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Original Research Article

Non obstructive versus obstructive coronary artery disease documented by coronary angiography: prevalence, diagnostic features in a single center experience

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ABSTRACT

Background: Coronary angiography often detects NOCAD. Stable angina or MI patients may have NOCAD, defined as less than 50% luminal diameter decrease by visual assessment on coronary angiography. The study was to determine the frequency of non-obstructive coronary artery disease in Al Hussain cardiac centre patients who underwent CAG and the differences in clinical presentation and associated morbidity between the two groups.
Methods: Cross-sectional research was done at Karbala's al-Hussaini cardiac centre. CAG data from 167 IHD-like patients between January and May 2021. NOCAD 42 individuals (stenosis <50%) were compared to 125 obstructive CAD patients (≥50% stenosis).
Results: Between January and May 2021, 167 individuals received CAG for diagnostic, therapeutic, elective, or emergency purposes. The study included 113 (67.7%) men and 54 (32.3%) women. Patients had an average age of 56.52±11.09 years, with a median of 58 years. Overall, 25.1% (n=42) of research participants had NOCAD. The frequency of INOCA was 29.4% and MINOCA 19.1%. Patients with NOCAD were younger than those with obstructive CAD ($p<0.05$). no significant gender, co morbidity, or clinical differences across groups.
Conclusions: We believe this is the first report of prevalence, risk factors, and clinical aspects in karbalai patients' cardiac care centre in Iraq. NOCAD patients are younger and their medical history, clinical features, ECG, and serum troponin are difficult to distinguish from OCAD.

Keywords: Coronary artery disease, Coronary angiography, Non-obstructive, Obstructive

INTRODUCTION

Ischemic heart disease (IHD) is the leading cause of death and morbidity worldwide in both men and women. Identifying obstructive coronary artery disease (CAD) in symptomatic patients is the current diagnostic and treatment paradigm for IHD. However, angiographic studies reveal that about two-thirds of women and one-third of men with stable IHD do not have obstructive CAD.[1] The coronary vasculature is composed of epicardial arteries, pre-arterioles, and arterioles, with the latter two forming the coronary microvasculature. The epicardial arteries provide little resistance when there is no significant stenosis. Pre-arterioles (100-500 μm) branch from these arteries and give rise to intramyocardial arterioles (about 100 μm), which account for the majority of coronary vascular resistance. Endothelial-dependent vasodilation regulates the proximal and larger arterioles, while medium-sized arterioles respond to pressure changes, and distal arterioles are influenced by metabolic activity.[2] Atherosclerosis begins with fatty streaks in the intima, characterized by lipid-laden macrophages (foam cells) and extracellular matrix. These can evolve into fibrous

plaques with a lipid core covered by a fibrous cap. The vasa vasorum, a network of micro vessels from the adventitial layer, supplies the outer arterial wall. As plaques grow, they develop their own microvascular network, which can hemorrhage and worsen the condition. Advanced lesions may contain necrotic lipid-rich cores and calcified regions, leading to coronary artery remodeling.[3] NOCAD is typically defined as stenosis of 50% or less in any major epicardial coronary artery. Despite the absence of significant stenosis, ischemia with no obstructive coronary arteries (INOCA) is linked to poor cardiovascular outcomes. It is increasingly recognized that many INOCA patients, especially women, have coronary vasomotor abnormalities or coronary microvascular dysfunction (CMD). CMD involves increased microvascular resistance and reduced coronary blood flow due to endothelial-dependent and independent processes, affecting nearly half of INOCA patients and often remaining undiagnosed and untreated.[4] CMD encompasses various abnormalities, including endothelial dysfunction, microvascular and epicardial spasm, and vasomotor abnormalities. Previously referred to as cardiac syndrome X, current evidence suggests that CMD patients have a significantly increased incidence of adverse cardiac events, such as myocardial infarction, heart failure, and sudden cardiac death.[9,10] Studies indicate that up to 49% of patients undergoing coronary angiography have no significant stenosis, and CMD may affect up to 60% of these patients. CMD often involves endothelial dysfunction and autonomic dysregulation, leading to vasospastic angina and myocardial ischemia. The autonomic nervous system, particularly adrenergic and muscarinic receptor pathways, plays a crucial role in coronary blood flow regulation, especially under stress.[5,6]

CMD can be diagnosed using invasive and non-invasive methods. Invasive methods include intracoronary acetylcholine testing and coronary flow reserve (CFR) measurement using Doppler or thermodilution techniques. Non-invasive techniques like positron emission tomography (PET) and cardiac magnetic resonance imaging (CMR) are also used. Treatment often involves standard anti-angina medications like beta-blockers and calcium antagonists. Novel treatments such as ivabradine and ranolazine show promise in improving symptoms and coronary flow reserve in CMD patients. Patients with MINOCA and INOCA syndromes are at increased risk for various cardiovascular diseases, including cerebrovascular accidents and heart failure with preserved ejection fraction. CMD and CAD often coexist, complicating the clinical management of IHD.[7,8] Aim of study is to study the prevalence, risk factors and clinical presentations between patients with non-obstructive CAD and obstructive CAD.

METHODS

This cross-sectional study was conducted at the Karbala Cardiac Center in Iraq, Kerbala, aiming to compare patients with non-obstructive coronary artery disease (<50% stenosis) and those with obstructive lesions (>50% stenosis). Prior to data collection, the following approvals and permissions were secured: Authorization from the Arab board of medical specializations. Consent from the hospital where the data was collected. Informed consent from the patients participating in the study. The study included 167 patients (113 males and 54 females) who were clinically diagnosed with ischemic heart disease (IHD) through clinical features, ECG, and serum troponin tests. These patients were admitted to the Karbala Cardiac Center and underwent coronary angiography (CAG) between January 2021 and May 2021. Patients of both genders who presented with clinical features and ECG findings indicative of IHD were considered for the study.

Inclusion criteria

Patients diagnosed with IHD, including myocardial infarction (MI), unstable angina (UA), and chronic stable angina. Patients undergoing elective CAG. Patients undergoing emergency CAG transferred from the cardiac care unit.

Exclusion criteria

Hemodynamically unstable patients whose data could not be collected. Uncooperative patients. Patients with incomplete data.

Data collection involved interviewing patients before assessment to gather demographic information and medical history using a specially designed questionnaire. Patients meeting the inclusion criteria were thoroughly evaluated through history-taking, clinical examination, and assessment of risk factors and comorbidities. Diagnostic tests included ECG, serum troponin tests, and CAG performed using a Philips machine. The type of chest pain or presentation regarding IHD was categorized into typical (central, heavy chest pain with characteristic radiations) and atypical presentations (left-sided chest pain associated with shortness of breath and palpitations).

Ethical considerations

After explaining the study's objectives and the type of information required during the interviews, all participating patients provided verbal informed consent. Confidentiality was maintained throughout the data collection, organization, analysis, and presentation processes. Patients' identities were protected by replacing their names with identifying numbers (file serial numbers).

Statistical analysis

It was conducted using SPSS® Software (version 26 for Windows 10®). Qualitative data were presented as numbers and percentages, while continuous numerical

data were presented as mean±standard deviation. The chi-square test was used to assess relationships between qualitative variables, and the student's t-test was used to compare continuous numerical variables between two populations. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 167 patients with IHD underwent coronary angiography were included in the study. 113 (67.7%) were males and 54 (32.3%) were females. As illustrate in figure (1A). 7 cases were excluded because of incomplete data. Age of participants ranged from (20-82) years, the mean age of patients (56.52±11.09) with median (58) years. The Age group of participants was presented in figure (1B).

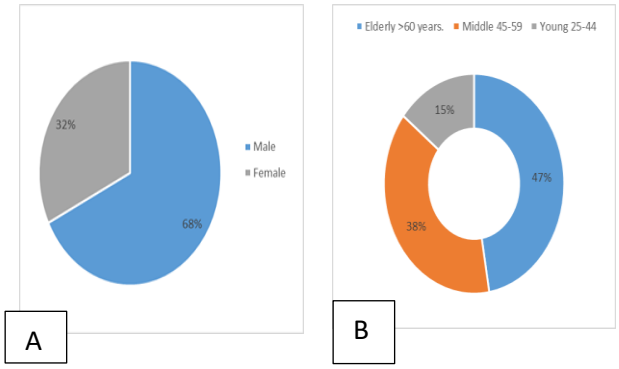

Figure 1: (A) Gender distribution of study participants, (B) age groups of participants. According to WHO classifications: young 25-44, middle 45-59, elderly >60 years.

The coronary angiography results were demonstrated that about 125 cases were with obstructive lesions (74.9%) while non-obstructive coronary arteries were 42 cases (25.1%), as shown in table 3 and figure 2.

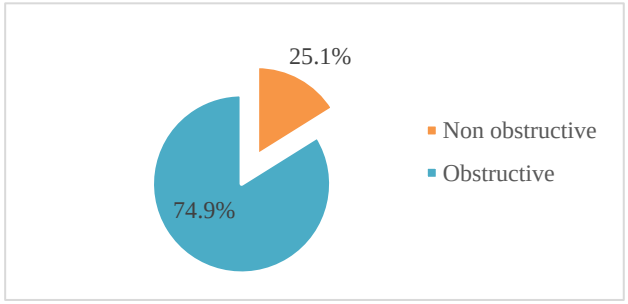

Figure 2: Angiographic results of participants.

Regarding the past medical history of study participants; results were shown that the commonest disorder was hypertension in (57.5%) of patients, followed by DM in (50.3%) of them, while smokers and negative past medical history was found in (43.1%) and (6%) respectively as presented in table 1.

Table 1: Past medical history of study participants.

Medical history		No. (%)	
History of DM	DM	84	50.3%
	No DM	83	49.7%
Hypertension	HTN	96	57.5
	No HTN	71	42.5
History of HT and DM	with	38	22.8
	Without	129	72.2
History of COPD	COPD	11	6.6
	No COPD	156	93.4
History of smoking within 5 years	Smoker	57	43.1
	Not Smoker	110	65.9
History of H.F	H. F.	27	16.2
	No history of H. F.	140	83.8
History of dyslipidemia	dyslipidemia	42	25.1
	No Dyslipidemia	125	74.9
No co morbidity and non-smoker	Yes	10	6
	No	157	94

Participants of Chronic stable angina were found to be 102 (61.7%) of total cases, among them, obstructive CAD observed in 70.6% and non-obstructive were 29.4%, as presented in figure 3

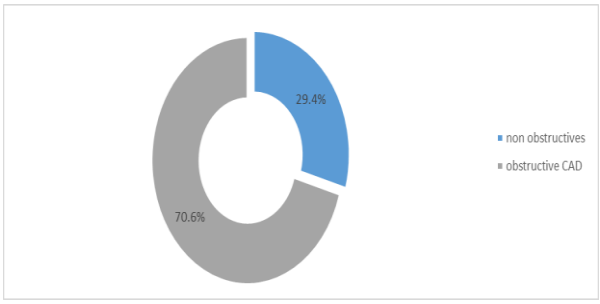

Figure 3: Angiographic results of stable angina participants.

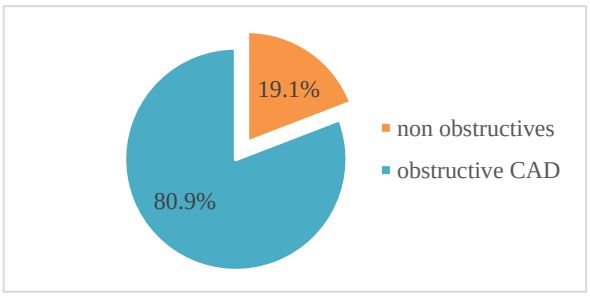

Figure 4: CAG results of MI participants.

By using the independent samples t-test there is significant difference between OCAD (median =60) and NOCAD (median =55), p value was 0.007. which means NOCAD patients were younger. As in table 2.

Table 2: age per years in association between obstructive CAD and NOCA.

Variables	Mean	S. D	P value
Obstructive CAD	57.85	10.199	0.002
NOCAD	52.57	12.747	

The results in Table 3 describe the characteristics of the study participants divided into two groups: those with obstructive coronary artery disease (CAD) based on angiography (CAG) and those without (NOCAD). In this study, results were shown that the majority of participants had obstructive CAD (74.9%) and males were more common in the study (67.7%). The table shown an even spread across three age groups: young (14.4%), middle-aged (38.3%), and older adults (47.3%). Typical chest pain was the predominant symptom (78.4%), regardless of the CAD status.

Table 3: The demographic and clinical characteristics of the study groups.

Variable	Category	No.	%
CAG results	Obstructive	125	74.9
	Non obstructive	42	25.1
Gender	Male	113	67.7
	Female	54	32.3
Age group	Young	24	14.4
	Middle	64	38.3
	Old	79	47.3
Symptoms at presentation	Typical chest pain	131	78.4
	Atypical chest pain	36	21.6
Type of IHD	Chronic stable angina	102	61.1
	Acute coronary syndrome	65	38.9
	Unstable angina	18	10.8
	NSTEMI	26	15.6
	STEMI	21	12.5
S. Troponin	Negative S. troponin	120	71.9
	Positive troponin	47	28.1

In Table 4, independent samples t-test was used to examine the mean differences in the frequency of comorbidities and risk factors in patients with obstructive CAD (OCAD) compared to those with non-obstructive CAD (NOCAD). Results were indicated that age was the only statistically significant variable (p value<0.05) between the two groups. The median age for patients with OCAD was 60 years old, while the median age for those with NOCAD was 55 years old. Results were shown an interesting finding included a trend towards large number of females in NOCAD group (33.3% vs. 66.7% in OCAD). While Smoking rates were higher in the NOCAD group (45.2% vs 30.4% in OCAD). Hypertension and Diabetes Mellitus were common in both groups. Overall, the table suggests that middle age is a key risk factor for NOCAD. While some other conditions like hypertension and diabetes are common among both OCAD and NOCAD groups.

Table 4: frequency of comorbidities and risk factors in Obstructive CAD and in NOCAD groups.

Variables	Obstructive CAD (n=125) (74.9%) N (%)	NOCAD (n=42) (25.1%) N (%)	P value
Gender, female	36 (66.7)	18 (33.3)	0.092
Age (in years), median (IQR)	60	55	0.007
Smoker	38 (30.4)	19 (45.2)	0.079
Hypertension	74 (59.2)	22 (52.4)	0.474
Diabetes mellitus	64 (51.2)	20 (47.6)	0.688
Diabetes mellitus with hypertension	31 (24.8)	7 (16.7)	0.277
Dyslipidaemia	34 (27.2)	8 (19.0)	0.292
Heart failure	18 (14.4)	9 (21.4)	0.296
COPD	10 (8.0)	1 (2.4)	0.204
No co morbidity and no smoking	8 (6.4)	2 (4.8)	0.699

Table 5: Assessment on admission among Obstructive CAD and in NOCAD groups.

Variables	Obstructive CAD (n=125) N (%)	NOCAD (n=42) N (%)	P value
Typical chest pain	95 (76.8)	35 (83.3)	0.373
Atypical chest pain	30 (23.2)	7 (16.7)	0.322
Serum troponin positive	38 (30.4)	9 (21.4)	0.263
Chronic stable angina	72 (57.6)	30 (71.4)	0.112
Acute coronary syndrome	53 (42.4)	12 (28.6)	0.112
MI	38 (30.4)	9 (22.8)	0.263
UA	15 (12.0)	3 (5.8)	0.192
STEMI	18 (14.4)	3 (8.1)	0.220
NSTEMI	20 (16.0)	6 (14.7)	0.791
ECG at admission anterior wall ischemia	60 (48.0)	19 (45.2)	0.756
Lateral wall ischemia	45 (36.0)	19 (45.2)	0.287
Nferior wall ischemia	36 (28.8)	12 (28.6)	0.977
Anterolaiteral wall ischemia	10 (8.0)	6 (14.3)	0.231

Table 5 shows findings on admission assessment among patients with obstructive coronary artery disease (OCAD) compared to those without obstructive CAD (NOCAD). There were no statistically significant differences between the two groups in most of the assessed variables. Patients have been categorized before undergoing coronary angiography into typical and atypical presentation. typical chest pain in OCAD group was 95 (76.8%) and in NOCAD group was 35 (83.3%). Chronic stable angina was a slightly higher rate in the NOCAD group. while Rates of MI were around 30.4% in OCAD and 22.8% NOCAD groups.

Unstable angina (UA) and ST-segment elevation myocardial infarction (STEMI) were less common than other presentations, also non-ST segment elevation MI (NSTEMI) rates were nearly similar between the two groups. Results were also shown that the presence of various ECG wall ischemia patterns (anterior, inferior, anterolateral) during admission assessment was similar between OCAD and NOCAD groups. these findings suggested that assessment on admission may not always be sufficient to differentiate between obstructive CAD and non-obstructive CAD. While some clinical suspicion might be raised by certain findings.

DISCUSSION

This study's sample size of 167 IHD patients is comparable to other studies. For instance, Lanza et al.'s study at the Institute of Cardiology, Università Cattolica del Sacro Cuore, Rome, Italy, involved 178 patients (9). Similarly, Bairey Merz et al. conducted a study with 185 patients at the Department of Cardiology, Gosford Hospital, Northern Sydney Central Coast Gosford, Australia (10). NOCAD: The prevalence of non-obstructive coronary artery disease (NOCAD) among patients who underwent coronary angiography (CAG) was 25.1% (Figure 2, Table 1). This finding aligns closely with Farrehi et al.'s study, which reported a NOCAD prevalence of 14.7%-22.0% across three southeastern Michigan hospitals and a composite sample from New York State.[11] INOCA: Among patients classified with ischemia with no obstructive coronary arteries (INOCA), the prevalence of stable angina pectoris without coronary artery obstruction was 29.4% (Figure 3). This is consistent with Ford et al report that at least one-third of angina patients undergoing invasive coronary angiography in some UK centers had no obstructive CAD.[12] It also aligns with Sucato et al literature review, which found that 20-30% of patients undergoing coronary angiography for chest pain suggestive of CAD had normal coronary angiograms.[13] MINOCA: The prevalence of myocardial infarction with non-obstructive coronary arteries (MINOCA) was 19.1% among all acute myocardial infarction (AMI) cases (Figure 4). This finding is consistent with Chow et al literature review, which confirmed that the prevalence of MINOCA in various studies ranged from 5%-25% of all MI events.[14] Age: Patients with NOCAD were significantly younger (mean age 52.57 years) compared to those with obstructive CAD (OCAD) (mean age 57.85 years). This age difference is consistent with Kissel et al cohort study in Canada and Pizzi et al meta-analysis published in AHA 2016, which used a larger sample size (15,16). Gender: The study found no significant sex differences between the NOCAD and OCAD groups (Table 3). This contrasts with the Women Ischemia Syndrome Evaluation (WISE) cohort study, which reported a higher prevalence of NOCAD in females, likely due to the higher proportion of women in WISE, increasing the women-to-men ratio.[17] Our study enrolled 54 females, which may appear small compared to the number of males but reflects efforts to avoid bias in sex-related NOCAD, given that most patients undergoing CAG at the Karbala Center for Cardiology were male.[18] The study observed no significant differences in symptoms between NOCAD and OCAD groups regarding typical or atypical chest pain, dyspnea, palpitations, and fatigability. This finding aligns with Mayala et al observational study in Wuhan, China, and Lanza et al literature review from the Cardiology Institute, Rome, Italy.[19,20] ECG changes: Anterior and inferior lead changes were more common in NOCAD, but there were no significant differences compared to OCAD patients (Table 4). This observation contrasts with only one study, which found more inferior lead changes in NOCAD, likely due to its smaller sample size.[21] The study found no significant differences in the prevalence of diabetes mellitus between the obstructive CAD and INOCA groups, consistent with Aribas et al systematic review.[22] However, Najib et al.'s retrospective study reported higher diabetes prevalence in obstructive CAD patients.[23] No differences were observed in the prevalence of hypertension between the NOCAD and OCAD groups, consistent with Pasupathy et al findings in Adelaide, Australia.[25] The same pattern was observed for dyslipidemia and heart failure, with no significant differences affecting the identification of NOCAD patients.[26] Traditional atherosclerosis risk factors such as hypertension, diabetes mellitus, and dyslipidemia were found to be associated with an increased risk of CMD.

CONCLUSION

The prevalence of NOCAD was 25.1%, with chronic stable angina and MI accounting for 29.4% and 19.1%, respectively, of their patient groups. NOCAD patients were generally younger. Clinical presentation and traditional risk factors were similar between NOCAD and obstructive CAD patients, making differentiation based on clinical features alone difficult. Non-traditional risk factors may also play a significant role.

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