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Effects of soleus push-up exercise on systemic immune-inflammatory index and blood lipid profile in coronary artery disease

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Abstract

Coronary artery disease (CAD) is closely associated with endothelial dysfunction and atherosclerosis, characterized by lipid accumulation in large artery walls. The systemic immune-inflammatory index is an emerging biomarker linked to cardiovascular disease progression. Soleus push-up exercises, targeting the soleus muscle (predominantly Type I fibers), may benefit patients with CAD. This study aimed to evaluate the effects of soleus push-up exercises on blood lipid profiles and systemic immune-inflammatory index in CAD patients. Forty-three CAD patients were enrolled and divided into 2 groups: 24 patients in the exercise group performed soleus push-up exercises, while 19 served as the control group with no exercise recommendations. Blood lipid profiles and systemic immune-inflammatory index were measured at baseline, 1 month, and 3 months. At the 1-month follow-up, the exercise group showed significantly lower total cholesterol levels and systemic immune-inflammatory index scores compared to the control group ($P < .005$). At the 3-month follow-up, the exercise group had significantly higher high-density lipoprotein cholesterol (HDL-C) levels ($P < .005$), and lower low-density lipoprotein cholesterol (LDL-C) and total cholesterol levels ($P < .005$) than the control group. The exercise group also exhibited significantly lower systemic inflammatory index (SII) scores at 3 months ($P < .001$). Soleus push-up exercises may positively influence blood lipid profiles and systemic immune-inflammatory index in CAD patients, highlighting a potential noninvasive approach for managing cardiovascular risk factors.

Abbreviations: BMI = body mass index, CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease, CVA = cerebrovascular accident, DM = diabetes mellitus, EDL = extensor digitorum longus, HDL = high-density lipoprotein, HF = heart failure, HT = hypertension, LDL = low-density lipoprotein, LVEF = left ventricular ejection fraction, N, L, P = neutrophil, lymphocyte, platelet, SII = systemic immune-inflammatory index, T. cholesterol = total cholesterol.

Keywords: coronary artery disease, endothelial dysfunction, exercise intervention, soleus push-up exercise, systemic immune-inflammatory index

1. Introduction

Coronary artery disease (CAD) constitutes a significant portion of the global health burden and originates from the occlusion of coronary arteries due to atherosclerosis, which is a pathophysiological process characterized by lipid accumulation within the intima matrix of large artery walls, initiated by endothelial dysfunction.[1,2] Various risk factors, such as genetic predisposition, infections, hypothyroidism, osteoporosis, chemotherapy and radiotherapy, psychological stress, smoking, hypertension, diabetes, dyslipidemia, advanced age, obesity, and a sedentary lifestyle, trigger the development of atherosclerosis.[3,4] Modifying these factors can prevent or slow the progression of atherosclerosis. Monitoring endothelial dysfunction and the associated systemic inflammatory response is crucial for managing this process. The systemic immune-inflammatory index (SII), computed by using platelet, neutrophil, and lymphocyte counts, was proposed as a biomarker for endothelial dysfunction and the development of cardiovascular diseases.[5,6]

Dyslipidemia plays a significant role in the development of CAD, defined by abnormalities in total cholesterol, LDL-C, HDL-C, and triglyceride levels.[7] Elevated LDL-C is related with the progression of atherosclerosis and an increased risk of CAD.[8] Therefore, managing dyslipidemia plays a very important role in preventing and treating CAD.

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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The soleus push-up exercise targets the soleus muscle, part of the triceps surae group in the calf. Comprising about 1% of body weight, the soleus muscle is predominantly composed of slow-twitch fibers (Type I) that adapt to oxidative metabolism. This muscle has a notably higher oxidative metabolism capacity than other muscles in the body. The soleus muscle sustains its oxidative metabolism using free glucose and fatty acids in the bloodstream rather than relying on glycogen stores for energy production. This feature makes it relatively less fatigable than other muscles.[9–13] Soleus push-up exercises are thought to have regulatory effects on blood glucose and lipid profiles, contributing to improvements in various conditions, including cardiovascular diseases.[9,14]

This study aims to investigate the effects of soleus push-up exercises on blood lipid profile and SII in patients with CAD.

2. Materials and methods

2.1. Patients

This prospective study involved patients diagnosed with CAD through angiographic coronary angiography performed in the catheter laboratory of our center between December 2023 and April 2024. Among these patients, those who did not attend their 1st and 3rd-month follow-ups, those with abnormal sedimentation rates, C-reactive protein levels, or White blood cell counts, and those with a history of rheumatic disease, trauma, cancer diagnosis, or acute or chronic infection were excluded. The remaining 43 patients constituted the study group. Among these patients, 24 were administered the soleus push-up exercise without any modification to their medical treatment or lifestyle, whereas 19 patients assigned to the control group did not undergo this exercise. Both groups were matched for age and gender, and evaluations were conducted at the 1st and 3rd months from the beginning of the study. Informed consent was obtained from all participants, and the study was approved by the medical ethics committee on October 10, 2023 (reference number 2023/10). The study process was carried out in line with the principles of the declaration of Helsinki and the good clinical practice guidelines.

2.2. Soleus push-up exercise protocol

The patients included in this study performed the soleus push-up exercise at least 3 times daily, lasting a minimum of 8 minutes each session, approximately 1 hour after meals, when postprandial glycemia and lipemia levels are expected to rise. The exercise protocol involved the patients seated with their legs positioned at a 90-degree angle to the floor and hands resting freely on their thighs. In this posture, while the toes and soles of the feet remained flat on the ground, the heels were raised and lowered repeatedly. The exercise was practically taught in a clinical setting, with brochures containing an exercise guide distributed to help patients remember to practice at home. Their adherence to the exercise regimen was regularly monitored, and corrective feedback was provided when necessary.

2.3. Medical and laboratory data measurements

In addition to demographic characteristics such as age and gender, anthropometric measurements, including height, weight, and body mass index (BMI), were recorded for the patients. The presence of chronic diseases such as diabetes mellitus (DM), hypertension (HT), heart failure (HF), chronic obstructive pulmonary disease (COPD), and cerebrovascular accident (CVA), along with any use of antilipidemic medications, were also noted. HT was defined as systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥90 mm Hg in at least 2 measurements or the use of any antihypertensive medication. DM was defined as fasting plasma glucose levels >126 mg/dL, glucose levels >200 mg/dL in any measurement, or the use of any antidiabetic medication. Left ventricular ejection fraction (LVEF) was measured using the modified Simpson method, and patients with LVEF ≤40% were classified as having HF.

Blood samples were collected from patients at the beginning of the exercise protocol and at the 1st and 3rd months to monitor blood lipid profile and systemic inflammatory index (SII) values. To obtain reliable results unaffected by daily metabolic changes, blood samples were drawn when the patients were in a rested state and had abstained from any fluid or solid food for at least 8 to 12 hours. Neutrophil (N), lymphocyte (L), and platelet (P) counts were measured through hemogram analysis, and systemic SII values were calculated using the formula $(N \times P)/L$. Lipid panel analyses measured LDL-C, HDL-C, and total cholesterol levels.

2.4. Statistical analyses

All data were analyzed using SPSS 21.0 software (IBM Corp., Armonk). Continuous variables are expressed as median or simple ranges if suitable, whereas categorical variables are summarized as counts and percentages. The Kolmogorov–Smirnov test was used to verify the normality of distribution for continuous variables and the one-sample *t*-test to compare biochemical parameter levels (mean ± SD) with reference ranges. A *P*-value of < .05 was considered significant. A priori power analysis could not be conducted owing to the unavailability. Therefore, a post hoc power analysis was performed to confirm that the current study has sufficient power (99%).

3. Results

The demographic characteristics of the patients are shown in Table 1. Among 24 patients who performed the soleus push-up exercise, 20 were male and 4 were female, with a mean age of 60.67 (range: 39–80) years. The control group comprised 19 patients, 16 male and 3 female, with a mean age of 65.89 (range: 48–80) years. Table 1 also presents the initial body mass index (BMI), HDL-C, LDL-C, total cholesterol levels, SII values, smoking status, presence of comorbidities such as DM, HT, HF, COPD, and CVA, and antilipidemic medication use. There were no significant differences in any of the variables examined between the patient and the control groups.

When analyzing the HDL-C and LDL-C values at the 1-month follow-up, no statistically significant differences were found between the groups. However, the mean total cholesterol values in the exercise group (162.2 ± 22.0 mg/dL) were significantly lower than those in the control group (181.8 ± 41.6 mg/dL; $P < .005$). Furthermore, the SII values at the 1-month follow-up were significantly lower in the exercise group (239.47 ± 7.7) compared to the control group (582.79 ± 270.93; $P < .005$) (Table 2).

At the 3-month follow-up, the mean HDL-C values in the exercise group (62.3 ± 10.7 mg/dl) were significantly higher than those in the control group (41.9 ± 11.2 mg/dL; $P < .005$). Additionally, the mean LDL-C values in the exercise group (56.6 ± 14.7 mg/dL) were significantly lower compared to the control group (87.7 ± 33.4 mg/dL; $P < .005$). The mean total cholesterol levels at the 3-month follow-up in the exercise group (150.1 ± 13.2 mg/dL) were also significantly lower than in the control group (176.0 ± 41 mg/dL; $P < .005$). Moreover, the SII values at the 3-month follow-up were significantly lower in the exercise group (213.4 ± 12.2) than in the control group (536.26 ± 55.99; $P < .001$) (Table 3).

Table 1

Demographic, clinical, and laboratory characteristics of the patients.

	Exercise group (n = 24) (mean ± SD)	Controls (n = 19) (mean ± SD)	*P*-value
Age (year)	60.67 ± 10.36	65.89 ± 8.86	.60
Gender (male)	20 (83%)	16 (84%)	.32
BMI (kg/m^2)	30.08 ± 5.23	28.39 ± 3.70	.31
LDL (mg/dL)	98 ± 37.2	95.8 ± 24.6	.13
HDL (mg/dL)	42 ± 14.2	41.3 ± 11.5	.38
T. CHOL (mg/dL)	170.7 ± 40.8	185.6 ± 30.4	.19
SII	347.3 ± 111.6	375.8 ± 136.2	.89
Smoking status (pack-years)	27.35 ± 4.70	30.03 ± 3.26	.51
Comorbidities			
DM	8	10	.15
HT	16	12	.64
HF	5	3	.40
COPD	4	2	.25
CVA	1	1	.72
Antilipidemic medications			
Atorvastatin	19 (79%)	14 (74%)	.27
Rosuvastatin	5 (21%)	5 (26%)	.21

BMI = body mass index, CVA = cerebrovascular accident, COPD = chronic obstructive pulmonary disease, DM = diabetes mellitus, HDL = high-density lipoprotein, HF = heart failure, HT = hypertension, LDL = low-density lipoprotein, SII = systemic immune-inflammatory index, SD = standard deviation, T.CHOL = total cholesterol.

Table 2

First-month follow-up parameters of the patients.

	Exercise group (n = 24) (mean ± SD)	Control group (n = 19) (mean ± SD)	*P*-value
HDL-C	52.9 ± 7.5	39.8 ± 11.8	.868
LDL-C	92.1 ± 38.0	86.7 ± 36.8	.529
T.CHOL	162.2 ± 22.0	181.8 ± 41.6	<.005
SII	239.47 ± 71.70	582.79 ± 270.93	<.005

HDL = high-density lipoprotein, LDL = low-density lipoprotein, SII = systemic immune-inflammatory index, SD = standard deviation, T.CHOL = total cholesterol.

Table 3

Third-month follow-up parameters of the patients.

	Exercise group (n = 24) (mean ± SD)	Control group (n = 19) (mean ± SD)	*P*-value
HDL-C	62.3 ± 10.7	41.9 ± 11.2	<.005
LDL-C	56,6 ± 14.7	87.7 ± 33.4	<.005
T.CHOL	150.1 ± 13.2	176.0 ± 41.0	<.005
SII	213.4 ± 12.2	536.26 ± 55.99	<.001

HDL = high-density lipoprotein, LDL = low-density lipoprotein, SII = systemic immune-inflammatory index, SD = standard deviation, T.CHOL = total cholesterol.

4. Discussion

To the best of our knowledge, this prospective study is the first to investigate the effects of soleus push-up exercises on patients with CAD. The results achieved in this study indicate that soleus push-up exercise may have beneficial effects on the blood lipid profile, endothelial dysfunction, and associated systemic immune-inflammatory response in patients with CAD. Figure 1 presents a graphical summary of our findings.

CAD is a chronic condition characterized by the narrowing or blockage of the coronary arteries that supply blood to the heart muscle, primarily due to atherosclerosis. Atherosclerosis is a complex vascular disease associated with endothelial dysfunction and chronic inflammation, characterized by the accumulation of lipids, inflammatory cells, and fibrous elements in the arterial walls.[2] Consequently, modulating inflammation has become a key target in the management of CAD.

Exercise plays a multifaceted role in preventing and managing atherosclerosis. It is well-known that regular physical activity positively impacts various atherosclerosis-related risk factors such as hypertension, dyslipidemia, and endothelial dysfunction. The anti-atherogenic effects of exercise are partly attributed to its ability to improve the lipid profile.[15] Exercise also enhances endothelial function, which is very important for vascular health. The endothelium plays a vital role in maintaining vascular tone and integrity, whereas dysfunction serves as a precursor to atherosclerosis. Physical activity supports endothelial nitric oxide production, which has vasodilatory, anti-inflammatory, and anti-thrombotic effects.

In addition to these direct cardiovascular benefits, exercise promotes the release of myokines – cytokines produced by muscle cells during contraction. These myokines exert systemic effects, including the modulation of immune response and potentially reducing inflammation associated with plaque formation in atherosclerosis.[16] Regular exercise also influences the immune system, which plays a critical role in the development and progression of atherosclerotic plaques. By modulating the function of cells within the innate immune system, exercise may impact immune responses and consequently affect plaque stability. Regular physical activity exerts an overall anti-inflammatory effect on the vascular endothelium, which protects against atherosclerosis.[17] Previous studies reported that regular physical activity enhances coronary flow reserve, improves coronary collateral circulation, slows the progression of atherosclerosis, and increases tolerance to ischemia.[18,19]

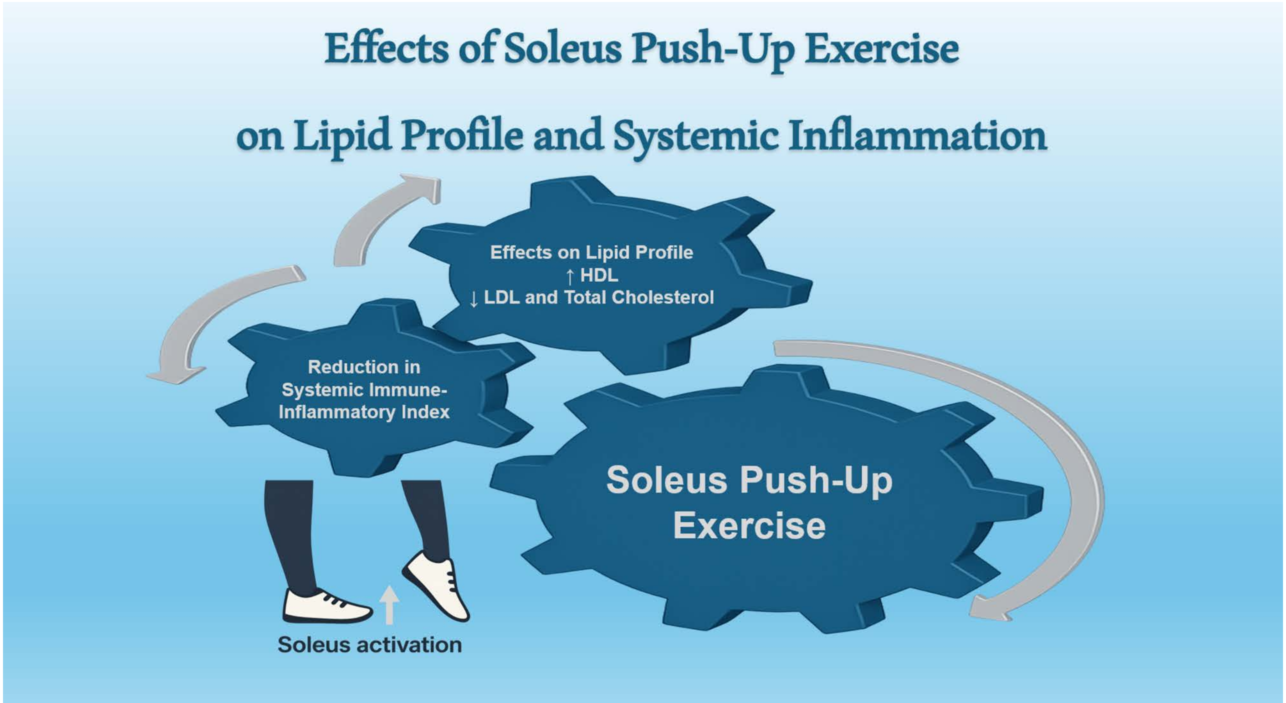

Figure 1. Graphical abstract illustrating the physiological effects of soleus push-up exercise on lipid profile and systemic inflammation.

The soleus muscle, located in the lower extremities, distinguishes from other muscle groups due to its physiological properties. This muscle contains slow-twitch fibers (Type I) that are resistant to fatigue and adapted for long-duration endurance activities. This contrasts with the extensor digitorum longus (EDL) and psoas muscles, which are designed for quicker, stronger movements and contain fast-twitch fibers (Type II). The slow-twitch fibers of the soleus muscle enable sustained activity due to their high oxidative metabolism capacity. Rich in mitochondria, myoglobin, and capillaries, these fibers significantly contribute to the muscle's endurance capacity.[20] In contrast, the fast-twitch fibers found in the EDL and psoas muscles are suited for anaerobic metabolism, providing rapid power output but tending to fatigue more quickly. The soleus muscle has a myo-connective structure that includes 3 intramuscular tendons, rarely seen in other muscle groups.[21] This complex structure helps the muscle absorb stress during prolonged activity without incurring damage. The gastrocnemius muscle, which shares a similar anatomical location with the soleus, is located superiorly to it. While the gastrocnemius is engaged in short-duration, high-power activities, the soleus is primarily active during prolonged, endurance-based tasks. During exercise, the soleus muscle relies on oxidative phosphorylation, using substrates like fatty acids and glucose for energy. Its high oxidative capacity and predominance of Type I fibers result in lower lactate production compared to muscles dominated by Type II fibers. Type I fibers utilize oxygen more efficiently to convert substrates into ATP, thereby minimizing lactate accumulation.[9,22] The ability of the soleus muscle to produce less lactate through aerobic metabolism while generating energy from carbohydrates and fatty acids suggests that it is more suitable for long-duration, repetitive exercise programs than other muscles.

In pathologies like HF and COPD, the oxidative capacity and perfusion of the soleus muscle are impaired, leading to significant reductions in strength and endurance. This functional decline can limit exercise tolerance and overall physical performance in affected individuals. Preserving the endurance capacity of the soleus muscle could thus play a crucial role in enhancing the efficacy of exercise interventions for cardiovascular conditions, such as CAD.[23] Consistent with clinical guidelines recommending at least 150 minutes of weekly exercise to protect against cardiovascular disease, patients in this study participated in an exercise protocol requiring a minimum of 150 minutes of weekly activity.[24]

The SII is a biomarker reflecting the balance between pro-inflammatory and anti-inflammatory forces in the body.[25,26] In the context of atherosclerosis, the SII has emerged as a potential prognostic tool for assessing the risk of adverse cardiovascular events.[5,6] Neutrophils are primary mediators of acute inflammation and contribute to the early stages of atherosclerotic plaque development. Beyond their role in hemostasis, platelets participate in inflammation and atherogenesis through growth factor release and immune cell recruitment. The lymphocytes, included in the SII calculation as the denominator, represent the regulatory arm of the immune response. A lower lymphocyte count, which indicates a higher SII, is associated with a more pronounced inflammatory state and an increased risk of plaque instability and rupture, leading to acute coronary events. Previous studies reported that a higher SII is correlated with increased severity of coronary artery disease and may predict poorer outcomes in patients experiencing acute myocardial infarction.[5,25,27] In a study conducted on the general population, a high SII was linked to elevated all-cause cardiovascular and cardio-cerebrovascular mortality.[28] Another study in patients with ST-elevation myocardial infarction highlighted the predictive value of SII in terms of mortality.[29] In summary, the SII serves as a valuable index for the clinical assessment of atherosclerosis, providing insights about the systemic inflammatory status of patients.

In this study, SII levels were lower in patients performing soleus push-up exercises at 1 and 3-month follow-ups when compared to those not exercising. This finding suggests that soleus push-up exercises may help reduce the immuno-inflammatory process in CAD patients, potentially slowing CAD progression.

Since the lipid profile plays a critical role in the pathogenesis of atherosclerosis, it is used to assess cardiovascular risk.[30,31] It is known that LDL-C, which infiltrates the endothelium and undergoes oxidative modification, can lead to endothelial dysfunction due to the pro-inflammatory nature of oxidized LDL-C. Conversely, HDL-C plays a protective role against atherosclerosis, facilitating the transport of cholesterol from peripheral tissues and plaques to the liver. This anti-atherogenic feature of HDL-C underscores the significance of the lipid profile's impact on atherosclerosis. Another component of the lipid panel, triglycerides, is also associated with atherosclerosis, albeit less directly than LDL-C.[32,33]

It was observed in this study that among patients performing soleus push-up exercises, average total cholesterol levels began to decrease from the 1st month of exercise, and by the 3rd month, LDL-C levels had decreased, while HDL-C levels had risen, reflecting positive effects on the lipid profile. These favorable effects suggest that they could be beneficial for CAD management.

In conclusion, this study emphasized the positive impacts of soleus push-up exercise on SII and the lipid panel in patients with CAD. However, these results need to be confirmed in further clinical studies with a larger number of patients and longer duration. Additionally, future studies should explore the effects of exercise on individuals with various demographic characteristics to better understand its impact across different populations. As a low-effort yet high-impact exercise, soleus push-up holds the potential to become a pivotal component in preventive and therapeutic strategies for cardiovascular health, offering an accessible and effective means to counteract the risks associated with sedentary lifestyles and improve overall quality of life.

Author contributions

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