Original Article

Prevalence of Coronary Artery Disease in Patients with Zero Calcium Score on Coronary CT Angiography

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ABSTRACT

Objective: To determine the frequency of coronary artery disease in suspected patients with zero calcium score on coronary CT angiography.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Cardiology, Ch. Pervaiz Elahi Institute of Cardiology, Multan 1-Aug-2017 to 31-Jan-2018.

Materials and Methods: A total number of 86 patients having age 18 to 65 years, with suspicion of coronary artery disease and having zero calcium score on CT angiography were included in this study. The data was analyzed through statistical analysis software (SPSS version 21.0). Qualitative variables e.g. gender, diabetes and presence of CAD was presented as frequency and percentage. Stratification of confounder variables was done. Post-stratification Chi-square test was applied.

Results: Mean age of study patients was 49.43±8.16 years. There were 71 (82.56%) male patients and 15 (17.44%) female patients. There were 37 (43.02%) diabetic patients. Coronary artery disease was diagnosed in 5 (5.81%) patients. while remaining 81 (94.19%) patients were having normal coronary arteries. There was no effect of age and gender on frequency of CAD. In diabetic patients, CAD was diagnosed in 4 patients and in only 1 patient without diabetes mellitus. Frequency of CAD was high in diabetics but statistically insignificant.

Conclusion: In our study, frequency of coronary artery disease in patients with zero calcium score on CT angiography was 5.81%.

Key Words: Coronary artery disease, coronary artery calcium score, CT angiography.

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INTRODUCTION

Coronary artery disease (CAD) is one of serious disease which has attained epidemic proportions and affecting people globally. Coronary artery disease (CAD) with an estimated 17.5million deaths worldwide in 2005 is a leading cause of mortality from non-communicable diseases.[1, 2]Cardiovascular disease is the most common cause of death in the UK, responsible for 238,000 deaths in 2002 or 39 % of all deaths. [3]. Countries with low-to-middle income share more than 80% of the global disease burden.[4] South Asians are among the highest susceptibility population with an alarmingly high incidence rate at younger age.[5]

Although there are no absolute figures available as yet on morbidity and mortality related to CAD in Pakistan, the anticipated prevalence is inordinately high and severe.[6] According to the National Health Survey, every third Pakistani over the age of 40 years is hypertensive and 20%population of ≥60 years of age is facing hypercholesterolemia.[7]

The disease has been controlled in the west through pharmacotherapy, proper medical treatment and life style modification,[8] however coronary artery disease (CAD) overall impact is greater in South Asians especially in Indo-Pakistani population and it affects the younger productive population of this continent[9] as well as has become one of the death leading cause. It includes comparatively lesser incidence of traditional risk factors and at the same time relatively higher prevalence of newer risk factors.[10,11]

Previous literature reported that in low and middle income countries, three fourth of global death is due to coronary artery disease. The World Health Organization (WHO) published its report and estimates that by 2020 the global number of CAD will rise from 7.1 in 2002 to 11.1 million.[12]

Coronary artery calcium (CAC) is present in only atherosclerotic arteries which helps to measure subclinical coronary artery disease .Coronary CT angiography helps to detect and quantify small amounts of CAC[(13)]. Electron beam chromatography-derived coronary artery calcium scores (CaSc) are directly

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associated with the number and severity of diseased vessels[14] However, hardly few studies of CaSc as a predictor of coronary artery disease have been conducted worldwide. Experts have concluded in their studies that a limited understanding exists regarding the utility of CAC as predictor of coronary artery disease. Larger data is needed to assess the clinical usefulness of CAC evaluations[15,16] Nevertheless, In previous literature a high variation from 2 to 32 % was reported in the incidence of obstructive CAD in patients with a CaSc of zero.[17]De Carvalho et al found 12.4% incidence of coronary artery disease in patients with zero CAC core.[18]

Recent studies have also shown that in patients with a CaSc of zero, obstructive CAD was found which was associated with increased cardiovascular events. Unfortunately no study has been reported in Pakistan and neighbor countries about the relationship of coronary artery disease (CAD) patients with zero calcium score on coronary artery CT angiography (CCTA). Although Pakistan reported higher prevalence of CAD and its risk factors.[19] The purpose of this study is to evaluate prevalence of coronary artery disease in patient with zero calcium score on coronary CT angiography. The results of this study will give us better estimates about the presence of CAD in suspected patients having zero CaSc on CCTA. Because CaSc is a potent marker of the presence or absence of CAD but in some cases it is not reliable and patients with zero CaSc are of having CAD. So this study will help us to get estimates that how many patients will be of having CAD.

MATERIALS AND METHODS

After informed consent eligible participants were selected who were referred from OPD for evaluation of possible CAD The research was initiated and data was only collected after approval from the Ethical and Scientific review committee, Ch. Pervaiz Elahi institute of cardiology, Multan. It was a Cross-sectional study and was conducted from 01-Aug-2017 to 31-Jan-2018. All Patient with suspicion of coronary artery disease with calcium score zero on CCTA, of either gender, age greater than 18 years of age and less than 65 and willing to give informed consent were included.

Patients with congenital heart disease, valvular heart disease, cardiomyopathy, cardiogenic shock ,previous Myocardial infarction and/or Coronary revasculari-zation, valvular or aortic surgery patient ,suspected acute coronary syndrome ,previous coronary artery bypass or stent implantation ,patient with known cognitive impairment, patients with acute or chronic kidney disease were excluded. The sample size calculated was 86.

Diagnosis of coronary artery disease was made on angiography reporting of the patients. All the angiographic procedures were performed by a senior cardiologist having a minimum of 5 years post-fellowship experience. I (the investigator) served assistant in all these procedures. Diagnosis of coronary artery disease was confirmed according to the findings given in operational definitions. Data regarding confounder variables e.g. diabetic history of the patients was also collected based on the previous history of patients.

The data was analyzed through statistical analysis software (SPSS version 21.0). Initially, the descriptive statistics was performed. The quantitative variables i.e. age was presented as mean ± SD. The descriptive variables i.e gender, diabetes and presence of coronary artery disease was measured and presented through frequency and percentages. Stratification of confounding variables e.g. age, gender and diabetes was done. Chi-square statistics was performed post-stratification. For all analysis P-value less than or equal to 0.05 was considered significant.

RESULTS

A total number of 86 patients were included in this study. Mean age of study patients was 49.43$\pm$8.16 years. The minimum age of study patients was 23 years and maximum age of study patients was 65 years (Table 4). There were more males as compared to the female patients. There were 71 (82.56%) male patients and 15 (17.44%) female patients in this study. Regarding diabetes mellitus, there were 37 (43.02%) diabetic patients and 49 (56.98%) non-diabetic patients in this study (Fig. 1).Coronary artery disease was diagnosed in 5 (5.81%) patients. while remaining 81 (94.19%) patients were having normal coronary arteries (Fig. 02).

Stratification of age of patients was performed. In patients having age <50 years, CAD was diagnosed in 2 patients and in patients having age $\geq$ 50 years, CAD was diagnosed in 3 patients. This difference in frequency of CAD in patients of different age groups was not statistically significant (p-value 0.68) [Table 5].

Stratification of gender was performed. In male patients, CAD was diagnosed in 3 patients. While in female patients CAD was diagnosed in 2 patients. This difference was not statistically significant (p-value 0.17) [Table 1].

Table No.1: Stratification of Gender of Patients.

Gender	Coronary Artery Disease		P-value
	Yes	No	
Male	3	68	0.17
Female	2	13	

Stratification of diabetes mellitus was also performed. In diabetic patients, CAD was diagnosed in 4 patients and in only 1 patient without diabetes mellitus. Frequency of CAD was high in diabetic patients as compared to the non-diabetic patients but this

difference was not statistically significant (p-value 0.08).

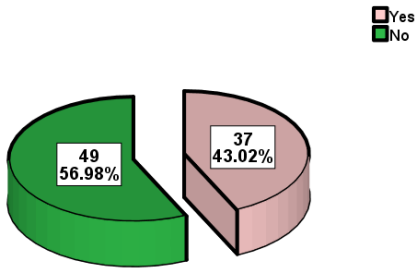

Figure No.1: Frequency of Diabetes Mellitus.

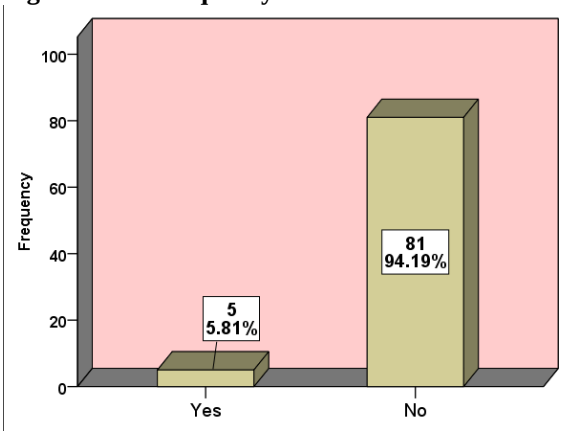

Figure No.2: Frequency of Coronary Artery Disease.

DISCUSSION

In this study, we found a low prevalence of coronary artery disease in patients with zero calcium score on CT angiography. The prevalence of coronary artery disease in patients with zero calcium score was 5.81% in our study. deCarvalho et al. found a very low prevalence of obstructive CAD (1.6 %) in the subset with a CaSc of zero. When considering the degree of stenosis, only 0.6% had a stenosis [≥70%).[18]Rubinshtein et al. found 7.0% prevalence of coronary artery disease in patients having zero calcium score on CT angiography.[16]

The prevalence and clinical significance of obstructive CAD on coronary CT angiography among patients with a calcium score of zero has been evaluated in several cohorts, but with conflicting results, depending on the population included. Data from Nieman et al.[10] the CONFIRM registry,[21] and Akram et al.[22] are in line with our results, with a low prevalence of obstructive CAD (2%, 3.5%, and 8.2 %, respectively).

In contrast, in the work of Harberlet al.[23] and Gottlieb et al[24], there was a high prevalence of CAD (32% and 19.4 %, respectively), which can be related to the fact that these studies included patients referred for conventional angiography, including patients with possible acute coronary syndromes.

There is no doubt that CTCA provides comprehensive assessment of CAD with demonstration of plaques with quantification of stenosis, thus providing greater accuracy for diagnosis and prognosis. CTCS, on the other hand is a relatively crude technique, but is much simpler to perform without the need for contrast and beta-blockers, as well requiring less time for reporting. The 2010 NICE chest pain guideline[26] had recommended CTCS as the initial test to rule out coronary disease in low-risk individuals, but the recently updated guidance advises CTCA as the first-line investigation for all patients with angina, independently of CTCS.[27] Our data suggest that even amongst patients with typical or atypical angina, as many as 50% will have a ZCS with an excellent prognosis.

Our data suggests that, although the absence of calcium does not exclude the presence of CAD, it was associated with a very low probability of obstructive lesions. This was especially true in cases of low and intermediate pretest CAD probability, as in the study from Werkhovenet al.[28] in which the prevalence of obstructive CAD, in the absence of calcium, was only 3.4 and 3.8 % in patients with low and intermediate pretest CAD probability, respectively. This is in line with the excellent prognosis that has been demonstrated for patients with a calcium score of zero.[29,30]

In this population of stable patients referred for evaluation of possible CAD that had a calcium score of zero, about 5.81% had obstructive CAD (≥50% stenosis). Therefore, and despite the known high negative predictive value of CaSc for coronary events, the absence of coronary artery calcification does not exclude the presence of coronary artery disease, but the prevalence of obstructive disease is very low.

CONCLUSION

In our study, frequency of coronary artery disease in patients with zero calcium score on CT angiography was 5.81%.

Author's Contribution:

Concept & Design of Study:	Tariq Abbas
Drafting:	Abubakr Ali Saad
Data Analysis:	Raheel Iqbal, Muhammad Amin
Revisiting Critically:	Tariq Abbas, Abubakr Ali Saad
Final Approval of version:	Tariq Abbas

Conflict of Interest: The study has no conflict of interest to declare by any author.

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