva-Gupta, M.V., 2020. The COronavirus Pandemic Epidemiology (COPE) consortium: a call to action. *Cancer Epidemiology and Prevention Biomarkers*, *29*(7), pp.1283-1289.

11: Greenhalgh, T., Javid, B., Knight, M. and Inada-Kim, M., 2020. What is the efficacy and safety of rapid exercise tests for exertional desaturation in covid-19. *Centre for Evidence-Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford*.

12: Levitan, R., 2020. The infection that's silently killing coronavirus patients. *The New York Times*,

13: Kabi, A., Mohanty, A., Mohanty, A.P. and Kumar, S., 2020. Post COVID-19 Syndrome: A Literature Review. *Journal of Advances in Medicine and Medical Research*, pp.289-295.

14: Tobin, M.J., Laghi, F. and Jubran, A., 2020. Why COVID-19 silent hypoxemia is baffling to physicians. *American journal of respiratory and critical care medicine*, *202*(3), pp.356-360.

15: Rahman, A., Tabassum, T., Araf, Y., Al Nahid, A., Ullah, M.A. and Hosen, M.J., 2021. Silent hypoxia in COVID-19: pathomechanism and possible management strategy. *Molecular biology reports*, pp.1-7.

16: Jounieaux, V., Rodenstein, D.O. and Mahjoub, Y., 2020. On Happy Hypoxia and on Sadly Ignored "Acute Vascular Distress Syndrome" in Patients with COVID-19. *American journal of respiratory and critical care medicine*, *202*(11), pp.1598-1599.

17: Chen, T., Wu, D.I., Chen, H., Yan, W., Yang, D., Chen, G., Ma, K., Xu, D., Yu, H., Wang, H. and Wang, T., 2020. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *bmj*, *368*.

Footnote may be given with Font size 10 of Times New Roman.

18: Ochs, M., Timm, S., Elezkurtaj, S., Horst, D., Meinhardt, J., Heppner, F.L., Weber-Carstens, S., Hocke, A.C. and Witzenrath, M., 2021. Collapse induration of alveoli is an ultrastructural finding in a COVID-19 patient. *European Respiratory Journal*, *57*(5).

19: Lari, A., Alherz, M., Nouri, A., Botras, L. and Taqi, S., 2020. Caution against precaution: A case report on silent hypoxia in COVID-19. *Annals of Medicine and Surgery*, *60*, pp.301-303

20**:**.' Couzin-Frankel, Jennifer. "The mystery of the pandemic's 'happy hypoxia'." (2020): 455-456.

21:. Vogel, D.J., Formenti, F., Retter, A.J., Vasques, F. and Camporota, L., 2020. A left shift in the oxyhaemoglobin dissociation curve in patients with severe coronavirus disease 2019 (COVID-19). *British journal of haematology*, *191*(3), pp.390-393

22**:** Dhont, S., Derom, E., Van Braeckel, E., Depuydt, P. and Lambrecht, B.N., 2020. The pathophysiology of 'happy'hypoxemia in COVID-19. *Respiratory research*, *21*(1), pp.1-9.

23**:**. Bahl, A., Van Baalen, M.N., Ortiz, L., Chen, N.W., Todd, C., Milad, M., Yang, A., Tang, J., Nygren, M. and Qu, L., 2020. Early predictors of in-hospital mortality in patients with COVID-19 in a large American cohort. *Internal and emergency medicine*, *15*(8), pp.1485-1499

24**:**. Mejía, F., Medina, C., Cornejo, E., Morello, E., Vásquez, S., Alave, J., Schwalb, A. and Málaga, G., 2020. Oxygen saturation as a predictor of mortality in hospitalized adult patients with COVID-19 in a public hospital in Lima, Peru. *PloS one*, *15*(12), p.e0244171

25**:** Vilarinho, R., Caneiras, C. and Montes, A.M., 2020. Measurement properties of step tests for exercise capacity in COPD: A systematic review. *Clinical rehabilitation*, p.0269215520968054.

26**:** Ni, M., Brown, L.G., Lawler, D. and Bean, J.F., 2017. Reliability, validity, and minimal detectable change of four-step stair climb power test in community-dwelling older adults. *Physical therapy*, *97*(7), pp.767-773.

27**:** Briand, J., Behal, H., Chenivesse, C., Wémeau-Stervinou, L. and Wallaert, B., 2018. The 1-minute sit-to-stand test to detect exercise-induced oxygen desaturation in patients with interstitial lung disease. *Therapeutic advances in respiratory disease*, *12*, p.1753466618793028

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