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# Diyabetik Olmayan ST Yükselmesiz Miyokard Enfarktüsü Hastalarında Serum Vaspin Düzeyi ile Koroner Arter Hastalığının Şiddeti Arasındaki İlişki

# Relationship Between Serum Vaspin Levels and the Severity of Coronary Disease Non-Diabetic Patients with Non-ST Elevation Myocardial Infarction

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**Öz**

**Giriş ve Amaç:** Vaspin bir adipositokin, serin proteaz inhibitörüdür ve obezite, insülin duyarlılığı, diabetes mellitus ve koroner arter hastalığı ile ilişkilidir. Vaspin ve koroner arter hastalığı arasındaki ilişki çeşitli çalışmalarda gösterilmiştir. Koroner arter hastalığı olan hastalarda bu değerin diyabetten bağımsız olup olmadığı ise bilinmemektedir. Ayrıca ST elevasyonsuz miyokard enfarktüslü (NONSTEMI) hastalarda vaspinin önemini gösteren bir çalışma yapılmamıştır. Bu çalışmada, diyabetik olmayan NONSTEMI hastalarında serum vaspin düzeyleri ile SYNTAX skoru ile belirlenen koroner arter hastalığı şiddeti arasındaki ilişkinin araştırılması amaçlanmıştır.

**Gereç ve Yöntemler:** NONSTEMI'li toplam 165 diyabetik olmayan hasta, kesitsel olarak çalışmaya dahil edildi. Serum vaspin seviyeleri ELISA yöntemi ile ölçüldü. SYNTAX skorları, anjiyografi sonuçlarına (çift kör) iki uzman operatör tarafından değerlendirildi. Hastalar çeyrekler arası aralık yöntemi ile SYNTAX skoruna göre üç gruba ayrıldı (Grup 1 SS <10, grup 2 10 ≤ SS≤22, grup 3 SS> 22).

**Bulgular:** Serum vaspin düzeyleri üç grup arasında anlamlı olarak farklı (p = 0,03) ve grup 1'de grup 3'e göre anlamlı olarak yüksek bulundu (p = 0,01). Grup 1 ve 2 ile grup 2 ve grup 3 arasında anlamlı fark bulunmadı. (p = 0, 52, p = 0.06). SYNTAX skoru ile serum vaspin seviyeleri arasında anlamlı ancak zayıf bir negatif korelasyon olduğu bulundu (r = -0.207, p = 0.008).

**Sonuç:** Vaspin, SYNTAX skoru ile negatif korelasyon göstermektedir ve diyabetik olmayan NONSTEMI hastalarında koroner hastalığın şiddetini göstermek için yararlı bir belirteç olabilir.

**Anahtar Kelimeler:** Diyabetik olmayan, NONSTEMI, SYNTAX, Vaspin.

**Abstract**

**Objectives:** Vaspin is an adipocytokine, serine protease inhibitor, correlated to obesity, insülin sensitivity, diabetes mellitus, and coronary artery disease. The association between vaspin and coronary artery disease was shown in several studies. Whether this value is independent of diabetes in coronary artery disease patients is not known. Also, a study that shows the importance of vaspin in patients with Non-ST elevation myocardial infarction

(NONSTEMI) is not conducted. This study aimed to investigate the relationship between serum vaspin levels and the severity of coronary artery disease, which is determined by the SYNTAX score, in nondiabetic patients with NONSTEMI

**Materials and Methods:** A total of 165 nondiabetic patients with NONSTEMI were included in this cross-sectional study. Serum vaspin levels were measured by the ELISA method. SYNTAX scores were evaluated by two expert operators blinded to the angiography results. Patients were divided into three groups according to the SYNTAX score by the interquartile range method (group 1 with SS <10, group 2 with 10 ≤ SS≤22, group 3 with SS> 22).

**Results:** Serum vaspin levels were found significantly different between three groups (p = 0,03) and significantly higher in group 1 than group 3 (p = 0,01).No significant difference was found between group 1 and 2 also group 2 and 3 (p = 0, 52, p = 0.06 ).It was found to be a significant but weak negative correlation between the SYNTAX score and serum vaspin levels (r = -0,207, p = 0.008).

**Conclusion:** Vaspin negatively correlates to SYNTAX score and maybe a useful marker to show the severity of coronary disease in nondiabetic patients with NONSTEMI

**Keywords:** NONSTEMI, Nondiabetic, SYNTAX, Vaspin.

## 1. Introduction

Coronary artery disease is the most common cause of death worldwide. Although many patients have similar traditional risk factors, coronary artery disease severity is not the same. This is because of the non-traditional risk factors such as homocysteine, lipoprotein-a, oxidative stress, adipocytokines, or genetic mutations. [1]. Adipose tissue acts as an endocrine gland by secreting adipocytokines. Some of these are pro-inflammatory and associated with insulin resistance, endothelial dysfunction, atherosclerosis, and increased cardiovascular risks [2-4]. Vaspin is an adipocytokine, serine protease inhibitor, correlated to obesity, insülin sensitivity, diabetes mellitus (DM), and coronary artery disease [5-8]

The Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) scoring system, which is calculated by evaluating the number of angiographic lesions, the location of the lesion, and its functional importance, is a validated scoring system that shows the severity of coronary artery disease [9]. It is demonstrated that vaspin levels may predict adverse cardiovascular events and mortality in patients with acute myocardial infarction [10]. But the study population consisted of diabetics and ST-elevation myocardial infarction (STEMI). A strong relationship between diabetes and vaspin may explain the predictive value of vaspin in these studies [9,10]. Whether this value is independent of diabetes in coronary artery disease patients is not known. Also, a study that shows the importance of vaspin in patients with NONSTEMI is not conducted. Therefore, this study aimed to investigate the relationship between serum vaspin levels and the severity of coronary artery disease determined with SYNTAX scores in non-diabetic patients with NONSTEMI.

## 2. Material and Methods

In this cross-sectional single-center study, 165 non-diabetic patients with NONSTEMI who underwent coronary angiography between 2016 -2017 were included. Ethical approval was obtained from the regional ethics committee (Approval no:215944, 07/06/2017), and each patient signed an informed consent form. All participants' rights were protected according to the Helsinki Declaration (2013). Echocardiography was performed on all patients. At the time of diagnosis, 3 mL of venous blood samples were taken from each patient. The samples were centrifuged, separated serums were stored at –80 °C, and serum vaspin levels were measured with the ELISA method by using East Biopharm Elisa kit. The reference range of vaspin was 50-10000 pg/ml

The exclusion criteria were as follows: Diabetes mellitus, advanced left ventricular dysfunction (EF <30%), history of coronary by-pass surgery, acute renal failure, end-stage renal failure (GFR <15 mL/min) requiring hemodialysis, advanced liver failure (Child-Pugh B, C), and active infection. NONSTEMI is defined as elevated cardiac troponin levels with one of the ST-T wave changes or pathological Q waves in the ECG report or newly detected wall motion abnormality with cardiac imaging. SYNTAX scores (SS) were evaluated by two expert operators blinded to the angiography results, and in case of any discrepancy, an opinion was sought from a third cardiologist. Most of the studies were divided patients into groups according to SS as; SS≤22, 22-32, and ≥32. However, when the patients were divided with this method in our study population, there would be no balanced distribution because 111 patients had SS ≤22. Therefore, patients were divided into three groups using the interquartile range (IQR) method: SS <10, 10 ≤ SS <22, and SS ≥ 22.

Statistics: SPSS (Statistical Package for Social Sciences, Chicago, Illinois) 21.0 program was used to analyze the variables. Normality analysis of the data was performed using the Kolmogorov–Smirnov test. Normally distributed numerical data were compared with Student's t-test. Categorical data were compared using the chi-square test. The relationship between the serum vaspin level and SS were analyzed using Pearson's correlation test. Quantitative variables are indicated as mean ± standard deviation. Furthermore, the median (minimum/maximum) and

categorical variables are shown as n (%). Variables were examined at a 95% confidence interval, and p <0,05 was considered significant.

## 3. Results and Discussion

*3.1. Results*

A total of 165 patients' mean age were 61,4 ± 10,4 years, and 68% were male. Hypertension and hyperlipidemia were found in 58% and 32,1% of patients, and 55,8% were active smokers. A significant difference was found between the groups in terms of age and EF (p <0,01, p <0,002). There was no significant difference between the groups in terms of hypertension, hyperlipidemia, gender, and smoking status (p >0,05). Previous myocardial infarction and percutaneous coronary intervention rates were similar (p = 0,12, p = 0,36). The demographic and clinical characteristics of the patients were shown in Table 1.

**Table 1.** Clinical characteristics of the patients.

| | SS<10 n=54 | 10≤SS<22 n=51 | SS≥22 n=60 | P value |
|---|---|---|---|---|
| **Age (mean± SD)** | 56,4 ± 12,6 | 62,5 ± 11,4 | 62,5 ± 12,4 | **0,01*** |
| **Male** | 33 (%60,5) | 44 (%73,6) | 41 (%67,4) | 0,33 |
| **BMI ($m^2$/kg)** | 27,2 ± 6,1 | 26,3 ± 5,3 | 26,7 ± 9,1 | 0,21 |
| **Hypertension** | 31 (%57,4) | 30 (%58,8) | 36 (%60) | 0,96 |
| **Hyperlipidemia** | 15 (%27,8) | 21 (%41,2) | 17 (%28,3) | 0,24 |
| **Smoking** | 27 (%50) | 31 (%60,8) | 34 (%56,7) | 0,53 |
| **Previous MI** | 15 (%27,8) | 6 (%11,8) | 12 (%20) | 0,12 |
| **Previous PCI** | 19 (%35,2) | 16 (%31,4) | 14 (%23,3) | 0,36 |
| **EF (%; mean ± SD)** | 55,2 ± 6,7 | 52,9 ± 7,8 | 49,9 ± 8,3 | **0,002**** |

*SS:SYNTAX score,BMI:Body mass index,MI:myocardial infarction,EF:Ejection fraction,PCI:Percutaneous coronary ınterventıon*

The mean LDL-C, CRP, hemoglobin, glucose, creatinine, and vaspin levels were 130,5 ± 41.8 mg/dL, 6,6 ± 6,1 mg/dL, 13,3 ± 1,9, 108,5 ± 22 mg/dL, 0,91 ± 0,23 mg/dL, and 386,5 ± 50,7 pg/mL, respectively. The mean vaspin value was 518,9 ± 66,8 pg/ml in SS <10 (group 1), 343,3 ± 45,7 in 10 ≤ SS 22 (group 2) and 281,1 ± 26,2 pg/ml in SS ≥ 22 (group 3). (Table 2). The total cholesterol, LDL-C, and creatinine levels of the patients were significantly higher in group 3 (p = 0,006, p = 0,01, p = 0,008, respectively). Creatinine values were significantly different between groups 1 and 3 (p = 0,001). Platelet count was significantly lower in group 3 (p = 0,02). Serum vaspin levels were found significantly different between groups (p = 0,03). When the binary groups were compared, only group-1 vaspin levels were significantly higher than group 3 (p = 0,01). No significant difference was found between group 1 and group 2 and between group 2 and group 3 in vaspin levels (p = 0,52, p = 0,06). (Table.2) (Figure.1)

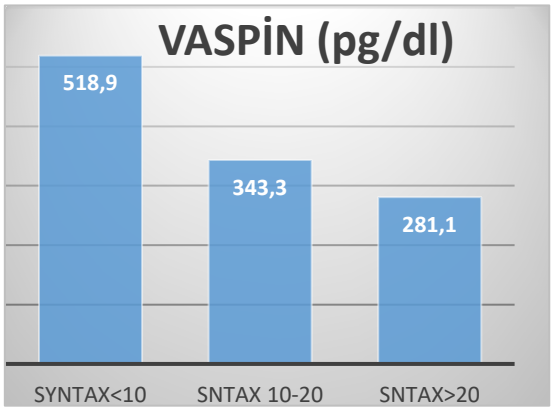


**Figure.1** Serum vaspin levels were found significantly different between groups (**p = 0,03**)

**Table.2** Laboratory findings of patients

| | **SS <10 (n=54)** | **10≤ SS<22 (n=51)** | **SS≥22 (n=60)** | **P-value** |
|---|---|---|---|---|
| Total cholesterol *(mg/dl;mean± SD)* | 175,4 ± 41,7 | 197,9 ± 49,7 | 196,1 ± 43,6 | **0,01*** |
| LDL-C **(***mg/dl; mean ± SD***)** | 116,2 ± 36,2 | 138,6 ± 47,6 | 136,7 ± 35,2 | **0,008**** |
| HDL-C **(***mg/dl; mean ± SD***)** | 37,8 ± 12,3 | 41,3 ± 10,6 | 36,7 ± 12,1 | 0,06 |
| Triglyceride **(***mg/dl; mean ± SD***)** | 187,8 ± 160,6 | 159,3 ± 89,2 | 185,7 ± 129,2 | 0,45 |
| Glucose (*mg/dl;mean± SD)* | 108,3 ± 61,3 | 100,7 ± 40,8 | 114,19 ± 51,5 | 0,38 |
| Creatinine *(mg/dl; mean ± SD)* | 0,84 ± 0,18 | 0,92 ± 0,21 | 0,98 ± 0,26 | **0,006*** |
| CK-MB *(ng/ml; mean ± SD)* | 32,6 ± 22,2 | 29,6 ± 27,6 | 34,1 ± 33,1 | 0,54 |
| Troponin **(***ng/ml; mean ± SD***)** | 0,30 ± 0,51 | 0,44 ± 0,57 | 0,54 ± 0,7 | 0,12 |
| Hemoglobin **(***gr/dl; mean ± SD)* | 13,1 ± 1,9 | 13,3 ± 1,8 | 13,5 ± 2 | 0,48 |
| CRP **(***mg/L; mean ± SD***)** | 6,4 ± 6,4 | 6,3 ± 5,4 | 7,0 ± 6,6 | 0,81 |
| Vaspin *(pg/ml; mean ± SD)* | 518,9 ± 66,8 | 343,3 ± 45,7 | 281,1 ± 26,2 | **0,03*** |

*Difference between group 1 and 2-3,**Difference between group 1 and 2 and 3

LDL-C: Low-density lipoprotein- cholesterol, HDL-C: High-density lipoprotein -cholesterol, CK-MB: Creatine kinase muscle-brain, CRP: C reactive protein

No significant differences were observed in other parameters between the groups (p>0,05).

In Pearson's correlation analysis, serum vaspin levels were found to be significantly negatively correlated to SS (r = -0,207, p = 0,008).

Of the 165 patients, 68 (41,1%) were diagnosed with single-vessel disease, 60 (35,7%) with the two-vessel disease, and 37 (23,2%) with multi-vessel disease. The mean SS was found 17,5 ± 11,4. The angiographic characteristics of the patients are shown in Table 3.

**Table 3.** Angiographic characteristics of patients

| **Number of critical coronary artery** | n=165 |
|---|---|
| One vessel | 68 (%41,1) |
| Two vessel | 60 (%35,7) |
| Multivessel | 37 (%23,2) |
| **Infarct related artery** | |
| Left Anterior Descending | 82 (%49,4) |
| Circumflex | 38 (%22,6) |
| Right coronary artery | 45 (%28) |
| **SYNTAX score (mean ± SD)** | 17,5±11,4 |

*3.2. Discussion*

A significant but weak negative correlation was found between serum vaspin levels and the extent and the severity of coronary artery disease in non-diabetic patients with NONSTEMI in this study. Serum vaspin levels significantly decreased in patients with a high SS. The possible reason for the low correlation coefficient between vaspin and SS in our study may be the lack of a strong effect of diabetes, insulin resistance to vaspin levels.

Systemic inflammation and adipokines production have been considered important mechanisms for the adverse effects on the vessel wall. Metabolites, cytokines, and adipocytokines like vaspin can target the liver. Changes in liver-derived lipoproteins, clotting factors, and inflammatory factors impact the vessel wall's atherogenic environment [11]. Studies have demonstrated the relationship between vaspin and atherosclerosis. Low vaspin levels were found to be a higher risk of coronary artery disease (CAD) [12]. In a study by Aust et al., no association was found between serum vaspin levels and stenosis severity in patients with carotid stenosis. However, it was found that low vaspin levels correlated to ischemic cerebrovascular events observed in the last six months [13]. In another study by Kadoglou et al., vaspin values were lower in coronary artery disease patients than in the healthy control group [14]. In the same study, a negative correlation was found between vaspin and the Gensini score, which indicates the severity of coronary artery disease. These findings are consistent with our results. Studies examining the relationship between vaspin and the severity of coronary artery disease are scarce. Serum vaspin levels were found to be significantly lower in patients with stenosis of more than 70% in a single vessel than in those without coronary stenosis [15]. A study by Zhang et al. compared acute coronary syndrome patients with patients having normal coronary arteries. Plasma vaspin levels were found to be significantly lower in patients with acute coronary syndrome [16]. In a study by Sathyaseelan et al., serum vaspin levels were compared in diabetic patients with and without acute coronary syndrome. Low serum vaspin levels were found to be an independent risk factor for coronary artery disease [17]. In contrast to our study, patients with acute coronary syndrome and stable patients were compared. Moreover, patients in that study had

diabetes. In another study, diabetic patients with and without coronary artery disease and the healthy control group were compared. In contrast to our study results and other studies, the lowest vaspin levels were found in the healthy control group. The highest levels were found in diabetic patients with coronary artery disease [18]. However, a significant positive correlation was found between serum vaspin levels and insulin resistance. The high level of vaspin in coronary artery patients may also be related to this high insulin resistance in patients with impaired diabetes regulation. In the Zhang et al. study, it was shown that the frequency of major cardiac adverse events was significantly higher in patients with low vaspin levels, and vaspin was an independent predictor of mortality in STEMI patients. In addition, increased vaspin levels may have a protective role in the recovery of ejection fraction. [10]. In a recent large patient population study, Xiang et al. showed that vaspin might be a valuable biomarker of major adverse cardiac events and improve risk stratification for acute myocardial infarction patients [19]. Moreover, Ji et al. showed that vaspin might be a useful marker to predict cardiovascular events in patients with stable coronary artery disease [20]. These findings are compatible with our study. To the best of our knowledge, the relationship between vaspin levels and the severity of coronary artery disease in non-diabetic patients with NONSTEMI was not conducted before.

The study's limitations are a single-center design, the limited number of patients, and the lack of follow-up data.

## 4. Conclusion

Vaspin negatively correlates to SS and may be a useful marker to show the severity of coronary disease in non-diabetic patients with NONSTEMI. However, multi-center studies with larger patient populations and follow-up need to reveal the relationship of vaspin with cardiovascular morbidity and mortality.

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All the authors of the study declare; there is no conflict of interest.

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