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ORIGINAL ARTICLE

Laboratory and Echocardiographic Parameters as Predictors of Coronary Artery Calcium Score Detected by Multislice Computed Tomography Coronary Angiography.

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ABSTRACT

Background: There are several methods for screening of cardiovascular diseases, among these, detection of calcium in coronaries by multislice computed tomography, which is widely used as a screening method. The aim of this study was the comparison between the total calcium as detected by echocardiography, ABO system and neutrophil lymphocyte ratio (NLR) as a predictor of coronary artery calcium score detected by multislice CT (MSCT).

Methods: 128 patients referred for MSCT angiography, with suspected coronary artery disease from January 2018 to August 2018. Patients were divided into three groups according to coronary artery calcium score (CACS), as measured by MSCT (group 1: CACS =0-99, group 2: CACS = 100-399 & group 3: CACS ≥400). Echocardiography, ABO system, CBC (NLR) and MSCT coronary angiography were done for all patients.

Results: There was a statistically significant difference between patients with blood group A and other blood groups as regards higher coronary calcium scores (by MSCT) ($p < 0.0001$). There was a positive significant correlation between cardiac calcium score (by echocardiography) and CAC score ($r= 0.712$, $p <0.0001$). Also, there was a positive significant correlation between N/L ratio and CAC score ($r= 0.433$, $p <0.0001$).

Conclusions: Multislice CT angiography plays a significant role in the prediction of atherosclerosis progression and cardiac events. NLR, cardiac calcium score and blood group A were found to be independent predictors for coronary calcium score.

Keywords: Atherosclerosis; Coronary artery calcium score (CACS); Neutrophil/lymphocyte ratio (NLR); CT coronary angiography, Cardiac calcium score.

INTRODUCTION

Coronary artery calcium score (CACS) reflects the presence and the degree of coronary atherosclerosis and has a free affiliation with cardiovascular events [1]. Calcification of different cardiac structures is common in elderly [2], and atherosclerosis and coronary artery disease have strong relation with mitral annular calcification (MAC) [3].Various diseases, especially cardiovascular diseases have been related to ABO blood groups [4].Inflammation plays a critical part in all stages of coronary artery disease (CAD) [5], and atherosclerosis has an inflammatory basic where leukocytes have a great role [6] Nowadays, neutrophil/lymphocyte ratio (NLR) has appeared as a new biomarker for inflammatory process [7]. Also, the NLR was associated with calcification and thrombus formation in coronary artery, therefore it was related with CAD and severity [8].

METHODS

Study Design: The current cross-sectional prospective study included 128 patients referred for multislice CT angiography, with suspected coronary artery disease (CAD), in the period between January 2018 and August 2018, the multi-detector computed tomography (MDCT) was done in Kobri el Kobba Military Hospital. Laboratory investigations performed according to Clinical Pathology Department Protocol in Zagazig University Hospitals. The study group was divided into three groups according to coronary artery calcium score (CACS); (group 1: CACS =0-99, group 2: CACS = 100-399 and group 3: CACS ≥400).***Inclusion Criteria***: All patients presenting by chest pain with low to intermediate pre-test probability (PTP) of CAD were included.

Exclusion Criteria: Patients with renal insufficiency (S. creatinine >1.5 mg/dl), previous

history of percutaneous coronary intervention (PCI) or previous coronary artery bypass graft (CABG), rheumatic heart disease, dye allergy, irregular heart rate like atrial fibrillation (AF) and frequent extra systoles, difficulties in performing CT, like inadequate breath holding and body weight over 130 kg, diagnosed as having acute coronary syndromes (elevated cardiac biomarkers and/or dynamic ECG changes), poor echocardiographic window and improper image quality, active infection or malignancies were excluded. ***Ethical Approvals:*** Written Informed consent was taken from patients to participate in the study. Approvals for performing the study was obtained from the Cardiology Department, Zagazig University Hospitals, Egypt after taking Institutional Review Board (IRB) approvals. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Procedures: All subjects in the study will be subjected to complete history taking, full general and local examination, laboratory investigations including serum creatinine, ABO blood group system (standard slide method was used, NLR (counted by division of neutrophil and lymphocyte count obtain by CBC).

Echocardiography A new echocardiographic calcium score was used to quantify the calcium in heart structures. This score depends on calcium in the aortic valve and root, mitral valve and annulus, and sub-mitral apparatus. We considered the presence of calcification when echo brightness more than normal valve tissue was seen [9].

Main Echocardiographic Score: Posterior annulus (by thirds, score 0-3), posterior mitral leaflet restriction (0,1), anterior annulus (0,1), anterior mitral leaflet restriction (0,1), MV calcification (0, 1 [mild], 2 [>mild]), subvalvular apparatus calcification (0,1) (Figure 1), AV calcification (0, 1 [nodule{s} in > 3 leaflets, 2 [nodules in 3 leaflets but nonrestrictive], 3 [restrictive]), and aortic root calcification (0,1).

Multislice CT Angiography: Coronary Calcium Scoring: The Agatston CACS [10] was used as a scoring system. It is derived by measuring the area of each calcific coronary artery lesion and multiplying it by coefficient of 1 to 4, depending on the maximum CT attenuation within that lesion; the CACS was classified into: No evidence of CAD: 0 calcium score, minimal: 1-10, mild: 11-100, moderate: 101-400, and severe: >400.

Statistical Analysis:All data were collected, tabulated, and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA) and MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi-Square test ($\chi 2$) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean ± SD (Standard deviation) for parametric and median and range for non-parametric data. One-way ANOVA test supplemented with LSD post hoc test was used to compare between more than two dependent groups of normally distributed variables while Friedman's test ranks test was used for non-normally distributed variables. Pearson's and Spearman's correlation coefficient were used for correlating normal and non-parametric variables respectively. Regression analysis using the stepwise method was used to identify the potential independent predictors for coronary calcium score. P value <0.05 was significant, P value <0.001 was highly significant, and P value >0.05 was non-significant.

RESULTS

As regards the ABO system of blood grouping, 50 patients were group A, 32 group B, 26 group O and 20 group AB. The study group was then divided into three groups according to coronary artery calcium score (CACS); (group 1: CACS =0-99, group 2: CACS = 100-399 and group 3: CACS ≥400): There was a statistically significant difference between the three groups as regard hypertension (p= 0.003).Also, patients with blood group A had higher coronary calcium scores than the other blood groups and represented the highest proportion of the patients with coronary calcium ≥ 400, with a high statistically significant difference (p < 0.001) (Table 1). Otherwise, other variables either did not show statistically significant difference among groups or the patients were divided into too small groups to draw a reasonable statistical conclusion.One-way ANOVA test was performed to compare means of age, N/L ratio, LDL, calcium level, cardiac and coronary calcium scores among three groups, (Table 2). According to the result of the test, patients with higher coronary artery calcium were older, had higher levels of N/L ratio, had a higher cardiac calcium score (p<0.0001), and higher serum calcium level (p<0.001). The overall mean±SD of all study population as regards the age, N/L ratio, calcium level, cardiac and coronary calcium scores are shown in (Table 3).Post Hoc analysis showed a high statistically significant difference was between groups (1&2), (1&3) but not between (2&3) (p<0.0001). As regards N/L ratio, the difference between groups 1&2 was significant (p<0.05), between groups 1&3 is highly significant (p<0.0001), between 2&3 is not significant (p>0.05). As regards serum calcium levels, the

statistical differences between groups (1&3), (2&3) were significant (p<0.05), but between 1&2 was not significant (p>0.05). And as regards cardiac calcium score the statistical difference among all groups was highly significant (p<0.0001).By doing multivariate regression analysis of all parameters that showed a statistically significant difference with coronary calcium score which included age, neutrophil lymphocyte ratio, calcium level, and cardiac calcium score, it has been proved that the neutrophil lymphocyte ratio and cardiac calcium score were the only independent predictor for coronary calcium score (p =0.001 & <0.0001 respectively), (Table 4). There was a strong positive correlation between N/L ratio and CACS, (r= 0.433, p <0.0001) (Figure 2), and a strong positive correlation between cardiac calcium score and CACS, (r= 0.712, p <0.0001) (Figure 3).

Table (1): ABO system among groups according to coronary artery calcium score (CACS):

Blood Group	Group 1: CACS =0-99	Group 2: CACS = 100-399	Group 3: CACS ≥400	X^2	P
Blood Group A	14 (28%)	12 (24%)	24 (48%)		
Blood Group B	24 (75%)	4 (12.5%)	4 (12.5%)		
Blood Group O	20 (77%)	0 (0%)	6 (23%)		
Blood Group AB	16 (80%)	2 (10%)	2 (10%)		
	1	2	3	X^2	P
Blood Group A	14 (28%)	12 (24%)	24 (48%)	29	< 0.0001*
Blood Group Non A	60 (77%)	6 (8%)	12 (33%)		

*P <0.0001 highly significant. CACS (coronary artery calcium score).

Table (2): One-way ANOVA test to compare the three groups according to age, N/L ratio, LDL, calcium, and cardiac calcium scores.

Variable	Group 1: CACS =0-99	Group 2: CACS = 100-399	Group 3: CACS ≥400	F	P
Age	50.7±9.7	60.44±10.8	62.4±8.7	20.99	<0.0001*
N/L ratio	1.54±0.44	1.90±0.31	2.03±0.6	14.41	<0.0001*
LDL	108.84±29.9	97.8±10.3	109.50±26.9	1.34	0.266
Ca level	8.82±0.8	8.7±0.8	9.29±0.7	7.13	0.001*
Cardiac Ca score	1.49±1.1	3.44±1.0	5.22±0.8	167.61	<0.0001*

*P <0.0001 highly significant. P<0.05 significant. CACS (coronary artery calcium score). N/L ratio (neutrophil/lymphocyte ratio). Ca (calcium).

Table (3): Age, N/L ratio, LDL, calcium level, cardiac and coronary calcium scores of the study population described as mean ± SD:

Parameter	Mean	Standard deviation
Age	55.3	11
N/L ratio	1.72	0.52
LDL-C	107.5	27.25
Calcium level	8.9	0.8
Cardiac calcium score	2.8	1.9
Coronary calcium score	1082.14	614.28

N/L ratio (neutrophil/lymphocyte ratio0. LDL-C (low density lipoprotein cholesterol).

Table (4): Multivariate regression analysis for parameter affecting coronary artery calcium score.

Variable	Odd's ratio	P
Age	1.45	0.150
N/L ratio	3.56	0.001*
Calcium level	1.38	0.170
Cardiac calcium score	7.76	< 0.0001*

*P <0.0001 highly significant. P<0.05 significant. N/L ratio (neutrophil/lymphocyte ratio).

Figure (1): Echo picture of papillary muscle calcification.

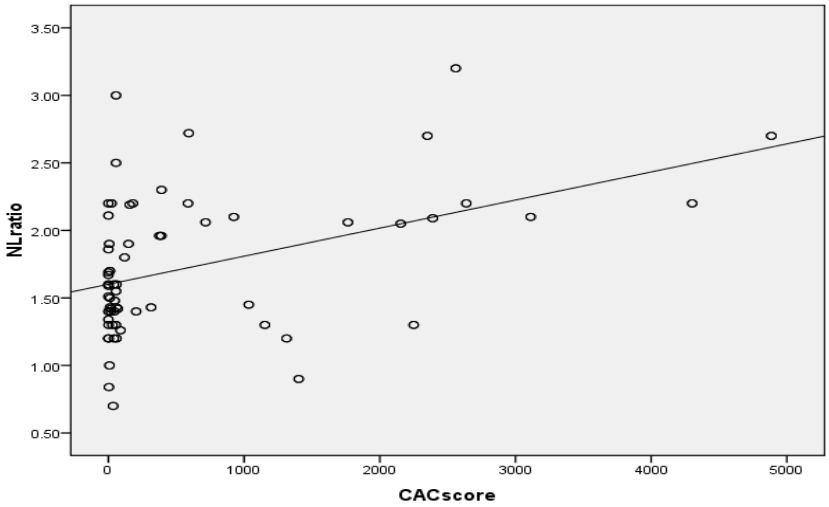

Figure (2): Correlation between N/L ratio and coronary artery calcium score (r= 0.433, p <0.0001).

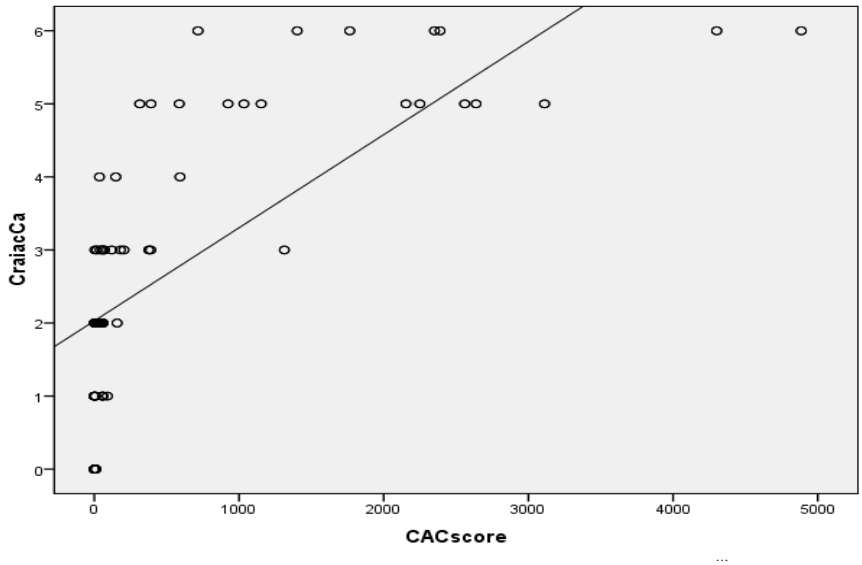

Figure (3): Correlation between cardiac calcium score and coronary artery calcium score (r= 0.712, p <0.0001).

DISCUSSION

In this study we evaluated the relationship between total cardiac calcium (Ca) detected by echocardiography, ABO system, neutrophil/lymphocyte ratio (NLR) and the severity of coronary artery calcium detected by multislice CT (MSCT) among patients presenting with chest pain with low to intermediate pre-test probability for coronary artery disease (CAD), aiming to decrease the burden cost and radiation and contrast exposure of multislice CT on patient, improve outcomes and decrease mortality rate of cardiovascular patients.

The risk of future coronary heart disease is increased as the total amount of calcium in the coronary arteries is increased [11]**.** The study population consisted of 128 patients, 118 (92.2%) were males with mean age of 55.3 ±11 years and mean coronary calcium score 1082.14 ±614.28. Regarding ABO, 39% of the patients were A, 25% were B, and 20.4% were O.

Since ABO blood groups and coronary artery calcium (CAC) had a close relation to atherosclerosis, the relationship needed more study. Although there are no available data regarding this relationship, the association of ABO blood groups with endothelial function has been studied.In our study, patients with blood group A tend to have higher coronary calcium scores than the other blood groups & represented the highest proportion of the patients with coronary calcium ≥ 400. However, Biswas et al. [12] found that AB blood group had decreased risk of CAD in healthy controls, while O blood group had increased risk of CAD. Teng et al [13] suggested that ABO blood group antigens may influence concentrations of inflammatory factors and lipid profiles, resulting in the incidence of cardiovascular disease. Therefore, they concluded that inflammation and dyslipidemia might be possible mechanisms to know the relation between ABO blood groups and CAC.In our study, we found that there was a highly significant difference in NLR as patients' group with CACS ≥ 400 were significantly higher in NLR compared to other patients' groups with CACS < 400. In consistence with our findings, Neves et al. [14] reported that calcium score, obtained from a standard echocardiographic examination was strongly correlated with CACS and it nicely predicts the presence of severe coronary calcification.Our results demonstrated that neutrophil lymphocyte ratio and cardiac calcium score were found to be independent predictors for coronary calcium score in the multivariate regression analysis. Other studies also found an independent correlation between the NLR and the CACS [15]. Drechsler et al [16] found that neutrophils had an important role in the formation and rupture of atherosclerotic plaques, in addition to that the increased cholesterol level in blood causes neutrophilia. Nowadays, a ratio reflecting acute episode of inflammation (neutrophilia) and acute physiological stress (lymphopenia) has started. Gibson et al. [7] demonstrated that the NLR as a good marker of inflammation, and in acute coronary syndrome, there is decrease in lymphocytes and increase in neutrophil.

CONCLUSIONS

Diagnosis of coronary artery disease can be done by MSCT, which is a reliable, and less-invasive method instead of invasive coronary angiography. Also, NLR, cardiac calcium score and blood group A were found to be independent predictors for coronary calcium score.

Conflicts of Interest: Nothing to declare.

Financial Disclosures: Nothing to declare.

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