

Original Article

Correlation of hs-CRP and the Duke Treadmill Score in the Cardiac Training Test

Muhamad Robiul Fuadi^{1*}, PhD; Rinta Prasetyanti¹, MD

ABSTRACT

Background: Risk stratification is the first step to prevent cardiovascular disease. Cardiac training tests perform it with the Duke Treadmill Score (DTS). The limitations and complications that may occur during cardiac training tests require alternative laboratory examinations. High-sensitivity C-reactive protein (hs-CRP) is an independent predictor of cardiovascular events. This study analyzed the relationship between hs-CRP and the Duke Treadmill Score.

Methods: This study has a cross-sectional, observational analytical design. Blood samples were taken from 40 patients who underwent cardiac training at Airlangga University Hospital and Telkom Laboratory in Surabaya, Indonesia. Patients' hs-CRP levels were measured by TMS 24i Premium Tokyo Boeki in the clinical pathology laboratory of Airlangga University Hospital.

Results: The average age of subjects was 43 years. Most subjects were male (60%) and had an increase in low-density lipoprotein cholesterol (92.5%). Hypertension was found in 22.5% of subjects. Most subjects were nonsmokers (70%), had a normal body mass index (82.5%), and did not have diabetic mellitus (82.5%). The mean hs-CRP level was 6.04 ± 9.79 mg/L. DTS results showed -5.13 ± 9.3 . There was a correlation between serum hs-CRP and DTS by Spearman analysis ($P = -0.85$ and $P < 0.05$).

Conclusions: Hs-CRP can be an alternative laboratory examination for stratifying cardiovascular event risks to cover DTS by cardiac training tests. (*Iranian Heart Journal 2026; 27(2): 47-53*)

KEYWORDS: high-sensitivity C-reactive protein; Duke Treadmill Score; cardiovascular disease; cardiac training test

¹ Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.

*Corresponding Author: Muhamad Robiul Fuadi, PhD; Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.

Email: muhamad-r-u-f@fk.unair.ac.id

Tel: +6281328712843

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The primary prevention of cardiovascular disease depends on the ability to identify high-risk individuals before the event's occurrence.¹ Risk stratification can increase effectiveness

in distributing effective prevention strategies related to cost-benefit and risk-benefit considerations. Cardiac training with electrocardiography (ECG) is a crucial examination for determining risk

stratification in cardiovascular events.² Several cardiac exercise test methods can be used as parameters for stratifying the risk of cardiovascular events. These are the Duke Treadmill Score (DTS), chronotropic incompetence, heart rate recovery, exercise-induced hypertension, exercise-induced hypotension, ventricular arrhythmia, and aerobic capacity.³ The DTS is one of the most powerful methods for risk stratification in cardiac exercise testing.⁴

Cardiac exercise testing is generally safe to perform; nonetheless, myocardial infarction and death have been reported and are estimated to occur in up to 1 per 2500 tests.⁵ The incidence of left bundle branch block induced by stress testing is reported in approximately 0.5% to 1% of all patients undergoing exercise testing.⁶ Cardiac training tests cannot be performed on all individuals, especially on sufferers with mobility impairments, severe arthritis, peripheral vascular disease, and neurological diseases.⁷ The limitations and complications that may occur during cardiac training tests require alternative laboratory tests as risk stratification for cardiovascular events.

Atherosclerosis is a major underlying process of cardiovascular disease, triggered by the accumulation of lipids in the artery walls and inflammation.⁸ Several inflammatory biomarkers can be used to describe the process of atherosclerosis formation. High-sensitivity C-reactive protein (hs-CRP) serves as an indicator of the ongoing inflammatory process in various diseases.⁹ Additionally, hs-CRP is a highly sensitive biochemical marker of CRP quantification, as an independent predictor of cardiovascular events.^{10,11}

This study aimed to analyze the relationship between hs-CRP levels and the DTS in patients undergoing cardiac training tests to determine the risk stratification of cardiovascular events with a view to improving disease prevention efforts.

METHODS

This cross-sectional, observational analytical study was conducted at Airlangga University Hospital and the Laboratory of Telkom Surabaya, Indonesia. TMS 24i Premium Tokyo Boeki performed the hs-CRP laboratory test with the immunoturbidimetric method. The research was carried out from November 2023 through December 2024. Subjects were patients who underwent a cardiac training test and agreed to be involved in this study. All subjects signed informed consent.

Subjects selected were aged between 18 and 65 years. Patients diagnosed with myocardial infarction, unstable angina, arrhythmia, aorta valve stenosis, acute aorta dissection, myocarditis, congestive heart failure, acute lung embolism, deep vein thrombosis, acute pericarditis, and endocarditis in medical record data were excluded from this study. In addition, patients with infectious disease; malignancy; and autoimmune, physical, or mental disorders that precluded cardiac exercise tests were excluded. Approval from the Ethics Committee of Airlangga University Hospital was obtained on March 25, 2024, (No. 049/KEP/2024). Informed written consent was acquired from all participants involved in this study.

Before the cardiac exercise test, patients received detailed explanations of the procedure and purpose of the examination, including the physical exercises to be carried out, their type and duration, symptoms and signs that may occur, and possible complications. Venous blood sampling for the hs-CRP laboratory test was carried out after participants signed the informed consent form. Patients were not allowed to eat or drink for 3 hours before the examination, but they were allowed to drink a small amount of water if some medications were needed to be taken. Subjects were not allowed to smoke for 3 hours before the test,

nor were they permitted to do heavy exercise on the same day as the examination. Further, β -blockers and nitrate drugs, which can decrease the heart rate and blood pressure response, were stopped 24 hours before the test.

Anamnesis and comprehensive assessments were necessary to obtain subject identity, history of stroke and ability to move, history of trauma or disease in the limbs that might interfere with movement, current medications, and daily physical activity or ability to estimate fitness levels. Cardiologists assessed and monitored subjects during the cardiac exercise test. It was ensured that the electrodes were installed and adhered strongly enough to subjects' skin. The area of subjects' skin where the electrode was to be attached was cleaned first. The Bruce protocol was employed to perform cardiac exercise tests.

Continuous ECG monitoring was performed during the test and recovery period to assess for changes in the ST segment and arrhythmias. The cardiac exercise test was performed to the patient's maximum capacity. Still, it could be stopped suddenly if chest pain, dizziness, shortness of breath, or abnormal findings on ECG occurred, along with changes in the patient's vital signs. ECG recording would continue during the examination until the cooling-down phase (5–10 minutes after physical exercise). Assessments during the examination were pulse rate, respiratory rate, blood pressure, ECG images, and the level of fatigue. The decision to stop the cardiac exercise test was one of the important functions of supervision. Subjects could ask to stop the test whenever they wanted. Absolute indications for stopping

the test were acute myocardial infarction, moderate-severe angina pectoris, ischemia, serious arrhythmias, signs of hypoperfusion, and neurological disorders.

The formula of the DTS was as follows³:

$$\text{DTS} = \text{Maximum exercise time (minutes)} - (5 \times \text{ST segment deviation in mm}) - 4 \times (\text{angina index})$$

- Exercise time: based on the standard Bruce protocol
- ST deviation: the maximum ST change (elevation or depression) in any lead except lead aVR
- Angina index: 0 points if no angina occurs, 1 point if nonlimiting angina occurs, and 2 points if angina occurs that limits exercise

Statistical analysis was performed using SPSS 26.0 software. Characteristics of the variables were analyzed with descriptive statistics. Correlations between hs-CRP and DTS were tested using the Spearman rank analysis. Statistical analysis used the confidence interval of 95%. Consequently, a *P* value of less than 0.05 was deemed statistically significant. A linear scatter plot between hs-CRP and the DTS was created using Microsoft Excel 2019.

RESULTS

Subjects involved in this study were 40 patients. The least hs CRP result was 0.24 mg/L, the maximum was 50.18 mg/L, and the mean was 6.04 mg/L with a standard deviation of 9.79 mg/L. The DTS had a mean of -5.13, a standard deviation of 9.3, a minimum of -24, and a maximum of 8. The characteristics of the studied subjects are presented in Table 1.

Table 1. Characteristics of the studied subjects

Characteristic	Total (No.,%)	hs-CRP (median, min-max in mg/L)	DTS (median, min-max)
Age (y)			
21-30	6 (15)	1.68 (0.24-4.11)	3.5 (-8-(6))
31-40	11 (27.5)	1.32 (0.45-10.28)	1 (-10-(8))
41-50	14 (35)	2.5 (0.98-32.64)	-10 (-24-(7))
51-60	9 (22.5)	4.78 (0.93-50.18)	-14 (-19-6)
Sex			
Male	24 (60)	3.27 (0.46-50.18)	-9 (-24-(7))
Female	16 (40)	1.25 (0-19)	1 (-19-(8))
Diabetic status			
DM	7 (17.5)	6.08 (0.46-19.15)	-13 (-23-(5))
non-DM	33 (82.5)	1.8 (0.24-50.18)	-3 (-24-(8))
Hypertension Status			
Hypertension	9 (22.5)	6.57 (1.06-50.18)	-12 (-24- (4))
Non-hypertension	31 (77.7)	1.57 (0.24-19.15)	-1 (-23-(8))
BMI			
Overweight	7 (17.5)	6.08 (0.77-50.18)	-12 (-24-(5))
Normal	33 (82.5)	1.84 (0.24-21.29)	-5 (-23-(8))
LDL Cholesterol Status			
High	11 (27.5)	6.15 (0.77-50.18)	-13 (-24-(5))
Elevated	26 (65)	1.55 (0.45-21.29)	-2 (-19-(8))
Normal	3 (7.5)	2.43 (0.24-4.11)	4 (-7-(6))
History of Smoking			
Smoking	12 (30)	2.47 (0.46-50.18)	-5.5 (-23- (6))
Non-smoking	28 (70)	1.99 (0.24-32.64)	-6 (-24-(8))

hs-CRP: high-sensitivity C-reactive protein; DTS: Duke Treadmill Score; DM: diabetes mellitus; BMI: body mass index; LDL: low-density lipoprotein

Older subjects had higher hs-CRP measurements and lower DTS values. Men had higher hs-CRP levels and lower DTS values than women. Similar findings were observed in subjects with diabetes mellitus (DM) compared with those without DM, hypertension compared with those without hypertension, normal body mass index (BMI) compared with overweight, and smoking compared with non-smoking. In general, the higher the low-density lipoprotein cholesterol (LDLc) value, the higher the hs-CRP value and the lower the DTS, except in the elevated category group, which had a lower mean hs-CRP value than the normal group.

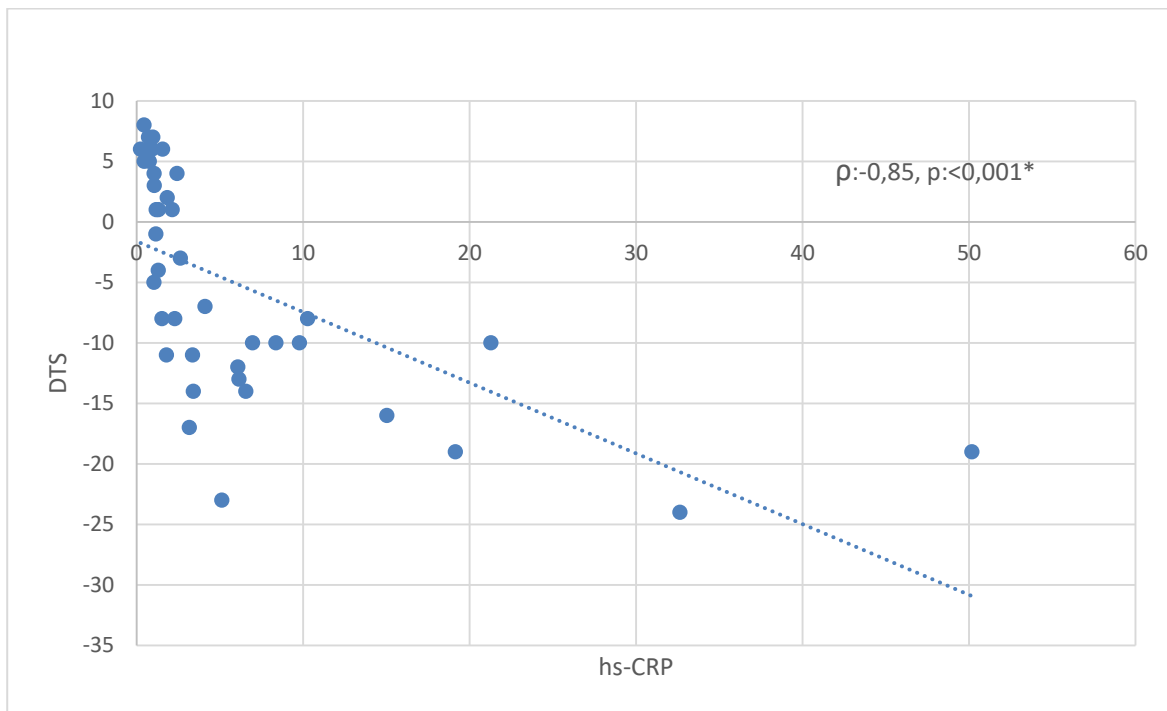
The relationship between hs-CRP and DTS values is shown in Figure 1. The Spearman analysis showed that the relationship had a rho (ρ) value of -0.85. A ρ value

approaching -1 indicated a strong negative relationship between hs-CRP and the DTS. DTS values decreased as the hs-CRP concentration increased. The relationship was also statistically significant ($P < 0.001$). In clinical implementation, hs-CRP and the DTS were divided into scoring categories for risk stratification and prognosis of cardiovascular events. Low risks of cardiovascular events were indicated by hs-CRP less than 1 mg/L, moderate risk by values between 1 and 3 mg/L, and high risk by greater than 3 mg/L. DTS scores fall into 3 categories: low risk (≥ 5), moderate risk (-10-4), and high risk (≤ 11).³ Table 2 shows the grouping of subjects based on the risk stratification of cardiovascular events, both in hs-CRP and the DTS. There was a concordance between hs-CRP and the DTS at low, moderate, and high risk of 80%.

Table 2. Correlation of hs-CRP with the DTS

hs-CRP	Duke Treadmill Score			
	Total (No., %)	Total (No., %)	Total (No., %)	Total
Low risk	8 (20)	-	-	8
Moderate risk	1 (2.5)	13 (32.5)	1 (2.5)	15
High risk	-	6 (15)	11 (27.5)	17
Total	9	19	12	40

Hs-CRP: high-sensitivity C-reactive protein

**Figure 1.** Linear scatter plot showing correlation between hs-CRP and the DTS

Hs-CRP: high-sensitivity C-reactive protein; DTS: Duke Treadmill Score

DISCUSSION

The results of the present study suggested that older age, male sex, DM, hypertension, and overweight BMI correlated with higher hs-CRP and lower DTS values. These variables are risk factors for cardiovascular disease that are already well-established. Control of these risk factors, especially DM, hypertension, and BMI, will reduce the risk of cardiovascular incidents.¹³

Subjects with high LDLc values had lower DTS and higher hs-CRP than subjects with elevated and normal LDLc values. Likewise, DTS values in subjects with elevated LDLc

were higher than those in normal subjects. The risk of cardiovascular disease has been reported to increase with a rise in blood LDLc levels.¹³ In this study, hs-CRP values in subjects with elevated LDLc had a lower median value than in subjects with normal LDLc. The use of antilipid therapy and differences in diets by subjects can affect this finding.

Subjects with a history of smoking had higher median hs-CRP values than those without smoking. The risk of cardiovascular disease has been reported to increase if there is a smoking habit.¹³ However, DTS values were high in patients with a history of

smoking compared with subjects without smoking. This study did not explore smoking history data in more detail, related to the amount, frequency, and duration of smoking in the studied subjects.

In this study, there was a correlation between hs-CRP and the DTS. The relationship was very strong. The relationship that occurred was opposite, indicated by the negative coefficient value, which means that if hs-CRP increases, then DTS will decrease. After grouping the risk stratification of cardiovascular events based on hs-CRP and DTS values, the agreement between the two parameters was also high, at 80%.

This study is in line with the study of Luo et al,¹⁴ who explored the possible relationship between endothelial dysfunction, systemic inflammation assessed by serum hs-CRP, and the DTS in patients with microvascular angina. Endothelial dysfunction and serum hs-CRP levels showed significant differences among the 3 groups according to DTS risk stratification. A negative correlation was found between DTS and hs-CRP levels.

This study is also aligned with the study of Long et al,¹⁵ who examined the relationship between endothelial dysfunction and inflammation in patients with cardiac syndrome X. The DTS was positively correlated with coronary flow reserve and negatively correlated with hs-CRP.

Endothelial dysfunction and systemic inflammation can impact exercise capacity and cardiovascular risk assessment related to the severity of myocardial ischemia. Inflammation damages the endothelial lining of blood vessels, disrupting normal blood flow regulation and contributing to decreased exercise performance. Endothelial dysfunction decreases nitric oxide production, which is required for smooth muscle relaxation and optimal blood flow distribution during physical activity.¹⁴ During exercise, coronary blood flow increases to meet the higher metabolic needs of the myocardium. The

limitation of coronary blood flow in response to the need to meet these needs quickly can cause electrocardiographic changes that affect the DTS.¹⁶

Moreover, hs-CRP is a sensitive marker of systemic inflammation and has been shown to predict future cardiovascular events. Elevated hs-CRP levels indicate a state of inflammation that contributes to endothelial dysfunction. In normal individuals, the endothelium has anti-inflammatory and antithrombotic properties, and regulates permeability to circulating molecules and vascular tone through a balance between the release of vasodilators, such as nitric oxide (NO). Endothelial dysfunction due to reactive oxygen species production reduces the bioavailability of NO, leading to reduced blood flow to the myocardium and muscles during exercise. Reduced blood flow decreases exercise capacity as reflected in the DTS score.¹⁷

This study provides a conclusion that hs-CRP values have a strong and significant negative correlation with the DTS in cardiac training tests. The relatively small number of subjects and the small proportion of subjects with low risk levels are limitations of this study. Furthermore, hs-CRP examinations can be used as an alternative to cardiac training tests in assessing cardiovascular risk.

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Conflict of Interest

The authors declare that they have no financial or personal relationships that could have improperly influenced them in writing this article.

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