

# Atherosclerosis burden and coronary artery lesion complexity in acute coronary syndrome patients

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## Abstract

**Background:** *Syntax score (SS) is a prognostic marker in patients with acute coronary syndromes (ACS). Carotid intima media thickness (CIMT) and cardio ankle vascular index (CAVI) are well known surrogate marker of atherosclerosis burden. But association between atherosclerosis burden and coronary artery disease (CAD) complexity in ACS patients has not been investigated yet.*

**Methods and Results:** *Consecutive patients with first time diagnosis of ACS (n = 172) were enrolled. SS, a marker of CAD complexity, was assessed by dedicated computer software. CIMT was examined by B-mode ultrasound. CAVI was assessed by VaSera VS-1000 cavi instrument. SS for low, intermediate and high tertiles of CIMT value were 10.1 ± 8.2 vs 11.4 ± ± 7.9 and 15.2 ± 8.8; p = 0.02). SS for normal, borderline and abnormal CAVI values were 4 ± 3.7 vs 11.1 ± 7.2 and 14.1 ± 9.1, respectively p = 0.009). Also, there was independent association between SS and CIMT (95% confidence interval [CI] 2.1–19, p = 0.014) and CAVI (95% CI 15–29, p = 0.021]. Neither traditional cardiovascular risk factor nor thrombolysis in myocardial infarction (TIMI) risk score was independent determinant of SS.*

**Conclusions:** *We have shown that patients with higher atherosclerosis burden have more complex coronary artery lesions. Also these patients may be identified early by using surrogate markers of atherosclerosis. Its clinical significance requires further research. (Cardiol J 2012; 19, 3: 295–300)*

**Key words:** acute coronary syndrome, cardio ankle vascular index, carotid intima media thickness, syntax score

## Introduction

Several studies have identified clinical and laboratory variables that correlate with a poor prognosis in patients with acute coronary syndromes (ACS) [1–4]. Baseline angiographic characteristics

add prognostic insight to clinical factors in the determination of cardiac ischemic events in patients with ACS [5]. The syntax score (SS) is a comprehensive angiographic scoring system that is derived entirely from the coronary anatomy and lesion characteristics [6–8]. It is an independent predictor of

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the one-year rates of death, cardiac death, myocardial infarction (MI), and target vessel revascularisation (TVR) in patients with ACS undergoing percutaneous coronary intervention (PCI) [9]. Also, SS can predict periprocedural myocardial necrosis during PCI that is associated with worse outcomes [10–12]. Therefore, identifying patients with complex coronary lesions may be important in terms of not only getting prognostic informations, but also taking measures in order to prevent and treat complications due to the coronary lesion complexity.

There is no study performed to find predictors of coronary artery disease (CAD) complexity, assessed by SS, in ACS patients. Thrombolysis In Myocardial Ischemia (TIMI) risk score is widely used as a prognostic marker that categorizes a patient's risk of death and ischemic events and provides a basis for therapeutic decision making [13]. Although association between TIMI risk score and CAD extent has been shown [14, 15], its relation to SS has not been investigated yet. So, in present study, we aimed to know whether well known surrogate markers of atherosclerosis, carotid intima media thickness (CIMT) and cardio ankle vascular index (CAVI), and TIMI risk score can provide predictive information on coronary lesion complexity in ACS patients.

## Methods

### Patients

Consecutive patients (n = 172) with non-ST segment elevation ACS undergoing coronary angiography and intervention were enrolled. ACS was diagnosed when an elevation of troponin T level (> 0.01 ng/mL in any sample during admission) and/or a typical creatine kinase-MB fraction (CK-MB) curve occurred, with or without ST/T changes in the electrocardiogram (ECG), in the absence of any other demonstrable cause for chest pain. All patients did not have any previous cardiovascular events or coronary revascularization.

Patients with a history of MI, valvular disease, acute or chronic heart failure, cardiomyopathy, systolic dysfunction, ejection fraction < 50%, renal, liver and neoplastic diseases were excluded. Patients with ST-elevation on the admission ECG were excluded. Patients were also excluded when the evolution of the ECG showed the development of a new left bundle branch block or new Q waves. Other exclusion criteria were known or suspected infectious or inflammatory conditions or need of urgent coronary angiography and intervention.

### Coronary angiography and syntax score

Coronary angiography was performed by the Judkins or Sones technique and analyzed by 2 experienced observers. Each angiogram was analyzed independently by 2 experienced interventional cardiologists who were blinded to the patient clinical data. In cases of disagreement, the decision of a third observer was obtained and the final decision was made by consensus. Each coronary lesion producing 50% diameter stenosis in vessels diameter 1.5 mm was scored separately and added together to provide the overall SS, which was calculated prospectively using the SS algorithm [8].

### Assesment of cardio ankle vascular index

CAVI was measured using a VaSera VS-1000 CAVI instrument (Fukuda Denshi Co. Ltd., Tokyo) by the methods described previously [16]. CAVI was measured in the morning after 12 h of fasting within 2 days before coronary angiography and intervention. Briefly, cuff were applied to the bilateral upper arms and ankles, with the subject supine and the head held in the midline position. After resting for 10 min, measurements were performed. Electrography, phonocardiography, and pressures and waveforms of brachial and ankle arteries were measured. Thereafter, ca-PWV and subsequently CAVI were calculated automatically.

### Assesment of carotid intima media thickness

Ultrasonography was performed with a Esaote Mylab50 equipped with a 7.5 MHz linear array imaging probe. The right common carotid artery (CCA) was examined with the patient lying supine, the head directed away from the side of interest, and the neck extended slightly. The transducer was manipulated so that the near and far walls of the CCA were parallel to the transducer footprint, and the lumen diameter was maximized in the longitudinal plane. A region 1 cm proximal to the carotid bifurcation was identified, and the CIMT of the far wall was evaluated as the distance between the lumen-intima interface and the media-adventitia interface. The CIMT was measured on the frozen frame of a suitable longitudinal image, with the image magnified to achieve a higher resolution of detail. The CIMT measurement was obtained from 4 contiguous sites at 1 mm intervals, and the average of the 4 measurements was used for analyses. All measurements were performed by the same investigator without knowledge of clinical and angiographic data.

The study was approved by the local bioethical committee and all patients gave their informed consent.

**Table 1.** Baseline and laboratory characteristics of study population (n = 172).

Age [years]	61 ± 11
Male gender	116 (68%)
Body mass index [kg/m <sup>2</sup> ]	27.6 ± 3.4
Dyslipidemia	74 (43%)
Diabetes	58 (34%)
Smoking	71 (42%)
Hypertension	86 (51%)
Systolic pressure [mm Hg]	154 ± 14
Diastolic pressure [mm Hg]	92 ± 7
TIMI risk score	3.6 ± 0.9
CAVI	9.2 ± 1.8
CIMT [mm]	0.84 ± 0.17
Syntax score	12.5 ± 8.5

ABI — ankle brachial index; CAVI — cardio ankle vascular index; CIMT — carotid intima media thickness; TIMI — thrombolysis in myocardial infarction

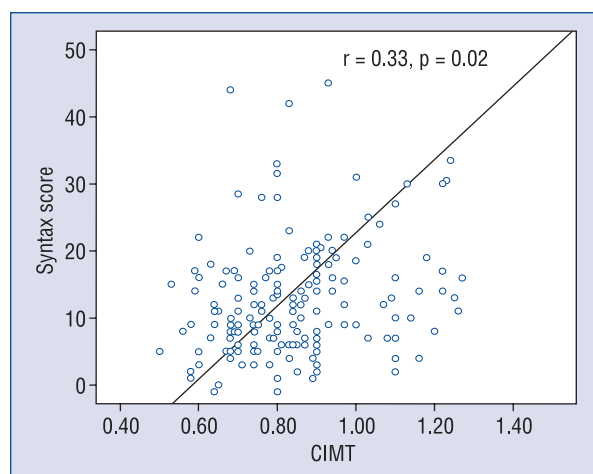
### Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables were expressed as percentage. An analysis of normality of the continuous variables was performed with the Kolmogorov-Smirnov test. The Spearman correlation analyse were used for assessing correlation between SS and other variables. In order to compare SS among CIMT, CAVI and TIMI risk score tertiles, Kruskal-Wallis test was performed. Man-Whitney U test was used as post hoc test after Kruskal-Wallis analyse. Statistical analyse was performed by using SPSS 14.0 and a p ≤ 0.05 (2-tailed) was considered significant.

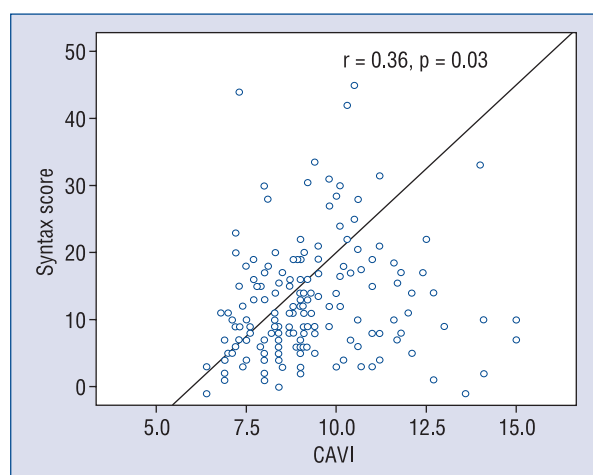
### Results

Clinical and demographic characteristics of all patients are listed in Table 1. Mean SS, CIMT and CAVI were 12.5 ± 8.5, 0.84 ± 0.17 and 9.2 ± 1.8, respectively.

The only significant correlation between SS and traditional cardiovascular risk factors was age (r = 0.26, p = 0.01). But it did not reach to significance in linear regression analyse (β = 0.11, p = 0.53). There was significant association between SS and CIMT (r = 0.33, p = 0.02) (Fig. 1) and CAVI (r = 0.36, p = 0.03) (Fig. 2). Linear regression analyze demonstrated independent association between SS and CIMT (95% confidence interval [CI] 2.1–19, p = 0.014) and CAVI (95% CI 15–29, p = 0.021) (Table 2).



**Figure 1.** Correlation analyse between carotid intima media thickness (CIMT) and syntax score.

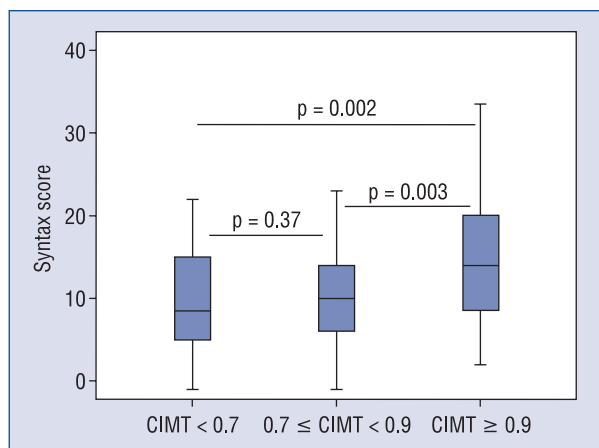


**Figure 2.** Correlation analyse between cardio ankle vascular index (CAVI) and syntax score.

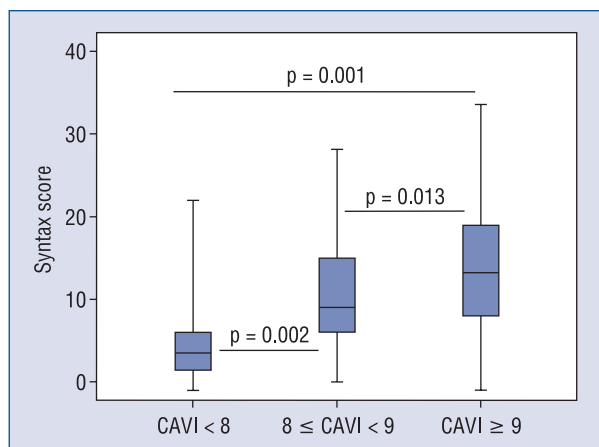
**Table 2.** Correlation and linear regression analyse of variables and syntax score.

	Correlation		Beta	Regression	
	r	p		p	95% CI
Age	0.26	0.01	0.11	0.53	-0.1–0.3
BMI	0.012	0.18	–	–	–
Dyslipidemia	0.21	0.37	–	–	–
Diabetes	0.14	0.21	–	–	–
Smoking	0.15	0.41	–	–	–
Hypertension	0.07	0.62	–	–	–
TIMI risk score	0.01	0.9	–	–	–
CAVI	0.36	0.03	0.29	0.021	15–29
CIMT	0.33	0.02	0.38	0.014	2.1–19

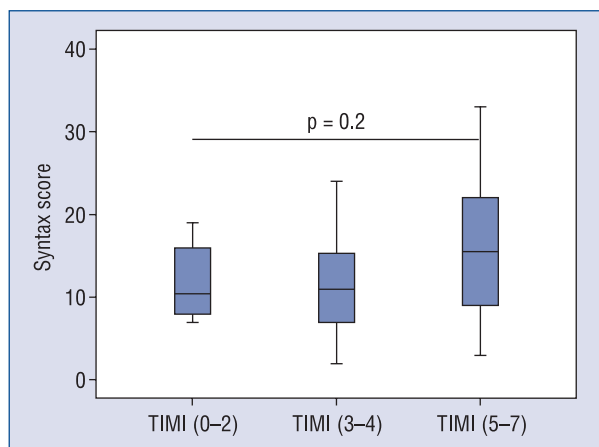
BMI — body mass index; CAVI — cardio ankle vascular index; CIMT — carotid intima media thickness; CI — confidence interval



**Figure 3.** Syntax scores in patients with different carotid intima media thickness (CIMT) values.



**Figure 4.** Syntax scores in patients with different cardio ankle vascular index (CAVI) values.



**Figure 5.** Syntax scores in patients by thrombolysis in myocardial infarction (TIMI) risk scores.

In order to impact of degree of atherosclerosis burden on CAD disease complexity, patients were divided into three groups according to the their CIMT and CAVI values. Number of patients with low (CIMT < 0.7 mm), intermediate (0.9 > CIMT ≥ 0.7 to) and high (CIMT ≥ 9) CIMT values were 34, 78 and 60, respectively. SS values according to the CIMT tertiles as follows: low and intermediate (10.1 ± 8.2 vs 11.4 ± 7.9, p = 0.37), low and high (10.1 ± 8.2 vs 15.2 ± 8.8, p = 0.002), intermediate and high (11.4 ± 7.9 vs 15.2 ± 8.8, p = 0.003) (Fig. 3).

As for relation between CAVI and CAD complexity, patients divided into three groups. Number of patients with normal (CAVI < 8), borderline (8 ≤ CAVI < 9) and abnormal (CAVI ≥ 9) CAVI values were 11, 71 and 90, respectively. SS for different CAVI categories as follows: normal and borderline (4 ± 3.7 vs 11.1 ± 7.2, p = 0.002), borderline and abnormal (11.1 ± 7.2 vs 14.1 ± 9.1, p = 0.013), normal and abnormal (4 ± 3.7 vs 14.1 ± 9.1, p < 0.001) (Fig. 4).

We also examined the relation between TIMI risk score and SS. Number of patients with low (TIMI [0-2]), intermediate (TIMI [3-4]) and high (TIMI [5-7]) TIMI scores were 12, 118 and 52, respectively. SS for low, intermediate and high TIMI scores were 11.8 ± 4.7, 11.9 ± 7.3 and 16 ± 9.2, respectively. Although there was a trend for higher SS for increased TIMI risk score, Kruskal-Wallis analyse did not reveal significant difference of SS between groups (p = 0.2) (Fig. 5).

## Discussion

In present study, we have found significant correlation between atherosclerosis burden and CAD complexity. Also, we have demonstrated that patients with severe degree of atherosclerosis have more complex coronary artery lesions. The other important finding is that neither traditional cardiovascular risk factors nor TIMI risk score can predict coronary artery lesion complexity.

SS is widely accepted as a CAD complexity marker and its prognostic value has been demonstrated in different clinical situations and patients with the highest tertile SS have significantly more major adverse cardiac events (MACE) [17-19]. SS has a role in the risk stratification of patients with STEMI having primary PCI and is a useful tool that provides additional risk stratification to known risk factors of long term mortality and MACE [20, 21]. Also, the clinical significance of SS has been shown in non-ST segment elevation ACS patients [9].

Morover, Wykrzykowska et al. [22] demonstrated independent predictive value of SS for MACE and mortality not only in selected patient groups but also in all CAD treated by PCI.

The worse prognosis and increased MACE in patients with higher SS may be explained by differences in clinical, angiographic and procedural characteristics. For clinical characteristics, patients with higher SS were older, more commonly had previous MI, diabetes and renal dysfunction [10, 21, 22]. These patients also presented with higher pulse rates, cardiogenic shock, and anterior STEMI. As for procedural and angiographic characteristics, implanted stents were longer, more likely to involve bifurcations and had increased rate of thrombosis in patients with higher SS [20, 21]. Procedure failure with TIMI 0/1 flow, low myocardial brush grade (MBG) and high corrected TIMI frame count (cTFC) were more common in the highest tertile SS [20, 21]. In addition, there was a significant positive association between SS and periprocedural myocardial necrosis during PCI that is associated with worse outcomes, including death [10–12].

Yet there is no study as to CAD complexity and CIMT in ACS patients, association between complex coronary and carotid artery plaques was investigated by few authors. Saito et al. [23] demonstrated significant association between complex carotid plaques and complex coronary stenoses. Kato et al. [24] investigated the relationship between ultrasonographic properties of the carotid artery and the angiographic features of coronary plaques and they found significant association between complex coronary plaques and positive carotid artery remodeling. Kalay et al. [25] found significant but weak correlation between CIMT and CAD severity determined by gensini score in ACS patients. But, in these studies coronary lesion complexity was defined by features of lesion morphology or culprit lesion that led to the cardiovascular event rather than SS. Recently, we and other authors have demonstrated significant association between CIMT and SS in stable CAD [26, 27].

Relation between CAVI and SS is less clear. Association between coronary atherosclerosis severity and CAVI has been shown [28–30]. Also, Horinaka et al. [31] demonstrated that CAVI could reflect plaque burden in the coronary artery. In addition, Mineoka et al. [32] found significant association between coronary artery calcification, well known marker of atherosclerotic burden, and CAVI. But, none of them considered SS as CAD complexity marker.

We did not find significant association between any traditional cardiovascular risk factors and CAD complexity apart from age event if these are well known risk factors for atherosclerosis. We can explain this situation by making assumption that cumulative rather than individual impact of traditional cardiovascular risk factors may be more important on CAD complexity. Also we did not demonstrate significant relation between TIMI risk factors and SS. This may be explained by the fact that some parameters of TIMI risk score such as aspirin use, anginal symptoms, ST segment depression or troponin elevation may not be related directly to the atherosclerotic process. A few researcher found significant association between TIMI risk score and number of diseased vessels, presence of intracoronary thrombus and impaired coronary flow. But none of these studies used SS as CAD complexity marker.

### Limitations of the study

Our study has several limitations. First, the population is relatively small. Also, we excluded patients with previous CAD. Therefore, our study does not represent all ACS patients. Since our study is cross sectional, we can not determine whether our patients with higher SS will face an increased risk of cardiovascular events. Even though it was statistically significant, this significance may be regarded weak or moderate when taking into account of coefficients of correlation analyse.

### Conclusions

We have demonstrated predictive value of atherosclerosis marker for CAD complexity in ACS patients independent from traditional cardiovascular risk factors and well known TIMI risk score. Further research is required to determine the clinical significance of atherosclerosis markers based risk stratification and treatment modalities in this patient population.

**Conflicts of interest:** none declared

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