HANG TUAH MEDICAL JOURNAL

www.journal-medical.hangtuah.ac.id

Research article

Submaximal Exercise in Hyperbaric-Hyperoxia and Ejection Fraction Change in Healthy Subjects

BENNY JOVIE[1], DJATIWIDODO EDI PRATIKNYA[2], I MADE PRASETYA KURNIAWAN[3]

[1]Faculty of Medicine, Hang Tuah University, Surabaya

[2]Marine Medicine Specialist, Faculty of Medicine, Hang Tuah University, Surabaya

[3]Department of Parasitology, Faculty of Medicine, Hang Tuah University, Surabaya

Alamat e-mail penulis korespondensi: bennyheart43@gmail.com

Abstract

Coronary artery disease (CAD) is a leading cause of global morbidity and mortality. An important parameter in assessing is the ejection fraction (EF. In recent decades, hyperbaric oxygen therapy (HBOT) has attracted attention as a non-pharmacological adjunct modality in the management of ischemic heart disease. Researchers aim to further investigate the effects of submaximal exercise in hyperbaric-hyperoxia on ejection fraction changes in healthy subjects, with the hope that this knowledge will be useful in patients with reduced cardiac ejection fraction in the future, particularly in those with coronary heart disease. This randomized controlled trial included 30 healthy male military personnel, randomized into a normobaric control group (n = 15) and a hyperbaric–hyperoxic group (n = 15). In the control group, EF grade worsened in 12 subjects after submaximal exercise (p = 0.001), whereas in the hyperbaric–hyperoxic group, EF grade improved in 10 subjects (p = 0.003). Post-test comparison between groups revealed a significant difference (p = 0.001). The conclusion of this study shows that Submaximal exercise in hyperbaric–hyperoxic conditions improved EF grading compared to normobaric conditions in healthy military personnel.

Keywords: ejection fraction, hyperbaric, hyperoxia, submaximal exercise

INTRODUCTION

Coronary artery disease (CAD) is a leading cause of global morbidity and mortality, with its pathophysiology based on coronary artery atherosclerosis and myocardial ischemia leading to left ventricular dysfunction. A crucial parameter in evaluating left ventricular function is the ejection fraction (EF), which indicates the heart's ability to effectively pump blood into the systemic circulation. A decreased EF is often an indicator of myocardial damage due to chronic ischemia or myocardial infarction and is a key prognostic factor in determining mortality and treatment options (McDonagh *et al*., 2021; Shams *et al.*, 2025).

Submaximal exercise is moderate-intensity physical activity, typically between 40–70% of maximal oxygen capacity (VO_2max), that stimulates the cardiovascular system without causing excessive stress. In healthy individuals, submaximal exercise increases cardiac output by increasing heart rate and ejection fraction, and improves tissue oxygen efficiency (Shushan et al., 2022). However, in patients with coronary artery disease (CAD), these compensatory mechanisms are often impaired due to decreased myocardial perfusion, reversible ischemia, and left ventricular dysfunction, characterized by reduced ejection fraction (LVEF) when activity increases (Shahid *et al*., 2025).

In recent decades, hyperbaric oxygen therapy (HBOT) has attracted attention as a non-pharmacological adjunct modality in the management of ischemic heart disease. The basic principle of HBOT is the administration of pure oxygen (FiO_2 100%) at a pressure greater than 1 atmosphere absolute (ATA), typically between 2–3 ATA, which increases the arterial partial pressure of oxygen (PaO_2) and significantly increases the dissolved oxygen content in plasma (Gušić et al., 2024). This hyperoxia condition results in increased oxygen diffusion to ischemic tissue, decreased edema, and modulation of oxidative stress and inflammation that can support myocardial viability and improve systolic function (Robins *et al*., 2025).

Physiologically, the decreased ejection fraction seen immediately after submaximal exercise and the decreased EF that occurs in coronary heart disease share many fundamental similarities. Both refer to impaired myocardial contractility caused by an imbalance between myocardial oxygen demand and coronary supply. In exercise situations, increased heart rate and oxygen demand pressures can exceed the heart's perfusion capacity, particularly when cardiac reserve is limited, resulting in transient ischemia or "cardiac fatigue," which reduces the ability of myocardial fibers to contract and increases residual systolic volume (ESV), ultimately reducing EF. In chronic coronary heart disease, arteriosclerosis and coronary stenosis persistently restrict blood flow to the heart muscle, leading to recurrent ischemia, ventricular remodeling, fibrosis, and permanent or progressive reduction in contractility. Both descriptions share fundamentally the same mechanism (insufficient supply relative to demand) but occur at different time scales and intensities. Therefore, researchers aim to further investigate the Effects of Submaximal Exercise in hyperbaric-hyperoxia on ejection fraction change in Healthy Subjects, with the hope that this knowledge will be useful in patients with coronary artery disease in the future.

METHOD

The type of research is a true experimental research design with a randomized control group, a pretest-posttest design, and the sampling technique used is simple random sampling. This research has been approved by the ethics board of the Faculty of Medicine, Hang Tuah University, Surabaya. This study is a pilot study with the population in this study being 30 soldiers of the Surabaya Marine Health Corps with the inclusion criteria for this study being male subjects, Indonesian Navy soldiers, healthy, aged 20-27 years, normal diagnostic physical tests, normal laboratory tests, normal ECG, normal blood pressure, normal pulse rate, able to perform physical tests adequately, and willing to participate in the study, and with exclusion criteria participants were unable to complete the study such as experiencing dizziness, seizures, severe ear pain, suffering from claustrophobia, history of ear infections, and history of upper respiratory tract infections. The treatment was given by exposure to pure oxygen (100%) given at a pressure of 2 ATA for 30 minutes every 1 x administration in a high-pressure air chamber, Comex Professional Deep Diving

Equipment series 9606, reference 407040, year of manufacture in 1996, obtained at Lakesla, Dr. Ramelan Naval Hospital, Surabaya.

This randomized controlled trial involved 30 healthy male military personnel using a single-blind method, where participants were randomized into a normobaric control group (n = 15) and a hyperbaric–hyperoxia group (n = 15). Before the treatment was carried out, the submaximal load was determined first. Then continued with pretest testing, namely the control group in a regular room and the experimental group in a hyperbaric chamber with a pressure of 2 ATA (adaptation was carried out first for 15 minutes). In each group, the warm-up began with a 60 RPM, unloaded cycle for 1 minute, after which the results were recorded (pre-experiment). Next, the load was increased to 1.5 kg for 12 minutes, and the results were recorded (post-experiment).

The recordings were conducted on both groups by specialist heart doctors. After the results are obtained, a grading will be carried out using the British Society of Echocardiography criteria. The data will be arranged using a grading scale as in Figure 1, with division using degrees, namely 1 for normal, 2 for borderline LVEF, 3 for Impaired LVEF, and 4 for severely impaired LVEF (Hudson & Stephen, 2020). After that, a statistical test will be carried out using SPSS version 22.0. The initial step will be a normality test, conducted using the Shapiro-Wilk test, to determine the data distribution. If the data is not normally distributed, the next step is to use non-parametric statistical tests, such as the Mann-Whitney and Wilcoxon tests. However, if the data show normality, the next step will be a homogeneity test using Levene's test, followed by parametric tests using the unpaired t-test and paired t-test.

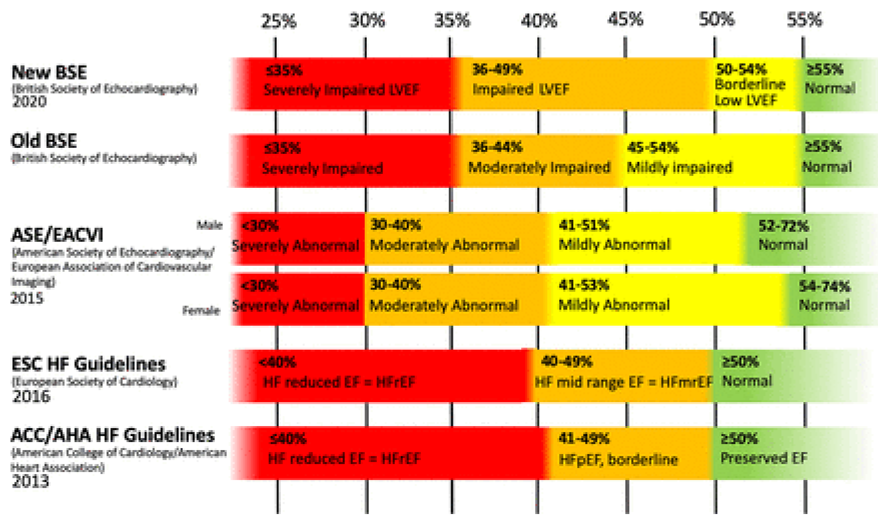

Figure 1. Ejection fraction grading (Hudson & Stephen, 2020)

RESULT

After conducting the research, the following results were obtained:

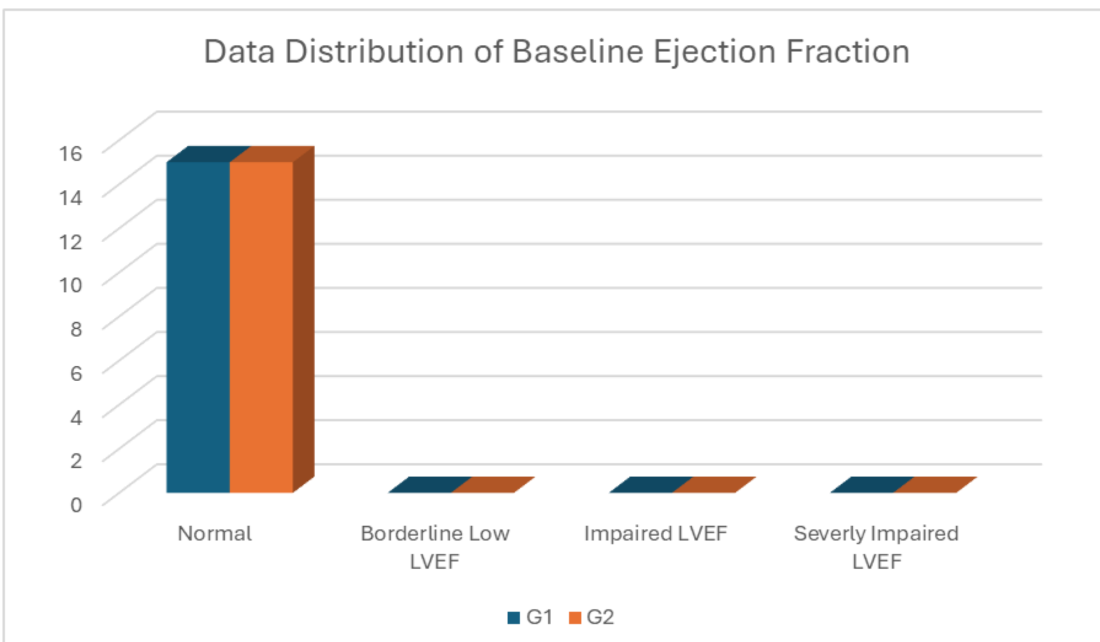

Figure 2. Data distribution of the ejection fraction baseline of research participants (G-1 is the control group, while G-2 is the experimental group).

The data above shows the baseline of the subject's ejection fraction, which obtained similar or homogeneous results in all subjects in both groups.

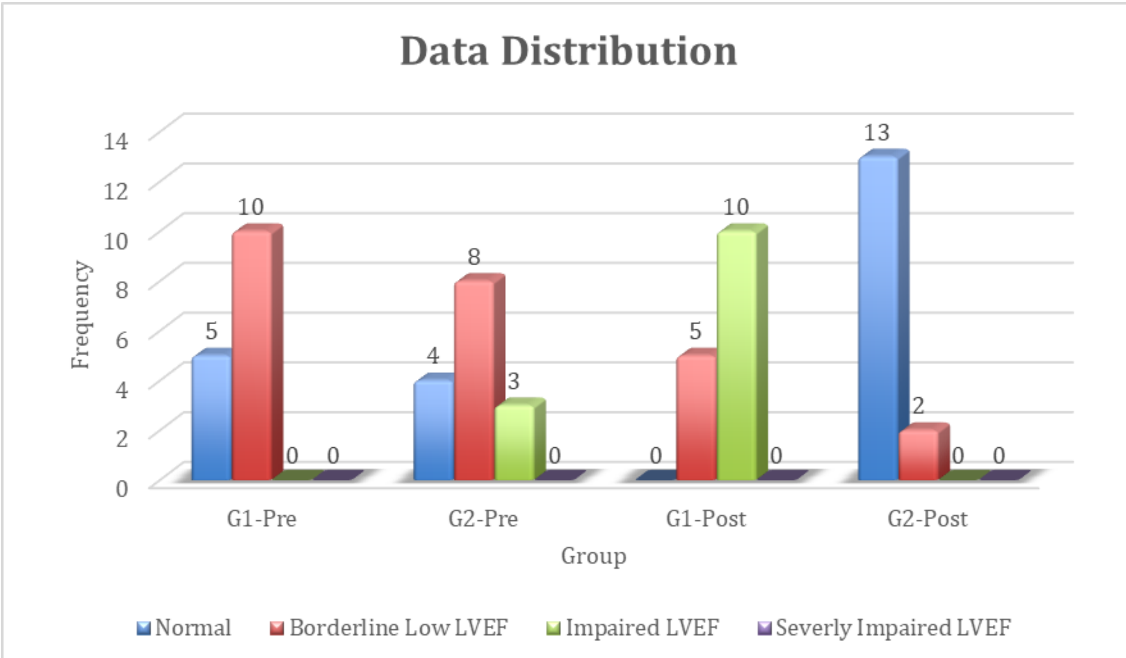

Figure 3. Data distribution of ejection fraction of research participants (G-1 is the control group, while G-2 is the experimental group).

In the research data above, it was found that, the control group in the pre-experiment had 5 subjects showing normal results (grade 1) and 10 subjects with borderline low LVEF results (grade 2), while in the post-experiment results at a glance it can be seen that there was an increase in grading, namely 5 subjects showed borderline low LVEF results (grade 2) and 10 people showed impaired LVEF results (grade 3). Then in the treatment group in the pre-experiment, 4 subjects showed normal results (grade 1), 8 subjects with borderline low LVEF results (grade 2), and 3 subjects showed impaired LVEF results (grade 3), while in the post-experiment results at a glance it can be seen that there was a decrease in grading, namely 13 subjects showed normal results (grade 1) and 2 subjects with borderline low LVEF results (grade 2).

Table 1. Data distribution of ejection fraction of research participants

Group		Mean	Median	Variance	Std. Deviation	Min	Max
Pre	G-1	1.67	2.00	0.238	0.488	1	2
	G-2	1.93	2.00	0.495	0.704	1	3
Post	G-1	2.67	3.00	0.238	0.488	2	3
	G-2	1.13	1.00	0.124	0.352	1	2

Description: G-1 is the control group, while G-2 is the experimental group.

The table above shows the distribution of cardiac ejection fraction based on grading. The results show an increase in the average grade in the control group from 1.67 to 2.67, while in the treatment group, there was a decrease from 1.93 to 1.13. In this experiment, 30 subjects were used; therefore, the next step is to test the normality of the data using the Shapiro-Wilk. The following results were obtained:

Table 2. Normality test result.

Group		Significance
Pre	G-1	0.001
	G-2	0.006
Post	G-1	0.001
	G-2	0.001

Description: G-1 is the control group, while G-2 is the experimental group.

The results of the normality test above showed a significant result, or $p < 0.05$, for all groups, indicating that the data were not normally distributed. The next step was to conduct a non-parametric statistical test using the paired Wilcoxon test. The results are shown in the following table.

Table 3. Non-parametric statistical test using the paired Wilcoxon test.

Group		Value
G1 Pre-Post	Negative Ranks	0
	Positive Ranks	12
	Ties	3
	Significance	0.001
G2 Pre-Post	Negative Ranks	10
	Positive Ranks	0
	Ties	5
	Significance	0.003

Description: G-1 is the control group, while G-2 is the experimental group.

The table above shows that in the control group, there was an increase in cardiac ejection fraction grading in 12 samples, and 3 samples showed the same pre- and post-results. Then, in the experimental group, there was a decrease in cardiac ejection fraction grading in 10 samples, and 5 samples showed the same pre- and post results. Furthermore, in both groups, the results obtained were $p < 0.05$, indicating a significant difference between the pre- and post-results, which can be interpreted as an effect of the treatment in both groups. To determine the differences between groups, a non-parametric statistical test using Mann-Whitney will be carried out.

Table 4. Non-parametric statistical test using Mann-Whitney.

Group	Value
Pre-test	0.283
Post-test	0.001

Description: G-1 is the control group, while G-2 is the experimental group.

The table above shows that there is a difference between the control and treatment groups in the post-test data, with a result of 0.001 or $p <0.05$. While in the pre-test group, the result shows 0.283, which is $p > 0.05$. This can be interpreted as indicating no difference in the data. This is because, in the pre-test, both groups were first screened through inclusion and exclusion criteria, so the results would not be significantly different.

DISCUSSION

Submaximal exercise is moderate-intensity physical activity, typically between 40 – 70% of maximal oxygen capacity (VO_2max), that stimulates the cardiovascular system without causing excessive stress. In healthy individuals, submaximal exercise increases cardiac output by increasing heart rate and ejection fraction, and improves tissue oxygen efficiency (Shushan *et al*., 2022). Physiologically, submaximal exercise produces characteristic hemodynamic and metabolic changes. Increased preload due to higher venous return during activity increases stroke volume, while increased sympathetic activity causes vasodilation in active muscles to maintain perfusion and oxygenation. At this stage, the left ventricular ejection fraction (LVEF) may increase slightly or remain unchanged due to increased myocardial contractility and optimized diastolic filling. However, in patients with heart disease, the LVEF will decrease due to the heart's inability to adapt to pumping blood (Dulaney *et al*., 2022).

Ejection fraction (EF) is an important parameter that describes the percentage of blood volume pumped out of the ventricles during one cardiac contraction cycle (systole) compared to the total blood volume contained in the ventricles at the end of diastole. Physiologically, EF reflects the systolic function of the ventricles, especially the left ventricle, which plays a major role in maintaining cardiac output and tissue perfusion. In healthy individuals, left ventricular EF is usually in the range of 55–70%, while a decrease in EF below 55% indicates impaired heart pump function. EF values <35% indicate severe systolic dysfunction, such as heart failure with reduced ejection fraction (HFrEF). Conversely, patients with EF ≥50% but with symptoms of heart failure are classified as having borderline low LVEF, where impairment occurs in ventricular relaxation (diastolic dysfunction) without significant contraction impairment (Shams *et al*., 2025). In this study, presented in Figure 2, the results in the control group showed 5 normal samples and 10 samples with borderline low LVEF in the pre-experiment, while in the post-experiment, 5 borderline low LVEF samples and 10 impaired LVEF samples were obtained. In the experimental group, 4 normal samples, 10 borderline LVEF samples and 3 impaired LVEF samples were obtained in the pre-experiment, while in the post-experiment, 13 normal samples and 2 borderline low

LVEF samples were obtained. Differences in EF between pre-exercise and post-submaximal exercise occur due to changes in loading conditions (preload & afterload), sympathetic response/contractility, changes in heart rate (and filling time), ventricular–vascular coupling, and the possibility of exercise-induced cardiac fatigue in some individuals (King, & Lowery, 2025).

High oxygen exposure at pressures greater than 1 ATA (hyperbaric hyperoxia) rapidly alters cardiopulmonary physiology by increasing the partial pressure of arterial oxygen (PaO_2) and modulating vascular tone. Hemodynamically, acute hyperoxia can induce systemic vasoconstriction in healthy subjects but shows a different response in patients with cardiopulmonary dysfunction, including a decrease in pulmonary vascular resistance that relieves right ventricular load and a potential increase in stroke volume during submaximal exercise (Müller *et al*., 2023; Tubek *et al*., 2021). In a hyperbaric environment, increased pressure increases the solubility of oxygen in the plasma, thus increasing tissue oxygenation regardless of changes in blood flow. This effect makes oxygen supply to working muscles more available at submaximal loads, with the potential to reduce heart rate and peak cardiac output requirements at a given work intensity. Furthermore, recent clinical evidence and meta-analyses suggest that hyperoxia/hyperbaric oxygen therapy (HBOT) interventions can improve left ventricular function in some populations, such as patients after myocardial reperfusion, which would theoretically be reflected as an increase in LVEF or stroke volume when the cardiac load is relatively low, such as in submaximal exercise (Hisamoto *et al*., 2025; Frontiers study, 2021). As in the research results above, in the control group, there was an increase in EF grading in the pre- and post-experiment, while in the experimental group, there was a significant decrease in grading due to the use of hyperbaric-hyperoxia, and there was a difference between the control and treatment groups in the post-test data. This is because in the hyperbaric chamber, there is more dissolved oxygen in the blood, and cellular responses occur (increased mitochondrial function/biogenesis, tissue perfusion), which together increase oxygen supply to the muscles and oxygen utilization so that submaximal work capacity, anaerobic threshold, and endurance increase compared to normal pressure. According to Henry's law, the amount of O_2 dissolved directly in the plasma increases drastically in addition to O_2 bound to hemoglobin. The result is an increase in CaO_2 (arterial O_2 content) and increased O_2 diffusion to active tissues so that the muscles receive more O_2 for aerobic metabolism at submaximal loads. This reduces dependence on anaerobic energy and delays lactate accumulation (Cannellotto *et al*., 2024).

When performing submaximal exercise in a hyperbaric-hyperoxic environment, cardiovascular adaptations occur, namely changes in afterload, preload, and myocardial oxygenation. Increased PaO_2 and dissolved oxygen can reduce the relative cardiac output requirement by increasing peripheral oxygen extraction and decreasing chemoreceptor signaling that modulates sympathetic drive. The result will be seen as a decrease in heart rate for the same workload and sometimes stabilization or a slight increase in stroke volume so that LVEF can appear to increase depending on the patient's baseline status. (Müller *et al*., 2023). In individuals with cardiopulmonary disease, hyperoxia/better oxygenation lowers pulmonary vascular pressure and reduces right ventricular load, which in turn may increase the preload contribution to the left ventricle and improve relative systolic function (expressed as an increase in LVEF or submaximal stroke volume) (Tubek *et al*., 2021).

CONCLUSION

This study demonstrates that submaximal exercise under hyperbaric–hyperoxic conditions leads to a more favorable change in left ventricular ejection fraction grading compared with normobaric exercise in healthy military personnel. In the control group, 12 subjects showed a worsening EF grade after exercise, whereas in the hyperbaric–hyperoxic group, 10 subjects improved to a better EF grade, with several shifting into the normal category (Wilcoxon test, $p<0.05$). These findings suggest a potential beneficial effect of hyperbaric–hyperoxic conditions on systolic function during submaximal exercise; however, larger multi-center studies are needed to confirm and generalize these results.

DAFTAR PUSTAKA

Cannellotto M, Yasells García A, Landa MS, 2024. Hyperoxia: effective mechanism of hyperbaric treatment at mild-pressure. International Journal of Molecular Sciences, 25, 2, 777. https://doi.org/10.3390/ijms25020777

Dulaney CS, Heidorn CE, Singer TJ, McDaniel J, 2023. Mechanisms that underlie blood flow regulation at rest and during exercise. Advances in Physiology Education, 47, 1, 26–36. https://doi.org/10.1152/advan.00180.2022

Gušić M, Stantić T, Lazić A, Andrašić S, Roelands B, Bogataj Š, 2024. Effects of hyperbaric oxygen therapy on recovery after a football match in young players: a double-blind randomized controlled trial. Frontiers in Physiology, 15. https://doi.org/10.3389/fphys.2024.1483142

Hisamoto K, Okubo N, Fujita M, Fukushima H, Okizuka Y, Yamanaka T, Matsui T, Morihara T, Hojo T, Fukuoka Y, Takahashi K, 2025. Mild hyperbaric hyperoxia improves aerobic capacity and suppresses cardiopulmonary stress during the maximal cycle-ergometer test. PLOS One, 20, 5, e0323885. https://doi.org/10.1371/journal.pone.0323885

Hudson S, Pettit S 2020. What is 'normal' left ventricular ejection fraction? Heart, 106, 18, 1445–1446. https://doi.org/10.1136/heartjnl-2020-317604

King J, Lowery DR, 2025. Physiology, cardiac output.

McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Čelutkienė J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Skibelund AK, 2021. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal, 42, 36, 3599–3726. https://doi.org/10.1093/eurheartj/ehab368

Müller J, Lichtblau M, Saxer S, Schneider SR, Appenzeller P, Bauer M, Hasler ED, Schwarz EI, Bloch KE, Ulrich S 2023. Hyperoxia improves exercise capacity in cardiopulmonary disease: a series of randomised controlled trials. ERJ Open Research, 9, 2. https://doi.org/10.1183/23120541.00563-2022

Pramana KAAP, Cahyani NGAMSD, Pintaningrum Y, 2025. Effect of hyperbaric oxygen therapy on LV function in CAD patients after reperfusion based on echo: a meta-analysis. British Journal of Cardiology. https://doi.org/10.5837/bjc.2025.017

Robins M, Falkson SR, Goldfarb J, Wyatt HA, 2025. Hyperbaric treatment of ischemia reperfusion injury.

Shahid M, Ibrahim R, Olagunju A, Mookadam M, Mookadam F, 2025. A contemporary review on heart failure with preserved ejection fraction: epidemiology, diagnosis, and management. Current Cardiology Reviews, 21, 1, e1573403X318646. https://doi.org/10.2174/011573403X318646240909072055

Shams P, Goyal A, Makaryus AN, 2025. Left ventricular ejection fraction.

Shushan T, McLaren SJ, Buchheit M, Scott TJ, Barrett S, Lovell R, 2022. Submaximal fitness tests in team sports: a theoretical framework for evaluating physiological state. Sports Medicine, 52, 11, 2605–2626. https://doi.org/10.1007/s40279-022-01712-0

Tubek S, Niewinski P, Paleczny B, Langner-Hetmanczuk A, Banasiak W, Ponikowski P, 2021. Acute hyperoxia reveals tonic influence of peripheral chemoreceptors on systemic vascular resistance in heart failure patients. Scientific Reports, 11, 1, 20823. https://doi.org/10.1038/s41598-021-99159-2