Medical Laboratory Journal
Online ISSN: 2538-4449
Golestan University of Medical Sciences

The effects of a special training program on cytochrome p450 gene expression and reactive oxygen species levels in patients with coronary artery bypass surgery

SeyedabdullahMousavi [1], Alireza Barari [1*], Asieh AbbassiDaloii [1]

1. Department of Sport Physiology, AyatollahAmoli Branch, Islamic Azad University, Amol, Iran
* Correspondence: Alireza Barari. Department of Sport Physiology, AyatollahAmoli Branch, Islamic Azad University, Amol, Iran. Tel: +989111277793;
Email: alireza54.barari@gmail.com

Abstract

Background: Significant economic consequences can lead to various problems and complications, including medical complications. Coronary artery disease (CAD), a serious health threat with increasing prevalence, is a major cause of death and mortality worldwide. This study aimed to investigate the effects of a special training program on cytochrome P450 (CYP) gene expression and reactive oxygen species (ROS) levels in patients with coronary artery bypass surgery.

Methods: This semi-experimental study was conducted on 16 patients who underwent coronary artery surgery in Babol City, Iran. The patients were selected using a random sampling method and divided into 2 groups: experimental and control groups. The experimental group engaged in an exercise program consisting of 3 sessions per week for a duration of 8 weeks. The expression levels of CYP and ROS genes were measured by the real-time polymerase chain reaction (PCR) method. The analysis was performed by comparing covariances and means.

Results: ROS gene expression levels significantly decreased in the experimental group than in the control group (P=0.003). However, there was no significant difference in P450 levels between the experimental and control groups (P=0.99).

Conclusion: Special exercises reduced ROS expression and increased P450 expression in patients who had coronary bypass surgery. There is a probability that special exercises, can effectively prevent heart damage by increasing antioxidant capacity and reducing ROS.

Article History

Received: 1 October 2020
Received in revised form: 1 May 2021
Accepted: 15 May 2021
Published online: 30 December 2023
DOI:10.29252/mlj.17.5.12.

Keywords

Steroid 15-beta-hydroxylase
ROS
Coronary artery bypass
Special training program

Article Type: Original Article

Introduction

Acute or chronic cardiovascular disease (CVD), particularly of myocardial origin, is among the leading causes of death worldwide (1). In addition to percutaneous coronary intervention, coronary artery bypass graft (CABG) surgery is the standard treatment, especially among those suffering from coronary artery stenosis (2). In 2003, CABG surgery was a commonly performed treatment for patients with coronary heart disease in the United States. Previous studies have shown that approximately 35 000 to 50 000 heart surgeries are performed annually in Iran (3). Heart surgery is a reliable way to improve myocardial blood flow, but it still has many postoperative side effects (4).

It is thought that hypertrophy, inflammation, and oxidative stress caused by hypoxia may play a prominent role in this phenomenon. Other possible stimuli are adipokines secreted by adipocytes, which reduce the bioavailability of NO and increase oxidative stress (5). Macrophages cause inflammation in adipose tissue and can also lead to impaired vascular contraction (6). The increased release of reactive oxygen species (ROS), for example, by NADPH oxidases and mitochondrial enzymes, leads to cardiac hypertrophy, fibrosis, and metalloproteinase activation, which potentially leads to the progression of heart disease (7). Studies have shown that free radicals are produced in a maximum of 3 to 5 minutes of reperfusion and lasting up to 3 hours, which significantly contributes to myocardial depression (8). We know that in cardiac surgery, the use of cardiopulmonary bypass exacerbates systemic ischemia and the release of free radicals (9). However, when ROS production exceeds the buffering capacity of the antioxidant defense systems in the heart, oxidative stress develops, resulting in cardiac dysfunction, ischemia-reperfusion injury, hypertrophy, cell death, and heart failure (HF) (10). Cardiopulmonary bypass is recognized to be responsible for activating neutrophils, a prominent source of primary systemic ROS. The impact of oxidative stress on postoperative outcomes among patients undergoing CABG surgery remains a controversial topic and an undeniable issue (10).

Cardiovascular disease, especially HF, suggests that molecular and genetic drugs may play a large role. In this situation, there is more evidence that cytochrome P450 (CYP) is involved in the onset, progression, and treatment of the disease (11). The CYP2B6 family appears to play an important role in HF pathogenesis. Cytochrome P450 enzymes are the most important enzymes involved in drug metabolism, accounting for approximately 75% of all different metabolic reactions (12). Aspromonte et al (2014) examined changes in cardiac CYP in HF patients. There are some pieces of evidence that CYP2B6 is involved in the onset, progression, and prognosis of CVD, particularly HF. Further studies are needed to elucidate the mechanisms by which CYP is used in the pathophysiology of HF, as well as the mechanism by which HF alters cardiac CYPs (13). In general, cardiac CYP2B6 and CYP11 mRNA levels and related enzyme activities usually increase in HF (14). Some studies have examined the molecular mechanisms by which these metabolites affect cardiomyocytes and blood vessels, leading to cardiac heart pathology and cardiac reconstruction. Patients who underwent complete reoperation not only survived for 5 years but also experienced an improvement in their overall survival time without angina (15).

Given the patient's need to achieve complete and rapid physical recovery after surgery to quickly normalize daily life activities (including returning to work), it seems necessary to adopt a healthy lifestyle and medication regimen for a lifetime. Cardiac rehabilitation (CR) typically involves a variety of interventions, such as regular exercise, healthy diet, medical treatment (eg, medication), managing risk factors with training, and coping with stress (16). Moderate-intensity exercise improves the performance of coronary patients; it may provide greater safety during unsupervised exercise. Also, low-intensity exercise increases the acceptance of training programs, especially for unhealthy and elderly patients (17, 18). Moholdt and coworkers compared moderate-intensity continuous exercise with intermittent aerobic exercise in the rehabilitation phase in CABG patients, showing an increase in VO2 in both subsets (19). In addition, there is limited research on the effect of CR on patients after CABG surgery. Accordingly, this study aimed to investigate the effects of a special training program on CYP2B6 gene expression and ROS levels in patients who had CABG surgery.

Methods

The study population included individuals who had undergone CABG surgery; at least 3 months had passed since their operation. After the voluntary participation of 16 patients to carry out this exercise program, initial evaluations and clinical examinations such as electrocardiography, echocardiography and exercise test were performed by a specialist doctor. These patients were then divided into 2 groups based on the results of the exercise test. The sample size was determined based on previous studies, the specific framework of the 2-month rehabilitation research, and the availability of facilities and equipment in rehabilitation centers (20). Inclusion criteria were physician permission, lack of motor restraint, and willingness to participate. Exclusion criteria were physician recommendation, absence from more than 3 exercise sessions, and lack of interest in participating in the study. During the study, none of the participants met the exclusion criteria.

Before starting the exercise program, all participants took part in a joint training session based on a pre-determined schedule for the rehabilitation program, and the research process was fully explained. They were then randomly divided into 2 groups. The participants engaged in 3 sessions per week involving special exercises. At the end of 8 weeks (3 sessions per week), they were tested again, and the exercise effects were examined in each group.

Our program was so similar to the program described by Wislowf et al. and the American College of Sports Medicine. According to the initial condition of them and the results of the recorded test, the heart rate and the level and intensity or speed of the treadmill for each patient were recorded on the exercise control sheet. Patients rested for 5 to 10 minutes, depending on individual weakness (21).

The strength training program was performed 3 times a week for 8 weeks (24 sessions) for the intervention group. The strength training recommendations provided by the American College of Sports Medicine were used in this study for those with CABG.

RNA was isolated from cells shortly after isolation and also after 1, 2, 3, and 5 days of culture using the SV Total RNA Isolation System (Promega, Mannheim, Germany) according to the manufacturer's recommendation. The quality of the isolated RNA was checked using a 1.0% agarose gel. Four micrograms of total RNA from each sample were used for the reverse transcription process. RNA and random primer were preheated for 10 minutes at 70 °C. The AMV Reverse Transcriptase 5X Reaction Buffer supplied with this enzyme has a composition of 250mM Tris-HCl, 40 U RNaseinhibitor, and 20 U AMV–RT (Promega) were added, and diethyl pyrocarbonate-treated water (Sigma) was added to a final volume of 20 µL. Next, reverse transcription was carried out for 60 minutes at 42 °C and stopped by heating to 95 °C for 5 minutes. The resulting complementary DNA (cDNA) was frozen at −20 °C until further experimentation.

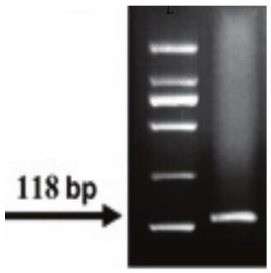
For the polymerase chain reaction (PCR) amplification of cDNA, a 25-µL reaction mixture was prepared containing 10× polymerase reaction buffer, 1.5 mm MgCl2, 0.4 nm dNTPs (Roche), 400 nm concentration of the 3′ and 5′-specific primers as shown in Table 1, 1 u Taq-polymerase (Roche), and 1 µL of cDNA.

Table 1. The sequence and characteristics of designed primers

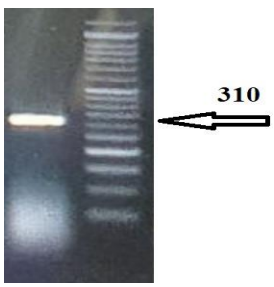
bp	Reverse (5′-3′)	Forward (5′-3′)	Gene
118	GAGTGGGTGTCGCTGTTGA	GGGAAACTGTGGCGTGAT	**GAPDH**
310	ACTGTGGGTCATGGAGAGCTG	GAGTTCTTCTCTGGGTTCCTG	**P450**

The polymerase chain reactions were performed in a thermal cycler using the following melting, annealing, and extension cycling conditions: denaturation for 30 seconds at 94 °C, annealing for 60 seconds at 57 °C, and extension for 60 seconds at 72 °C (29 cycles) for CYP isoforms and GAPDH. DNA contamination was checked for by direct amplification of RNA extracts prior to conversion of RNA to cDNA, and any possible contamination could be excluded. The polymerase chain reactions were performed within the linear range of amplification, separated using a 1.8% agarose gel, stained with ethidium bromide, and photographed on a transilluminator (Figure 1). A semiquantitative measurement was done using NIH Image version 1.62. The ROS production rate was determined in 50 µL capillary blood by means of a recently developed electron paramagnetic resonance (EPR) microinvasive method (21).

The Shapiro-Wilk test was used to test the normal distribution of the data. The Levene test was used to determine the variance homogeneity test. For intragroup changes, the t statistical model was used for dependent groups. Also, the parametric test of analysis of covariance (ANCOVA) was used for differences between groups; subsequently, the Bonferroni test was used. Statistical analyses were performed using SPSS version 20 (SPSS Inc, Chicago, IL, USA). P values less than 0.05 were considered statistically significant (Figure1).



The agarose gel image of the GAPDH gene: the left column is the ladder, and the right column is the corresponding band of one of the samples identified at the 118-bp position.



The agarose gel image of the P450 gene: the right column is the ladder, and the left column is the corresponding band of one of the samples identified at the 310-bp position.

Figure 1. Agarose gel electrophoresis image

Results

Anthropometric indices of correlation to the research subjects in control and intervention groups are reported in Table 2.

Table 2. The Mean and SD of the individual characteristics

Variable group		Control-Patient	Exercise
Age (year)	Pretest	51.60±5.07	47.20±7.12
Height(cm)	Pretest	166.40±10.69	181±3.31
Weight (kg)	Pretest	91.12±8.63	81.86±5.48
	Posttest	91.12±8.63	81.86±5.48
HR (per minute)	Pretest	82.60±5.07	78.80±11.21
	Posttest	80±4.89	72.80±5.80
SBP (mm Hg)	Pretest	132.40±7.36	131.60±8.50
	Posttest	129±6.55	124.6±5.36
DBP (mm Hg)	Pretest	80.2±7.95	76.44±8.56
	Posttest	79.4±5.54	72.8±7.01
BFP	Pretest	29.12±4.12	26.86±4.96
	Posttest	31.14±3.8	25.4±4.34

Abbreviations: HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; BFP, body fat percentage.

A dependent *t* test, which was used to assess the intragroup changes in P450 expression between the control and intervention groups, revealed that the factor level in the posttest stage did not exhibit statistical significance when compared to the pretest stage(P=0.583). Also, there was an increase in the level of P450 expression in the intervention group during the posttest stage compared to the pretest stage, but the difference did not reach a statistically significant level(P=0.082).

The results showed that the ROS level in the posttest stage had a significant decrease compared to the pretest stage in the intervention group (P=0.005). The ROS gene expression in the control group in the posttest stage did not show a significant change compared to the pretest stage (P=0.21). The data analysis revealed that the control and exercise groups did not have a significant difference in P450 gene expression (P=0.003; Tables 2-4). The results of this research showed that there was a significant increase in P450 level changes in the intervention group. Also, the level of reactive oxygen species (ROS)decreased significantly in the intervention group, but these indicators were not significant in the control group.

Table 3. Covariance analysis results of p450 expression in both groups

	Total of squares	*Degree offreedom*	*Mean of squares*	*F*	Significance
Modified model	111.23	2	555.11	056.3	0.097
P450 (pretest)	507.12	1	507.12	308.3	0.0102
Group	769.12	1	769.12	377.3	0.99

Table 4. Covariance analysis results of the ROS level in both groups

	Total of squares	*Degree offreedom*	*Mean of squares*	*F*	*Significance*
Modified model	848.45	2	924.22	504.19	*0.001
ROS (pretest)	885.22	1	885.22	471.19	0.068
Group	530.19	1	530.19	616.16	*0.003

Discussion

The current study investigated the effect of specialized physical exercises on CYP and ROS expression among individuals who had undergone CABG surgery. According to the data analysis, the intervention group showed a significant decrease in ROS gene expression compared to the control group; however, there were no significant differences in P450 changes between the intervention and control groups. An increase observed in changes in the intervention group was during the posttest stage compared to the pretest stage; however, this increase did not reach a statistically significant level. The intragroup analysis results showed that the ROS level within the intervention group exhibited a significant decrease in the posttest stage than in the pretest stage. They stimulate ROS production in the vessels. ROS levels, such as superoxide and hydrogen peroxide, are identified in CVD and congestive heart failure (CHF) patients (22). Physical activity is a major factor of CR in patients with coronary artery disease (CAD). Cardiac rehabilitation improves the patient's physical condition after cardiac operation and surgery; it reduces the risk of cardiovascular problems (23). Increased oxygen consumption through exercise can lead to mild and tolerable oxidative stress, which can increase the capacity of antioxidant systems. This idea was used for CR, which aimed to improve exercise capacity and physical performance (24). In general, after CR, a slight decrease was seen in oxidative stress parameters, such as peroxide and thiobarbituric acid reactive substances (TBARS)levels, indicating a positive effect of CR on plasma antioxidant activity. If glutathione (GSH) levels do not decrease as a result of short-term exercise, the level of thiol groups is likely to

be higher. It has previously been shown that exercise reduces plasma GSH levels, and moderate exercise reduces it slightly. Also, CR increased the GSH concentration1 hour after exercise compared to the baseline time (before exercise). The plasma system slightly affected the antioxidant property. These changes are maintained for at least 6 months after the completion of CR; it helps to effectively improve exercise outcomes in cardiovascular patients (25,26). Increased plasma superoxide dismutase (SOD)activity and improved brachial artery endothelial performance were also found in CAD patients after 12 weeks of special exercises (27). The amplification of the immune system and antioxidant enzymes can indirectly reduce the product of lipid peroxidation. Some of these parameters were well related to each other. However, in these interventions, both plasma antioxidant capacities were reported to be high, and the reduction in CR-induced oxidative stress was not sufficient to alter the levels of carbonyl groups. However, longer exercise (6 months) in HF patients showed a decrease in oxidative protein (28). The results showed that P450 changes in the intervention group did not differ significantly from the control group. The process of incremental changes was observed in the intervention group in the posttest stage compared to the pretest; it did not reach a significant level. Moreover, regarding these 2 key metabolic ways, there is further evidence for the importance of endogenous P450 metabolites, such as aldosterone, androgens, cortisol, sex hormones, and thromboxane, in maintaining vascular homeostasis. In addition, there is further evidence that shows CYP is involved in the disease onset, progress, and treatment. There is a connection between CYP and CVD expression, such as hypertension, CAD, stroke, HF, cardiomyopathy, and arrhythmia. Cytochrome P450 is a wonderful family of hemoproteins that are the final oxidase of the oxidase system, involved in the transfer of endogenous proteins and xenobiotics. Cytochrome P450 enzymes are the most important enzymes involved in drug metabolism, accounting for approximately 75% of total metabolic reactions. Human CYPs are encoded by 57 different CYP genes identified in the human genome (29). Cytochrome P450 enzymes also play an important role in the metabolism of endogenous compounds, such as steroids, fat-soluble vitamins, fatty acids, and biogenic amines (30). Cytochrome P450 enzymes are important in cardiovascular physiology; their ability to metabolize arachidonic acid to epoxyacids and hydroxyacids in maintaining cardiovascular health, is clear. Activity of specific CYP enzyme and hydrolases can alter the delicate balance between synthesis of hydroxyeicosatetraenoic (HETEs) and epoxyeicosatrienoic acids (EETs). Several neuro-hormonal pathways are activated in HF patients, a complex clinical syndrome that marks the end stage of CVD. Cortisol, angiotensin II, aldosterone, norepinephrine, epinephrine, and parathyroid hormone levels increase at different stages of HF. In addition to activating the hormonal nerve, the pathophysiology of HF includes an increase in oxidative stress in several organs, stimulatory immune state, and inflammatory phenotype (31). The CYP family seems to play an important role in the pathogenesis of HF (32,33). On the other hand, EETs have anti-inflammatory properties. They are considered a useful anti-inflammatory treatment strategy. The inhibition of Soluble Epoxide Hydrolase (SHE) can reduce inflammation and prevent cardiac damage and cardiac dysfunction (34). Physical activity increased the expression level of the P450 gene in the exercise group, but these incremental changes did not reach a significant level.

Conclusion

Special exercises significantly reduced ROS production and increased P450 expression in patients who had CABG surgery. It is possible that exercise can prevent heart damage by increasing antioxidant capacity and decreasing ROS.

Acknowledgement

We are grateful to Babol University of Medical Sciences for coordinating the implementation of this research.

Funding sources

The financial resources of this article were personally provided by the PhD student and no financial support was received from any company or organization.

Ethical statement

Ethical code: IR.IAU.M.REC.1398.02.

Conflicts of interest

This research was performed at the personal expense of the doctoral student and did not receive any financial support. Additionally, there are no conflicts of interest associated with this article.

Author contributions

This article is part of the doctoral thesis of Mr. Seyyed Abdullah Mousavi and Mr. Alireza Berari is the supervisor of thesis and correspond author of this article and Asieh Abbassi Daloii is co-advisors for this thesis.

References

1. Nuhu F, Bhandari S. Oxidative Stress and Cardiovascular Complications in Chronic Kidney Disease, the Impact of Anaemia. Pharmaceuticals (Basel). 2018;11(4):103. [View at Publisher] [Google Scholar] [DOI] [PMID]
2. Zordoky BNM, El-Kadi AOS. Modulation of cardiac and hepatic cytochrome P450 enzymes during heart failure. Curr Drug Metab. 2008;9(2):122-8. [View at Publisher] [Google Scholar] [DOI] [PMID]
3. Ghroubi S, Elleuch W, Abid L, Abdenadher M, Kammoun S, Elleuch MH. Effects of a low-intensity dynamic-resistance training protocol using an isokinetic dynamometer on muscular strength and aerobic capacity after coronary artery bypass grafting. Ann Phys Rehabil Med. 2013;56(2):85-101. [View at Publisher] [Google Scholar] [DOI] [PMID]
4. Gao FJ, Yao KP, Tsai CS, Wang KY. Predictors of health care needs in discharged patients who have undergone coronary artery bypass graft surgery. Heart Lung. 2009;38(3):182-91. [View at Publisher] [Google Scholar] [DOI] [PMID]
5. Greenstein AS, Khavandi K, Withers SB, Sonoyama K, Clancy O, Jeziorska M, et al. Local inflammation and hypoxia abolish the protective anticontractile properties of perivascular fat in obese patients. Circulation. 2009;119(12):1661-70. [View at Publisher] [Google Scholar] [DOI] [PMID]
6. Withers SB, Agabiti-Rosei C, Livingstone DM, Little MC, Aslam R, Malik RA, et al. Macrophage activation is responsible for loss of anticontractile function in inflamed perivascular fat. Arterioscler Thromb Vasc Biol. 2011;31(4):908-13. [View at Publisher] [Google Scholar] [DOI] [PMID]
7. Sorescu D, Weiss D, Lassègue B, Clempu RE, Szöcs K, Sorescu GP, et al. Superoxide production and expression of nox family proteins in human atherosclerosis. Circulation. 2002;105(12):1429-35. [View at Publisher] [Google Scholar] [DOI] [PMID]
8. Valko M, Morris H, Cronin MT. Metals, toxicity and oxidative stress. Curr Med Chem. 2005;12(10):1161-208.[View at Publisher] [Google Scholar] [DOI] [PMID]
9. Lazzarino G, Raatikainen P, Nuutinen M, Nissinen J, Tavazzi B, Di Pierro D, et al. Myocardial release of malondialdehyde and purine compounds during coronary bypass surgery. Circulation. 1994;90(1):291-7. [View at Publisher] [Google Scholar] [DOI] [PMID]
10. Liu C, Cao F, Tang QZ, Yan L, Dong YG, Zhu LH, et al. Allicin protects against cardiac hypertrophy and fibrosis via attenuating reactive oxygen species-dependent signaling pathways. J Nutr Biochem. 2010;21(12):1238-50. [View at Publisher] [Google Scholar] [DOI] [PMID]
11. Sim SC, Ingelman-Sundberg M. Update on allele nomenclature for human cytochromes P450 and the Human Cytochrome P450 Allele (CYP-allele) Nomenclature Database. Methods Mol Biol. 2013;987:251-9. [View at Publisher] [Google Scholar] [DOI] [PMID]
12. Nelson DR, Zeldin DC, Hoffman SMG, Maltais LJ, Wain HM, Nebert DW. Comparison of cytochrome P450 (CYP) genes from the mouse and human genomes, including nomenclature recommendations for genes, pseudogenes and alternative-splice variants. Pharmacogenetics. 2004;14(1):1-18. [View at Publisher] [Google Scholar] [DOI] [PMID]
13. Zhang K, Wang J, Zhang H, Chen J, Zuo Z, Wang J, et al. Mechanisms of epoxyeicosatrienoic acids to improve cardiac remodeling in chronic renal failure disease. Eur J Pharmacol. 2013;701(1-3):33-9. [View at Publisher] [Google Scholar] [DOI] [PMID]
14. Michaud V, Frappier M, Dumas MC, Turgeon J. Metabolic activity and mRNA levels of human cardiac CYP450s involved in drug metabolism. PloS One. 2010;5(12):e15666.[View at Publisher] [Google Scholar] [DOI] [PMID]
15. Sellke FW, Ruel M. Vascular growth factors and angiogenesis in cardiac surgery. Ann Thorac Surg. 2003;75(2):S685-90. [View at Publisher] [Google Scholar] [DOI] [PMID]
16. Deb S, Wijeysundera HC, Ko DT, Tsubota H, Hill S, Fremes SE. Coronary artery bypass graft surgery vs percutaneous interventions in coronary revascularization: a systematic review. JAMA. 2013;310(19):2086-95.[View at Publisher] [Google Scholar] [DOI] [PMID]
17. Hambrecht R, Wolf A, Gielen S, Linke A, Hofer J, Erbs S, et al. Effect of exercise on coronary endothelial function in patients with coronary artery disease. N Engl J Med. 2000;342(7):454-60. [View at Publisher] [Google Scholar] [DOI] [PMID]
18. Schumacher B, Peecher P, Von Specht BU, Stegmann T. Induction of neoangiogenesis in ischemic myocardium by human growth factors: First clinical results of a new treatment of coronary heart disease. Circulation. 1998;97(7):645-50. [View at Publisher] [Google Scholar] [DOI] [PMID]
19. Moholdt TT, Amundsen BH, Rustad LA, Wahba A, Løvø KT, Gullikstad LR, et al. Aerobic interval training versus continuous moderate exercise after coronary artery bypass surgery: a randomized study of

cardiovascular effects and quality of life. Am Heart J. 2009;158(6):1031-7. [View at Publisher] [Google Scholar] [DOI] [PMID]
20. Osailan A, Abdelbasset WK. Exercise-based cardiac rehabilitation for postcoronary artery bypass grafting and its effect on hemodynamic responses and functional capacity evaluated using the Incremental Shuttle Walking Test: A retrospective pilot analysis. J Saudi Heart Assoc. 2020;32(1):25-33. [View at Publisher] [Google Scholar] [DOI] [PMID]
21. Mrakic-Sposta S, Gussoni M, Montorsi M, Porcelli S, Vezzoli A. A quantitative method to monitor reactive oxygen species production by electron paramagnetic resonance in physiological and pathological conditions. Oxid Med Cell Longev. 2014;2014:306179. [View at Publisher] [Google Scholar] [DOI] [PMID]
22. Fukuda T, Kurano M, Fukumura K, Yasuda T, Iida H, Morita T, et al. Cardiac rehabilitation increases exercise capacity with a reduction of oxidative stress. Korean Circ J. 2013;43(7):481-7. [View at Publisher] [Google Scholar] [DOI] [PMID]
23. Wan S, Leclerc JL, Vincent JL. Inflammatory response to cardiopulmonary bypass: Mechanisms involved and possible therapeutic strategies. Chest. 1997:112(3):676-92. [View at Publisher] [Google Scholar] [DOI] [PMID]
24. Church TS, Lavie CJ, Milani RV, Kirby GS. Improvements in blood rheology after cardiac rehabilitation and exercise training in patients with coronary heart disease. Am Heart J 2002;143:349-55. [View at Publisher] [Google Scholar] [DOI] [PMID]
25. Fukuda T, Kurano M, Fukumura K, Yasuda T, Iida H, Morita T, et al. Cardiac rehabilitation increases exercise capacity with a reduction of oxidative stress. Korean Circ J. 2013;43(7):481-7. [View at Publisher] [Google Scholar] [DOI] [PMID]
26. Linke A, Adams V, Schulze PC, Erbs S, Gielen S, Fiehn E, et al. Antioxidative effects of exercise training in patients with chronic heart failure: Increase in radical scavenger enzyme activity in skeletal muscle. Circulation. 2005;111(14):1763-70. [View at Publisher] [Google Scholar] [DOI] [PMID]
27. Davies SW, Duffy JP, Wickens DG, Underwood SM, Hill A, Alladine MF, et al. Time-course of free radical activity during coronary artery operations with cardiopulmonary bypass. J Thorac Cardiovasc Surg. 1993;105(6): 979-87. [View at Publisher] [Google Scholar] [DOI] [PMID]
28. Meirelles LR, Matsuura C, Resende ADC, Salgado ÂA, Pereira NR, Coscarelli PG, et al. Chronic exercise leads to antiaggregant, antioxidant and anti-inflammatory effects in heart failure patients. Eur J Prev Cardiol. 2014;21(10):1225-32. [View at Publisher] [Google Scholar] [DOI] [PMID]
29. Bleau AM, Levitchi MC, Maurice H, Du Souich P. Cytochrome P450 inactivation by serum from humans with a viral infection and serum from rabbits with a turpentine-induced inflammation: The role of cytokines. Br J Pharmacol. 2000;130(8):1777-84. [View at Publisher] [Google Scholar] [DOI] [PMID]
30. Bièche I, Narjoz C, Asselah T, Vacher S, Marcellin P, Lidereau R, et al. Reverse transcriptase-PCR quantification of mRNA levels from cytochrome (CYP)1, CYP2 and CYP3 families in 22 different human tissues. Pharmacogenet Genomics. 2007;17(9):731-42. [View at Publisher] [Google Scholar] [DOI] [PMID]
31. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009;360(10):961-72.[View at Publisher] [Google Scholar] [DOI] [PMID]
32. Imig JD, Hammock BD. Soluble epoxide hydrolase as a therapeutic target for cardiovascular diseases. Nat Rev Drug Discov. 2009;8(10):794-805. [View at Publisher] [Google Scholar] [DOI] [PMID]
33. Lavie CJ, Milani R V, Ventura HO, Messerli FH, Murgo JP. Cardiac rehabilitation, exercise training, and preventive cardiology research at Ochsner Heart and Vascular Institute. Tex Hear Inst J. 1995;22(1):44-52. [View at Publisher] [Google Scholar] [PMID]
34. Church TS, Lavie CJ, Milani RV, Kirby GS. Improvements in blood rheology after cardiac rehabilitation and exercise training in patients with coronary heart disease. Am Heart J. 2002;143(2):349-55. [View at Publisher] [Google Scholar] [DOI] [PMID]

How to Cite:
Mousavi SA, Barari A, Abbassi Daloii A. The effects of a special training program on cytochrome p450 gene expression and reactive oxygen species levels in patients with coronary artery bypass surgery. 2023;17(5):12-5.