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Research Article

Visfatin Related to the Severity of Non-ST-Segment Elevation Acute Coronary Syndrome: A Retrospective Study of 164 Patients at a Tertiary Chest Pain Center

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Acute coronary syndrome (ACS) poses a pervasive threat to individuals grappling with cardiovascular afflictions, manifesting as unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI), or sudden cardiac death, depending on vascular obstruction's extent and location. NSTEMI, closely linked to substantial morbidity and mortality, has become the primary cause of hospitalization in ischemic heart disease patients. Swift prognostication of non-ST-segment elevation acute coronary syndrome (NSTE-ACS) is crucial, necessitating the identification of precise markers. This study, conducted from January 2020 to March 2021, explored the correlation between serum visfatin levels and NSTE-ACS severity. A total of 164 patients undergoing coronary angiography were enrolled, with a control group ($n = 55$) exhibiting less than 50% coronary stenosis. NSTE-ACS patients were categorized based on angiography outcomes into single-vessel ($n = 41$), double-vessel ($n = 28$), and multivessel ($n = 40$) groups. Serum visfatin levels, meticulously quantified, showed significant elevation in NSTE-ACS patients ($n = 109$) compared to the control group ($n = 55$) ($P < 0.01$). Visfatin correlated positively with the GRACE score ($r = 0.397$, $P < 0.01$). In the multivessel disease group, visfatin levels were notably higher ($P < 0.01$). After adjusting for cardiovascular risk factors, visfatin emerged as an independent predictor of affected coronary arteries (OR 0.205; 95% CI 0.032–0.378; $P = 0.02$). Receiver-operating characteristic (ROC) curves demonstrated enhanced prognostic ability when combining visfatin with age, hypertension, and diabetes for multivessel disease (AUC: 0.839, sensitivity: 65.0%, specificity: 89.7%, $P < 0.001$). Elevated serum visfatin in NSTE-ACS patients suggests its role as an independent harbinger for the number of affected coronary arteries, potentially indicating severity in NSTE-ACS patients.

1. Introduction

Acute myocardial infarction (AMI) is a sudden and severe narrowing of the coronary arteries supplying the myocardium due to various reasons, resulting in necrosis of the myocardium due to a severe lack of blood supply, and there are two types of acute ST-segment elevation myocardial infarction (STMI) and acute non-ST-segment elevation myocardial infarction (NSTEMI). Non-ST-segment elevation acute coronary syndrome (NSTE-ACS) is the severe type of acute coronary syndrome (ACS) that leads to death and it becomes the main cause of hospitalization in patients with ischemic heart disease [1, 2]. Therefore, finding biological markers for effective prediction in the early stage of NSTE-ACS and then taking measures to achieve satisfactory therapeutic effects has always been a hot topic in academic research. In recent years, studies have found that visfatin plays an important role in the occurrence and outcome of ACS [3–5]. This study intends to observe the difference of serum visfatin levels between NSTE-ACS patients and control group, then to explore the relationship between visfatin and the number of diseased coronary artery. Through this study, we hope to have a better guidance in diagnosis and treatment of patients with NSTE-ACS.

2. Methods

A total of 164 Chinese patients (121 males and 43 females, mean age 64.7 ± 10.19 years) who admitted to the cardiology ward of Hainan Western Central Hospital from January 2020 to March 2021 were recruited for this study. The diagnostic criteria of NSTE-ACS patients ($N = 109$) complies with (Guideline and consensus for the management of patients with non-ST-elevation acute coronary syndrome (2016)) released in China [6]. The comparative cohort ($N = 55$) comprised individuals who underwent coronary angiography within the corresponding hospitalization duration, evidencing coronary artery stenosis of less than 50% and negative troponin levels. Exclusion criteria as follows: 1. current infection; 2. valvular heart disease, myocarditis, cardiomyopathy, congenital heart disease; 3. hyperthyroidism or hypothyroidism; 4. severe hepatic and renal insufficiency; and 5. malignancy and hematological system diseases. This study was approved by the ethical committee of Hainan West Central Hospital, and the protocol was compliant to the Declaration of Helsinki. Each study patient provided written informed consent before enrollment.

The information on demographic and clinical characteristics, including age, gender, body mass index (BMI), smoking status, history of hypertension, history of diabetes was obtained at initial admission. Peripheral venous blood was collected from all participants in the next morning (fasting for 8 hours) after admission to detect the creatinine and lipid profile (total cholesterol, triglyceride, high-density lipoprotein-C, low-density lipoprotein-C). All indicators were measured in laboratory of our hospital.

Precoronary angiography, morning blood samples (after an 8-hour fast) were obtained from peripheral veins and centrifuged at 3000r/min for 10 minutes. We followed the methods of Chen et al. [7, 8]. The supernatant was divided and refrigerated at −70°C for uniform detection of visfatin. Human visfatin detection kit (Cat. No.: EK-003-80) was purchased from Phoenix Pharmaceuticals in the United States, serum concentration of visfatin was determined by enzyme-linked immunosorbent assay according to the product instructions.

GRACE score is recommended in guidelines to facilitate the management of patients who present with acute coronary syndromes. There are eight criteria including ST segment deviation, age, heart rate, systolic blood pressure, creatinine, Killip class, cardiac arrest at admission, and elevated biomarkers of necrosis [9].

All participants underwent coronary angiography in this study. Coronary artery stenosis was imaged by multiple projections and the severity of coronary atherosclerotic lesion was judged by at least two expert cardiologists independently. The diagnosis of coronary artery disease was according to a stenosis of more than 50% in at least one main coronary artery. According to the number of diseased coronary artery vessel, NSTE-ACS patients were divided into single-vessel disease group, double-vessel disease group and multivessel disease group.

Normally distributed data was expressed as mean ± standard deviation and skewed data were expressed as median with interquartile range. The student's t-test was applied for intergroup comparisons of normally distributed data, and the Mann–Whitney U test for comparisons of skewed data. Multiple groups comparisons of normally distributed data and skewed data were performed with the analysis of variance and the Kruskal–Wallis H test, respectively. Categorical variable was determined as number (percentage) and analyzed by the chi-square statistic test or Fisher exact test. Univariate regression was used Pearson's linear correlation to assess the association between visfatin and GRACE score. Multivariate logistic regression was used to determine the independent predictor of the number of diseased coronary artery. The value of visfatin for predicts multivessel disease was estimated in Receiver-operating characteristic (ROC) curves. Candidate variables with a P value < 0.2 on univariate analysis were included in multivariable model. Statistical analysis was performed using SPSS software (version 22, SPSS, Chicago, IL). A P value of <0.05 was considered to indicate statistical significance.

3. Results

The baseline clinical characteristics of control group and subgroup of coronary lesions were summarized in Table 1. There were no discernible discrepancies among the four groups regarding gender, age, smoking status, history of hypertension, history of diabetes, BMI, total cholesterol, triglyceride, and low-density lipoprotein-C (all $P > 0.05$). Nevertheless, noteworthy disparities were noted in high-density lipoprotein-C and creatinine (all $P < 0.05$).

Patients with NSTE-ACS had higher serum visfatin levels than control group ($P < 0.01$, Table 2) and visfatin positively correlated with GRACE score ($r = 0.397$, $P < 0.01$, Figure 1).

Visfatin elevated with the number of diseased coronary artery. The levels of visfatin in the subgroup of coronary lesions (single-vessel, double-vessel and multiple-vessel disease group) significantly higher than control group ($P < 0.05$). Visfatin in multivessel disease group significantly higher than single-vessel disease group ($P < 0.01$), but there was no statistically significant difference between single-vessel disease group and double-vessel disease group, and double-vessel disease group and multivessel disease group ($P > 0.05$). Table 3.

Multivariate logistic regression was used to determine the independent predictor of the number of diseased coronary artery. After adjustment for gender, age, smoking, diabetes, hypertension, BMI, triglycerides, total cholesterol, high-density lipoprotein-C, low-density lipoprotein-C, creatinine, and GRACE score, visfatin remained was an independent predictor of the number of diseased coronary artery (OR 0.205; 95% CI 0.032–0.378; $P = 0.02$, Table 4).

The ROC curves showed that visfatin values being predictive of the multivessel disease above the threshold of 9.619 ng/ml with a 0.659 area under curve (AUC) (95% CI 0.548–0.769, $P = 0.006$) and a 47.5% sensitivity and 82.4% specificity. In order to improve the sensitivity for predicting multivessel disease, we combined visfatin with hypertension and diabetes into the model which showed a 0.839 AUC

Table 1: Comparison of clinical data between control group and subgroup of coronary lesions.

Variable	Control ($n = 55$)	NSTE-ACS ($n = 109$)			P value
		Single-vessel disease group ($n = 41$)	Double-vessel disease group ($n = 28$)	Multivessel disease group ($n = 40$)	
Male (n, %)	33 (60.0%)	32 (78.0%)	22 (78.6%)	30 (75.0%)	0.156
Age (years)	66.87 ± 9.45	62.66 ± 11.44	61.43 ± 9.69	66.30 ± 9.49	0.054
Smoking (n, %)	17 (30.9%)	18 (43.9%)	15 (53.6%)	18 (45.0%)	0.208
Diabetes (n, %)	8 (14.5%)	5 (12.2%)	5 (17.9%)	12 (30.0%)	0.180
Hypertension (n, %)	21 (38.2%)	19 (46.3%)	11 (39.3%)	23 (57.5%)	0.273
BMI (kg/m^2)	23.40 (21.90, 25.30)	23.80 (22.05, 26.25)	24.40 (22.60, 25.97)	24.40 (22.01, 26.15)	0.563
Triglycerides (mmol/L)	1.29 (1.01, 1.65)	1.13 (0.84, 1.76)	1.40 (1.03, 1.86)	1.52 (1.14, 1.94)	0.102
Total cholesterol (mmol/L)	4.22 ± 0.91	4.02 ± 0.89	4.29 ± 1.02	4.11 ± 0.96	0.604
High-density lipoprotein-C (mmol/L)	1.17 (0.98, 1.40)	1.07 (0.96, 1.22)	0.96 (0.82, 1.16)	0.92 (0.79, 1.04)	<0.01
Low-density lipoprotein-C (mmol/L)	2.46 (2.05, 2.86)	2.61 (2.09, 2.93)	2.86 (2.18, 3.46)	2.66 (2.05, 3.14)	0.335
Creatinine (μmol/L)	68 (59, 85)	73 (65, 83)	79.5 (70, 93)	79 (68, 98)	0.023

BMI, body mass index.

Table 2: Comparison of visfatin levels between control group and NSTE-ACS.

Variable	Control ($n = 55$)	NSTE-ACS ($n = 109$)	P value
Visfatin (ng/ml)	6.74 (5.76, 7.53)	7.67 (6.67, 9.64)	<0.01

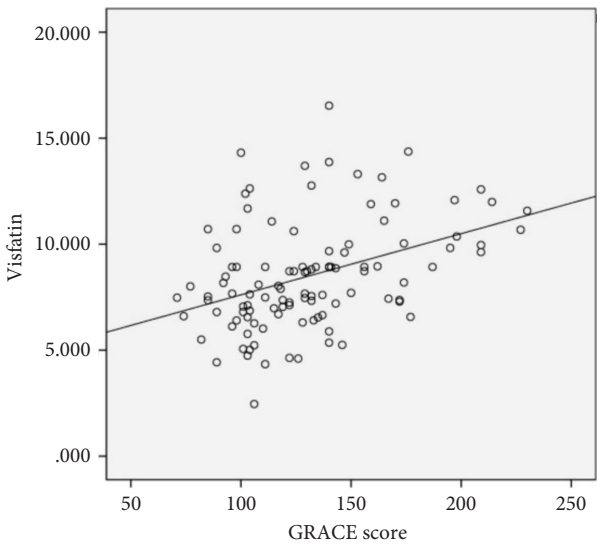

Figure 1: Correlation between serum visfatin levels and GRACE score.

Table 3: Comparison of visfatin levels between control group and subgroup of coronary lesions.

Variable	Case (n)	Visfatin (ng/ml)
Control group	55	6.74 (5.76, 7.53)
Single-vessel disease group	41	7.46 (6.48, 8.92)[a]
Double-vessel disease group	28	8.10 (6.58, 8.92)[a]
Multivessel disease group	40	8.87 (7.24, 11.98)[ab]

[a]Compared with control group, $P < 0.01$. [b]Compared with single-vessel disease group, $P < 0.01$.

Table 4: Independent predictors for the number of diseased coronary artery by multivariable logistic regression.

Variable	OR	95% CI	P value
Diabetes	0.170	0.069–0.418	<0.01
Hypertension	0.263	0.120–0.577	0.005
Visfatin	0.205	0.032–0.378	0.020

Adjustment for gender, age, smoking, diabetes, hypertension, BMI, triglycerides, total cholesterol, high-density lipoprotein-C, low-density lipoprotein-C, creatinine and GRACE score.

(95% CI 0.764–0.914, $P < 0.01$) with a sensitivity of 65.0% and a specificity of 89.7% (Figure 2).

4. Discussion

Visfatin, a novel adipocyte factor, also recognized as Pre-B cell colony-enhancing factor [PBEF] and nicotinamide phosphoribosyltransferase (Nampt) [10], manifests ubiquitous expression and secretion within adipose tissues, liver, myocardial cells, and immune cells [10, 11]. Past research has elucidated visfatin's pleiotropic nature [12–16]. Numerous studies have established its linkage to metabolic disorders, including obesity, type 1 and 2 diabetes, and polycystic ovary syndrome [12]. Furthermore, investigations have suggested its involvement in autoimmune diseases, potentially designating it as a pivotal biomarker and therapeutic target for rheumatoid arthritis [13]. Notably, Yan and colleagues discerned a correlation between elevated visfatin levels and a dismal clinical prognosis among colorectal cancer patients [14]. Recent studies have brought to light an elevated plasma visfatin level's association with an augmented risk of myocardial infarction [15, 16]. Given visfatin's nexus with a multitude of previously mentioned disease factors, discerning its role as a biomarker for gauging NSTE-ACS severity mandates meticulous categorization of patients presenting with multiple co-morbidities. The establishment of comprehensive categorization criteria warrants further investigation. Furthermore, the influence of medications and lifestyle choices on adipose tissue, liver, cardiomyocytes, and immune cells underscores the urgency of formulating appropriate quantitative scoring criteria. This shall be the focal point of future research endeavors.

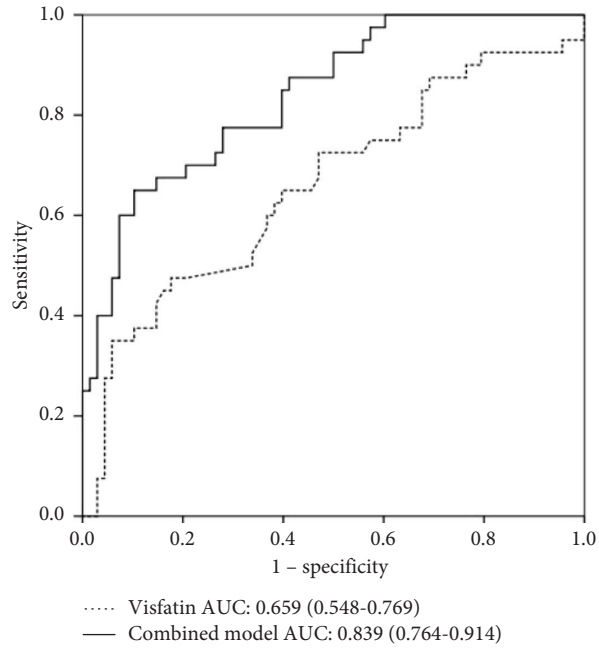

Figure 2: Receiver-operating characteristic curves of visfatin and combined model for predicting multivessel disease.

To the best of our knowledge, this study constitutes the inaugural exploration of the relationship between serum visfatin levels and NSTE-ACS. Our present findings suggest that patients afflicted with NSTE-ACS exhibit elevated serum visfatin levels compared to the control group. The latest guidelines emphasize the close interrelation between NSTE-ACS prognosis and risk stratification, predominantly assessed by the GRACE score [17]. For high-risk patients, prompt coronary angiography becomes imperative, with interventional therapy contingent upon the results [6]. Our discovery underscores a positive correlation between visfatin

and the GRACE score. Detecting visfatin levels may enhance risk stratification and enable the assessment of NSTE-ACS severity.

Our study unequivocally demonstrates an elevation in visfatin levels commensurate with the number of diseased coronary arteries, with the multivessel disease group exhibiting significantly higher levels compared to the single-vessel disease group. Multivariate logistic regression analysis, even after adjusting for traditional risk factors, establishes visfatin as an independent predictor of the number of diseased coronary arteries. For every increment of 1 ng/ml in visfatin concentration, the risk of augmented coronary artery lesions increases by 0.205 times. Receiver Operating Characteristic (ROC) curves highlight visfatin's specificity (82.4%) but reveal a lower sensitivity (47.5%) in predicting coronary multivessel disease. The addition of age, hypertension, and diabetes to the visfatin model elevates specificity and sensitivity to 89.7% and 65.0%, respectively. The area under the curve (AUC) for predicting coronary multivessel disease improves from 0.659 to 0.839. The combined model markedly enhances the ability to predict coronary multivessel disease, conferring significant clinical value.

Current literature corroborates several key aspects of visfatin's mechanisms in coronary atherosclerotic heart disease. Firstly, visfatin potentially contributes to atherosclerosis through vascular inflammation. Prior studies have reported visfatin's capacity to activate nuclear factor- (NF-) kappaB, thereby promoting the release of interleukin (IL)-1, IL-6, tumor necrosis factor-alpha (TNF-a), and other inflammatory factors [18, 19]. In monocytes of patients afflicted with acute coronary syndrome, visfatin messenger RNA expression markedly increases, correlating positively with inflammatory factors and the antioxidant enzyme superoxide dismutase (SOD)-2 [20]. Secondly, visfatin may play a role in atherosclerosis progression via participation in vascular remodeling. It can mediate vascular proliferation by enhancing endothelial synthesis and secretion of vascular endothelial growth factor (VEGF) and its related receptor (VEGFR-2) [21]. Researchers have also demonstrated that visfatin can increase matrix metalloproteinases (MMPs) expression, promoting collagen degradation and elevating the plaque vulnerability index [22]. Overexpression of visfatin has been observed in smooth muscle cells and foam cells, contributing to the instability of atherosclerotic plaques in acute myocardial infarction patients [23, 24].

Several limitations merit consideration in this study. Firstly, it is grounded in single-center data with a limited sample size. While this ensures stringent adherence to recruitment criteria, a larger, multicenter study would furnish more conclusive insights. Secondly, the cross-sectional nature of the study precludes the measurement of other inflammatory markers. Subsequent research endeavors should encompass representative inflammatory factors and longitudinal follow-up to delve into visfatin's prognostic attributes in NSTE-ACS.

The realm of adipocytokines harbors a plethora of entities, and visfatin, a burgeoning adipocytokine, exhibits the capacity to be secreted in various locales beyond adipose tissue. Its multifaceted biological role encompasses a wide spectrum, encompassing pivotal involvement in metabolic syndrome, type 2 diabetes, obesity, as well as the progression and rupture of atherosclerotic plaques, vascular endothelium impairment, and the activation of the inflammatory response in coronary heart disease. Although the pathophysiology and mechanistic underpinnings of visfatin remain enigmatic, further exploration of endolipids promises to illuminate the role of these molecules in glucose and lipid metabolism, obesity, atherosclerosis formation, and rupture. Additionally, it holds the potential to provide a fresh perspective on comprehending the development, pathogenesis, diagnosis, and treatment of coronary heart disease. The findings of this study underscore a close nexus between visfatin and illness severity in NSTE-ACS patients, thereby aiding clinicians in charting the course of disease progression and devising efficacious treatment strategies in its nascent stages.

5. Conclusion

In summation, serum visfatin levels are elevated in NSTE-ACS patients, demonstrating a positive correlation with the GRACE score. Furthermore, visfatin emerges as an independent predictor of the number of diseased coronary arteries, signifying its potential as a novel biomarker for assessing the severity of NSTE-ACS patients.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflicts of Interest

All authors declare that they have no conflicts of interest.

Authors' Contributions

MF Zheng and F Xiao conceptualized and designed the study. ZW Wu provided administrative support. ZW Wu, CQ Liu, MF Zheng, and F Xiao provided provision of study materials or patients. MF Zheng and F Xiao contributed to collection and assembly of data. MF Zheng, F Xiao, and ZW Wu contributed to data analysis and interpretation of the study. All authors wrote the manuscript and approved the final version of the manuscript.

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