



The Correlation between High Sensitive C-reactive Protein Levels and Gensini Score in Diabetes Patients

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Abstract

Edited by: Igor Spiroski
Citation: Rotty L, Wantania F, Wowor R. The Correlation between High Sensitive C-reactive Protein Levels and Gensini Score in Diabetes Patients. Open Access Maced J Med Sci. 2023 Jan 23; 11(B):212-215. https://doi.org/10.3889/oamjms.2023.11099
Keywords: Coronary artery disease; hsCRP; Gensini score; Diabetes
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Received: 11-Oct-2022
Revised: 28-Nov-2022
Accepted: 13-Jan-2023
Copyright: © 2023 Linda Rotty, Frans Wantania, Ribka Wowor
Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist
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BACKGROUND: Coronary artery disease is a disease caused by atherosclerotic plaques in the coronary arteries. The severity of coronary artery disease can be assessed objectively by coronary angiography. Many prospective studies have shown that inflammatory biomarkers with high sensitivity C-reactive protein (hsCRP) are independent predictors of cardiovascular events.

AIM: The aim of this study was to determine the correlation of hsCRP and Gensini score in subjects with coronary artery disease and diabetic patients.

METHODS: This study used an analytical observational design with a cross-sectional study to see the correlation between hsCRP and Gensini score in coronary artery disease subjects. The total sample was 40 subjects with a diagnosis of coronary artery disease and diabetes. Examination of angiography and hsCRP levels was performed on all subjects.

RESULTS: A total of 40 diabetic patients were included in the analysis. The mean age in this study was 57.98 ± 8.71 years old. The mean Gensini score in this study was 63.90 ± 40.79 years old. The median hsCRP level in this study was 13.05 (0.3–245.6). There was a significant correlation between hsCRP levels and the Gensini score ($r = 0.346$, $p = 0.029$).

CONCLUSION: There was a significant positive relationship between hsCRP levels and Gensini score, where an increase in the hsCRP value was also followed by an increase in the Gensini score; therefore, the hsCRP value can be used to assess the degree of coronary artery disease lesions.

Introduction

Coronary artery disease (CAD) is the leading cause of death in the USA (one of five deaths) and worldwide (one of five deaths) [1]. Nowadays, in Indonesia, CAD can be seen as a prevalent cardiovascular disease. Results of a survey conducted by the Indonesian Ministry of Health showed that CAD prevalence in Indonesia continues to increase year after year. Moreover, starting in the 2000s down to date, it can be confirmed that causes of death in Indonesia have shifted from infectious diseases to cardiovascular diseases (including CAD) [2].

Coronary artery disease is a disease caused by atherosclerotic plaques in the coronary arteries. The severity of coronary artery disease can be assessed objectively by coronary angiography. Many prospective studies have shown that inflammatory biomarkers such as high sensitivity C-reactive protein (hsCRP) are independent predictors of cardiovascular events [3].

Angiography examination is not readily available in all regional general hospitals yet in

Indonesia. With this in mind, hsCRP can become an alternative for screening diabetic patients who may have extensive but asymptomatic atherosclerotic lesions. Based on the high prevalence of diabetes mellitus (DM) and CAD cases in North Sulawesi, we are interested to find the correlation between hsCRP and the extent of atherosclerotic lesions in type 2 DM patients.

Methods

This study used an analytical observational design with a cross-sectional study to evaluate the relationship between hsCRP and Gensini score in CAD-diabetic subjects. This research was conducted in a span of 6 months from October 2021 to May 2022 at Prof. dr. R.D. Kandou Hospital in Manado, Indonesia. Consecutive sampling was performed. This study involved patients aged ≥18 years with both coronary artery disease and diabetes, who underwent coronary arteriography procedure. Patients with active infection, cancer, and whom refused to participate

were excluded from the study. Eligible patients were given the informed consent form, interviewed for basic characteristics, and then undergone laboratory testing. In this study, 40 samples were obtained from subjects with coronary heart disease and diabetic patients who met inclusion and exclusion criteria. The calculated minimum sample was 30 patients, which determined using minimum sample size equation for correlation test with assumed correlation coefficient of 0.5. Angiography and hsCRP level measurement were performed on all subjects. HsCRP levels were obtained by venous blood samples using immunoturbidimetric method. Gensini score was used to determine the lesion severity of CAD. Objective criteria: 1 point for $\leq 25\%$ stenosis, 2 points for 26–50% stenosis, 4 points for 51–75% stenosis, 8 points for 76–90% stenosis, 16 points for 91–99% stenosis, and 32 points for 100% stenosis; then multiplied by the multiplication factor of each part of the artery affected and the final scores are summed. Examination method: Coronary angiography obtained the number of lesions, the degree of stenosis, and the location of the coronary vessels which were, then, calculated based on the scheme published by Gensini. Gensini score was used to assess coronary artery atherosclerotic disorder, number of stents inserted, type of stent, and total length of stent used based on elective coronary angiography by assessing the affected blood vessels [4]. This study has been approved by Research Ethics Committee of Prof. Dr. R. D. Kandou Hospital (Number: 131/EC/KEPK-KANDOU/VII/2021).

Data analysis was supported with Statistical Package for the Social Science (SPSS) version 25. Data will be described descriptively. Normality test was conducted using Shapiro–Wilk test. Pearson or Spearman correlation test was used to determine the correlation between hsCRP and Gensini score.

Results

The mean age in this study was 57.98 ± 8.71 years old. The majority of respondents in this study were male (90%). The mean Gensini score in this study was 63.90 ± 40.79 years old. The median hsCRP level in this study was 13.05 (0.3–245.6). Detail on research subjects' characteristics is shown in Table 1.

Table 1: Characteristics of research subjects

Variable	N	Min	Max	Median	Average	SD
Age (years)	40	43	77	-	57.98	8.71
Hb (g/dl)	40	9.6	19.6	13.5	13.67	0.27
WBC ($\times 10^9/L$)	40	5.6	15.4	9.3	9.04	2.23
Platelet ($\times 10^9/L$)	40	162	448	260-13.05	265.08	59.61
Gensini score	40	8	182		63.90	40.79
hs-CRP (mg/dL)	40	0.3	245.6		-	-

N: Number of samples, SD: Standard deviation.

Sample distribution based on coronary angiography results

This study found of coronary angiography result of CAD triple vessel disease was 16 cases (40%) later followed with CAD double-vessel disease that was 13 cases (32.5%), CAD one vessel disease was 11 cases (27.5%). The angiography results are shown in Table 2.

Table 2: Sample distribution based on coronary angiography results

Coronary angiography results	N	Percentage
CAD one-vessel disease	11	27.5
CAD double-vessel disease	13	32.5
CAD triple-vessel disease	16	40

N: Number of samples.

Correlation analysis between hsCRP and Gensini score

The data normality was tested using Shapiro–Wilk and showed an abnormal distribution of data ($p < 0.05$) on the hsCRP value. The correlation between hsCRP and Gensini score was assessed by Spearman's test (Table 3) and the value of $r = 0.346$ with $p = 0.029$. Therefore, there was a weak and significant positive correlation between hsCRP and Gensini score. The higher the Gensini score, the higher the hsCRP value will be, and vice versa.

Table 3: Correlation between hsCRP and Gensini score

Variable	N	Correlation coefficient*	Significance*
hsCRP – Gensini Score	40	0.346	0.029

*Spearman's test, N: Number of samples.

Discussion

The mean age of the patients who enrolled in this study is 57 years old. This result was in accordance with research conducted at Dr. Kariadi Hospital, Semarang. They found that the mean age of patients with coronary artery disease that underwent coronary angiography was 56.25 years old and as many as 107 patients (83.60%) aged ≥ 45 years [5] Rachmawati *et al.* also found in their study that more than 60% respondents with CAD were aged ≥ 45 years old [6].

The majority of respondents in this study were male. This result was similar with study conducted by Wicaksono *et al.* with as much as 87.5% participants was male [7]. Moreover, research conducted by Hosseini *et al.* also found that patients who underwent angiography and had at least 50% stenosis in either one vessels blood were male [8]. Elderly was associated with higher risk to develop CAD. The incidence of CAD was started rising in above 40 years old population. The risk to develop cardiocerebrovascular disease

increased in age 55 years for male and 65 years old for female. Woman above 65 years old had the same risk with male from the same age [9]. In general, male was associated more with cardiovascular disease compared to female. However, postmenopausal women had increased risk of coronary heart disease. It was related with the decrease of estrogen hormone, which played a role in protecting the blood vessel from triggering vascular damage that happened in atherosclerosis. Premenopausal women were protected by estrogen that played a role in increasing high-density lipoprotein (HDL) levels [10]. Study conducted by Otaki *et al.* that involved 1635 adults young (≤ 45 years old) showed that male gender was strong predictor for CAD [11].

In this study, a positive correlation was found with a weak but statistically significant relationship between hsCRP and Gensini score ($r = 0.346$ with $p = 0.029$). Gensini score is a validated score to describe the coronary angiography result which evaluating the extent of coronary artery stenosis degree; therefore, it may correlate with CAD. A study by Masood *et al.* was aiming to evaluate the connection between Gensini score and risk group according to hsCRP level and found that there was significant correlation between severity arterial stenosis that assessed using angiography Gensini score and hsCRP [12]. Research conducted by Ahmed *et al.* on vascular inflammation and angiographic severity of CAD in young Asian Indians reported that high hsCRP is related to higher risk of severity in coronary lesion on young adult using the Gensini score ($r = 0.66$ with $p < 0.01$) [13]. The positive correlation between hsCRP level and Gensini score also demonstrated by Jia *et al.*, which assessed 238 patients with CAD ($r = 0.128$; $p = 0.049$) [14]. Piranfar *et al.* also found that higher hsCRP was found in higher severity of artery stenosis (moderate and severe) compared to patients with mild stenosis ($p < 0.010$). Therefore, it can be concluded that hsCRP may significantly correlated with coronary atherosclerosis severity [15].

High sensitivity C-reactive protein is an acute phase reactant that mainly produced in liver due to stimulation from proinflammatory cytokines. Using very sensitive method, we can check hsCRP in very low levels. However, hsCRP protein is not just a marker for chronic systemic inflammation, but also by direct involvement in the process of atherosclerosis, because hsCRP can amplify the anti-inflammatory response through complement activation, tissue damage, and cell endothelium activation. All those inflammatory response may lead to change in morphology of heart blood vessels [3], [16].

High sensitivity C-reactive protein has longer half-life in plasma and now considered as a mediator or as sign from atherothrombotic disease. Moreover, it is a predictor for strong incident in cardiovascular event. Inflammation is one of the descriptions of atherosclerosis. There is a strong link association

between the incident of inflammation and the incident of atherothrombotic. High sensitivity C-reactive protein may detect low-grade inflammation and can predict the cardiovascular event on coronary heart disease [3].

Conclusion

There was a significant correlation between hsCRP levels and Gensini score in CAD diabetic patients, where the higher the Gensini score, the higher hsCRP levels will be. Therefore, hsCRP levels can be used as an assessment of the degree of coronary heart disease lesions.

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