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Correlation between B-type Natriuretic Peptide and Syntax Score in Patients of Multivessel Coronary Artery Disease Presented with Acute Coronary Syndrome

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ABSTRACT

Background: The SYNTAX score measures the architectural complexity of coronary artery disease (CAD), whereas B-type natriuretic peptide (BNP) is a biomarker of ventricular stress and ischemia. It is yet unknown how they work together to treat multivessel CAD in patients with acute coronary syndrome (ACS). **Aim**: To assess correlation between SYNTAX score and plasma BNP levels in multivessel CAD patients who present with ACS. **Patients and Methods:** This prospective study included 60 ACS patients admitted to Zagazig University Hospital and El-Agouza Police Hospital. All patients underwent BNP measurement and coronary angiography with SYNTAX scoring. Patients were divided into two groups: Group 1 (non-multivessel CAD) and Group 2 (multivessel CAD). Clinical characteristics, risk factors, lesion complexity, BNP, and SYNTAX score were compared. **Results:** Multivessel disease (MVD) patients were older and predominantly male, with higher prevalence of diabetes, dyslipidemia, smoking, obesity, and LVH. They also showed significantly lower hemoglobin and higher creatinine levels. Complex lesion characteristics were more frequent in MVD group. BNP levels were markedly higher in MVD group and increased with number of diseased vessels, there was a statistically significant increase in BNP level with progression of CAD, worsening of lesion characteristics and increase in complexity and severity of lesions. BNP correlated strongly with SYNTAX score in the total cohort and within subgroups. **Conclusion:** BNP levels indicate the degree and complexity of CAD in ACS patients and correspond with the SYNTAX score. When combined with SYNTAX, BNP may be a straightforward supplementary tool for risk assessment and revascularization strategy guidance.

Keywords: B-type natriuretic peptide (BNP); SYNTAX score; Multivessel coronary artery disease; Acute coronary syndrome; Lesion complexity; Risk stratification.

INTRODUCTION

B-type natriuretic peptide (BNP) in particular has become one of the most promising indicators for evaluating heart function. BNP levels have been thoroughly investigated as indicators of asymptomatic left ventricular dysfunction and early heart failure, and they are commonly increased in heart failure patients [(1)].

According to recent experimental and clinical research, myocardial ischemia also causes the production of BNP, with the degree of increase according to the severity of the ischemia. Furthermore, BNP has been demonstrated to offer independent predictive information for mortality in individuals with acute coronary syndromes (ACS), irrespective of troponin status [(2)]. Because of the increasing interest in enhancing risk stratification techniques, the predictive relevance of BNP in ACS is still being actively studied [(3)]. There is ongoing discussion on the best revascularization techniques for individuals with coronary artery disease (CAD), especially when multivessel disease (MVD) is present. In this regard, a number of randomized trials have contrasted coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) [(4)].

To inform decision-making, precise measurement of the structural disease burden is crucial for patients with complex CAD, such as those with left main involvement or three-vessel disease. In order to compare PCI and CABG in de novo multivessel or left main CAD, the SYNTAX (SYNergy between PCI with TAXUSTM and Cardiac Surgery) experiment was created. The creation of the SYNTAX score, an angiographic instrument that evaluates lesion number, location, and complexity to comprehensively characterize the coronary vasculature, was a major result of this trial. Higher SYNTAX scores have been linked to worse clinical outcomes, such as higher rates of major adverse cardiac and cerebrovascular events (MACCE) after one year, and are indicative of more complex disease [(5)].

This study intends to examine the relationship between BNP levels and the SYNTAX score in patients presenting with ACS, because B-type natriuretic peptide (BNP) has been consistently linked to the diagnosis and prognosis of ACS, but its relationship with the anatomical extent and severity of coronary lesions in multivessel CAD is still unclear.

AIM OF THE WORK

The aim of this study is to determine BNP levels and calculate SYNTAX scores in patients with multivessel CAD presenting with ACS, and to evaluate the relationship between BNP concentrations and the angiographic severity and complexity of coronary lesions.

PATIENTS AND METHODS

A total of 60 consecutive patients diagnosed with acute coronary syndrome (ACS) who were admitted to the Cardiology Departments of Zagazig University Hospital and El-Agouza Police Hospital were enrolled in this prospective observational study.

Ethical considerations:

The study protocol was reviewed and approved by the Local Medical Research and Ethics

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Committee of the Faculty of Medicine, Zagazig University , and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion in the study.

Inclusion criteria:

Enrollment was open to patients with ACS manifesting as ST-segment elevation myocardial infarction (STEMI), unstable angina (UA), or non-ST-segment elevation myocardial infarction (NSTEMI). The most recent European Society of Cardiology guidelines were used to define the diagnostic criteria for UA, NSTEMI, and STEMI (ESC) guidelines [6,7].

Exclusion criteria:

Patients with any of the following were excluded:

1. Moderate to severe left ventricular dysfunction.
2. End-stage renal disease.
3. Atrial fibrillation.
4. History of pulmonary embolism.
5. Significant valvular heart disease.

Age, sex, and coronary artery disease risk factors, such as obesity (BMI >30 kg/m^2), smoking, hypertension, diabetes mellitus, and dyslipidemia, were all included in the comprehensive history that was taken [8]. Every patient underwent a thorough physical checkup. A routine 12-lead surface ECG was performed on all patients at arrival in order to detect arrhythmias and ischemia abnormalities. A GE Vivid 9 ultrasound machine (GE Healthcare, Chicago, USA) with a 1.7–4 MHz transducer was used to perform two-dimensional transthoracic echocardiography with Doppler. In order to evaluate regional wall motion anomalies, evaluate left ventricular systolic function (fractional shortening (FS) and ejection fraction (EF)), and rule out valvular heart disease using color Doppler, examinations were conducted in the standard left lateral position. Complete blood count, random blood glucose, serum urea and creatinine, liver function tests, and lipid profiles were among the standard laboratory tests. At admission, cardiac biomarkers such as troponin and creatine kinase-MB (CK-MB) were tested. EDTA-anticoagulated blood samples were subjected to a quantitative immunofluorescence assay to determine the levels of plasma BNP. The results were given in pg/mL. Every patient had a coronary angiography. Two skilled interventional cardiologists used the verified online SYNTAX score calculator to determine the SYNTAX score while being blind to the BNP values. The mean of the two readings was taken into account in the event of a discrepancy.

B-type natriuretic peptide (BNP) Assay

A sandwich enzyme-linked immunosorbent assay (ELISA) kit, which is based on the idea of antibody capture and detection using a horseradish peroxidase (HRP)-conjugated anti-BNP antibody, was used to quantify the quantities of BNP in plasma. The detection range, for example, was 4–48 ng/L, while the assay sensitivity was X pg/mL. Every step was carried out in compliance with the manufacturer's guidelines. BNP concentrations were calculated by interpolating using a standard calibration curve, and optical density was measured at 450 nm using a microplate reader. Where necessary, the results were adjusted for dilution factors [9].

Coronary Angiography and SYNTAX Score Calculation

A diagnostic coronary angiography was performed on each patient. Using the online SYNTAX calculator, the angiographic data were examined and each patient's SYNTAX score was determined. The score uses the American Heart Association's (AHA) 16-segment model to measure lesion complexity by adding up the weighted scores for all coronary lesions with >50% diameter stenosis in arteries larger than 1.5 mm [10]. Two skilled interventional cardiologists who were blind to the BNP values agreed on the final SYNTAX score.

Two groups of the study population were created: Group 1 (non-multivessel patients) comprised individuals with one or two-vessel disease, CAD treated medically, and normal coronary angiography. Patients with angiographically verified multivessel CAD were included in Group 2 (Multivessel patients). The association between BNP levels, SYNTAX score, and the existence of more severe and complex coronary lesions was assessed by comparing the two groups.

Statistical Analysis

IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA) was used to analyze the data. While quantitative variables were presented as mean ± standard deviation (SD) for normally distributed data or as median and interquartile range (IQR) for non-normally distributed data, qualitative variables were expressed as frequencies and percentages. The Kolmogorov–Smirnov test was used to test for normality. The independent Student's t-test for quantitative variables with a normal distribution, the Mann-Whitney U test for variables with an abnormal distribution, and the Chi-square test or Fisher's exact test for categorical variables were used to compare groups. Statistical significance was defined as a two-tailed p-value <0.05.

RESULTS

In this study, 60 ACS patients had coronary angiography, BNP testing, and SYNTAX score computations. Patients were split into two equal groups based on angiographic results: Group 1 (non-multivessel CAD; n = 30) and Group 2 (multivessel CAD; n = 30).

Patients in the multivessel group were more likely to be males (80% vs. 53.3%) and substantially older (63.6 ± 10.6 vs. 54.8 ± 9.9 years). The two groups' admission diagnoses (STEMI vs. NSTE-ACS) did not differ significantly (Table 1).

Table (1): Comparison between the two studied groups according to demographic data

	Non MV (n = 30)		MV (n = 30)		Test of Sig.	p
	No.	%	No.	%		
Age (years) Mean ± SD.	54.77 ± 9.85		63.63 ± 10.62		t=3.352*	0.001*
Sex					χ^2	p
Male	16	53.3	24	80.0	χ^2= 4.800*	0.028*
Female	14	46.7	6	20.0		
STEMI	7	23.3	4	13.3	1.002	0.317
NSTE-ACS	22	73.3	26	86.7	1.667	0.197

IQR: Interquartile range, SD: Standard deviation, χ^2: Chi square test , t: Student t-test

*: Statistically significant at $p \leq 0.05$, IQR: Interquartile range, SD: Standard deviation, χ^2: Chi-square test, t: Student's t-test, STEMI: ST-segment elevation myocardial infarction, NSTE-ACS: Non-ST-segment elevation acute coronary syndrome, MV: Multivessel, Non-MV: Non-multivessel, p: Probability value (significance level).

Multivessel patients were more likely to have diabetes mellitus (80% vs. 46.7%), dyslipidemia (96.7% vs. 73.3%), smoking (66.7% vs. 30%), obesity (53.3% vs. 20%), and diastolic dysfunction/LVH (73.3% vs. 43.3%) (Table 2).

Table (2): Comparison between the two studied groups according to risk factors of CAD

	Non MV (n = 30)		MV (n = 30)		χ^2	p
	No.	%	No.	%		
HTN	19	63.3	20	66.7	0.073	0.787
DM	14	46.7	24	80.0	7.177*	0.007*
DLP	22	73.3	29	96.7	6.405*	FEp=0.026*
Smoking	9	30.0	20	66.7	8.076*	0.004*
Obesity	6	20.0	16	53.3	7.177*	0.007*
DD/LVH	13	43.3	22	73.3	5.554*	0.018*

χ^2: **Chi square test**, FE**: Fisher Exact,** *: Statistically significant at $p \leq 0.05$

HTN: Hypertension, DM: Diabetes mellitus, DLP: Dyslipidemia, DD/LVH: Diastolic dysfunction / Left ventricular hypertrophy, χ^2: Chi-square test, FE: Fisher's Exact test.

In multivessel patients, serum creatinine was significantly higher (0.95 ± 0.21 vs. 0.83 ± 0.21 mg/dL, and hemoglobin levels were significantly lower (12.8 ± 2.2 vs. 14.0 ± 1.7 g/dL). Troponin and CK-MB levels did not differ significantly between the 2 groups (Table 3).

Table (3): Comparison between the two studied groups according to laboratory parameters (Hb level, creatinine, and cardiac biomarkers)

	Non MV (n = 30)	MV (n = 30)	t	p
Hb level (gm/dl) Mean ± SD.	13.96 ± 1.73	12.83 ± 2.23	2.195*	0.032*
Creatinine (mg/dl) Mean ± SD.	0.83 ± 0.21	0.95 ± 0.21	2.250*	0.028*
Troponin (ng/ml) Mean ± SD.	3.12 ± 0.30	4.19 ± 1.09	328.50	0.072
CKMB (IU/L) Mean ± SD.	29.61 ± 5.67	35.15 ± 5.59	359.0	0.178

IQR: **Interquartile range** SD: **Standard deviation** **t: Student t-test**

*: Statistically significant at $p \leq 0.05$, Hb: Hemoglobin, SD: Standard deviation, IQR: Interquartile range, t: Student's t-test.

Of the 60 patients, 30 (50%) had multivessel CAD (Table 4).

Table (4): Distribution of the studied cases

	No.	%
Normal CAG/CAD for medical ttt	4	6.67
1 VD	9	15
2 VD	17	28.33
MVD	30	50

CAG: Coronary angiography, CAD: Coronary artery disease, VD: Vessel disease, MVD: Multivessel disease.

Total occlusion, bifurcation lesions, ostial lesions, long lesions >20 mm, calcification, tortuosity, and widespread disease/small vessels were all more common in the multivessel group, which also had considerably higher lesion complexity (Table 5).

Table (5): Comparison between the two studied groups according to lesions characteristics

	Non-MV (n = 30)		**MV (n = 30)**		χ^2	**p**
	No.	**%**	**No.**	**%**		
Total occlusion	7	23.3	18	60.0	8.297*	0.004*
Bifurcation	4	13.3	20	66.7	17.778*	<0.001*
Ostial lesion	2	6.7	10	33.3	6.667*	<0.001*
Thrombus	5	16.7	5	16.7	0.0	1.000
Lesion length > 20 mm	20	66.7	28	93.3	6.667*	0.010*
Calcification	6	20.0	14	46.7	4.800*	0.028*
Tortuosity	3	10.0	10	33.3	4.812*	0.028*
Diffuse disease / small vessels	5	16.7	15	50.0	7.500*	0.006*

χ^2: Chi square test ***:** Statistically significant at $p \leq 0.05$

χ^2: Chi-square test

MV: Multivessel, VD: Vessel disease, SD: Standard deviation

Patients in group 1 had significantly less mean SYNTAX scores (10.67±7.27) compared to those in group 2 (27.35±5.75) (Table 6).

Table (6): Comparison between the two studied groups according to SYNTAX score

	Non MV (n = 30)	**MV (n = 30)**	**U**	**p**
Syntax Mean ± SD.	10.67 ± 7.27	27.35 ± 5.75	35.0*	<0.001*

IQR: Interquartile range, SD: Standard deviation, U: Mann Whitney test, *: Statistically significant at $p \leq 0.05$

IQR: Interquartile range, SD: Standard deviation, U: Mann–Whitney test, MV: Multivessel

Mean BNP levels in patients in groups 1 and 2 were 142.07 ± 33.01 pg/ml and 212.97 ± 24.25 pg/ml respectively. The two groups' BNP levels differed in a way that was statistically significant (Table 7).

Table (7): Comparison between the two studied groups according to BNP level

	Non MV (n = 30)	**MV (n = 30)**	**t**	**p**
BNP (pg/ml) Mean ± SD.	142.07 ± 33.01	212.97 ± 24.25	9.481*	<0.001*

IQR: **Interquartile range**, SD: **Standard deviation**, **t: Student t-test**, *: Statistically significant at $p \leq 0.05$

BNP: B-type natriuretic peptide, SD: Standard deviation, IQR: Interquartile range, t: Student's t-test.

As CAD worsened and the number of coronary arteries affected increased, the BNP level increased statistically significantly **(Table 8)**.

Table (8): Relation between BNP level and coronary vessels involved

	N	BNP (pg/ml)			F	p
		Min. – Max.	Mean ± SD.	Median		
Normal CAG/CAD for medical ttt	4	69.0 – 89.0	77.75 ± 8.38	76.50	66.564*	<0.001*
1 VD	9	118.0 – 180.0	138.8 ± 20.35	134.0		
2 VD	17	120.0 – 182.0	158.9 ± 20.31	166.0		
Multi vessel	30	181.0 – 258.0	212.97 ± 24.25	207.50		

F: **One way ANOVA test,** *: Statistically significant at p ≤ 0.05, BNP: B-type natriuretic peptide, VD: Vessel disease.

Patients with more complex lesions, such as total blockage, bifurcation, ostial, lengthy lesions >20 mm, calcification, tortuosity, and widespread disease, had significantly higher BNP values (Table 9).

Table (9): Relation between BNP and complexity and severity of the lesions in total sample (n = 60)

	N	BNP (pg/ml)			t	p
		Min. – Max.	Mean ± SD.	Median		
Total occlusion	25	150.0 – 254.0	203.3 ± 28.90	198.0	4.486*	<0.001*
Bifurcation	24	120.0 – 258.0	208.0 ± 31.30	206.0	4.991*	<0.001*
Ostial lesion	12	170.0 – 254.0	210.5 ± 31.16	210.50	2.964*	0.004*
Thrombus	10	120.0 – 243.0	182.7 ± 34.80	187.0	3.389	<0.001*
Lesion length > 20 mm	48	120.0 – 258.0	190.6 ± 36.54	186.50	5.349*	<0.001*
Calcification	20	147.0 – 258.0	207.4 ± 32.53	207.50	4.430*	<0.001*
Tortuosity	13	166.0 – 258.0	201.4 ± 27.66	190.0	2.937*	0.006*
Diffuse disease / small vessels	20	166.0 – 258.0	200.85 ± 27.84	190.0	3.529*	0.001*

SD: **Standard deviation** **t: Student t-test** *: Statistically significant at p ≤ 0.05
BNP: B-type natriuretic peptide, SD: Standard deviation, t: Student's t-test.

BNP level and SYNTAX score were positively correlated in both groups and the entire sample (r = 0.843* in non-MV, r = 0.632* in MV, and r = 0.632* in the complete sample) **(Figure 1).**

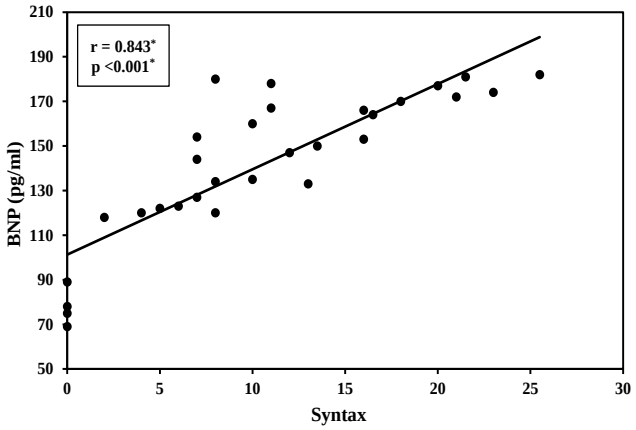

Figure (1a): Correlation between BNP and Syntax in Non MV group

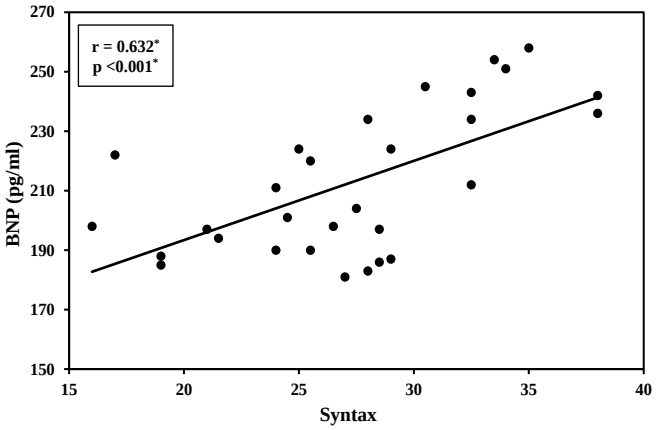

Figure (1b): Correlation between BNP and Syntax in MV group

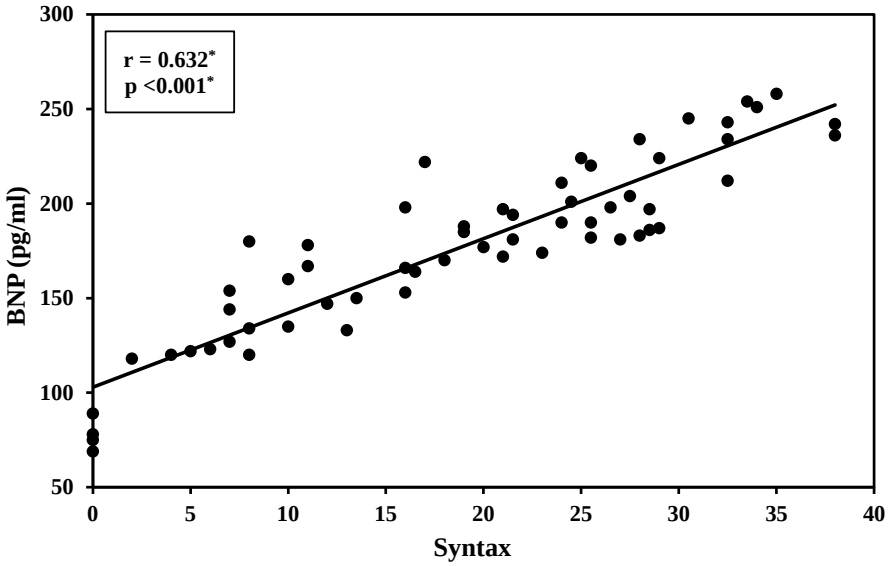

Figure (1c): Correlation between BNP and Syntax in Total sample.

DISCUSSION

Patients in group (1) in the current study were between the ages of 38 and 73, with a mean age of 54.77 ± 9.85 years, and those in group (2) were between the ages of 44.0 and 83.0, with a mean age of 63.63 ± 10.62 years.

Group 1 consisted of 14 patients (46.7%) who were females and 16 patients (53.3%) who were males. In contrast, 6 patients (20%) were females and 24 patients (80%) were males in group (2).

The presence of more severe and complex coronary lesions was statistically significantly correlated with older age, male gender, and the extension of CAD (P = 0.028).

Age and gender are non-modifiable risk factors for CAD, and its prevalence rises in both men and women after the age of 35. According to **Burke *et al.* [11],** men are more at risk than women, which is consistent with the study of **Sanchis-Gomar *et al.* [10]**. The reason for this could be that estrogen is believed to prevent coronary vasoreactivity and to stabilize plaque by reducing inflammation in atherosclerosis. Men and women differ in terms of CAD burden, risk factors, plaque types, and clinical aspects, according to **Kim *et al.* [12].** These differences emphasize the necessity of specialized treatment and diagnostic strategies for CAD in both sexes. It's also critical to acknowledge that women have lower rates of drug prescriptions, longer diagnostic turnaround times, and delays in treatments and surgeries. Raising awareness of sex differences and prejudice is necessary to address these problems, as is involving more women in clinical research to collect more comprehensive data on the cardiovascular health of women.

Regarding diagnosis of patients on admission

Patients who presented with STEMI included 7 (23.3%) of group (1) and 4 (13.3%) of group (2) in the current study. Patients who presented with NSTE-ACS comprised 22 (73.3%) of group (1) and 26 (86.7%) of group (2).

Patients who presented with STEMI or NSTE-ACS did not significantly correlate with the presence of more severe and complex coronary lesions or the extension of CAD (P = 0.197).

In contrast to our research, **Khan *et al.* [13]** shown that patients with NSTEMI had a more extensive degree of coronary artery disease than those with STEMI. A total of 100 consecutive MI patients had their angiographic data collected; 50 of these patients had STEMI (Group I: 45, female: 5), and the remaining 50 patients had NSTEMI (Group II: 38, female: 12). Eighty percent of the patients with NSTEMI had multi-vessel disease, whereas only twenty percent of the patients with STEMI had multi-vessel illness, with the remaining eighty percent having single-vessel disease.

Due to the small sample size, there was no difference in the occurrence of more severe and complex coronary lesions or the extension of CAD between patients who presented with STEMI and NSTE-ACS in our investigation.

Regarding Risk factors of CAD

The following were CAD risk variables in the current study:

- There were 19 (63.3%) hypertension patients in group (1) and 20 (66.7%) in group (2).
- There were 14 (46.7%) diabetic patients in group (1) and 24 (80%) in group (2).
- There were 22 (73.3%) and 29 (96.7%) dyslipidemic individuals in groups (1) and (2), respectively.
- There were nine (30%) smokers in group (1) and twenty (66.7%) in group (2).

Six patients (20%) in group (1) and sixteen patients (53.3%) in group (2) were obese.

Twenty-two (73.3%) patients in group (2) and thirteen (43.3%) patients in group (1) had echocardiographic findings of DD/LVH.

Risk factors, such as DM (FEP=0.026), DLP (P=0.007), smoking (P=0.004), obesity (P=0.007), and LVH (P=0.018), were statistically significantly associated with the presence of more severe and complex coronary lesions and the extension of CAD, but there was no significant association between hypertension and CAD extension (P=0.787).

Regarding HTN

Malakar *et al.* [14] indicated that hypertension is a significant risk factor for CAD because to the oxidative and mechanical stress it places on the artery wall, which is contrary to our findings. Additionally, **Thomopoulos *et al.*** [15] showed that a significant absolute risk reduction in CAD-related events occurred when the systolic and diastolic blood pressures were reduced by more than 10 mmHg and 5 mmHg, respectively.

Regarding DM

According to one research, a 0.5% decrease in HbA1C was associated with a 20% hazard risk reduction (95% CI 4-33%) for major cardiovascular events [16]**.** Patients on peptidase-4 inhibitors, GLP-1 agonists, and SGLT-2 inhibitors were included in this meta-analysis of 12 cardiovascular outcomes trials. Furthermore, compared to individuals without diabetes, diabetic patients who present with NSTEMI are likely to have more severe and widespread coronary artery involvement [17]**.** Therefore, aggressive risk factor reduction by lifestyle modifications and medication, along with routine check-ups, may help reduce cardiovascular mortality and morbidity in diabetic patients both before and after acute coronary syndrome.

Regarding DLP

According to one research, statins lower the risk of major cardiovascular events [18]**.** Treatment with a moderate-intensity statin reduced the absolute risk of CAD by 2.7%, while treatment with a high-intensity statin reduced the absolute risk of CAD by 4.1%. Additionally, because it provides an extra cardiovascular risk stratification value, LDL-C has lately emerged as one of the most reliable predictors of ASCVD [19]**.** People with CAD frequently have higher LDL values, which seem to positively correlate with an increased overall risk of experiencing a catastrophic cardiovascular event. These figures demonstrate how important LDL is for effectively controlling cardiometabolic risk.

Regarding Smoking

According to a meta-analysis [20], smoking increased the risk of cardiovascular disease in patients over 60 by 37% for former smokers and by double for current smokers, which is consistent with our study. Additionally, current smoking was found to be significantly associated with subclinical coronary atherosclerosis as measured by CCTA [21]**.** Furthermore, non-calcified plaque was linked to past smoking, suggesting an increased risk of cardiovascular disease.

Regarding Obesity

As per the findings of one study by **Garcia-Labbé *et al.*** [22]**,** obesity is linked to more complex, elevated, and high-grade atherosclerotic coronary artery lesions. It also raises the risk of developing other CAD risk factors, such as diabetes mellitus, hypertension, and hyperlipidemia.

Regarding LVH

According to one research, LVH is a risk factor for CAD in hypertensive individuals, and it is also associated with CAD in normotensive patients [23]. This correlation's pathophysiology may be because people with LVH have a number of factors that can lower myocardial oxygen delivery, cause coronary atherosclerosis, and ultimately result in CAD. Potential explanations include elevated blood viscosity, platelet abnormalities, coronary artery abnormalities, and a prothrombotic state. In addition to these factors, people with LVH have larger LV cavities, greater LV masses, and higher LV wall stress, which raises their myocardial oxygen demand.

Regarding Hb level

Patients' hemoglobin levels in groups (1) of the current study varied from 10.90 to 17.10 gm/dl, with a mean of 13.96 ± 1.73 gm/dl and in group (2) it ranged from 10.0 to 17.40 gm/dl, with a mean of 12.83 ± 2.23 gm/dl.

A statistically significant correlation was found between the presence of more severe and complex coronary lesions and a lower Hb level and the expansion of CAD (P = 0.032).

According to our research, anemia has been linked to the onset of coronary artery disease or a poor prognosis for patients with the condition. This is because anemia reduces the amount of oxygen delivered to the myocardium and lowers blood viscosity, which can result in an increase in venous return and, ultimately, preload. According to **Lanser *et al*.** [24], anemia was also linked to the severity of the condition, as seen by more advanced stenosis in CAG, a higher risk of cardio-cerebrovascular events, and elevated levels of inflammatory markers. Underlying inflammation and immunological activation may be the primary cause of the correlation between anemia and the severity and outcome of the disease.

Regarding Creatinine level

Patients' creatinine levels in groups (1) and (2) of the current study ranged from 0.50 to 1.30 mg/dl with a mean of 0.83 ± 0.21 mg/dl and 0.60 to 1.30 mg/dl with a mean of 0.95 ± 0.21 mg/dl, respectively.

Higher creatinine levels and the presence of more severe and complex coronary lesions were statistically significantly correlated with the extension of CAD (P=0.028).

Briasoulis and Bakris [25] demonstrated that individuals with even slightly lower GFR (30–60

ml/min) are more likely to develop obstructive CAD, which is consistent with our findings. As renal function deteriorates, the risk rises. Stages III–V of advanced chronic kidney disease (CKD) have been compared to CAD risk. In patients with chronic kidney disease (CKD), the prevalence of conventional cardiovascular risk factors such diabetes, hypertension, and hyperlipidemia is quite high. CAD's severity and scope, however, are out of proportion to the conventional risk factor profile. The coronary artery calcium (CAC) score is an independent predictor of cardiac events in both the general population and individuals with chronic kidney disease (CKD), according to research by **Kramer *et al.* [26].** Depending on the stage of CKD, the prevalence of CAC ranges from 13.9% in stages I and II to 83% in stages III and V. According to **Cai *et al.* [27]**, pro-inflammatory cytokines (interleukin-6, tumor necrosis factor-α, monocyte chemotactic protein-1) and inflammatory markers (C-reactive protein) rise in plasma as renal function declines. This, along with decreased nitric oxide synthesis, plays a significant role in escalating oxidative stress, endothelial dysfunction, and atherosclerosis.

Regarding Cardiac Biomarkers

Troponin levels in patients in groups 1 and 2 of the current investigation ranged from 0.01 to 45.0 ng/ml with a mean of 3.12 ± 8.30 ng/ml and 0.01 to 46.20 ng/ml with a mean of 4.19 ± 9.09 ng/ml, respectively. Patients in group (1) had CKMB levels ranging from 5.10 to 76.40 IU/L with a mean of 29.61 ± 15.67 IU/L, while those in group (2) had levels ranging from 13.50 to 69.0 IU/L with a mean of 35.15 ± 15.59 IU/L.

The low sample size may have contributed to the lack of a significant correlation between the presence of more severe and complex coronary lesions and the level of cardiac biomarkers and the extension of CAD (P= 0.178).

In contrast to our research, cardiac biomarkers in the acute environment revealed that STEMI patients had higher levels of myocardial dysfunction and inflammation than NSTEMI patients. Both STEMI and NSTEMI patients had similar prognoses based on these biomarkers. The circulating cardiac biomarkers are crucial for enhancing risk stratification for incident cardiovascular disease, but their findings do not support treating STEMI and NSTEMI patients differently based on their biomarker concentrations. Additionally, patients with a significant rise in hs-cTnI levels may have more severe coronary artery lesions than those with a slight rise, according to research by **Chen *et al.* [28].** Higher SYNTAX scores are correlated with elevated hs-cTnI levels, suggesting that NSTEM patients have more complex anatomy. Furthermore, there is a moderate linear relationship between SYNTAX scores and hs-cTnI levels.

As anticipated, the group of patients with multivessel CAD had statistically significant more severe and complex lesions.

One research by **Feldman *et al.* [29]** demonstrated that, in comparison to single-vessel disease (SVD), multivessel disease (MVD) is associated with a worse prognosis, more complications, longer hospital stays, a higher incidence of Major Adverse Cardiovascular Events (MACCEs), such as myocardial infarction, stent thrombosis, ischemic stroke, and all-cause death during hospitalization, and a higher in-hospital mortality. Additionally, it was acknowledged by **He *et al.* [30]** that specific characteristics of coronary artery lesions make intervention more difficult. An increased chance of further ischemia episodes and poorer cardiovascular outcomes are linked to complex lesions. Based on their angiographic characteristics, these lesions are grouped. Bifurcation lesions, calcified lesions, in-stent restenosis, chronic complete occlusions, and graft interventions are some of these characteristics.

Regarding SYNTAX score

Patients in group 1 of the current study had SYNTAX scores ranging from 00.0 to 25.5 with a mean of 10.67 ± 7.27, while patients in group 2 had scores ranging from 16.0 to 38.0 with a mean of 27.35 ± 5.75. Higher SYNTAX scores and the presence of more severe and complex coronary lesions were significantly correlated with the extension of CAD.

A "one-size-fits-all" approach to reflexively treat MVD is no longer justified; instead, individualized decisions regarding the best revascularization strategy are required, taking into account the complexity of coronary anatomy, patient comorbidities, the operator's experience, and the patient's preferences and expectations. **Dawson *et al.* [31]** in the FAME 3 Trial (Angiography vs. Fractional Flow Reserve for Multivessel Assessment) discussed how the Syntax Score (SS), which measures coronary intricacy, alters how revascularization strategy affects patient outcomes during PCI or CABG. Using an SS or Functional Syntax Score (FSS) threshold in the mid- rather than low 20s, a larger percentage of patients with MVD without left main involvement can be detected with equal results with PCI compared with CABG.

Regarding BNP

BNP levels in patients in groups 1 and 2 of the current investigation ranged from 69.0 to 182.0 pg/ml with a mean of 142.07 ± 33.01 pg/ml and 181.0 to 258.0 pg/ml with a mean of 212.97 ± 24.25 pg/ml, respectively.

An increase in the number of coronary arteries affected and the progression of CAD were significantly correlated with an increase in BNP levels (P<0.001).

In line with our research, **Goyal *et al.* [32]** found that widespread coronary atherosclerosis and multi-vessel disease are linked to elevated BNP levels in the blood. BNP was directly correlated with the severity of coronary disease: when the measurement was restricted to the 1-vessel group, they found that patients with left anterior descending artery (LAD) involvement had

significantly higher BNP than patients with other coronary artery involvement. Significant progressive differences were also evaluated between the 1-vessel, 2-vessel, and 3-vessel groups. Moreover, **Zhang *et al.* [33]** demonstrated that NT-proBNP has been extensively employed as a prognostic marker in heart failure and CAD, reflecting neurohormonal activation and myocardial stress in addition to elevated IL-6 and TAGs as predictors of CAD progression, offering fresh perspectives on the metabolic and inflammatory processes propelling disease progression. These results highlight how crucial it is to incorporate new biomarkers into clinical practice in order to enhance risk assessment and develop individualized treatment plans.

Regarding correlation between BNP and Syntax (complexity and severity of the lesions)

Increases in BNP levels were significantly correlated with worsening lesion features as well as an increase in the lesions' complexity and severity. In both groups and the entire sample, there was a positive connection between the BNP level and SYNTAX score ($P<0.001$) ($r = 0.843$* in non-MV, $r = 0.632$* in MV, and $r = 0.632$* in the complete sample).

The study of **Sarak *et al.* [34]** demonstrated that the degree, complexity, and severity of coronary atherosclerosis as determined by the SYNTAX score were independently correlated with the NT-ProBNP levels in patients who had myocardial infarction upon admission.

The study of **Chen *et al.* [35]** also found that the SYNTAX score had a positive correlation with NT-proBNP and that it might predict the prognosis of patients with AMI in addition to reflecting the degree, severity, and complexity of coronary atherosclerosis.

LIMITATIONS

Subjective angiographic complexity interpretation and interobserver diversity in how various operators interpret the SYNTAX score.

When compared to other scoring systems that use clinical parameters, the SYNTAX score has a poor predictive value and a lesser capacity to predict death.

The study was restricted to two locations; thus, the findings cannot be applied to the entire Egyptian community. Despite the relatively small study population, our sample was carefully characterized and chosen based on clinical and angiographic criteria.

CONCLUSION

According to this study, more widespread CAD was substantially correlated with male sex, diabetes, dyslipidemia, smoking, obesity, anemia, CKD, and older age. In ACS patients, there was a positive correlation between BNP levels and SYNTAX score; higher values indicated more severe and complicated coronary lesions.

RECOMMENDATIONS

In multivessel CAD patients with ACS, BNP and SYNTAX score may enhance risk stratification. To improve anatomical and functional assessment and direct individualized treatment, larger research using cutting-edge modalities like IVUS, FFR, and iFR are advised.

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Competing interests

The authors declare that they have no competing interest.

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