

Acute Coronary Syndrome with Normal or Near-Normal Coronary Angiography: Prevalence and Clinical Outcomes among Yemeni Patients

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Abstract

Background: Nonobstructive acute coronary syndrome or acute coronary syndrome with normal or near-normal coronary angiography (ACSNONCA) occurs in 10% to 25% of patients undergoing coronary angiography and in up to 6% of patients with troponin-positive ACS. Prevalence of ACSNONCA and its clinical outcomes were not discussed in previous studies in Yemen.

Aim of Study: Our study aimed to compare demographic and clinical findings and prognosis in patients who have ACS with stenosis <50% (Group I) with patients who have ACS with critical obstructive disease, requiring percutaneous coronary intervention (Group II).

Patients and Methods: The total population (n=327) was divided according to the angiographic findings into: Group I (stenosis <50%) with 114 patients (14.8%) and Group II (stenosis >50%) with 213 patients (27.6%). During the period January 2010 through September 2015, patients were admitted at Algamhoria Teaching Hospital, Aden and undergone cardiac catheterization in Cardiac Surgery Center at Althawra Hospital, Sana'a.

Results: Group I Patients (stenosis <50%) were significantly younger were more likely to be female, younger, with fewer risk factors, compared to Group I Patients. We isolated and defined two subgroups within Group I: Group IA: Patients with normal angiograms (n=60, 52.6%) and Group IB patients with stenosis of 20-50% (n=54, 47.4%). Patients with stenosis of 20%-50% were relatively older males, with an increasing frequency of nondiabetic, with a history of chronic heavy chewing and with a worse prognosis, during long-term evaluation.

Follow-up data revealed that myocardial infarction was found in 1.8% of Group IA and in 5.2% of Group IB patients. Follow-up revealed no deaths in Group IA patients and two cardiac deaths (3.7%) in Group IB patients.

Conclusions: Prognosis of patients with nonobstructive stenosis was significantly better than that of patients with

critical obstructive stenosis. However, patients with stenosis of 20-50% had a worse prognosis than did those with normal coronary arteries.

Key Words: Acute coronary syndrome – Normal or near-normal coronary angiography.

Introduction

ACUTE coronary syndrome (ACS) with normal or near-normal coronary angiography (ACSNNOCA) is a frequently occurring condition with a heterogeneous pathogenesis [1]. This refers to patients, clinically presenting with acute typical anginal pain, atypical ECG and elevated ischemic markers but without significant coronary artery stenosis [2]. ACSNNOCA or nonobstructive ACS occurs in 10% to 25% of patients undergoing coronary angiography and in up to 6% of patients with troponin-positive ACS, including unstable angina (UA) or non-ST segment elevation myocardial infarction (NSTEMI) [3,4,5].

Although this problem is associated with adverse outcomes, its clinical importance remains underestimated [6]. Nonobstructive coronary lesions can be defined as atherosclerotic plaques that would not be expected to obstruct blood flow. Although such lesions have been characterized incorrectly as “insignificant” in the medical literature [7-10], yet different studies have noted that the majority of plaque ruptures and resultant myocardial infarctions (MIs) arise from nonobstructive plaques [4,11]. Previously, Scheffold and colleagues developed the concept of an insubstantial but malignant stenosis that has a pathogenesis and prognosis resembling that of ACS with coronary stenosis substantial enough to warrant PCI [12].

In Yemen, Khat chewing has been established as an independent risk factor for ACS. Different authors have reported a higher incidence of non-obstructive ACS among khat chewing [13,14]. The First and Second Gulf Registries of Acute Coronary Events (Gulf RACE-1 & 2) from 6 Middle Eastern countries including Yemen have recently shown that Khat chewing is associated with worse outcome in patients with acute coronary syndrome (ACS), compared with non-Khat users who are mainly from different Gulf populations [13,15]. More than 20 million people on the Arabian Peninsula and East Africa chew the fresh leaves and young stems from the plant khat for their euphoric properties [16]. Cathinone, cathine and norephedrine, alkaloids contained in the plant are structurally and functionally similar to amphetamine [17]. Cathinone is the principal active constituent of khat responsible for the stimulant effects that have led khat to be known as a 'natural amphetamine' [18]. Fresh khat is reported to contain an average of 36mg cathinone, 120mg cathine and 8mg norephedrine per 100g leaves [19]. Khat has direct effects on the cardiovascular system due to indirect sympathomimetic activity of cathinone [16], causing clear increases in heart rate and blood pressure in humans. An Ethiopian study showed that the prevalence of hypertension was significantly higher among Khat chewers, compared to Khat non-chewers [20].

During the last decade, studies have been focused on clinical, pharmacological and experimental topics, related to ACS and khat chewing. These included clinical and therapeutic outcomes of ACS patients, with a history of khat chewing, dose-response relationship between the quantity of khat chewed and risk of MI and the effect of drugs used for management of ACS in khat chewers [16,21,22]. However, few studies recently attempt to concentrate on relationship between khat chewing and angiographic findings. In a recent study, Al-Motarreb and others have assessed outcomes among MI patients, with history of khat chewing, who had nonobstructive lesion on angiography [21,22,23].

Pharmacodynamic and pathophysiological mechanisms of khat on the cardiovascular system are related to the actions of the most active khat alkaloids, cathinone and cathine. These amphetamine-like compounds are responsible for the sympathomimetic and catecholamine effects that play an essential role in the pathogenesis of Khat-induced cardiovascular complications, particularly ACS. These mechanisms include Khat induced tachycardia and arterial hypertension, Khat induced vasospasm and thrombogenicity, cathinone effect of catecholamine-induced platelet aggregation,

hypercoagulability and premature coronary atherosclerosis. Some of these effects, like tachycardia, arterial hypertension, coronary vasospasm and khat-induced thrombosis have been proved and supported by direct pharmacological experimental investigations [24-27]. However; a cathinone effect of catecholamine-induced platelet aggregation, hypercoagulability and premature coronary atherosclerosis were hypothesized by the fact that amphetamine-like compounds, similar to cathinone have been shown to induce similar effects [28,29,30].

In the current study, we aimed to explore the prevalence and clinical outcomes of ACS with normal or near-normal coronary angiography among Yemeni patients presenting with symptoms and signs of UA or NSTEMI.

Aim of study:

- To compare demographic and clinical findings and prognosis in patients who have ACS with stenosis less than 50% (Group I) with patients who have ACS with critical obstructive disease, requiring percutaneous coronary intervention (Group II).
- To evaluate the clinical outcomes in patients with stenosis less than 50% (Group I).

Patients and Methods

Study population:

A total of 773 ACS patients were recruited for the study during the period January 2010 through September 2015. Patients were admitted at Algamhoria Teaching Hospital, Aden and undergone cardiac catheterization in Cardiac Surgery Center at Althawra hospital, Sana'a.

The total population was divided according to the angiographic findings into:

- Group I: The study group included 114 patients (14.8%) with stenosis less than 50% and
- Group II: The control group included 213 patients (27.6%) with critical stenosis >50% (Fig. 1).

Within the first group (n=114), we defined two subgroups:

- Group IA: Patients with normal angiograms (n=60, 52.6%) and
- Group IB Patients with stenosis 20-50% (n=54, 47.4%).

Excluded patients:

Excluded patients from the study involved patients with ST-segment-elevation myocardial infarction (STEMI); false diagnosis of STEMI as

indicated by pacemaker rhythm or bundle-branch block upon electrocardiography (ECG); single vessel coronary disease; Takotsubo-like left ventricular cardiomyopathy); renal failure defined here as elevation of creatinine (>2.5mg/dl or >220 ~~µmol/L~~); infectious disease (clinical signs, C reactive protein > 100mg/L).

Electrocardiographic evaluation:

All ECGs were evaluated for ST-segment depression ($\geq 0.05\text{mV}$), Q waves, and T-wave inversion ($\geq 0.1\text{mV}$). New onset atrial fibrillation was estimated as a clinical and prognostic characteristic.

Coronary angiography:

Angiographic definitions were considered with standard angiographic descriptions [31,32]. Nonobstructive ACS (ACS NNOCA) was defined as a coronary artery stenosis 20%, greater but less than 50% in the left main coronary artery or a stenosis 20%, or greater but less than 70% in any other epicardial coronary artery [31]. Obstructive CAD was defined as any stenosis 50% or greater in the left main coronary artery, 70% or greater in any other coronary artery, or both. No apparent ACS was defined as all coronary stenosis less than 20% or luminal irregularities [31]. Intraluminal thrombus was defined as an intraluminal-filling defect separate from the adjacent vascular wall, an ulcer was defined as a breakdown of the plaque surface, and vasospasm was defined as a stenosis that could be

reversed by the application of nitrates [32]. Takotsubo-like left ventricular cardiomyopathy was defined as hypokinesia or akinesia from the mid-portion to the apex of the left ventricle together with hyperkinesia in the base [33].

Outcomes:

The mean follow-up duration was 12.2 months (range, 10-42 months) in Group I patients and 11.1 months (range, 4-40 months) in Group II patients. Follow-up data were obtained by periodic outpatient visits and reviewing the patient's clinic records. Anginal class by Canadian Cardiovascular Society (CCS) was noted, and events were identified as myocardial infarction or cardiac decomposition or as those requiring re intervention or rehospitalization. While primary outcome was the 1-year hospitalization for MI, secondary outcomes included 1-year all-cause death and 1-year cardiac mortality. Mortality was measured using VA vital status data.

Statistical analysis:

Demographics characteristics (age, sex, parameters of Khat chewing) and CAD risk factors (hypertension, hyperlipidemia, diabetes, persistent smoking) were estimated and described as number & percentage. Continuous variables were expressed as mean \pm SD. Comparisons for continuous variables were performed using Student's *t*-test. All *p*-values were 2-tailed, and a *p*-value <0.05 was considered statistically significant.

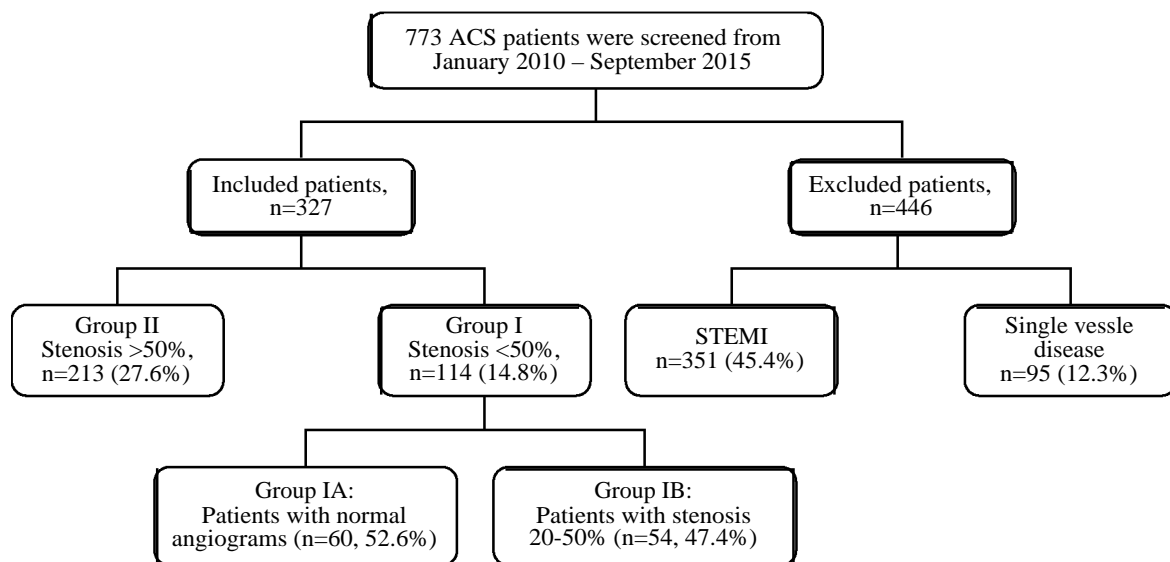


Fig. (1): Study design: Of 773 ACS patients who were screened, 446 patients were excluded: 351 (45.4%) with STEMI and 95 (12.3%) with single vessel disease. The total population (n=327) was divided according to the angiographic findings into: Group I (stenosis <50%) with 114 patients (14.8%) and Group II (stenosis > 50%) with 213 patients (27.6%). Furthermore, Group I was divided to two subgroups: Group IA: patients with normal angiograms (n=60, 52.6%) and Group IB patients with stenosis 20-50% (n=54, 47.4%).

Results

Demographic and clinical characteristics:

As shown in Table (1), patients with nonobstructive disease (Group I) were compared to patients with critical obstructive disease (Group II) in terms of demographic and clinical features, characteristic for ACS with unstable angina / NSTEMI. As compared to control, mean of age in the study group was 53.43 years v/s 66.54 years, males were ~35% v/s 78.9%, age >65 years-14.04% v/s 29.11%, two or more cardiovascular risk factors - 18.3% v/s 65.7%.

Significant differences between the two groups of patients were found in relation to history of CAD or PCI and history of previous myocardial infarction, and with regard to diabetes mellitus. No significant differences were found between the study group and control concerning hyperlipidemia, hypertension nor regarding persistent smoking.

Paraclinical characteristics of patients with nonobstructive ACS, compared to those with obstructive ACS.

Laboratorial variables analysis showed a significant difference between the study group patients, compared with the control in term of troponin I and CRP. Hyperlipidemia was found to be more frequent in the study group but with no significant difference (Table 2).

According to the ACS register of our clinic during the study period, 538 patients were with positive troponin, of them 37 patients (6.88%) were with nonobstructive lesions.

ECG study revealed a significant frequency of ST-segment depression, T wave inversion and arrhythmias in Group I, compared to Group II. Arrhythmias included sinus tachycardia, paroxysmal supraventricular tachycardia, new onset atrial fibrillation, atrial & ventricular ectopic beats, left anterior hemiblock and atrioventricular blocks (AVB I, II degree). Less significantly, ST-segment elevation was found to be more frequent in the control in compare to control study group (Table 2). Echocardiographic results showed that global left ventricular (LV) wall hypokinesia was found only in the control. Mean LV ejection fraction was 50.36% in patients with nonobstructive disease, v/s 45.09% in patients with nonobstructive disease (Table 2).

Angiographic findings:

As we mentioned above, the study population involved 327 patients. Angiographically they were divided into two groups:

Group I (stenosis <50%) with 114 patients (14.8%) and Group II (stenosis >50%) with 213 patients (27.6%). We found normal angiograms (undetectable atherosclerosis, Group IA) in 60 patients (52.63%) and stenosis between 20 and 50% (nonobstructive atherosclerosis, Group IB) in 54 patients (47.37%).

Coronary artery angiographic analysis of Group IB patients showed that 58% of lesions were located mainly in the left anterior descending coronary artery, 29% in the right coronary artery and 13% in the right circumflex artery. These nonobstructive lesions were distributed as single vessel disease (53%), double vessel disease (33%) and three-vessel disease (14%).

Patients with critical obstructive lesions (Group II) were distributed as double vessel disease (48.83%), three vessel disease (38.02%) and left main disease (13.15 %). Patients with single vessel disease >50% were excluded from the control.

Prognosis of patients with nonobstructive ACS, compared to patients with obstructive ACS:

Follow-up data were obtained by periodic outpatient visits and reviewing the patient's clinic records. The mean follow-up duration was 12.2 months (range, 10-42 months) in Group I patients and 11.1 months (range, 4-40 months) in Group II patients. Follow-up data were obtained by periodic outpatient visits and reviewing the patient's clinic records. As shown in Table (3), follow-up data revealed significant differences between the two groups, concerning therapy with aspirin, clopidogrel and warfarin, incidence of anginal episodes during follow-up and anginal status by Canadian Cardiovascular Society (CCS) or by Braunwald's guides for unstable angina. Myocardial infarction was observed in 1.8% of Group I patients and in 5.2% of Group II patients ($p < 0.05$). Rehospitalization, revascularization and cardiac decomposition were observed in 14.9%, 1.8% and 3.5% of Group I and in 62.4%, 4.7% and 17.3% of Group II patients, respectively. All deaths and cardiac death cases were observed in 3.5% and 1.8% of Group I patients and in 5.6% and 4.2% of Group II patients, respectively.

Analysis of mortality causes in Group I showed that two patients died due to cardiogenic shock following MI and the other 2 patients died at hospital of noncardiac causes (malignancy). Table (3).

Table (1): Demographic and clinical characteristics of patients with nonobstructive ACS (Group I), compared to patients with obstructive ACS (Group II).

Characteristics	Group I	Group II	p-value
No of patients	114	213	Significant
History of CAD, n (%)	49 (42.9)	155 (77.7%)	Significant
History of MI, n (%)	8 (7.0)	32 (15.0%)	Significant
History of CABG, n (%)		14 (6.6%)	Significant
History of PCI, n (%)	12 (10.5)	86 (40.4%)	Significant
Mean of age (years)	53.43	66.5	Significant
Age ≥65 years, n (%)	16 (14.0)	62 (29.1 %)	Significant
Male gender	40 (35.1)	168 (78.9%)	Significant
Risk factors ≥2	22 (19.3)	140 (65.7)	Significant
DM	20 (17.5)	104 (48.8%)	NS
HTN	45 (39.4)	130 (61.0%)	NS
Hyperlipidemia	61 (53.5)	86 (40.4%)	NS
Persistent smoking	42 (36.8)	104 (48.8%)	Significant
Khat chewing	51 (44.7)	168 (78.8%)	Significant
Heavy Khat chewing during last week	21 (18.4)	106 (49.8%)	Significant
Heavy Khat chewing prior to attacks	18 (15.8)	86 (40.4%)	Significant

CAD : Coronary artery disease.
 MI : Myocardial infarction.
 CABG : Coronary artery bypass grafts.
 PCI : Percutaneous coronary intervention.
 DM : Diabetes mellitus.
 HTN : Arterial hypertension.
 NS : Nonsignificant.

Table (2): Paraclinical characteristics of patients with nonobstructive ACS (Group I), compared to patients with obstructive ACS (Group II).

Characteristics	Group I	Group II	p-value
Number of patients	114	213	
Elevated CRP (n, %)	38 (33.3)	121 (56.8)	NS
Dyslipidemia (n, %)	61(53.5)	86 (40.4)	NS
ST depression >0.05mV (n, %)	34 (29.8)	127 (59.6)	Significant
ST elevation >0.05mV (n, %)	35 (30.7)	67 (31.5)	NS
T wave inversion ≥0.1mV (n, %)	31(27.2)	116 (54.5)	Significant
Arrhythmias (n, %)	30 (26.3)	115 (54.0%)	Significant
SWMA (n, %)	37 (32.5)	78 (36.6%)	NS
Patients with LVEF <35% (n, %)	0	75 (35.2%)	Significant*
Mean LVEF%	50.6	45.1	Significant

CRP : C reactive protein.
 SWMA : Segmental wall motion abnormality.
 LVEF : Left ventricular ejection fraction.
 NS : Nonsignificant.
 Significant*: p-value of 0.001.

Table (3): Prognosis of patient with nonobstructive ACS (Group I), compared to patients with obstructive NSACS (Group II).

Characteristics	Group I	Group II	p-value
Number of patients	114	213	
Therapy with aspirin, clopidogrel or warfarin, n (%)	52 (45.6)	197 (92.5)	Significant
Absence of angina during follow-up, n (%)	85 (74.6)	110 (51.6)	Significant
Angina pectoris CCS class III- IV, n (%)	6 (5.2)	18 (8.5)	NS
MI during follow-up, n (%)	2 (1.8)	11 (5.2)	Significant
All deaths n (%)	4 (3.5)	12 (5.6)	NS
Cardiac deaths n (%)	2 (1.8)	9 (4.2)	Significant
Rehospitalization, n (%)	17 (14.9)	133 (62.4)	Significant
Cardiac decompensation, n (%)	2 (1.8)	10 (4.7)	Significant
PCI or CABG during follow-up, n (%)	4 (3.5)	37 (17.3)	Significant

MI : Myocardial infarction.
 PCI : Percutaneous coronary intervention.
 CABG : Coronary artery bypass grafts.
 NS : Nonsignificant.

Clinical and prognostic characteristics of Group I patients (with nonobstructive ACS):

Further analysis of Group I revealed significant differences between the two subgroups: Group IA (n=60, 52.6%) within normal angiography and Group IB (n=54, 47.4%) within stenosis of 20-50% (Table 4). Group IA patients who had normal angiography were younger (mean age, 47.2 years ± 16.2) than were IB patients within coronary stenosis of 20-50% (mean age, 59.6 years ± 11). Compared to Group IB, Group IA patients were mostly female (83.3% vs. 42.6, p-value <0.5) and presented with fewer cardiovascular risk factors (for hypertension 38.33% vs. 40.741%, for hyperlipidemia 42.9% vs. 66.7%). Exception was observed in DM, as it occurred more frequently in Group IB in 23.3% vs. 11.1 % in Group IA patients. Age ≥65 years was found in 6.7% of Group IA and in 22.2% of Group IB patients.

Significant differences between the two subgroups of patients were found regarding Khat chewing, heavy Khat chewing prior to anginal attacks or during last week before attacks. Khat chewing was more frequently found in Group IB-patients (~ 74% vs 18.3%). History of heavy Khat chewing prior to anginal attacks or during the last week was found to be higher in Group IB patient-rather than Group IA patients (27.8 % vs. 5%, and 31.5% vs. 6.7%, respectively). Troponin and CRP studies revealed significant differences between these two subgroups. (Table 4) ST depression and T wave inversion were observed in both subgroups without significant difference.

Follow-up data revealed significant differences between the two subgroups of patients within nonobstructive ACS. Therapy with aspirin, clopidogrel and warfarin, incidence of anginal episodes during follow-up and advanced anginal class by Canadian Cardiovascular Society CCS or by Braunwald's guides were significantly more frequent among Group IB than among Group IA patients (Table 5).

Rehospitalization was noted more frequently among Group IB than among Group IA patients (27.7% vs. 3.3%). Cardiac decompensation was observed only in Group B patients (3.7%). Revascularization was found in 1.7% of Group IA and in 5.6% of Group IB patients. MI, all deaths and cardiac death were only observed among Group IB patients in 3.7%, 7.4% and 3.7%, respectively. (Table 5).

Table (4): Demographic, clinical and paraclinical characteristics of nonobstructive ACS patients with normal angiography (Group IA), compared to patients with non-obstructive ACS patients with stenosis 20-50% (Group IB).

Characteristics	Group IA	Group IB	p-value
No of patients	60	54	
History of CAD	19 (31.7)	30 (55.6%)	NG
History of MI	2 (3.3)	6 (11.1)	NG
Mean age/years	47.2	59.6	Significant
Age >65 years	4 (6.7)	12 (22.2%)	Significant
Male gender	9 (16.7)	31 (57.4%)	Significant
≥2 risk factors	7 (11.7)	15 (27.8 %)	Significant
DM	14 (23.3)	6 (11.1)	Significant
HTN	23 (38.3)	22 (40.7%)	NG
Hyperlipidemia	25 (41.7)	36 (66.7%)	NG
Persistent smoking	21 (34.9)	21 (38.9%)	NG
Khat chewing	11 (18.3)	40 (74.1)	Significant
Heavy Khat chewing during last week	4 (6.7)	17 (31.5)	Significant
Heavy Khat chewing prior to attacks	3 (5.0)	15 (27.8 %)	Significant
Elevated Troponin I	16 (26.7)	21 (38.9)	NG
Elevated CRP	16 (26.7)	22 (40.7%)	NG
ST depression >0.05mV	13 (21.7)	21 (38.9)	NG
T wave inversion 0.1mV	16 (26.7)	15 (27.8)	NG
Arrhythmias	14 (23.3)	21 (38.9)	NG
Mean LVEF%	52.1	49.2	Significant

CAD : Coronary artery disease.

MI : Myocardial infarction.

DM : Diabetes mellitus.

HTN : Arterial hypertension.

CRP : C reactive protein.

LVEF : Left ventricular ejection fraction.

Table (5): Prognosis of patients with nonobstructive ACS with normal angiography (Group IA), compared to patients with nonobstructive ACS patients with stenosis 20-50% (Group IB).

Characteristics	Group IA	Group IB	p-value
No of patients	60	54	
Therapy with aspirin, clopidogrel or warfarin, n (%)	13 (21.7)	39 (72.2)	Significant
No angina during follow-up	56 (93.3)	30 (55.6)	Significant
Angina pectoris CCS class III- IV	1 (1.7)	5 (9.2)	Significant
MI during follow-up	0 (0.0)	2 (3.7)	Significant
All deaths	0 (0.0)	4 (7.4)	Significant
Cardiac deaths	0 (0.0)	2 (3.7)	Significant*
Readmission to hospital	2 (3.3)	15 (27.7)	Significant
Cardiac decompensation	0 (0.0)	2 (3.7)	Significant*
PCI or CABG during follow-up	1 (1.7)	3 (5.6)	Significant

MI : Myocardial infarction.

PCI : Percutaneous coronary intervention.

CABG : Coronary artery bypass grafts.

Significant*: p-value of 0.001.

Discussion

The characterization and outcomes of unstable angina (UA)/NSTEMI patients who present with ACS, but angiographically with nonobstructive lesions remain debatable. Lack of longitudinal outcomes data on nonobstructive ischemic syndromes is a principal cause behind the limitation and controversy of data, needed for understanding their risks for adverse cardiac implications [8].

This study aimed to define the demographic and clinical features of patients with nonobstructive ACS and to evaluate their long-term prognosis, compared with patients with critical obstructive ACS. A main goal was to analyze the association between khat chewing and the clinical and prognostic trends of nonobstructive ACS patients.

Our results supported the concept that nonobstructive CAD is not (insignificant) but somewhat is associated with a significant risk for cardiovascular morbidity and mortality, especially in association with Khat chewing. After we carefully excluded other causes of ACS, based on Braunwald's guides for diagnosis and evaluation of UN/NSTEMI, we observed this phenomenon at a rate of 15%. This finding agrees well with other the findings of other studies [9,23].

Compared with the control (obstructive ACS, Group II), patients with nonobstructive ACS (Group I) were more likely to be female, younger, with fewer risk factors. They had less frequent prior history of MI, and coronary revascularization.

Females in the nonobstructive group were three times more than those with obstructive ACS. Patients with nonobstructive lesions showed markedly an increasing frequency of nondiabetic patients, although dyslipidemia was found to be more, compared with the control group. While Khat chewing was found more frequently in patients with critical obstructive disease, further subanalysis of Group I revealed a significant increasing of khat chewing in patients with stenosis of 20-50% (IB), compared to patients with normal angiography (IA).

Demographic, clinical and prognosis of nonobstructive ACS:

Further subanalysis of Group I patients (ACSNNCA) revealed two subgroups with different characteristics and outcomes. This subdivision of the ACS patients with nonobstructive stenosis might help in understanding the pathogenesis of this syndrome, especially in patients who use regularly khat. More than half of Group A had normal coronary arteries without any suspected atherosclerosis, while the rest showed signs of atherosclerosis (20-50% diameter stenosis).

Demographic and clinical data, especially risk factors comparative analysis of these two subgroups was an effective approach to evaluate the angiographic and prognostic tendencies in the nonobstructive ACS group. Patients in Group IA (with normal angiograms) were younger female with fewer cardiovascular risk factors (mean of age-47.23 years). In contrast, Group IB patients were older male with an increasing frequency of nondiabetic patients and khat chewers (mean of age-59.62 years). However, diabetes and khat chewing were to be found more determining factors that define the angiographic trends and differences in these two subgroup. Diabetes occurred less frequent in IB patients, who had stenosis of 20-50%, (11.12% against 23.33% for patients with normal angiography. While history of khat chewing, heavy chewing prior anginal attacks, heavy chewing during anginal presentation, and related hypertension were frequent in the male patients with nonobstructive lesions, all of these findings were not characteristic for the females in both subgroups of the study group population.

The prognosis of patients with nonobstructive ACS seems to be better than that of patients with critical obstructive ACS; although Group IB patients, who had stenosis of 20-50% had a worse prognosis than did those with normal coronary arteries (Group IA). In our study cardiac death and cardiac decompensation occurred in both IA and IB groups, however, cardiac death and myocardial

infarction were found only in patients with stenosis of 20-50%, compared to patients with normal coronary angiograms. These findings were consistent with new large multicenter studies [8]. In an American national cohort of patients undergoing elective coronary angiography, nonobstructive CAD, compared with no apparent CAD, was associated with a significantly greater 1-year risk of MI and all-cause mortality [8]. Regarding khat chewing, our results were also consistent with previous studies of the GULF RACE 2 study [15].

Although Khat chewing was found less frequently in patients with nonobstructive disease, further subanalysis revealed a significant increasing of khat chewing in patients with stenosis 20-50% (Group IA), compared to patients with normal angiography (Group IB). Khat chewing was observed in 74.1% of Group IB and in 18.3% of Group IA patients. Heavy Khat chewing prior to attacks was found in 27.8 % of Group IB and in 5% of Group IA patients.

A relatively recent Yemeni study tried to investigate the angiographic anatomy of MI patients, divided into three subgroups: Diabetic and khat chewers, khat chewers and nondiabetic, and diabetic and non-khat users [34]. This study showed that, 58% of the second investigated group (khat chewers and nondiabetic) had insignificant lesions with stenosis <50%, including normal coronary arteries (44%) in compare to the other two groups who were diabetic [34].

We could suggest that chronic khat use is a possible cause of nonobstructive ACS, induced by vasospasm [24-27]. Our basic findings are consistent with the pharmacodynamic and pathophysiological mechanisms of khat on the cardiovascular system- Chronic and heavy khat use might induce or exacerbate ACS in khat chewers [35]. Probably, this is due to a long-term exposure to hyperfunction of catecholamines, systemically released during cathinone metabolism. At this point, we accept the coronary vasospasm as a possible cause of nonobstructive ACS in khat chewers presenting with UA/NSEMI, who had < 50% stenosis. Majority of these patients were relatively older nondiabetic men with evidence of long standing khat chewing.

Finally, we can characterize Group IIB patients with stenosis of 20%-50% as a distinct group that differ entirely from Group IIA patients with normal coronary angiograms. Patients with stenosis 20%-50% were relatively older males, with an increasing frequency of nondiabetic, with a history of chronic heavy chewing and with a worse prognosis, during long-term evaluation.

Limitations:

Our basic data were collected retrospectively, so procedural and operative data on coronary angiography were limited. Lack of advanced investigations, like cardiac magnetic resonance imaging (MRI) to exclude myocarditis in patients with normal angiography; for this purpose, we used our possible routine methods. However, well-designed study plan, and the availability of full sized previous clinical patients' records, in our center. Future prospective studies, involving patients from multiple hospitals and cardiac centers are needed.

Conclusions:

- 1- Patients with nonobstructive were approximately 14% of all ACS patients, screened during the study period.
- 2- The prognosis of patients with nonobstructive ACS seems to be better than that of patients with critical obstructive ACS.
- 3- Subdivision of patients with nonobstructive ACS appears to be reasonable: Group IB patients with stenosis of 20-50% had different demographic, clinical and prognostic characteristics, compared to Group IA patients with normal angiography.

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المتلازمة التاجية الحادة غير الإنسدادية الانتشار والنتائج السريرية لدى مرضى يمينيين

تحدث المتلازمة التاجية الحادة غير الإنسدادية في ١٠٪ إلى ٥٢٪ من المرض الذين يجرون تصويراً صغياً للشرايين التاجية وإلى ما يربو ٦٪ من مرضى المتلازمة التاجية الحادة موجبي التروپونين. رغم إنها لم تحز على الاهتمام الكافي إلا أن الأهمية السريرية لهذه المتلازمة تكمن في أنه مرتبطة بمضاعفات خطيرة منها حدوث الاحتشاء القلبي والوفاة بعد أقل من عام من تشخيصها. الانتشار والنتائج السريرية للمتلازمة التاجية الحادة غير الإنسدادية لم يدرس بالتفصيل في اليمن حتى الآن.

هدف الدراسة: مقارنة مرضى المتلازمة التاجية الحادة غير الإنسدادية (بنسبة انسداد أقل من ٥٠٪) بمرضى المتلازمة التاجية الحادة الإنسدادية (بنسبة انسداد أكثر من ٥٠٪) إضافة إلى تقييم النتائج السريرية لمرضى المتلازمة التاجية الحادة غير الإنسدادية.

طرائقية البحثو المرضى: شملت الدراسة ٣٢٧ مريضاً، تم تقسيمهم إلى مجموعتين حيث ضمت الأولى ١١٤ مريضاً ممن بينت القسطرة اعتلالاً تاجياً بانسداد وعانى أقل من ٥٠٪ وشملت المجموعة الثانية على ٢١٣ مريضاً بانسداد وعانى حرج أعلى من ٥٠٪. تم إجراء الدراسة في الفترة من يناير ٢٠١٠ حتى سبتمبر ٢٠١٥ حيث تم ترقيده المرضى في مستشفى الجمهورية التعليمي في عدن وتم اجاء التصوير الصبغى للشرايين التاجية في مركز جراحة القلب في صنعاء.

الدراسة: بينت الدراسة أن المرضى من المجموعة الأولى في الأغلب أقل سناً ومن الإناث وبأقل عوامل الخطورة للإصابة، على خلاف المرضى من المجموعة الثانية. تم تقسيم المجموعة الأولى إلى مجموعتين:

١- المجموعة الأولى أ وتشمل المرضى الذين بينت القسطرة عدم وجود أى تغيرات وعائية أو عية قلبية طبيعية.

٢- المجموعة الأولى ب وتحتوى على المرضى الذين لديهم انسداد من ٢٠٪ إلى ٥٠٪.

نتائج: تقسيم مرضى المجموعة الأولى إلى مجموعتين بينت أن المجموعة ب التي تشمل المرضى بانسداد من ٢٠٪ إلى ٥٠٪ تتكون في الأغلب من مرضى رجال بسن عمرية متقدمة ونسبة محدودة من مرضى السكرى ومرتفعة جداً من المتعاطيين للقات نتائج تقسيم المرضى إلى مجموعتين بينت أن المجموعة الثانية التي تشمل المرضى بانسداد أقل من ٥٠٪ تتكون في الأغلب من مرضى رجال بسن عمرية متقدمة ونسبة محدودة من مرضى السكرى ومرتفعة جداً من المتعاطيين للقات. حدث الاحتشاء القلبي بنسبة ١٠.٨٪ في مرضى المجموعة الأولى (أ) وبنسبة ٥.٢٪ في مرضى المجموعة الأولى (ب) نتائج المتابعة بينت أيضاً حدوث وفيات في مرضى المجموعة الأولى (ب) بنسبة ٣.٧٪، بينما لم تسجل وفيات في مرضى المجموعة الأولى (أ).

الاستنتاجات: تنبؤ المرضى الذين لديهم انسداد أقل من ٥٠٪ أفضل من تنبؤ المرضى بانسداد وعانى حرج أعلى من ٥٠٪. بالنسبة للمرضى الذين لديهم انسداد أقل من ٥٠٪، فانتنبؤ المرضى الذين لديهم انسداد من ٢٠٪ إلى ٥٠٪ أسوأ من تنبؤ المرضى بأوعية قلبية طبيعية.