Assessment of Coronary Slow Flow, Cystatin C, and Body Mass Index in Female Candidates for Diagnostic Coronary Artery Angiography

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Abstract
Introduction: Evidence indicates that the associations between coronary slow flow (CSF), cystatin C (Cys C), and body mass index (BMI) are unclear. Therefore, the purpose of our study was to determine the association among the above-mentioned parameters in female patients.
Methods: This was a descriptive-analytical study and the participants were those who were referred to the Shohada Cardiovascular Center of Urmia in 2015-2016. The participants were measured by a quantitative method under angiography (corrected TIMI frame count, CTFC) for CSF assessment, followed by evaluating physiological indices and the serum Cys C by the enzyme-linked immunosorbent assay. Finally, Pearson correlation coefficient test was used to analyze the correlations among CTFC, Cys C, and BMI, and a significance level of P < 0.05 was used for this test.
Results: Sixty-six female patients (mean age: 57.01 ± 8.25 years) took part in this study. The correlations among Cys C with CTFC, and BMI (r = -0.189, $P = 0.128$ and r = 0.044, $P = 0.724$, respectively) and BMI with CTFC (r = -0.178, $P = 0.153$) were not meaningful in female patients' who were candidates for angiography.
Conclusion: In general, the results suggested that serum Cys C cannot be considered as a predictive biomarker for the prognostic stratification of CSF and BMI in female patients aged 34-73 years who were candidates for angiography.
Keywords: Angiography, Cystatin C, Slow coronary flow, Body mass index

Introduction

In angiography, coronary slow flow (CSF) is characterized by the slow passage of contrast in the lack of any obstructive coronary artery disease (CAD) or microvascular resistance dysfunction.[1,2] Inflammatory indices, endothelial dysfunction, small vessel disease, and atherosclerosis are associated with the etiology of the CSF and cardiovascular disease (CVD) risk indices.[3-6] In other words, the CSF pathogenesis is multifactorial. Microvasculature abnormalities, endothelial dysfunction, increased inflammatory indices, the anatomical factors of epicardial arteries, and atherosclerosis are related to the CSF.[7] Thrombolysis in the myocardial infarction (TIMI) score is used to evaluate the coronary blood flow, which represents the speed and full passage of the contrast agent injected into the coronary arteries.[8] The TIMI index is a reperfusion strategy qualitative method.[8,9] The corrected TIMI frame count (CTFC) is a quantitative method for assessing the TIMI flow grading system[9-11] and represents the count of the elapsed angiographic frames until the contrast material arrives in the distal bed of coronary arteries.[9]

On the other hand, cystatin C (Cys C) is an

important biomarker for prognostic stratification in acute coronary syndrome (ACS) patients[12,13] and is secreted by all nucleated cells.[14] Recent studies have reported that the high Cys C serum is a marker of CAD and unfavorable prognosis in patients with ACS.[15-18] It seems that Cys C is a prognostic marker in CVDs and death.[15-18] It has been shown that serum Cys C is correlated with congestive heart failure, various subgroups of atherosclerotic diseases such as CAD and peripheral disease,[15-18] and body mass index (BMI).[19] In addition, another study reported that higher BMI is independently related to the high Cys C.[19] Thus, the present study assessed the associations between CTFC, serum Cys C, and BMI in female patients' referring to the Shohada Cardiovascular Center in Urmia.

Methods
Subjects
This study was performed using a descriptive-analytical design at Urmia University of Medical Sciences, Iran. All sedentary female (aged 34-73 years old) CSF candidates for angiography referring to our center (from 2015 to 2016) were the statistical population of our study. Among the participants, 66 patients were selected for evaluation.

Inclusion Criteria
The inclusion criteria included being female patients (aged 34-73 years) candidate for angiography referring to the Shohada hospital of Urmia from 2015 to 2016, having no history of angiography or CVD, and having no history of diseases in other body systems such as liver, central nerve system, and kidneys.

Exclusion Criteria
The exclusion criteria were a history of previous CVD (e.g., myocardial infarction), unstable angina pectoris, and systolic or diastolic heart failure which is diagnosed by echocardiography that the left ventricular injection of less than 40% is defined as systolic heart failure. Further, other criteria included a history of heart valve disease, kidney failure, liver failure, malignancy, coronary anomalies, ectasia, and slow coronary flow with more than 30% stenosis in major coronary arteries.

Angiography
After obtaining inform consent, 66 female patients were selected by convenience non-random sampling,[20] followed by determining demographic and physiological parameters by an interview, a wall-meter (Beurer, Germany), a digital scale (Beurer, Germany), and the kg/m² formula for age, height, weight, and BMI, respectively. The participants were evaluated through performing the standard coronary angiography with at least 4 and 2 facets of left and right coronary arteries by the Judkins technique via the angiography system, respectively (Siemens Medical Systems, Forchheim, Germany).

Cystatin C Measurement
Five milliliters of blood samples withdrawn in fasting at the morning was used to determine the serum Cys C using the enzyme-linked immunosorbent assay (ELISA) kit (DZ133C-K, Diazyme, Germany) by ELISA (Stat Fax˙4200, USA).

Data Analysis
Data were expressed as the mean ± standard deviation (SD) and checked for normality using the Kolmogorov-Smirnov test. Furthermore, Pearson correlation coefficient was applied to determine the correlations between Cys C, CTFC, and BMI among female patients. Eventually, data were analyzed by SPSS software, version 23.0. The statistical significance was considered at $P < 0.05$ for the two-tailed test.

Results
Table 1 presents the mean of demographic and physiological characteristics in female patients. Based on the data (Table 2), there was no significant correlation among Cys C with CTFC and BMI in patients ($P > 0.05$). Moreover, MBI and CTFC were not correlated in female patients ($P > 0.05$). The scatter plots of Cys C, CTFC, and BMI in female patients are shown in Figure 1.

Discussion
The current study aimed to investigate the correlations among CTFC, serum Cys C, and BMI in female patients referring to the Cardiovascular Center of Shohada hospital in Urmia. Our findings indicated that there was no significant correlation among CTFC, serum Cys C, and MBI in patients, which is consistent with the results of some previous studies[21-23] while contradicts those of other studies.[23-25] For instance, El Telbani demonstrated that the association among blood glucose and serum Cys C in diabetic patients was not statistically significant.[21] Additionally, Hosseini-Kakhk et al reported that the

Table 1. The Mean of Physiological Specifications in Female Candidates of Angiography

| Variable	Age (y)	Height (m)	Weight (kg)	BMI (kg/m²)
Mean ± SD	57.01 ± 8.25	1.57 ± 0.14	72.00 ± 7.60	29.42 ± 4.33

Note. SD: standard deviation; BMI: body mass index.

Table 2. Pearson's Correlation Coefficient Between Cys C, CTFC, and BMI in Female Candidates of Angiography

Variables	CTFC		BMI	
	R	P	r	P
Cys C	-0.189	0.128	-0.044	0.724
BMI	-.178	.153	-	-

Note. Cys C: cystatin C; BMI: body mass index; CTFC: corrected TIMI frame counts.

$P < 0.05$: Significant correlation;
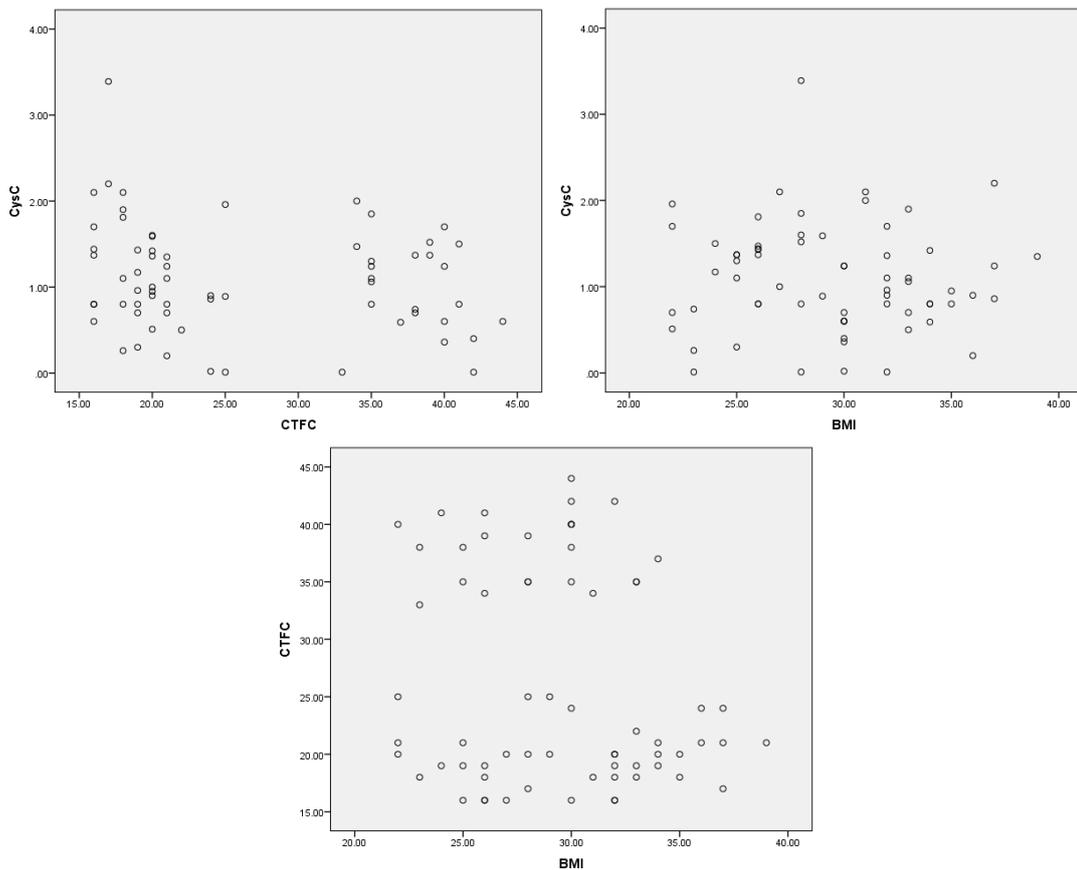
Figure 1. 2-D Scatter Plot of (Cys C vs. CTFC, Cyst C vs. BMI, and CTFC vs. BMI) in Female Candidates of Angiography. *Note*. Cys C: cystatin C; CTFC: corrected TIMI frame counts; BMI: body mass index.

correlation among BMI and Cys C in obese females with an average of 21 years and 32 kg/m^2 was not significant.[22] Furthermore, Afsargharehbagh et al suggested that the correlations among CSF with BMI and Cys C were not significant in male patients aged 34-73 years.[23]

In contrast, Ying et al found a significantly positive correlation among the serum Cys C and BMI in a Chinese population with metabolic syndrome.[24] Similarly, Tasal et al demonstrated that serum Cys C has a positive correlation with CTFC and the number of vessels with CSF.[25] The association between high Cys C and high BMI among American adults without clinically recognized chronic kidney disease was independently significant in another study.[19] Likewise, Luc et al revealed that serum Cyst C significantly predicted the incidence of ischemic coronary events in 50-59-year-old men.[26]

Our results are similar to those of the studies by El Telbani[21] and Hosseini-Kakhk et al[22] in terms of similar parameters, same participants, and same indices such as metabolic patients and the assessment of serum Cys C and BMI in obese female, respectively. Contrarily, different methods of assessment for CSF,[25] age and gender differences of the subjects,[26] the classification of BMI according to the World Health Organization,[19,24] as well as the control of patients' interventional factors in terms

of traditional risk factors including smoking, metabolic diseases, family history of CVD, and hypertension in other studies[24,25] may be the possible inconsistency reasons among these studies including ours.

The findings of our study indicated that Cys C had no relationship with cardiovascular risk factors such as CTFC and BMI, which is inconsistent with previous results. This probably indicates that the Cys C index cannot be considered as an important biomarker for the cardiovascular system in female patients with CSF. Additionally, our results revealed that Cys C had no significant relationship with body composition indices such as BMI in female patients aged 34-73 years. However, some studies reported an association between CVD, serum Cys C, and BMI.[18,27-30] For instance, Amer and Curry noted a positive correlation between serum Cys C and BMI in adults with normal renal function.[30] In a prospective study on cardiac patients, Batra et al[31] also described a link between Cys C and risk of CAD. In contrast, a recent study reported that lower Cys C serum is related to the CAD and vascular dilatation compared to CSF patients.[32] Similarly, Abisi et al[33] found that the lower serum Cys C in the aneurysm wall is associated with high cathepsin activity in patients with the aortic occlusive disease. Cys C is positively associated with the

atherosclerotic disease while negatively associated with CAD.[31-33] In other words, the results of previous studies related to Cys C and CAD are contradictory.[31-33] In the current study, the cut-off level of Cys C was set at 0.69 mg/L whereas this value was set at 0.001 mg/L (or 922 ng/mL) in the study by Tasal et al,[25] indicating that there was a weak non-significant correlation between serum Cys C and CTFC compared to the other studies. On the other hand, it is likely that the laboratory kits of different companies affect the sensitivity of Cys C serum in terms of its accuracy of measurement.

Strengths and Limitations

The identification of CAD risk factors such as Cys C serum as a possible biomarker in CSF and its correlations with CTFC and BMI were the strengths of our study. In contrast, the low number of participants can be considered as a limitation.

Conclusion

In general, the findings of this study indicated that the correlations between CTFC, serum Cyc C, and BMI in female patients aged 34-73 years referring to Shohada Cardiovascular Center in Urmia were not significant, and further studies are needed in this regard.

Ethical Approval

This study was approved by the Ethics Committee of Urmia University of Medical Sciences, Urmia, Iran (Code: ir.umsu.rec.1395.233).

Conflict of Interest Disclosure

None.

Informed Consent

Informed written consent was obtained from all the patients.

Authors' Contribution

NAA: Conceptualization, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing.

RA: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software,Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing.

AN: Validation, Visualization, Writing - original draft, Writing - review & editing.

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SG: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Visualization, Writing - original draft, Writing - review & editing.

AM: Validation, Visualization, Writing - original draft, Writing - review & editing.

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