Nesfatin-1 levels in patients with slow coronary flow

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Abstract

Background: Nesfatin-1 is a novel anorectic neuropeptide with potent metabolic regulatory effects.

Aim: We aimed to evaluate the relationship between nesfatin-1 levels and slow coronary flow (SCF).

Methods: A total of 60 consecutive patients with SCF and 60 consecutive patients with normal coronary flow (NCF) were enrolled into the study. Nesfatin-1 level was measured from blood serum samples using enzyme-linked immunosorbent assay test.

Results: Serum nesfatin-1 levels were significantly lower in the SCF group compared to the NCF group (p < 0.001). Low levels of nesfatin-1 were found to be significantly and independently associated with the SCF (odds ratio 0.982, 95% confidence interval 0.969–0.995, p = 0.005).

Conclusions: The results of this study showed that serum nesfatin-1 level was lower in the SCF group than in the NCF group. Nesfatin-1 could play a role in the pathogenesis of SCF phenomenon with mechanisms such as inflammation and endothelial dysfunction. Further studies are needed to determine the relation between SCF and nesfatin-1.

Key words: inflammation, nesfatin-1 protein, human, coronary circulation

Kardiol Pol 2018; 76, 2: 401–405

INTRODUCTION

Slow coronary flow (SCF) is an important coronary angiographic phenomenon characterised by delayed progression of angiographic contrast media in the coronary arteries in the absence of obstructive coronary artery disease (CAD) [1]. The incidence of SCF ranges between 1% and 7% among patients who undergo coronary angiography [1]. It is known that SCF is associated with angina pectoris, myocardial infarction, sudden cardiac death, and life-threatening arrhythmias [2, 3]. Behind this entity, there may be secondary factors like coronary artery stenosis, coronary artery ectasia, coronary artery spasm, valvular heart disease, and connective tissue disorders [4], but the underlying pathophysiological mechanisms of primary SCF have not yet been clearly demonstrated. Potential underlying mechanisms like microvascular dysfunction, endothelial dysfunction, vasomotor dysfunction, small vessel dysfunction, diffuse atherosclerosis, inflammation, oxidative stress, and increased platelet aggregability have been evaluated so far [1–4]. Neuropeptide Y, a chemical mediator released from the adipose tissue, is thought to play a role in this phenomenon by causing increased resting resistance; "cardiac syndrome Y" has even been proposed as a name [5].

Nesfatin-1 was discovered by Oh et al. [6] in 2006. They showed that nesfatin-1 is secreted from the hypothalamic nuclei, which are responsible for controlling appetite. It was initially evaluated as a satiety molecule involved in decreasing appetite and regulating metabolism. Maejima et al. [7] showed that acute and chronic anorexigenic effects of nesfatin-1 occur through the melanocortin system. Subsequently it was found that nesfatin-1 influences growth and differentiation of the adipose tissue, inflammation, thermoregulation, pancreatic insulin secretion, glucose homeostasis in the liver, nutrient

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Received: 26.07.2017 Accepted: 05.10.2017 Available as AoP: 27.10.2017

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intake in the brain, sleep, fear, anxiety, stress, glucose homeostasis; regulation of gastric emptying, gastric acid secretion, gastric motility, and reproductive functions [8].

Dai et al. [9] have shown that serum nesfatin-1 levels were lower in individuals with acute myocardial infarction (AMI) compared to the angina pectoris group and the control group, in a study involving 156 individuals. In addition, plasma nesfatin-1 levels were inversely correlated with high sensitivity C reactive protein (hs-CRP), neutrophil percentage, and Gensini score in the AMI group. They reported that low levels of nesfatin-1 may have an important role in the development of AMI [9].

It has been shown that nesfatin-1 has an effect on inflammation and CAD [9]. Chemical mediators released from adipose tissue and inflammation have a role in the development of SCF [5]. This study aimed to evaluate the relationship between nesfatin-1 and SCF.

METHODS Study population

Between October 2016 and March 2017, 2568 patients who underwent coronary angiography due to clinical suspicion or myocardial ischaemia demonstrated by exercise stress testing or myocardial perfusion scintigraphy were evaluated at Turkiye Yuksek Ihtisas Training and Research Hospital. Two groups were created. Sixty consecutive patients showing SCF with normal coronary artery anatomy were selected as the patient group (SCF group), and 60 consecutive patients with a normal coronary flow (NCF) pattern showing normal myocardial blushing and clearing were considered as the control group.

We obtained a detailed medical history from all patients and performed a complete physical examination. The patients were evaluated by means of 12-lead electrocardiography. Two experienced specialists performed a detailed transthoracic echocardiography of all the patients. The diagnosis of hypertension was made by a systolic blood pressure of 140 mmHg or higher, or a diastolic blood pressure of 90 mmHg or higher by at least three different measurements, or the use of anti-hypertensive medication. The diagnosis of diabetes mellitus was established by a fasting blood glucose of 126 mg/dL or higher, or the use of anti-diabetic medication. Hyperlipidaemia was defined as total cholesterol levels of 200 mg/dL or higher, or a history of statin use except in the last three months. Patients who were smoking before hospitalisation were accepted as smokers.

Patients with known CAD, acute coronary syndrome, peripheral arterial disease, congestive heart failure with an ejection fraction < 55%, history of surgical or interventional cardiovascular procedure, stroke, pulmonary hypertension, valvular heart disease, cardiomyopathies, myocarditis, pericarditis, hepatic or renal dysfunction, chronic inflammatory diseases, malignancies, active infections, and endocrine or metabolic disorders except diabetes mellitus were excluded from the study. Patients taking antiaggregants, anticoagulants, corticosteroids, statins in the last three months, anti-oxidant vitamins, and alcohol were also excluded from the study.

The study protocol was approved by the local Ethics Committee and written, informed consent was taken from all patients. The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice and International Conference on Harmonisation guidelines.

Coronary angiography

Two experienced interventional cardiologists blinded to the clinical characteristics of the patients performed coronary angiography using the standard Judkins technique. Iohexol was used as a non-ionic contrast agent during coronary angiography in all patients and control subjects. During coronary angiography, the contrast agent was manually injected as 6-10 mL at each position. Visualisation of the coronary arteries was obtained in standard planes. Coronary flow rates of all subjects were documented using the Thrombolysis in Myocardial Infarction (TIMI) frame count (TFC) method described by Gibson et al. [10]. The TFCs of the left anterior descending (LAD) and circumflex (Cx) arteries were assessed in either the right anterior oblique projection with caudal angulations or the left anterior oblique projection with cranial angulations, and that of the right coronary artery (RCA) [11] usually in straight left anterior oblique projection. The initial frame was defined as the frame in which concentrated dye occupies the full width of the proximal coronary artery lumen, touching both borders of the lumen, and forward motion down the artery. The final frame is defined as the frame when the leading edge of the contrast column initially arrives at the distal end. The last frames used for the LAD, Cx, and RCA were those in which the dye first entered the moustache segment, the distal bifurcation segment, and the first branch of the posterolateral artery, respectively. The final count was then subtracted from the initial count and the exact TFC was calculated for the given artery. The TFC of the LAD artery was corrected by dividing the final count by 1.7. Due to different durations required for normal visualisation of coronary arteries, the corrected cutoff values were 36.2 ± 2.6 frames for LAD, 22.2 ± 4.1 frames for Cx, and 20.4 \pm 3.0 frames for the RCA, as has been reported previously in the literature [10]. Patients with a TFC greater than two standard deviations from the normal published range for any one of the three vessels were assigned to SCF patients. The mean TFC for each patient and control subject was calculated by adding the TFCs for LAD, Cx, and RCA and then dividing the obtained value by three.

Laboratory measurements

Samples were taken from the antecubital vein at the admission of patients to the hospital. Basal creatinine level, white blood cell count, platelet count, and haemoglobin concentration were measured. The morning after admission to the hospital,

Parameters	Patients with NCF (n = 60)	Patients with SCF (n = 60)	р
Age [years]	54.9 ± 9.5	55.8 ± 8.9	0.566
Body mass index [kg/m²]	27.5 ± 3.3	27.3 ± 4.0	0.752
Female	24 (40.0%)	25 (41.7%)	0.853
Diabetes mellitus	9 (15.0%)	10 (16.7%)	0.803
Arterial hypertension	20 (33.3%)	19 (31.7%)	0.845
Dyslipidaemia	19 (31.7%)	22 (36.7%)	0.564
Family history	7 (11.7%)	11 (18.3%)	0.306
Smoking	22 (36.6%)	33 (55.0%)	0.044

Table 1. Baseline characteristics of the study groups (n = 120)

Data are given as mean ± standard deviation or number (percentage); NCF — normal coronary flow; SCF — slow coronary flow

lipid profile and other biochemical parameters were measured using standard techniques. Peak and basal levels of troponin and creatinine kinase myocardial band levels were measured.

Blood samples to be used for nesfatin-1 measurement were centrifuged immediately and serum samples were stored at -80°C until the day of analysis. Serum nesfatin-1 levels were measured using a commercial enzyme-linked immunosorbent assay (ELISA) kit (Sensitivity: < 10 pg/mL; Assay range: 31.2–2000 pg/mL; Boster Immunoleader, USA) as recommended by the manufacturer's protocol.

Statistical analysis

All statistical analyses were performed using SPSS for Windows version 19.0 (SPSS, Chicago, IL, USA). For the descriptive statistics of the data, mean, standard deviation, rate, and frequency values were used. The Kolmogorov-Smirnov test was used to evaluate whether the distribution of continuous variables was normal. For the analysis of parametric data, Student's t-test was used. For the analysis of non-parametric data, the Mann-Whitney U test was used. The χ^2 test was used to compare the categorical variables between groups. For correlation analysis, Pearson correlation analysis was used. Logistic regression analysis was used to determine the impact of variables. Standardised beta coefficients and 95% confidence intervals (CI) were calculated. Statistical significance was defined as p-values < 0.05.

RESULTS

Baseline clinical and demographic characteristics of the study population are shown in Table 1. There was statistically no significant difference between groups in terms of age, body mass index, gender, diabetes mellitus, hypertension, dyslipidaemia, and family history status. The number of smokers was significantly higher in the SCF group compared to the NCF group (p = 0.306).

The laboratory findings of the patients and controls are shown in Table 2. Hs-CRP levels were significantly different between two groups (p = 0.030). Serum nesfatin-1 levels were significantly lower in the SCF group compared to the NCF group (p < 0.001).

To determine the possible confounding factors for SCF, multistep logistic regression analysis was performed. In multivariate logistic regression analysis, low level of nesfatin-1 was found to be significantly and independently associated with the SCF (odds ratio 0.982, 95% CI 0.969–0.995, p = 0.005; Table 3).

DISCUSSION

It was revealed that nesfatin-1 levels were significantly lower in patients with SCF phenomenon than in patients with angiographically normal coronary artery, in the present study. A strong negative relationship was demonstrated between nesfatin-1 levels and SCF measured with corrected TFCs.

The underlying pathophysiological mechanisms of primary SCF have not been overtly shown until now. Yucel et al. [12] found that medial hypertrophy, myointimal proliferation, endothelial degeneration with changes of myofibrillar degenerative foci, and lipofuscin deposits on electron microscopy can cause endothelial dysfunction in patients with SCF [12]. Coronary adrenergic hyperactivity due to increased sympathetic activity may be the cause of reduction in coronary blood flow and angina. Higher adrenalin and noradrenalin levels have been determined in SCF patients compared to individuals with NCF [11]. So, it is possible to say that may have a role in the pathogenesis of SCF. An improvement in microvascular tone and coronary flow with microvascular vasodilators suggesting a functional increase in microvascular resistance in patients with SCF was also reported by Kurtoglu et al. [13]. Many studies have shown that inflammation is one of the main factors leading to SCF [14].

Some studies in the last decade have demonstrated that pathological functions of adipose tissue can be associated with increased cardiovascular disease risk, not only due to the effect of the hypothalamus nucleus [6] on the regulation of cardiovascular function but also by activating the autocrine/paracrine/endocrine pathway of chemical mediators

Parameters	Patients with NCF (n = 60)	Patients with SCF (n = 60)	р
Glucose [mg/dL]	115.4 ± 44.1	122.1 ± 59.7	0.490
Creatinine [mg/dL]	0.98 ± 0.2	1.05 ± 0.4	0.266
Uric acid [mg/dL]	5.8 ± 2.1	5.6 ± 1.7	0.580
WBC count [10³/mm³]	9.8 ± 2.4	10.3 ± 2.6	0.269
Haemoglobin [g/dL]	13.4 ± 1.7	13.7 ± 1.5	0.255
Platelet count [10 ³ /mm ³]	236.4 ± 62.4	231.2 ±56.8	0.671
Total cholesterol [mg/dL]	184.0 ± 79.6	191.1 ± 77.4	0.615
Triglyceride [mg/dL]	124.0 (80.0–190.0)	123.5 (78.25–161.25)	0.683
LDL-cholesterol [mg/dL]	113.1 ± 57.3	116.0 ± 58.7	0.790
HDL-cholesterol [mg/dL]	41.0 (33.5–48.0)	43.5 (35.0–49.0)	0.820
Hs-CRP [mg/L]	3.1 (1.2–4.6)	4.9 (2.5–6.5)	0.030
Nesfatin-1 [pg/mL]	128.1 ± 31.8	108.5 ± 30.8	< 0.001
LVEF [%]	58.0 ± 4.9	58.5 ± 5.1	0.599
TFC-LAD	38.6 ± 9.8	16.8 ± 3.9	< 0.001
TFC–Cx	27.9 ± 7.4	12.1 ± 4.7	< 0.001
TFC-RCA	28.6 ± 6.6	11.6 ± 4.1	< 0.001
TFC-mean	31.7 ± 6.2	13.5 ± 4.0	< 0.001

Table 2. Comparisons of laboratory findings, TIMI frame counts and nesfatin-1 levels

Data are given as mean ± standard deviation, number (percentage) or median (interquartile range); Cx — circumflex artery; HDL — high-density lipoprotein; Hs-CRP — high-sensitivity C-reactive protein; LAD — left anterior descending artery; LDL — low-density lipoprotein; LVEF — left ventricular ejection fraction; NCF — normal coronary flow; RCA — right coronary artery; SCF — slow coronary flow; TIMI — Thrombolysis in Myocardial Infarction; TFC — TIMI frame count; WBC — white blood cells

Table 3. Multivariate logistic regression analysis predicting slow coronary flow

	Univariable OR (95% Cl)	р	Multivariable OR (95% Cl)	р
Smoking	2.111 (1.016–4.385)	0.045	1.834 (0.847–3.972)	0.124
Hs-CRP	1.127 (1.008–1.261)	0.036	1.099 (0.982–1.230)	0.100
Nesfatin-1	0.980 (0.967–0.992)	0.002	0.982 (0.969–0.995)	0.005

CI — confidence interval; Hs-CRP — high-sensitivity C-reactive protein; OR — odds ratio

released from adipose tissue like nesfatin-1 [15]. Nesfatin-1 is primarily a satiety hormone [6]. Intracerebroventricular injection of this peptide to rats or intraperitoneal application to mice has decreased food intake in some studies [6]. Recently, a close relationship has been reported between this peptide and diabetes [16], polycystic ovary syndrome [17], psychiatric disorders [18], or neurogenic diseases [19].

Bonnet et al. [20] have revealed an association between inflammation of the brainstem and hypothalamus and activation of neuron expressing nesfatin-1. One of the most important pathophysiological mechanisms of SCF is inflammation, and recent studies have shown anti-inflammatory and anti-oxidant effects of nesfatin-1 [21]. It has been demonstrated that intravenous nesfatin-1 application induces vasoconstriction via inhibition of nitric oxide production and causes high blood pressure [22]. Ayada et al. [23] have demonstrated that chronic peripheral infusion of nesfatin-1 decreases endothelial nitric oxide synthesis especially in chronic restraint stressed rats. Dai et al. [9] have shown that plasma nesfatin-1 levels were substantially decreased in patients with AMI. In addition, plasma nesfatin-1 levels are negatively associated with C-reactive protein and neutrophil percentage, which are important predictors of SCF development, in patients with AMI [9]. Osaki et al. [24] showed that 6-hydroxydopamine, which makes chemical sympathectomy, could increase nesfatin/NUCB2 expression in the subcutaneous fat tissues. So, it may be possible to infer that sympathetic activity could suppress nesfatin-1 expression. Increased sympathetic activity is also closely associated with endothelial dysfunction [25].

Limitations of the study

The present study is a cross-sectional study with a relatively small sample size. We did not measure nesfatin-1 levels after discharge and do not have data on major adverse cardiovascular events during follow-up. Therefore, our results should be verified in a multi-centre prospective longitudinal studies on a larger sample size. The limitations of this study should be considered when interpreting the results.

CONCLUSIONS

In conclusion, the results of this study showed that serum nesfatin-1 level was lower in the SCF group than in the NCF group. Low levels of nesfatin-1 could play a role in the pathogenesis of SCF phenomenon with mechanisms such as inflammation and endothelial dysfunction. Further studies are needed to determine the relation between SCF and nesfatin-1.

Conflict of interest: none declared

References

- Wang X, Nie SP. The coronary slow flow phenomenon: characteristics, mechanisms and implications. Cardiovasc Diagn Ther. 2011; 1(1): 37–43, doi:10.3978/j.issn.2223-3652.2011.10.01, indexed in Pubmed: 24282683.
- Beltrame JF, Limaye SB, Horowitz JD. The Coronary Slow Flow Phenomenon – A New Coronary Microvascular Disorder. Cardiology. 2002; 97(4): 197–202, doi: 10.1159/000063121, indexed in Pubmed: 12145474.
- Mangieri E, Macchiarelli G, Ciavolella M, et al. Slow coronary flow: Clinical and histopathological features in patients with otherwise normal epicardial coronary arteries. Cathet Cardiovasc Diagn. 1996; 37(4): 375–381, doi: 10.1002/(sici)1097-0304(19960 4)37:4<375::aid-ccd7>3.0.co;2-8, indexed in Pubmed: 8721694.
- Oktay V, Arat Özkan A. Coronary slow flow. Turk Kardiyol Dern Ars. 2016; 44(3): 193–195, doi: 10.5543/tkda.2016.72429, indexed in Pubmed: 27138306.
- Fineschi M, Bravi A, Gori T. The. Int J Cardiol. 2008; 127(3): 358–361, doi: 10.1016/j.ijcard.2007.06.010, indexed in Pubmed: 17651842.
- Oh IS, Shimizu H, Satoh T, et al. Identification of nesfatin-1 as a satiety molecule in the hypothalamus. Nature. 2006; 443(7112): 709–712, doi: 10.1038/nature05162, indexed in Pubmed: 17036007.
- Maejima Y, Sedbazar U, Suyama S, et al. Nesfatin-1-regulated oxytocinergic signaling in the paraventricular nucleus causes anorexia through a leptin-independent melanocortin pathway. Cell Metab. 2009; 10(5): 355–365, doi: 10.1016/j.cmet.2009.09.002, indexed in Pubmed: 19883614.
- Aydin S. Multi-functional peptide hormone NUCB2/nesfatin-1. Endocrine. 2013; 44(2): 312–325, doi: 10.1007/s12020-013-9923-0, indexed in Pubmed: 23526235.
- Dai H, Li X, He T, et al. Decreased plasma nesfatin-1 levels in patients with acute myocardial infarction. Peptides. 2013; 46: 167–171, doi: 10.1016/j.peptides.2013.06.006, indexed in Pubmed: 23806888.
- Gibson CM, Cannon CP, Daley WL, et al. TIMI Frame Count: A Quantitative Method of Assessing Coronary Artery Flow. Circulation. 1996; 93(5): 879–888, doi: 10.1161/01.cir.93.5.879, indexed in Pubmed: 8598078.

- Yazici M, Demircan S, Durna K, et al. The role of adrenergic activity in slow coronary flow and its relationship to TIMI frame count. Angiology. 2007; 58(4): 393-400, doi: 10.1177/0003319707305118, indexed in Pubmed: 17652227.
- Yucel H, Ozaydin M, Dogan A, et al. Evaluation of plasma oxidative status in patients with slow coronary flow. Kardiol Pol. 2013; 71(6): 588–594, doi: 10.5603/KP.2013.0122, indexed in Pubmed: 23797431.
- Kurtoglu N, Akcay A, Dindar I. Usefulness of oral dipyridamole therapy for angiographic slow coronary artery flow. Am J Cardiol. 2001; 87(6): 777–779, doi: 10.1016/s0002-9149(00)01503-4, indexed in Pubmed: 11249903.
- Li JJ, Xu Bo, Li ZC, et al. Is slow coronary flow associated with inflammation? Med Hypotheses. 2006; 66(3): 504–508, doi: 10.1016/j.mehy.2005.09.028, indexed in Pubmed: 16288834.
- Feijóo-Bandín S, Rodríguez-Penas D, García-Rúa V, et al. Nesfatin-1: a new energy-regulating peptide with pleiotropic functions. Implications at cardiovascular level. Endocrine. 2016; 52(1): 11–29, doi: 10.1007/s12020-015-0819-z, indexed in Pubmed: 26662184.
- 16. Li QC, Wang HY, Chen Xi, et al. Fasting plasma levels of nesfatin-1 in patients with type 1 and type 2 diabetes mellitus and the nutrient-related fluctuation of nesfatin-1 level in normal humans. Regul Pept. 2010; 159(1-3): 72–77, doi: 10.1016/j.regpep.2009.11.003, indexed in Pubmed: 19896982.
- Deniz R, Gurates B, Aydin S, et al. Nesfatin-1 and other hormone alterations in polycystic ovary syndrome. Endocrine. 2012; 42(3): 694–699, doi: 10.1007/s12020-012-9638-7, indexed in Pubmed: 22367584.
- Ari M, Ozturk OH, Bez Y, et al. High plasma nesfatin-1 level in patients with major depressive disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2011; 35(2): 497–500, doi: 10.1016/j. pnpbp.2010.12.004, indexed in Pubmed: 21163317.
- Aydin S, Dag E, Ozkan Y, et al. Nesfatin-1 and ghrelin levels in serum and saliva of epileptic patients: hormonal changes can have a major effect on seizure disorders. Mol Cell Biochem. 2009; 328(1-2): 49–56, doi: 10.1007/s11010-009-0073-x, indexed in Pubmed: 19262995.
- Bonnet MS, Pecchi E, Trouslard J, et al. Central nesfatin-1-expressing neurons are sensitive to peripheral inflammatory stimulus. J Neuroinflammation. 2009; 6: 27, doi: 10.1186/1742-2094-6-27, indexed in Pubmed: 19778412.
- 21. Ozturk CC, Oktay S, Yuksel M, et al. Anti-inflammatory effects of nesfatin-1 in rats with acetic acid induced colitis and underlying mechanisms. J Physiol Pharmacol. 2015; 66(5): 741–750, indexed in Pubmed: 26579580.
- Yamawaki H, Takahashi M, Mukohda M, et al. A novel adipocytokine, nesfatin-1 modulates peripheral arterial contractility and blood pressure in rats. Biochem Biophys Res Commun. 2012; 418(4): 676–681, doi: 10.1016/j.bbrc.2012.01.076, indexed in Pubmed: 22293188.
- Ayada C, Turgut G, Turgut S, et al. The effect of chronic peripheral nesfatin-1 application on blood pressure in normal and chronic restraint stressed rats: related with circulating level of blood pressure regulators. Gen Physiol Biophys. 2015; 34(1): 81–
 –88, doi: 10.4149/gpb_2014032, indexed in Pubmed: 25504061.
- Osaki A, Shimizu H, Ishizuka N, et al. Enhanced expression of nesfatin/nucleobindin-2 in white adipose tissue of ventromedial hypothalamus-lesioned rats. Neurosci Lett. 2012; 521(1): 46–51, doi: 10.1016/j.neulet.2012.05.056, indexed in Pubmed: 22641054.
- Lee MGY, Hemmes RA, Mynard J, et al. Elevated sympathetic activity, endothelial dysfunction, and late hypertension after repair of coarctation of the aorta. Int J Cardiol. 2017; 243: 185–190, doi: 10.1016/j.ijcard.2017.05.075, indexed in Pubmed: 28545853.

Cite this article as: Kuyumcu MS, Kuyumcu A, Yayla Ç, et al. Nesfatin-1 levels in patients with slow coronary flow. Kardiol Pol. 2018; 76(2): 401–405, doi: 10.5603/KPa2017.0210.