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PREVALENCE OF FLUOROSCOPIC CALCIUM IN PATIENTS WITH CORONARY ARTERY DISEASE AND ITS ASSOCIATION WITH VARIOUS RISK FACTORS

Clinical Research

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ABSTRACT

Background: Coronary artery calcification (CAC) is a predictor of coronary artery disease (CAD) and closely related to the predictor of future cardiac events.

Objective: To assess the prevalence of fluoroscopic calcium in patients with CAD and to determine its association with various coronary risk factors.

Methods: The CAC measurement was conducted by visual identification during fluoroscopy. The study subjects were allocated into two group, according to the presence (+) or absence (-) of CAC. The Syntax score was calculated from the results of coronary angiography.

Results: Out of 846 patients, 236 patients represented CAC(+). The mean±SD age of the total study patients was 61±5.8 years with a male preponderance of 415(71.2%). Systolic/diastolic blood pressure was 132±24/80±13mm Hg in CAC(+) patients. The present study finding elucidated that diabetes (Adjusted Odds Ratio [OR], 8.52, 95% confidence interval [CI], 6.2-12.5, P=0.02), hypertension (OR, 5.52, 95% CI, 3.2-8.4, P=0.03), and Syntax score (OR, 12.40, 95% CI, 8.82-16.56; P=0.001) were more prevalent in CAC(+) group compared to CAC(-) group. Those patients with family history of CAD had significant CAC as compared to those without CAD family history (OR, 3.32, 95% CI, 2.8-5.3, P=0.04).

Conclusion: The prevalence of CAD among diabetic and hypertensive patients undergoing coronary calcification is significant. Therefore, screening of CAC should be considered in such patients for the better identify of their risk of cardiovascular complications.

KEYWORDS

Coronary artery calcification; coronary artery disease; Fluoroscopy; Syntax score

Introduction

Cardiovascular disease is the leading cause of morbidity and mortality globally. Even previous asymptomatic subjects of coronary artery disease (CAD) develops severe cardiac event. Hence, Cardiologists were interested in developing a screening method to define the risk factor of the primary cardiac event. Coronary artery calcification (CAC) is the accumulation of calcium in atherosclerotic plaques, and serves an indicator of coronary atherosclerosis (Burke et al., 2001; Rifkin, Parisi, & Folland, 1979; Wexler et al., 1996). It is also a subclinical predictor tool of future coronary events (Detrano et al.). It can be detected by fluoroscopy, multi-slice computed tomography (CT), and intravascular sonography (Erdogan, Altin, & Altunkan).

Risk factors for CAC are similar to those for CAD, and it includes male sex, older age, chronic kidney disease, smoking, DM, hypertension, peripheral arterial disease, family history of CAD, etc (Erdogan et al.). A growing number of evidence have been emerged for identifying the essential application of CAC in the assessment of cardiac event risk differentiation (Chen et al.; Liu et al.). The use of conventional coronary angiography is the globally acceptable method in diagnosing CAD due to its better temporal resolution, thus facilitating the accurate measurement of the degree of coronary stenosis. However, this practice remains invasive, inconvenient and expensive for patients. Conversely, the CAC quantification is most commonly accepted criteria using fluoroscopy, which is widely used in a routine clinical setting as a noninvasive method.

A large body of evidence point towards the association between diabetes mellitus, dyslipidemia, obesity, hypertension, family history of coronary artery disease, or smoking and quantification of 10-year coronary event risk events but their relationship with CAC presence has not been fully determined in symptomatic patients. The European Calcific Coronary Artery Disease (EURO-CCAD) findings support an association between flow-limiting lesions prevalence and severity of the CAC score (Henein et al., 2013; Nicoll et al., 2016). Also, there were no studies in the literature to be explored any association exists between CAC and either the severity or extent of CAD.

The objective of the present study was to find out the prevalence of fluoroscopic calcium in patients with CAD and its association with various risk factors.

Material and Method

Study design and patient population

From January 2012 to May 2013, a total of 846 patients were recruited at department of Cardiology, Government T. D. Medical College, Alappuzha, Kerala, India. All patients provided written informed consent before enrollment, and the study protocol was approved by the local ethical committee. The patient characteristics and baseline data were recorded. A detailed physical assessment was performed including past medical history. Cardiovascular risk factors were recorded. Hypertension was categorized based on their blood pressure exceeding 140/90 mmHg in at least three measurements, or identified based on previous medical records.

All patients underwent coronary angiography and allocated into two groups, according to the presence or absence of CAC. The CAC(+) group consisted of 236 patients with mean age of 61±5.8 years. While, the CAC(–) group consisted of 610 patients with mean age of 59±5.8 years. The severity and extent of coronary atherosclerosis were calculated using Syntax score. The exclusion criteria included the unsatisfactory visualization of the coronary arteries, calcification of the aortic valve or mitral annuli, constrictive pericardial disease, and chronic kidney disease.

Patient Catheterization and Determining CAC Calcification

All patients were catheterized percutaneously via either the right femoral artery or the right radial artery using the standard technique. Patients were screened in two orthogonal views to detect CAC before contrast injection. Siemens Axiom Artis Zee floorVC14 I machine was used for fluoroscopy and angiogram. During clinical procedures, two experienced cardiologists interpreted each coronary angiogram.

The synergy between percutaneous coronary intervention with Taxus and cardiac surgery (Syntax) score was calculated based on the American Heart Association classification of the coronary artery tree modified for the arterial revascularization therapy study (Austen et al., 1975; Serruys et al., 1999; Sianos et al., 2005). The Syntax score was applied to quantify the characteristic of coronary vasculature concerning the location, number, and identified the complexity of

angiographically obstructive lesions. The Syntax score was calculated using an online available website (www.syntaxscore.com) and recorded all morphological features of each lesion. A lesion is defined as significant if it causes ≥ 50% luminal obstruction by visual estimation in vessels with a diameter ≥1.5 mm. To aid in the generation of Syntax scores, at least 5 different planes of view were obtained for each patient (right anterior oblique caudal, right anterior oblique cranial, left anterior oblique cranial, left anterior oblique caudal, and anteroposterior cranial).

Statistical Analysis

All data were analyzed using SPSS version 16 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as means±SD, and categorical variables as percentages. The two groups (CAC +/-) were compared by unpaired Student's *t*-tests for continuous variables and by Pearson's $\chi 2$ analysis for categorical variables. Binary logistic regression analysis was performed to identify independent predictors of significant CAC. For all statistical analyses, a P value of < 0.05 was considered statistically significant.

Results

Baseline, lesion and procedural characteristics

The clinical characteristics, laboratory variables and the Syntax scores for the 610 subjects with CAC(–) and the 236 CAC(+) patients are presented in Table 1. Gender, smokers, systolic and diastolic BP, urea and creatinine levels were not significantly different between the CAC(+) and CAC(–) groups. There was a significant association between diabetes mellitus, hypertension, family history of CAD patients and low high-density lipoprotein (HDL) levels with CAC. The patient with diabetes was seen more frequently (44% vs. 25%; P=0.002) in CAC(+) group. Hypertension was more common among the CAC(+) than CAC(-) group (44% vs. 38%, P=0.002). Also CAC(+) group had a higher mean Syntax score compared to CAC(–) group (25±5.2 Vs 12±5.2, P=0.001). The levels of blood urea, creatinine, total and low-density lipoprotein cholesterol were similar in the two groups, but level of HDL cholesterol (40 mg/dl vs. 48 mg/dl; P< 0.05) was significantly lower in the CAC(+) group than in the CAC(–).

Table 1: Baseline clinical and laboratory characteristics in subjects with coronary artery calcification CAC(+) and without coronary artery calcification CAC(–)

Clinical and Hemodynamic Data	CAC(-) (n= 610)	CAC(+) (n= 236)	Value of p
Age (years)	59±6.7	61±5.8	0.123
Male (%)	415(68%)	168(71.18%)	0.134
Systolic BP (mm Hg)	132±24	136±28	0.154
Diastolic BP (mm Hg)	80±13	84±15	0.140
Diabetes Mellitus (%)	152(25%)	104(44%)	0.002
Hypertension (%)	238(38%)	103(44%)	0.030
Dyslipidemia (%)	177(29%)	80(34%)	0.08
Cigarette smoking (%)	214(35%)	90(38%)	0.125
Family history of CAD (%)	49(8%)	40(17%)	0.027
Total Syntax score	12±4.3	25±5.2	0.001
Blood urea (mg/dl)	31±15.6	35±18.7	0.122
Serum creatinine (mg/dl)	1.1±0.7	1.2±0.6	0.234
Random blood sugar (mg/dl)	138±46	143±62	0.134
Triglyceride (mg/dl)	195±39	199±49	0.165
LDL cholesterol (mg/dl)	125±38	130±38	0.245
HDL cholesterol (mg/dl)	48±14	40±10	0.034
Total cholesterol (mg/dl)	164±68	166±67	0.232

LDL: low-density lipoprotein, HDL: high-density lipoprotein

Finally, the logistic regression analysis identified diabetes mellitus (OR, 8.52; 95%CI, 6.2-12.5; P=0.020), hypertension (OR, 5.52; 95%CI, 3.2-8.40; P=0.032), family history of CAD (OR, 3.32; 95%CI, 2.8-5.3; P=0.040), and Syntax score (OR, 12.40; 95%CI, 8.82-16.56; P=0.001) as independent predictors of the CAC phenomenon (Table 2).

Table 2: Binary logistic regression analysis to identify predictors of coronary artery calcification (CAC)

Parameter	Adjusted Odds Ratio	95% CI Of Adjusted Odds Ratio	p Value
Diabetes Mellitus	8.52	6.2-12.5	0.020
Hypertension	5.52	3.2-8.40	0.032
Family history of CAD	3.32	2.8-5.3	0.040
Syntax score	12.4	8.82-16.56	0.001

Discussion

Coronary artery calcification occurs shortly after fatty streak formation (Stary, 1990), a finding that should be detectable by microscopic methods (Doherty & Detrano, 1994). The CAC consists of small clumping of crystalline calcium amid a core of lipid particles in the atherosclerotic plaque (Doherty & Detrano, 1994; Stary, 1990; Stary et al., 1995). Thus, it has become well known that potentiating of active calcification in the coronary arteries is a biomarker of atherosclerosis, and that CAC does not exist on normal vessel walls (O'Rourke et al., 2000). However, a clinically more relevant point pertains to the severity and extent of atherosclerosis. Consequently, we focused on whether coronary calcification is also an indicator of the severity and extent of atherosclerosis, as well as its presence with various risk factors. Screening for evidence of CAC is done to evaluate patients with chest pain, to screen asymptomatic subjects, and to follow the progression of coronary atherosclerosis. Coronary artery calcification can be identified using either fluoroscopy or computed tomography. Of these, fluoroscopy is the more frequently used technique. The sensitivity of fluoroscopy in determining significant stenosis (greater than 50% occlusion) in patients with CAC has ranged from 40% to 79%, and its specificity from 52% to 95% (Detrano & Froelicher, 1987; Detrano, Salcedo, Hobbs, & Yiannikas, 1986; Wexler et al., 1996).

The results of this study provide several new insights. In this contest, our results revealed that there was no association between the presence of CAC and age, gender, cigarette smoking. However, there was a strong association between CAC and other CAD risk factors such as diabetic mellitus, hypertension, HDL cholesterol profile, or a family history of CAD.

In contrast to these data, Fathala et al., 2017 have represented that a strong association between CAC score and age, male sex and diabetes mellitus, whereas no association between CAC score and hypertension, family history of CAD, obesity, hypercholesterolemia, or smoking determined by single-photon emission computed tomography (Fathala et al., 2017). In agreement with the study by Nicoll et al., diabetes was significantly associated with the presence of CAC (Nicoll et al., 2016).

We identified a significant difference between diabetic and non-diabetic patients in terms of CAC. Next finding of our study was that the frequency of coronary calcification was significantly higher in hypertensive patients. In two previous studies, coronary calcification was found to be associated with hypertension, but the incidence observed in both studies were chronic renal failure patients enrolled, in whom widespread calcification is not an unusual finding (Austen et al., 1975; Megnien, Simon, Lemariey, Plainfosse, & Levenson, 1996). In the present study, patients have family history of CAD elucidated significant positive CAC(+) than the negative CAC (17% vs. 8%, P=0.02). Serum levels of HDL cholesterol (40 mg/dl vs. 48 mg/dl; P< 0.05) were significantly lower in the CAC(+) group than in the CAC(–).

Finally perhaps the most important and pioneering finding of this study pertained to the Syntax score, a known measure of both the severity and extent of coronary artery disease. The CAC(+) group had a higher Syntax score as compared to CAC(-) group (25 vs 12, P=0.001).

Moreover, the frequency of coronary calcification was no different in smokers compared to non-smokers. Also, there was no gender effect, the calcification ratio being no different between males and females. In terms of dyslipidemia, the results of some studies suggested that higher electron beam computed tomography (ECBT) CAC scores observe in higher LDL cholesterol patients associated with lower HDL-Cholesterol (Orakzai, Nasir, Blaha, Blumenthal, & Raggi, 2009). In our study, Total cholesterol and LDL levels were elevated in CAC(+) patients, but it was not significant. HDL cholesterol was significantly lower in CAC(+) patients compared to CAC(-) patients.

Our analysis has shown that the fluoroscopic detection of CAC may predict CV risk event in patient. In conclusion, our results emphasized that the hypertension, HDL, diabetes mellitus, family history of CAD and Syntax score (the extensiveness of coronary artery disease) is an independently associated with the presence of CAC. Clearly, the

usefulness and application of this relationship warrant further clinical investigation.

Limitations

The evaluation of coronary artery calcium was conducted in a single center. Detection of CAC via fluoroscopy is a less sensitive method than computed tomography. Despite of 846 enrolled patients, the present study may not necessarily provide data reflecting overall tendencies in Indian individuals.

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