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CORRELATION OF PENTRAXIN-3 LEVELS WITH GENSINI SCORE IN ACUTE CORONARY SYNDROME

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Abstract
Background: Acute coronary syndrome (ACS) continues to be a major cause of morbidity and mortality throughout the world. Inflammation plays an important role at every stage of development of atherosclerosis. Pentraxin3 (PTX3) is the newly identified acute phase reactant, PTX3 Proteins are expressed in vascular endothelial cells and macrophages. Thus, the level can reflect the presence of blood vessel inflammation. The severity of coronary artery stenosis can be calculated through Gensini score through coronary angiongraphy.
Aim : Find out the relationship of pentraxin 3 levels with Gensini scores in acute coronary syndrome
Methods: Sampling was carried out during june - July 2019. The total population of the study included 61 people suffering from ACS. The entire population was examined by Pentraxin 3 and calculated the severity of coronary artery stenosis with Gensini score through angiography. The study was conducted after obtaining ethical approval and informed consent.
Result And Discussion: Pentraxin 3 levels were obtained with median value of 0.59 (0.06-22.96). The Gensini score was obtained with median value of 62.00 (2.00 – 113.00). The Spearman Rank Test, there was no significant relationship between the Pentraxin 3 levels and the Gensini score r = 0,250 dan p = 0,052 .
Conclusion and Suggestion: There was no significant relationship between the Pentraxin 3 levels and the Gensini score. Further research needs to be done by considering the sampling time for the PTX-3 examination given the variation in the time of the attack when coming to the hospital between study subjects so that more stringent patient detection is needed.

Keywords: Acute coronary syndrome, Pentraxin 3, Gensini score.

Introduction
Coronary arterial disease is a global problem both in the country both developed and developing countries. Coronary arterial disease (CAD) is the leading cause of morbidity and mortality in the world despite advances in treatment of patients with acute myocardial infarction and all efforts to spread the prevention of this disease in the general population. (Benjamin EJ et al, 2019) Coronary heart disease occurs when the coronary arteries that supply the myocardium harden and narrow. This occurs due to the inflammatory process and the accumulation of cholesterol in the walls of coronary arteries called *atherosclerosis.* The process of atherosclerosis that continues will cause the lumen of the coronary arteries to narrow, so that blood flow will be obstructed. Heart muscle that lacks oxygen supply due to decreased blood flow causes symptoms in the form of chest pain or heart attack. (National Institutes of Health, 2019)

Pentraxin3 (PTX3) is a newly identified acute phase reactant, characterized by a multimeric cyclic structure. Many cell types such as macrophages, dendritic cells, neutrophils, adipose cells, fibroblasts, and vascular endothelial cells produce PTX3 in response to inflammatory signals. PTX3 is independently associated with the risk of damage to blood vessels. Serum PTX3 concentrations have been shown to increase in patients with macrovascular complications such as diabetes mellitus, unstable angina, heart failure, and cardiovascular disease. (Garlanda C et al, 2015; Diniz SN et al, 2014).

There are several scoring systems used to assess the severity of coronary artery stenosis. Research by Neeland *et al*. showed that from several scoring systems on the severity of coronary artery stenosis assessed through angiography it was found that the Gensini scoring system had the highest level of correlation with the severity of coronary artery stenosis as assessed through angiography. (Neeland IJ *et al*, United States 2012)

This study aims to analyze the relationship of PTX3 levels with Gensini scores in patients with acute coronary syndrome (ACS).

Methods

This study was a cross-sectional observational study conducted at the Haji Adam Malik General Hospital in Medan with permission from the Research Ethics Committee of the Faculty of Medicine, University of North Sumatra-RSHAM. Subjects were recruited from May to July 2019 in sequence. Inclusion criteria were patients who were clinically confirmed as Acute Coronary Syndrome and underwent percutaneous coronary intervention. While the exclusion criteria are patients with cancer, liver disease, thyroid disease, chronic kidney disease.

Research Procedures

Clinical and demographic characteristics of subjects treated in the ED with acute myocardial infarction as a work diagnosis were recorded. Blood samples were taken from all subjects when entering. The sample is then placed in a clot activator containing a tube to obtain serum and kept at an optimal temperature and frozen until examination. Pentraxin 3 levels were measured using Bioassay Technology Laboratory reagent kits with the principle of Enzyme-linked immunosorbent assay. Gensini scores were assessed based on the results of percutaneous coronary intervention.

Statistical analysis

The characteristics of the research subjects are presented in tabulated form and described. The relationship ofPTX3 levels with Gensini scores in ACS patients usedcorrelation *Pearsontest* if the data were normally distributed. If the data are not normally distributed, *Correlation Spearman rank test* was used. All statistical tests with $p < 0.05$ were considered significant.

Results

A total of 61 patients with acute coronary syndrome were included in this study consisting of 46 (75.4%) males and 15 (24.6%) females as presented in table 1.

Table 1. Descriptive Data by Gender

VARIABLE		N	%	age
Gender	Male	46	75.4%	(36-81)
	Female	15	24.6%	(39-83)

Of all study participants had a median age of 59 years. With the youngest age is 36 years and the oldest age is 83 years. At the initial measurement the study population was obtained the median value of PTX3 was 0.59 with a minimum value of 0.06 and a maximum value of 22.96. While the median Gensini score is 62 with a minimum value of 2 and a maximum value of 113 (Table 2)

Table 2. Descriptive Data by Age, PTX3, Gensini Score

Variable	Median
Age	59.00 (36-83)
PTX3 level (ng/mL)	0.59 (0.06-22.96)
Gensini Score	62.00 (2.0-113.0)

The Mann Whitney U test was used to assess the comparison of Homocysteine levels with the severity of AMI associated with Gensini scores, p value = Gensini 0.003 was obtained (Table 2). This shows that there is a significant difference between Homocysteine levels in groups with low gensini scores (mild atherosclerosis) and groups with high gensini scores (severe atherosclerosis).

Spearman correlation test shows there is no relationship between PT. Gensini scores with (r = 0.250)) and (p = 0.052) (Table 3).

Table 3. Correlation between Pentraxin3 and GENSINI Score

variable	levels of PTX3		
	n	**r**	**p**
Score GENSINI	61	0.250	**0.052 ***

***** Spearman correlation test

By using the Mann Whitney test to assess the comparison of Pentraxin 3 levels with the severity of SKA associated with the Gensini score, the value of p = 0.109 was obtained. This shows that there is no significant difference between PTX 3 levels in the group with mild atherosclerosis and the group with severe atherosclerosis. (Table 4)

Table 4. Comparison of Pentaxin 3 Levels with Gensini Scores in Groups with Severe Atherosclerosis and Mild Atherosclerosis

Variable	Severity of IMA		Value p Value of
	Mild **(Gensini Score 1-29)** **Median (Min-Max)**	**Atherosclerosis Severe Atherosclerosis** **(Gensini Score ≥ 30)** **Median (Min-Max)**	
PTX 3 level (ng/mL)	3.11 (0.06 –11.80)	0.59 (0.06–22.96)	0.109 *

* Mann Whitney Test

Discussion

Median age of patients in this study is 59 years. With the youngest age is 36 years and the oldest age is 83 years. This is consistent with the theory which states that before the age of 40 years, rarely occur serious illness while from the age of 40 to 60 years, the incidence of myocardial infarction increased fivefold. Age is a risk factor for CHD where increasing age increases the risk of CHD. The older the age, the greater the emergence of plaque that sticks to the wall and causes disruption of blood flow through it. (Pencina M et al, United States 2019)

Coronary heart disease in men is two times greater than in women there are several things that cause men more potentially affected by coronary heart disease, among others, the lifestyle of modern men with indiscriminate eating habits , drinking alcohol, and smoking habits and the presence of high stress factors in men that trigger hypertension which is a risk factor for CHD. (Pencina M et al, United States 2019)

Spearman correlation test statistic test showed that there was no significant relationship between Gensini score and PTX level 3 r = 0.250 and p = 0.052. The Mann Whitney test also obtained a comparison of Pentraxin 3 levels with the severity of ACS related to the Gensini score obtained p = 0.109. This shows that there is no significant difference between PTX 3 levels in the group with mild atherosclerosis and the group with severe atherosclerosis.

PTX3 in proatherogenic events can be associated with the possibility of an increased inflammatory status in the walls of blood vessels, which can contribute to atherogenic processes. (Rossini et al., 2013) In contrast, transgenic PTX3 overexpression has been found to produce greater resistance to lipopolysaccharide toxicity and

abrasions and puncture secretions. There is also evidence that PTX3 can modulate inflammation-related tissue damage. (Inoue, Kodama and Daida, 2012)

Other evidence shows that PTX3 provides an important role in modulating the cardiovascular system in humans and in experimental models. (Dubin et al., 2012). In particular, there are conflicting opinions regarding the effect of PTX3 on cardiovascular disease (CVD) because some observations show the protective effect of PTX3 cardiovascular disease. (Fornai et al., 2016)

PTX3 has also been found to provide a protective effect against atherosclerosis. As a relationship between PTX3 and P-selectin cell adhesion molecules in atherosclerotic lesions. Maybe PTX3 uses some of these effects through association with protein. For example, neutrophils in P-selectin in venules at the site of infection or injury receive signals for the release of PTX3 and stimulate PTX3 production and then selectively bind Pselectin expressed locally by paracrine, whereas the separation of this complex is slowed by increasing binding avidity due to the multimeric nature of PTX3. PTX3. As more neutrophils are produced, they release more PTX3, which then binds more P-selectin molecules. This is a local negative feedback system that reduces neutrophil tethering, accelerates rolling, and increases immune system detachment. Indeed, PTX3 expression has been found to reduce the number of neutrophils in P-selectin in vitro in a concentration-dependent manner, whereas PTX3 injection in vivo has been shown to reduce the number of neutrophils in rat thrombin-stimulated mesenteric venules due to competitive PTX3 inhibitors between P-selectin and P-selectin glycoprotein 1 (PSGL-1) bond. (Inoue, Kodama and Daida, 2012)

In this study PTX3 illustrates no correlation with Gensini scores because of several things such as natural processes of inflammation and drug interventions obtained at the beginning of an attack that might affect the effects or the inflammatory process. This can lead to suboptimal PTX3 results. PTX3 is time dependent, it requires serial retrieval in ACS cases to better illustrate the overall PTX3 results.

The Gensini score illustrates long-term occlusion in the coronary arteries due to chronic processes, while a PTX 3 set only illustrates the response of inflammation at the time of (acute) events in the process of comparing coronary lesions in this study.

Conclusion

There is no significant relationship between Gensini scores with Pentraxin 3 levels with Gensini scores in Acute Coronary Syndrome patients. Pentraxin 3 levels cannot be used as a marker of severity in patients with acute coronary syndrome.

Limitations and Recommendations

There are some limitations of this study such as limited samples, no follow-up after the patients were discharged, no subgroup analyzes and time variations when collecting blood samples for serum pentraxin-3 levels. Further studies can recruit more representative samples of the population with longer follow-up, so the exact prognostic significance of serum pentraxin-3 may be useful.

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