Research Article

Prediction of Cardiovascular Events in Patients with Isolated Coronary Artery Ectasia

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Abstract

Background: Coronary artery ectasia is abnormal dilatation of a segment of coronary artery to 1.5 times or more the size of adjacent normal segment, in patients with CAE the adverse outcomes could be anticipated from their risk profiles using risk scoring systems like metabolic and Framingham risk scoring systems.

Objective: to determine the risk factors and predictors of adverse cardiovascular events in patients with coronary artery ectasia without obstructive CAD using metabolic syndrome risk score and Framingham risk score.

Methods: The study was conducted on 187 patients, 36 patients with angiographic evidence of isolated coronary artery ectasia and 151 controls. All patients were subjected to detailed history, physical examination, laboratory investigations, electrocardiography, conventional echocardiography, diagnostic coronary angiography and follow up by metabolic, Framingham risk scores and TIMI flow.

Results: We used M$S and FRS to stratify the risk of all the patients. However, none of them showed any significant difference between the 2 groups. However, in correlating between these different scores and the different ectatic segments in number and sizes; only TIMI flow had the significant correlation (P <0.001). TIMI flow was the main significant variable when correlating to the incidence of cardiovascular events (P <0.001). However, FRS and M$S had no significant correlation to it (P 0.6)

Conclusion: TIMI flow was the main significant predictor of cardiovascular events in patients with coronary artery ectasia however, FRS and M$S had no role in prediction or risk stratification in CAE patients.

Keywords: Coronary artery ectasia; FRS; MSS; TIMI flow

Introduction

Coronary Artery Ectasia (CAE) is the abnormal dilatation of a segment of coronary artery to 1.5 times or more the size of adjacent normal segment of the artery. The incidence of coronary artery ectasia has been reported to be 0.3 to 5.3% of patients undergoing coronary angiography [1]. Twenty to 30% of cases of coronary ectasia are considered congenital and the others are acquired. Of the acquired cases, 50% are attributed to atherosclerosis while 10% to 20% are associated with inflammatory and connective tissue diseases (like Ehlers-Danlos syndrome, Kawasaki disease and scleroderma), syphilis, and bacterial infections [2].

Because CAE renders patients to higher risk of myocardial ischemia irrespective of the extent of stenosis, more studies characterizing this understudied disease entity are necessary to further improve management. We hypothesize that the cardiac events outcomes in patients with coronary artery ectasia could be predicted [3]. Framingham Risk Scoring System (FRS) and metabolic syndrome risk score are also a simple and feasible methods that can be used for prediction of obstructive coronary artery disease in patients with coronary artery ectasia and also in the detection of its severity [4,5]. Previous studies founded non-significant correlation between CAE group and control group as regarding criteria of metabolic syndrome risk score; DM, HTN, TG and HDL [6].

Framingham risk score have no relation with CAE, it only predicts severity of CAD, the hazard ratios remained elevated on adjusting for Framingham Risk Score, 2.9 (2.3 to 3.7) for men and 3.0 (2.0 to 4.4) for women. It was associated with approximately twice the 10-year total mortality, cardiovascular mortality and major coronary event rate compared with the overall rate in each Framingham category [7]. Some researches stated that, using the TIMI frame count method, patients with CAE in the left anterior descending and left circumflex arteries had significantly lower flow velocity than control patients [8].

We aimed to determine the risk factors and predictors of adverse cardiovascular events in patients with coronary artery ectasia without obstructive CAD using metabolic syndrome risk score and Framingham risk score.

Material and Methods

Patient Population

This study was study conducted on a convenient sample of 187 patients admitted at Menoufia University Hospital with angiographic evidence of isolated coronary artery ectasia. The patients were classified into 2 groups according to CA result into group I, 36 patients with coronary artery ectasia and 151 subjects represents control group II matched for age and sex. This study was done between September 2019 to March 2020. Sample was calculated to be 187 patients (151 patients as control group and 36 patients as ectasia group) using open EPI program with test power 80%, CI 95%.

The study protocol was formally reviewed and approved by the ethics committee for human research at Menoufia Faculty of Medicine with informed consent obtained from all participants prior to commencement of the study after thorough explanation of the study objectives.

Inclusion Criteria

Adult male or female >18 years' old who underwent elective coronary angiography revealing isolated coronary artery ectasia in the absence of obstructive coronary artery lesions and without evidence of prior acute coronary syndrome.

Exclusion Criteria

Patients with, significant valvular diseases more than mild, non-ectatic coronary arteries, pericardial diseases, significant atrial or ventricular arrhythmias other than sinus rhythm, congenital heart diseases, cardiomyopathy heart disease and previous acute coronary syndrome prior to the first coronary angiography were excluded from our study. After exclusion of non-responders, drop out participants and those with exclusion criteria, 187 subjects completed the study (this number was considered suitable enough sample for statistical analysis with significant results and correlations).

Methods

All patients were subjected to detailed history, including CAD risk factors, physical examination, Electrocardiography (ECG) to detect ST segment and T wave abnormalities.

Blood samples were collected before cardiac catheterization. Patients fasted for >12 hours before cardiac catheterization. Blood was collected either from the antecubital vein or indwelling catheter into Two 3.2% trisodium citrate tube after discarding the initial 3 ml of blood. Serum was separated by centrifugation at 2000g for 15 minutes and stored at -70°C. Complete blood picture, serum creatinine, bleeding profile and total lipid profile were measured.

Conventional Echocardiography measure of the left ventricle geometry (LVEDD, LVESD, IVSd, PWDd and EF by m-Mode) and wall motion abnormalities using Philips Echo machine and the results were done blindly by two echo experts as recommended by American Society of Echocardiography [9].

Diagnostic coronary angiography was performed using the percutaneous femoral approach by Sildenger technique. Right and left coronary angiography were performed using multiple projections and analysis was done by professional interventionists who were blind to the cases. CAD severity was assessed by Gensini score as giving a severity score to each coronary stenosis.

The vessel diameter was calculated quantitatively in case of conflicts about CAE. The CAEs are defined based on the criteria used in the Coronary Artery Surgery Study. According to the angiographic definition used in that study, a vessel is considered to be ectasic when its diameter is ≥1.5 times that of the adjacent normal segment in segmental ectasia [10]. Isolated CAE was defined as CAE without significant coronary artery stenosis. The severity of isolated CAE was determined according to the Markis classification [11].

Finally, follow up by TIMI flow, M$S and Framingham risk score for major adverse cardiac events as follow:

1. Framingham Risk Scoring (FRS) is a multivariable risk factor algorithm that is used to calculate the 10-year risk of the major cardiovascular events. FRS uses these factors; age, sex, total cholesterol level, HDL level, systolic blood pressure, if on antihypertensive medications, presence of diabetes mellitus, smoking and any known cardiovascular disease.

2. Metabolic Syndrome Scoring (MSS) is a score from 0 to 5 which is calculated according to the presence of any of the following factors; (1) elevated waist circumference: ≥90 cm in men or ≥80 cm in women; (2) elevated TGs: ≥1.7 mmol/L (150 mg/dl) or on drug treatment for elevated TGs; (3) reduced HDL-C: <1.03mmol/L (40 mg/dl) in men or <1.3 mmol/L (50 mg/dl) in women or on drug treatment for reduced HDL-C; (4) elevated blood pressure: SBP ≥130 mmHg or DBP ≥85 mmHg or on antihypertensive drug treatment in a patient with

a history of hypertension; and (5) elevated fasting glucose: ≥5.6 mmol/L (100mg/dl) or on drug treatment for elevated glucose.

3. TIMI flow as follow, TIMI 0 - no perfusion, TIMI 1 - penetration without perfusion, TIMI 2 - partial perfusion and TIMI 3 - complete perfusion

Statistical Analysis

Statistical analysis was performed using Statistical Package for The Social Sciences Version 22 (IBM Corp., Armonk, NY, USA). Quantitative data are expressed as means and standard deviations. P-Value ≤ 0.05 was considered to indicate significance. Correlation analysis assesses the strength of association between two variables. Multiple logistic regression analysis was used to detect the associations between lipid profile and both maternal and neonatal complications.

Results

According to the angiographic data, these patients were divided into 2 groups; 36 patients with isolated coronary artery ectasia (CAE) and 151 patients with normal coronary artery matched for age and sex; Table 1.

	CAE (N=36)	Control (N=151)	P Value
Age	53.2±6.9	53.8±9.4	0.6
Gender:			
Male	26(71.4%)	73(48.3%)	0.01
Female	10(28.4%)	78(51.7%)	
Risk Profile:			
HTN	17(47.2%)	67(44.4%)	
DM	9(25%)	89(58.9%)	
Dyslipidemia	17(47.2%)	67(44.4%)	0.02
Smoking:			<0.001
Smokar	18(50%)	27(17.9%)	0.02
Ex-Smokar	2(5.6%)	15(9.9%)	<0.001
Non-Smokar	16(44.4%)	109(72.2%)	

Table 1: Demographic data and risk factors among the studied groups.

As depicted in Table 1, there were no significant differences between the CAE and the control groups in relation to age (53.2±6.9, 53.8±9.4 years old P value=0.6). Male gender is significantly more prevailed in CAE group than in control group [26(71.4%), 73(48.3%) respectively P value=0.01].

Hypertension, dyslipidemia and diabetes mellitus were more prevailed in the CAE group (17 47.2%, 17 47.2% and 20 55.6% respectively) than in the control group (67 44.4%, 67 44.4% and 42 27.8% with P value=0.02, <0.001, 0.02 respectively); (Table 1, Figure 1).
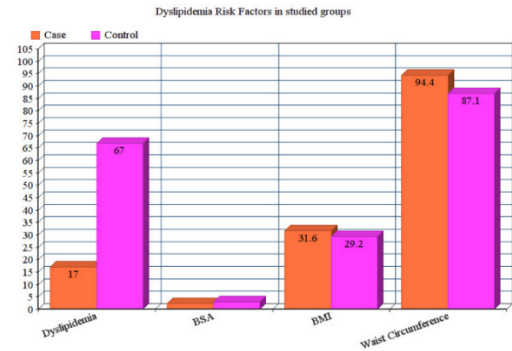
Figure 1: Risk factors among the studied groups.

We used M$S (Metabolic Syndrome Score) and FRS (Framingham Risk Score) to stratify the risk of all the patients. However, none of them showed any significant difference between the 2 groups; (Table 2).

	CAE (N=36)	Control (N=151)	P Value
Metabolic S Score (MSS):			
0	4(11.1%)	13(8.6%)	
1	10(27.8%)	23(15.2%)	
2	6(16.7%)	39(25.8%)	
3	4(11.1%)	33(21.9%)	0.2
4	9(25%)	21(13.9%)	
5	3(8.3%)	22(14.6%)	
Framingham Risk Score % (FRS)	13.1±12.1	10.3±9.2	0.12

Table 2: Risk stratification of the studied groups.

By analyzing the angiographic data of the patients; the prevalence of coronary artery ectasia as illustrated by MARKIS5 classification, showed that the affection of one vessel with ectasia (MARKIS5 class 4) is more likely to happen than that of the 3 vessels (MARKIS5 class 1) [18(50%) versus 12(33.3%) respectively]. There were variable sized of the different ectatic segments which varies from 3 to 6 mm, but the most common ectasia size was

4.00mm [16(44.4%)] and the second most common was 4.5mm [6(16.7%)]; (Figures 2,3).
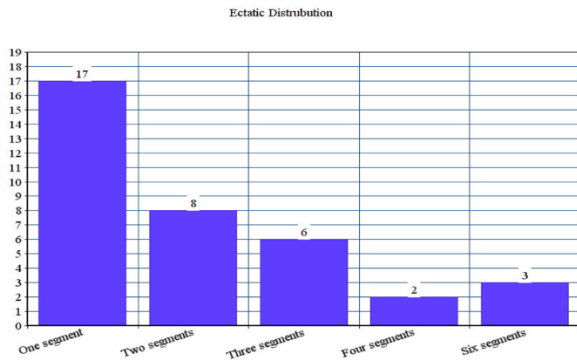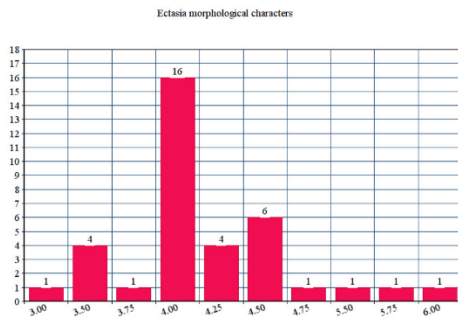

Figure 2: Prevalence of ectasia.

Figure 3: Ectasia morphological characters.

LAD artery was the most common artery to be affected with ectasia especially in the proximal segment [80.6%], then RCA in the second place especially in the proximal segment [38.9%], and

lastly comes LCX with equal incidence in both the proximal and the middle segments. (Table 3).

Affected Vessel	Number	Percentage %	Mean of ectatic size (mm)
LM	0	0	0
LAD	34	94.5	
Proximal	29	80.6	4.1
Mid	4	11.1	4.5
Distal	1	2.8	3.5
LCX	20	55.6	
Proximal	10	27.8	4.1
Mid	10	27.8	4.3
Distal	0	0	0
RCA	25	69.4	
Proximal	14	38.9	4.3
Mid	8	22.2	4.3
Distal	3	8.3	4.3

Table 3: Localization of ectasia in coronary arteries.

There was a significant correlation between TIMI flow and FRS (P value=<0.05), and also between FRS and M$S (P value=<0.001), but it was absent between M$S and TIMI flow. However, in correlating between these different scores and the different ectatic segments in number and mean sizes; only TIMI flow had the significant correlation (P value=<0.001). In addition, the FRS had a significant correlation with the highest ectatic segment sizes (P value=<0.05); (Tables 4, 5).

	M$S		FRS		TIMI grade	
	r	p	r	p	r	p
M$S	1	<0.001	0.61	<0.001	-0.14	**<0.42**
FRS	0.61	<0.001	1	<0.001	-0.35	<0.05
TIMI grade	-0.14	**<0.42**	-0.35	<0.05	1	<0.001

Table 4: Relation of angiographic data to FRS, MSS and TIMI grade.

	Highest ECT		Lowest ECT		Mean ECT		N. of ectatic segments	
	r	p	r	p	r	p	r	p
M$S	0.34	<0.05	0.32	**0.06**	0.24	**0.16**	0.24	**0.16**
FRS	-0.57	<0.001	-.053	<0.001	-0.49	0.004	-0.49	0.004
TIMI grade	-0.13	**0.46**	-0.8	**0.64**	-0.03	**0.88**	0.03	**0.88**

Table 5: Relation of ectasia to cardiovascular diseases risk scores.

There was a significant correlation between the two groups as regarding cardiovascular events with P value=<0.001. TIMI flow was the main significant variable when correlating to the incidence of cardiovascular events (P value=<0.001) as 4 patients with MACEs had TIMI flow 1, 11 had TIMI flow 2 and 1 had TIMI flow 3. However, FRS mean and SD was 10.4±9.2 and 14.4±14.6 between the two groups and had no significant correlation to it (P value=0.6) as well as M$S with (P value=0.6); (Table 6, Figure 4).

	Cardiovascular events		P value
	Yes (N.16)	No (N.171)	
Group			
Control	1(6.2%)	150(87.7%)	<0.001
CAE	15(93.8%)	21(12.3%)	
M$S			
0	2(12.5%)	15(8.8%)	
1	3(18.8%)	20(11.7%)	
2	5(31.3%)	38(22.2%)	
3	1(6.3%)	36(21.1%)	0.6
4	4(25%)	25(14.6%)	
5	1(6.3%)	37(21.6%)	
TIMI grade			
1	4(25%)	0	
2	11(68.8%)	5(2.9%)	<0.001
3	1(6.3%)	166(97.1%)	
FRS mean %	14.4±14.6	10.4±9.2	0.6

Table 6: Correlation between cardiovascular events and different scores.
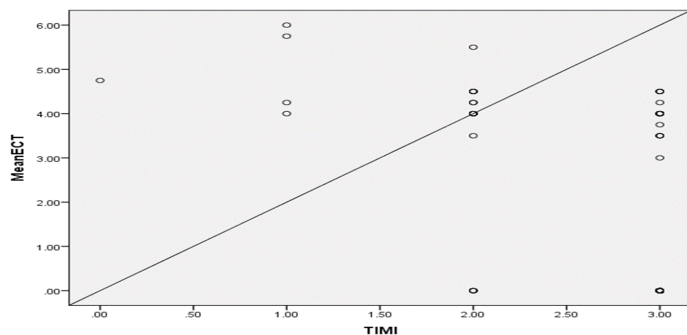
Figure 4: Relation between mean ectasia size and TIMI frame count.

TIMI flow is also significantly correlated to the type and the total number of cardiovascular events (P value=<0.001). There are 3 types of TIMI flow; TIMI 3 flow (18 cases) and only 1 of them had unstable angina, TIMI 2 flow (14 cases) and 8 of them had unstable angina, 2 had inferior STEMI, 13 had stroke, 2 had SVT and 3 had paroxysmal AF and TIMI 1 flow (4 cases) and all of them had unstable angina, 1 had anterior STEMI, 3 had inferior STEMI and3 had arrhythmias, (Table 7).

	TIMI grade flow			P Value
	1(N.4)	2(N.14)	3(N.18)	
Angina:				
Yes	4(100%)	8(57%)		<0.001
No	0	6(43%)		
MI				
No	0	12(86%)	18(100%)	
Anterior	1(25%)	0	0	<0.001
Inferior	3(75%)	2(14%)	0	
Stroke:				
Yes	0	13(92.9%)	0	**0.39**
No	4(100%)	1(7.1%)	18(100%)	
Arrhythmias				
None	1(25%)	9(64.3%)	18(100%)	
PAF	1(25%)	2(14.3%)	0	
PVCs	1(25%)	0	0	<0.001
SVT	0	3(21.4%)	0	
VT	1(25%)	0	0	
Total events number:				
0	0	4(28.8%)	17(94.4%)	
1	0	2(14.4%)	1(5.6%)	<0.001
2	1(25%)	6(42.4%)	0	
3	3(75%)	2(14.4%)	0	

Table 7: TIMI grade risk scoring in individual cardiovascular events.

Discussion

Coronary Artery Ectasia (CAE) has been defined as localized or diffuse non-obstructive lesions of the epicardial coronary arteries, with a luminal dilation ≥ 1.5 times of the normal adjacent

segments or vessel diameter. Isolated CAE has been defined as CAE without significant coronary artery stenosis. This abnormal dilatation of coronary arteries can cause angina pectoris and even myocardial infarction due to vasospasm, dissection or thrombus in patients without coronary artery disease [10]. Previous studies have demonstrated that inflammation, neurohormonal process and cardiovascular risk factors are associated with development of CAE. Although it has been suggested that CAE is a variant of O-CAD, a definitive link between atherosclerosis and ectasia has not been confirmed [12].

It is a prospective study that included 187 patients divided into two groups, 36 subject in the first group as CAE group and 151 in control group, we studying their demographic, clinical and angiographic data obtained from the follow up visits for an average of 33 months until December 2018. In our study as regarding demographic data there were no significant differences between the CAE and the control groups in relation to age (53.2±6.9, 53.8±9.4 years old P value=0.6). Male gender is significantly more prevailed in CAE group than in control group [26(71.4%), 73(48.3%) respectively P value=0.01].

This was concordant with a previous study by Puri, et al., which stated that the incidence of CAE worldwide was higher in men than in women (2.2:0.5%) [13]. As regarding age, our results are concordant with Sultana, et al. the result of study which showed that coronary ectasia was unrelated to age [14].

Our results stated that hypertension, dyslipidemia and diabetes mellitus were more prevailed in the CAE group (17 47.2%, 17 47.2% and 20 55.6% respectively) than in the control group (67 44.4%, 67 44.4% and 42 27.8% with P value=0.02, <0.001, 0.02 respectively). In concordance with our results as regarding hypertension, Adiloglu, et al. found it to be more frequent in ectatic patients [15]. However, Bakr, et al. stated that there was no significant difference between group of CAE and normal subjects as regards the prevalence of hypertension [16].

As regarding DM, Fujiwara, et al. and Androulakis et al reported significant independent association between CAE and diabetes mellitus. This was concordant with our study results [17,18]. Meanwhile for dyslipidemia, similar to our results, Gunes et al and Sudhir et al were concordant with our study [19,20]. However, reported that they did not show any relation between CAE and dyslipidemia [21]. Our results stated that CAE is more common in LAD then RCA, but Brunetti et al and Doi et al, stated that CAE is more common in RCA (93%) than left coronaries (36%) with MARKIS classification mean and SD 2.0±1.0 with total number of affected segments 2.1±1.2 and this was discordant to our results [6,22].

In our results there was a significant correlation between TIMI flow and FRS (P value=<0.05), and also between FRS and M$S (P value=<0.001), but it was absent between M$S and TIMI flow. However, in correlating between these different scores and the different ectatic segments in number and mean sizes; only TIMI flow had the significant correlation (P value=<0.001). In addition, the FRS had a significant correlation with the highest ectatic segment sizes (P value=<0.05)

We also founded that TIMI flow was the main significant variable when correlating to the incidence of cardiovascular events (P value=<0.001). However, FRS and M$S had no significant correlation to it (P value=0.6) Mavrogeni, et al. stated that controls had significantly higher peak flow velocity (p < 0.001) and lower TIMI frame count (p < 0.001) in both RCA and LAD, compared to patients with CAE. In patients with CAE, there was a negative correlation between flow velocity and TIMI frame count measurements (r = − 0.74, p < 0.001) [23].

A study by Senen, et al. stated that in patients with coronary artery ectasia, the TIMI frame count of the RCA was higher than that of the left anterior descending and left circumflex coronary artery (51 ± 17 vs. 42 ± 11 and 44 ± 15, respectively, P less than 0.05). They also have shown increased TIMI frame counts in patients with isolated coronary artery ectasia [24].

In concordance with our results, Doi, et al. founded non-significant correlation between CAE group and control group as regarding criteria of Metabolic syndrome risk score; DM, HTN, TG and HDL with p values 0.1, 0.2, 0.6 and 0.7 respectively [6] and also in previous studies –in concordance with our results- Framingham risk score have no relation with CAE, it only predicts severity of CAD [7].

Limitations

In our study, it was conducted on a small number of patients and the definition of coronary arteries disease was based on angiographic views y 2D X-ray, we did not use IVUS or FFR which may interfere with the decision of the interpretation of coronary angiography.

Conclusion

Patients with coronary artery ectasia the adverse outcomes could be anticipated from their risk profiles. So we founded that the application of the established risk scoring systems like TIMI risk score could anticipate the future risk profiles of these patients. Metabolic risk scoring system and Framingham risk scoring system has nothing to do in prediction of MACE in isolated CAE patients.

Recommendations

Further studies on a large number are more needed. We can use TIMI flow grades to predict cardiovascular events in patients with coronary artery ectasia.

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