Relationship between Inflammation Markers and Stenosis Degrees in Stable Coronary Heart Disease

by Sefri Noventi Sofia

Submission date: 13-May-2023 02:32PM (UTC+0700)
Submission ID: 2092004933
File name: s-degrees-in-stable-coronary-heart-disease-5e5659bb1bb69.pdf.pdf (196.48K)
Word count: 4321
Character count: 23398

ISSN: 13412051
Volume 25, Issue 02, February, 2020

Relationship between Inflammation Markers and Stenosis Degrees in Stable Coronary Heart Disease

Edward Kurnia Setiawan Limijadi[1], Ariosta[1], Banundari Rachmawati[1], Sulistiyati Bayu Utami[2], and Sefri Noventi Sofia[2]

Department of Clinical Pathology of Medical Science Faculty of Diponegoro University, Central Java, Indonesia[1]
Department of Cardiology of Medical Science Faculty of Diponegoro University, Central Java, Indonesia[2]

Abstract— Stable coronary heart disease is the highest cause of death. This situation involves neutrophils and lymphocytes described by the neutrophil lymphocyte ratio (NLR) in inflammation. Inflammation makes an increase in acute phase protein C-reactive protein (CRP) and serum amyloid A (SAA), both of which also play a role in coronary artery stenosis. The degree of stenosis is measured by Gensini scores through invasive angiography. The relationship between the three hematological parameters and the degree of coronary artery stenosis needs a further investigation. A cross sectional study involving 35 stable coronary heart patients was calculated according to the formula of the sample size with inclusion and exclusion criteria. Examination of NLR was done by comparing absolute neutrophil counts, moreover absolute lymphocytes was examined by using a hematology analyzer. CRP levels were examined by the hs-CRP method and SAA levels were examined by using the ELISA principle. The Gensini score was used to assess coronary artery stenosis. The Spearman relationship test was used to analyze between variables. $p < 0.05$ was considered significant. There is a significant positive relationship between NLR and SAA but no correlation between CRP and NLR and SAA. There is a significant positive relationship between NLR and SAA with Gensini scores. There is no relationship between CRP and Gensini score. NLR is a simple parameter and SAA is a biomolecular parameter, both of which increase with increasing weight coronary artery stenosis, in stable CHD patients, it can be used for evaluation of stable CHD patients.

Keywords: Neutrophil lymphocyte ratio, C-reactive protein, amyloid A serum, gensini score, stable coronary heart disease.

Introduction

Cardiovascular disease is currently one of the main and first causes of death in both developed and developing countries [1,2]. The World Health Organization estimates that there are around 17.9 million deaths each year due to cardiovascular disease which is estimated at 31% of the world's population [3]. This shows that cardiovascular disease will continue to dominate mortality in the future. The prevalence of coronary heart disease diagnosed by doctors in Indonesia according to the 2013 Basic Health Research Agency for Health Research and Development was 0.5% or estimated at around 883,447 people [4].

Coronary heart disease is cardiovascular disease or heart and blood vessel disease caused by narrowing of the coronary arteries due to the process of atherosclerosis. One manifestation of coronary heart disease is stable coronary heart disease. Stable coronary heart disease refers to patients who have been diagnosed with coronary heart disease or those who are suspected of suffering from coronary heart disease who do not experience changes in acute symptomatic status at this time [5-7]. Dyslipidemia is one of the risk factors for the incidence

of stable coronary heart disease, because it plays an important role in the process of forming atherosclerosis in blood vessels which can lead to stable coronary heart disease [8,9]. Stable coronary heart disease is also known as chronic inflammation. Previous studies have shown that inflammatory symptoms are associated with the severity of stable coronary heart disease and worsening cardiovascular outcomes [10-12]. An increase in leukocytes count shows that there are infections and inflammation that play a role in atherogenesis, the development of ruptured atherosclerotic plaques and thrombosis. The process of atherogenesis is an inflammatory process in which neutrophils are a marker of nonspecific inflammation and lymphocytes as regulatory markers [13,14]. Neutrophil lymphocyte ratio (NLR) is an independent prognostic factor in coronary heart disease which is also influenced by the condition of hypercholesterolemia, metabolic syndrome and diabetes and hypertension. Neutrophil lymphocyte ratio can also be a predictor of mortality in cardiovascular disease [15]. Previous studies have shown a relationship between NLR and the severity of stenosis in stable coronary heart disease based on coronary angiography results [16]. There were significant differences in NLR in the group with a higher Gensini score than the group with a lower Gensini score [17].

C-Reactive Protein (CRP) is one of the acute reactant phase proteins produced by the liver as a marker of systemic inflammation and increases in various types of injuries. Previous research has shown that CRP is not only a sign of inflammation but can play an active role in atherogenesis. Syed SH, et al. (2013) conducted a study on the relationship between CRP levels and the severity of stenosis in patients with coronary heart disease. The results of the study prove that there is a significant positive relationship between CRP levels and the severity of stenosis in the group of patients with coronary heart disease [18]. High sensitivity CRP examination techniques have been developed to detect lower serum CRP levels than previous laboratory methods and are known as highly sensitive CRP (hs-CRP) methods. This technique can be used to assess the risk of heart disease associated with atherosclerotic chronic vascular inflammation [19,20]. Serum Amyloid A (SAA) is also an acute phase reactant protein produced by the liver which appears as a chronic and acute inflammatory response. In acute inflammation, SAA levels can increase to 1000-fold. Some evidence suggests that SAA plays a role in the pathophysiology of coronary stenosis, namely SAA is found as apolipoprotein in HDL particles and plays a role in acute modification of cholesterol transport during physiological stress. SAA also shows the chemotactic impact on monocytes. Previous research proved that there were significant differences in SAA levels between subjects with coronary stenosis and without coronary stenosis [21].

Coronary heart disease is stable with chronic inflammation, therefore laboratory parameters used in this study were NLR, CRP and SAA as markers of inflammation in stable coronary heart disease, where the three parameters influence the occurrence of atherosclerosis [17,21]. Neutrophil lymphocyte ratio and CRP can be important measures of inflammation in stable coronary heart disease because they are cost effective, easily available and can be easily calculated. The SAA parameter is a laboratory examination that is expected to detect early the occurrence of chronic processes in stable coronary heart disease. Moreover, determination of the degree of stenosis used in this study was based on the degree of coronary stenosis quantitatively obtained from the results of coronary angiography or cardiac catheterization because it is easier, more done and more applicable [22]. These things encourage researchers to prove the relationship between NLR and SAA levels with the degree of stenosis in stable coronary heart disease.

2. Methods

Analytical descriptive study with cross sectional approach was conducted on 35 stable coronary heart patients at Dr. RSUP Kariadi Semarang. The study was conducted in February to October 2018. Samples were taken by consecutive sampling where subjects were selected non-randomly in March to May 2018 who met the inclusion and exclusion criteria of the study. Inclusion criterias were above 40 years old, normal body

temperature and willing to take part in the study. On the other hand, exclusion criterias were patients with acute coronary syndrome, infection, undergoing chemotherapy, hematological malignancy, chronic liver disease, lysis and jaundice serum.

The patient's identity and other matters related to treatment and other risk factors were identified by history and looking at the patient's medical record. Blood was taken using 3 cc EDTA and plain tubes for each patient. A plain tube was left for 30 minutes to get the serum and then centrifuged 3000 rpm for 5 minutes then examined the levels of CRP and SAA. EDTA blood was examined using hematology analyzer to obtain absolute neutrophil counts and absolute lymphocyte counts. NLR was calculated manually by dividing between absolute neutrophil counts and absolute lymphocyte counts with a cut off value of <2.5. CRP levels were examined by the hs-CRP method, the examination using the ELISA principle with a cut off value of <5 mg / l, as well as SAA levels with a cut off value of <6 ng / mL. The degree of stenosis of stable coronary heart disease patients was determined based on the Gensini score by two SF and SLY cardiologists to assess the degree and extent of the atherosclerotic plaque area (Neeland et al., 2012).

Data analysis used the nonparametric correlation test with the Spearman test. Significance was expressed at $p < 0.05$. All research respondents were requested to give written informed consent and patient's identity was confidential. This research was approved by the Health Research Ethics committee of the Faculty of Medicine Diponegoro University/RSUP Dr. Kariadi Semarang

Results

The characteristics of the subject of this study can be seen in table 1.

Table 1. Characteristics of research subjects

Subject Characteristics	Median (min-max)
Age (year)	56 (43-78)
Height (cm)	160 (150-176)
Weight (kg)	61 (48-85)
IMT (kg/m$^{2)}$	24,2 (17,0-31,2)
Systolic pressure (mmHg)	135 (100-170)
Diastolic pressure (mmHg)	80 (65-100)
Hb (g/dl)	13,0 (11,0-17,40)
Leukocyte count (x10^3/ μl)	7,28 (3,24-13,20)
Neutrophils count (x10^3/ μl)	4,17(0,76-7,18)
Lymphocyte count (x10^3/ μl)	2,12(1,33-3,54)
NLR	1,78(0,29-4,61)
Platelet count (x10^3/μl)	246 (171-381)
Fasting blood glucose (mg/dl)	125 (75-390)
Total cholesterol (mg/dl)	158 (104-283)
LDL (mg/dl)	105 (60-190)
Triglyceride (mg/dl)	116 (60-216)
HDL (mg/dl)	41 (13-67)
CRP (mg/l)	1,5 (0,50-6,54)
SAA (ng/ml)	25,97 (14,43-56,23)
Gensini Score	42,5 (0-151)

Description: min: lowest value, max: highest value

Table 1. shows that the research subjects with more male gender were 21 respondents (60%) compared to women which amounted to 14 respondents (40%). The median age of the study subjects was 56 years with a range of 43-78 years. Media values of NLR, CRP levels, SAA levels and Gensini scores in the study subjects were 1.78; 1.5 mg / l; 25.97 ng / ml and 42.5. The median CRP and NLR in this study were still below the cut-off value, while the SAA level exceeds the cut-off value.

Distribution of risk factors in the subject of this study were presented in the following table 2.

Table 2. Risk factors for stable CHD in study subjects

Risk Factor	Number (Person)	Percentage (%)
Diabetes mellitus	17	48,57
Hypertension	16	45,71
History of active smokers	14	40,00
Dyslipidemia	10	28,57

The research subjects had diverse risk factors with at least one risk factor in one patient, there were also 2 to 4 risk factors in one patient when added together, the risk factors for the most stable emergence of coronary heart disease were diabetes mellitus.

The body mass index of the subject of this study was classified and presented in the following table 3. The most body mass index of the research subjects was in the normal category (42.86%) even though there were 18 overweight research subjects (52.43%). It was possible for these patients to know their condition before being diagnosed with stable coronary heart disease, so they regulated their eating patterns that could affect body weight.

Table 3. Body mass index of research subjects

IMT	Number (Person)	Percentage (%)
Underweight	2	5,71
Normal	15	42,86
Overweight	7	20,00
Obese	11	31,43

The correlation between inflammation parameters were done. There was a significant moderate positive (r=0.628; p=0.000) between NLR and SAA. No correlation between CRP and NLR, and so did CRP and SAA. The relationship between NLR values and SAA levels with Gensini scores showed a moderate positive relationship with a significance of 0.000. This states that there is a significance moderate positive relationship between NLR values (0.593) and SAA levels (0.584) with the degree of coronary stenosis. The more severe coronary stenosis occurs in a person, the higher the NLR value and SAA level. There is no relationship between CRP levels and Gensini scores.

4. Discussion

The results of this study have a correlation between NLR and the degree of stenosis. Neutrophil/lymphocyte ratio (NLR), according to the research, has been used as a marker for systemic inflammation, cardiovascular disease, cancer that is easy and quite inexpensive [24]. NLR is reported to be related to the severity of heart disease and its clinical output. Sahin, et al. (2013) reported that there was a relationship between NLR and the severity of coronary heart disease, where high NLR was a poor prognostic factor in SKA patients.

Furthermore, NLR is referred to as a free predictor of stable CHD severity because it is significantly associated with a Gensini score that increases with an increase in NLR [25]. The process of atherogenesis is an active inflammatory process with important actions from functional and dysfunctional leukocytes. Neutrophils provide an important role both in eliminating infarction or in platelet leukocyte aggregate formation and in reperfusion injury in coronary heart disease [26,27].

Neutrophil lymphocyte ratio can also be a predictor of mortality in cardiovascular disease. The results of this study are in line with previous studies which showed that there was a relationship between NLR and the severity of stenosis in stable coronary heart disease based on coronary angiography results. There were significant differences in NLR in the group with a higher Gensini score than the group with a lower Gensini score [26-28].

The results of this study indicate that there is no significant relationship between CRP and the degree of coronary stenosis. Parameter CRP is a parameter for acute inflammation. This study took samples in stable CHD where the inflammation was chronic. Increased CRP synthesis in plasma is likely to increase but the amount is not large, so the level is not enough to give a sign of acute inflammation. In addition, the condition of stable CHD atherosclerosis is better than unstable CHD. This is due to atherosclerotic plaque in patients with stable CHD without rupture even though the Gensini score in the study subjects was more than 20 indicating a heavy blockage. The resulting inflammation is chronic and patients do not have prominent symptoms [29].

C-Reactive Protein (CRP) is one of the acute reactant phase proteins produced by the liver as a sign of systemic inflammation and increases in various types of inflammation. This parameter is widely used as a predictor of someone having a high risk of blockage of the coronary arteries [30,31]. Induction of CRP formation in high conditions is caused by an acute inflammatory state that occurs in a person due to atherosclerosis by proinflammatory cytokines. CRP plays an important role in atherogenesis including complement activation, lipid uptake by macrophages, spurring the release of proinflammatory cytokines, inducing tissue factors, endothelial dysfunction, and inhibiting nitric oxide production [32]. CRP levels increase at the 19th hour of onset of inflammation and reach a peak in plasma at 24-48 hours [33].

The test results of the relationship between SAA levels and the degree of coronary stenosis in this study was positively significant. This value indicates that the increase in SAA levels is directly proportional to the severity of the degree of coronary stenosis. Chronic inflammatory reactions that occur in stable CHD induce liver to synthesize SAA in response to cytokines produced by macrophages, namely tumor necrosis factor-α (TNF-α), interleukin -1 (IL-1), interleukin-6 (IL-6) [34,35]. This acute phase protein can also be used as a marker of chronic inflammation that is different from CRP which increases in acute inflammation especially in unstable coronary heart disease after 12 hours of symptom onset [36]. Amyloid A serum induces monocytes and procoagulant factors in inflammation faster than CRP [37].

Other conditions, namely SAA, are also produced by monocytes/ macrophages, vascular muscle cells, and endothelial cells which results in increased levels of SAA with the course of inflammation caused by atherosclerosis of the coronary arteries. Amyloid A serum is degraded in the liver which in a state of inflammation both chronic and acute will decrease, so that SAA levels will be high [38]. This is the basis that SAA levels are higher and are significantly related to the degree of coronary stenosis compared to CRP levels.

Some evidence shows that SAA plays a role in the pathophysiology of coronary stenosis. SAA is found as apolipoprotein in HDL molecules and shows the chemotactic effects of monocytes and T lymphocytes. The SAA molecule allows vascular damage and induces the expression of metalloproteinase (MMP) matrix which causes atherosclerosis [39].

Amyloid A serum moves the apo A-1 from HDL to form larger and denser HDL molecules thereby it reduces the ability to catalyze cholesterol esterification. The SAA-HDL bond is not able to prevent LDL oxidation, and even strengthens the occurrence of foam cells and then becomes a fatty streak which is the beginning of the development of coronary stenosis. The SAA molecule can be distributed not only in HDL but also in LDL particles.

The SAA bond with LDL has been found to be formed from oxidative interactions between SAA and LDL that are catalyzed by ROS. The bond stimulates the formation of proteoglycans that contribute to the formation of atherosclerotic plaques. Early emergence of small plaques with small extracellular lipid content and cholesterol esters and thick fibrous capsules with stable plaque characteristics give rise to stable coronary levels beginning to increase [40-43].

This study did not analyze the effect of risk factors for stable CHD on research variables. Further research can take meaningful variables in this study to be able to be analyzed in a stable CHD population with only specific risk factors and taking into account these risk factors in variable analysis.

5. Conclusion

NLR is a simple parameter that can be conducted, while SAA is a biomolecular parameter, both of which increase with increasing weight coronary artery stenosis in stable CHD patients, it can be used for evaluation of stable CHD patients.

6. Ethical clearance

This study has been received ethical approval by Ethics Committee of Diponegoro University, Semarang, Indonesia.

7. Disclosures

The authors have no conflict of interest.

8. Funding

The authors are responsible for study funding without any involvement of grant, sponsorship, or another resources of funding.

9. Legends

Table 1. Characteristics of research subjects

Table 2. Risk factors for stable CHD in study subjects

Table 3. Body mass index of research subjects

10. References

[1] Nichols M, Townsend N, Scarborough P, Rayner M. 2013. Cardiovascular disease in europe: epidemiological update. Eur. Heart J. 34: 3028–34.

[2] Santulli, G. 2013. Epidemiology of cardiovascular disease in the 21 st century : updated numbers and updated facts. J. Cardiovasc. Dis.1: 1–2.

[3] World Health Organization. Cardiovascular disease. Available at: https://www.who.int/cardiovascular_diseases/en/. Assessed Desember 28, 2018.

[4] Kementrian Kesehatan RI. Riset Kesehatan Dasar (Riskesdas). 2013: 1–384.

[5] Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, et al.2013. ESC guidelines on the management of stable coronary artery disease – addenda. Eur. Heart J. 34: 2949–3003.

[6] Fihn SD, Blankenship JC, Alexander KP, Bittl JA, Byrne JG, Fletcher BJ, et al. 2014. 2014 ACC / AHA / AATS / PCNA / SCAI / STS Focused Update of the GuidekGuideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease. Circulation 130: 1749-67.

[7] Dai X, Whitehead JB, Forman DE, Alexander KP. 2016. Stable ischemic heart disease in the older adults. J Geriatr Cardiol 13(2): 109-14.

[8] Badimon L, Padró T, Vilahur G. 2012. Atherosclerosis, platelets and thrombosis in acute ischemic heart disease. Eur. Heart Journal 1: 60–74.

[9] Niroumand S, Khajedaluee M, Rezaiyan MK, Abrishami M, Juya M, Khodaee G, et al. 2015. Atherogenic Index of Plasma (AIP): A marker of cardiovascular disease. Med. J. Islam Repub. Iran 29: 627–35.

[10] Libby, P. 2012. Inflammation in atherosclerosis. Journal of the American heart association 32: 2045-51.

[11] Prajapati JH, Sahoo S, Nikam T, Shah KH, Mahareya B, Parmar M. 2014. Association of high density lipoprotein with platelet to lymphocyte and neutrophil to lymphocyte ratios in coronary artery disease patients. Journal of Lipids: 1-8.

[12] Cicek G, Açıkgöz SK, Yayla Ç, Kundi H, İleri M. White blood cell count to mean platelet volume ratio: A novel and promising prognostic marker for st-segment elevation myocardial ınfarction. Cardiol. Journal 23: 225–35.

[13] Sahin D, Elbazan Z, Gur M, Yildiz A, Akpinar O, Icen YK, et al. 2013. Neutrophil to Lymphocyte Ratio Is Associated With the Severity of Coronary Artery Disease in Patients With ST-Segment Elevation Myocardial Infarction. Angiology 64(6):23-9.

[14] Varol E, Aksoy F, Bas HA, Ari H, Ozaydin M. 2014. Mean platelet volume is elevated in patients with low high-density lipoprotein cholesterol. Angiology 65(8): 733-6.

[15] Balta S, Celik T, Mikhailis D, Ozturk C, Demirkol S, Aparci M, et al. 2015. The Relation Between Atherosclerosis and the Neutrophil – Lymphocyte Ratio. Clinical and Applied Thrombosis/Hemostasis: 1-7.

[16] Arbel Y, Finkelstein A, Halkin A, Birati EY, Revivoa M, Zuzut M, et al. 2012. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. Atherosclerosis 225: 456–60.

[17] Zhang G, Chen M, Yu ZMM, Wang XD, Wan ZQQ. 2014. Relation between neutrophil-to-lymphocyte ratio and severity of coronary artery stenosis. Genet. Mol. Res.13: 9382–9.

[18] Syed SH, Al Masri AA. 2013. Relationship of high sensitivity C-reactive protein with presence and severity of coronary artery disease. Pak J Med Sci. 29(6): 1425–9.

[19] Dubey RK, Dhakal N, Das BKL, Pandey NK, Baral N, Lamsal MH, et al.2013. C- Reactive Protein in patients with nstemi acute coronary syndrom. Journal of Universal College Of Medical Sciences 1: 1–5.

[20] Madjid M, Fatemi O. 2013. Components of the complete blood count as risk predictors for coronary heart disease. In depth review and update. Texas Heart Institute Journal: 17–29.

[21] Sudana G, Setyawati, Sukorini U 2015. Perbedaan bermakna kadar serum amiloid a antara stenosis koroner dibandingkan bukan stenosis koroner. IJCPML. 21(3): 231-6.

[22] Knudtson M. 2014. Coronary Scoring Systems A Historical Perspective. p.1–33. Available at: http://www.approach.org/pdfs/.../History_of_Coronary_Scoring_March2014.pdf. Accessed December 15, 2018.

[23] Neeland IJ, Patel RS, Eshtehardi P, Dhawan S, McDaniel MC, Rab TS, et al. 2012. Coronary angiographic scoring systems: An evaluation of their equivalence and validity. Am. Heart J. 164(4): 547–52.

[24] Aydin M, Yilmaz A, Donma AM, Tulubas F, Demirkol M, Erdogan M, et al. 2015. Neutrophil/lymphocyte ratio in obese adolescents. North Clin Istanbul 2(2):87-91.

[25] Datta RK, Rashid MM, Azam MG, Ulubbi MS, Siddiqui MKR, Karmaker P, et al. 2015. Association between Neutrophil to Lymphocyte Ratio and Severity of Coronary Artery Disease in Chronic Stable Angina. BanglaJOL 10(2):164-70.

[26] Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. 2008. Association Between Admission Neutrophil to Lymphocyte Ratio and Outcomes in Patients With Acute Coronary Syndrome. Am. J. Cardiol. 102: 653–7.

[27] Bugan B, Onar LC. 2014. The Neutrophil-to-Lymphocyte Ratio. Clin. Appl. Thromb. 20: 341–2.

[28] Carbone F, Nencioni A, Mach F, Vuilleumier N, Montecucco F. 2013. Pathophysiological role of neutrophils in acute myocardial infarction. Thrombosis and Haemostasis 110(2): 1-14.

[29] Chen ZW, Chen YH, Qian JY, Ma JY, Ge JB. 2014. Validation of a Novel Clinical Prediction Score for Severe Coronary Artery Diseases before Elective Coronary Angiog raphy. Plos One 9(4):1-8.

[30] Faraj M, Salem N. C-Reactive Protein. Available at: https://www.intechopen.com/books/blood-cell-an-overview-of-studies-in-hematology/c-reactive-protein. Accessed 4 Agustus 2017.

[31] Strang F, Schunkert H. 2014. C-Reactive Protein and Coronary Heart Disease:All Said—Is Not It?. Mediators of Inflammation, Hindawi Publishing Corporation. p 1-7.

[32] ShrivastavaAK, Singh HV, Raizada A, Singh SK. 2015. C-reactive protein, inflammation and coronary heart disease. EHJ 67, 89–97.

[33] Choudhury M, Devagourou V. 2017. Biomarkers of Atherosclerosis: Is the Evaluation Essential Preoperatively?. Atheroscler 2(3):1-5.

[34] Regina E, Peggy B, Melanie K, Sabine Z, Jutta MW, Andre s, et al. 2015. Acute phase serum amyloid A induces proinflammatory cytokines and mineralization via toll-like receptor 4 in mesenchymal stem cells. J SCR 15:231-9.

[35] Lisa RT, Maria CDB, Ailing J, Preetha S, Victoria PN, Laura DH. 2017. Serum Amyloid A3 is a High-density lipoprotein-associated acute phase protein. J. Lipid Res. 59(2):339-47.

[36] Auer J, Berent R, Lassnig E, Eber B. 2002. C-reactive protein and coronary artery disease. Jpn Heart J 43:607-19.

[37] Hong C, Changjie S, Ikuko E, Jesse G, Wendy J, Ben F, et al. 2007. Serum Amyloid A Induces Monocyte Tissue Factor. J Immunol 178:1852-60.

[38] Susan H, Changjie S, Carolyn LG, Ben F, Paul KW. 2013. A role for acute-phase serum amyloid A and highdensity lipoprotein in oxidative stress, endothelial dysfunction and atherosclerosis. Redox Report 14:5, 187-96.

[39] Zhu Y, Xian X, Wang Z, Bi Y, Chen Q, Han X. 2018. Research Progress on the Relationship between Atherosclerosis and Inflammation. Biomolecules;8(3):2-11.

[40] Malle E, Beer FC. 1996. Human serum amyloid A (SAA) protein: a prominent acute-phase reactant for clinical practice. Eur. J. Clin. Invest. 26: 427–35.

[41] Kotani K, Satoh N, Yamada T, Gugliucci A. 2010. The potential of serum amyloid A–LDL as a novel biomarker for cardiovascular disease risk. Clin. Lipidol. 5: 489–95.

[42] Zewinger ME, Drechsler C, Kleber ME, Dressel A, Riffel J, Triem S, et al. 2015. Serum amyloid A:

High-density lipoproteins interaction and cardiovascular risk. Eur. Heart Journal 36: 3007–16.

[43] Thompson JC, Colton J, Thompson J, Wilson PG, Yoder MH, Webb N, et al. 2015. A brief elevation of serum amyloid A is suffi cient to increase atherosclerosis. J. Lipid Res. 56:286-93.

This work is licensed under a Creative Commons Attribution Non-Commercial 4.0 International License.

View publication stats

Relationship between Inflammation Markers and Stenosis Degrees in Stable Coronary Heart Disease

ORIGINALITY REPORT

8%	6%	3%	5%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Submitted to Teerthanker Mahaveer University Student Paper	2%
2	epag.springeropen.com Internet Source	1%
3	Submitted to Udayana University Student Paper	1%
4	journals.plos.org Internet Source	1%
5	www.ncbi.nlm.nih.gov Internet Source	<1%
6	www.hindawi.com Internet Source	<1%
7	www.pharmateca.ru Internet Source	<1%
8	farmalkes.kemkes.go.id Internet Source	<1%
	research-information.bris.ac.uk	

9	Internet Source	<1%
10	link.springer.com Internet Source	<1%
11	1filedownload.com Internet Source	<1%
12	Submitted to Universitas Diponegoro Student Paper	<1%
13	worldwidescience.org Internet Source	<1%
14	www.atlantis-press.com Internet Source	<1%
15	www.nalchbp.org Internet Source	<1%
16	Submitted to Donau Universität Krems Student Paper	<1%
17	forschung.medunigraz.at Internet Source	<1%
18	www.frontiersin.org Internet Source	<1%
19	Gilberto Vargas-Alarcon, Oscar Perez-Mendez, Gabriel Herrera-Maya, Cynthia Garcia-Sanchez et al. " and Gene Polymorphisms Are Associated with High-Density Lipoprotein	<1%

Subclasses and Acute Coronary Syndrome ", Lipids, 2018
Publication

20 T. Ono, K. Azuma, A. Kawahara, J. Akiba, T. Kakuma, S. Chitose, H. Umeno. " Pre-treatment CD8 tumour-infiltrating lymphocyte density predicts distant metastasis after definitive treatment in patients with stage III/IV hypopharyngeal squamous cell carcinoma ", Clinical Otolaryngology, 2018 <1%
Publication

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	Off		