

Frequency of Non Obstructive Epicardial Coronary Arteries in Patients with Typical Cardiac Chest Pain

Jha Ashish¹, Jamwal Naveen², Tiwari Bhuwan C.³, Misra Mukul⁴, Vijay Sudarshan K.⁵, Jha Manish K.⁶

Abstract

Background: Coronary angiography is often found to be normal in patients with typical cardiac chest pain. There is limited data from India on frequency of normal coronary angiogram in patients undergoing coronary angiography. **Aims and Objectives:** To evaluate the frequency of normal coronaries in patients with typical cardiac chest pain. **Material and Methods:** This is a registry based retrospective analysis of all the patients undergoing coronary angiography for suspected coronary artery disease in a tertiary care hospital in north India over a period of 3 yrs. **Results:** During the study period 3975 patients underwent coronary angiography, out of which 573 patients (14.41%) were found to have no significant obstructive coronary artery disease (coronary artery stenosis <50%). Presenting diagnosis was unstable angina in 73.8%, stable angina in 14.8, Non-ST Elevation MI in 5.6% and ST Elevation MI in 4.4%. Coronary angiogram was completely normal in 82% of patients. Slow flow and other evidences of endothelial dysfunction were seen in 14.8 % of patients. Coronary ectasia or aneurysm was seen in 0.9% and re-canalized artery with no significant residual coronary stenosis was seen in 0.3% of patients. Mortality at 1 yr follow-up in these patients was 0.2%. **Conclusions:** Angiography was found to be normal in 1 out of 7 patients with suspected cardiac origin chest pain. These patients had a very low mortality at 1 yr follow-up on optimal medical management. In spite of normal coronary arteries these patients should be put on optimal medical therapy.

Keywords: ACS-Acute Coronary Syndrome; NSTEMI- Non ST Elevation MI; STEMI -ST Elevation MI; MVA - Microvascular Angina; CAG: Coronary Angiography, DAPT- Dual Anti-platelet Therapy; PCI- Percutaneous Coronary intervention.

Authors Affiliation

^{1,2}Assistant Professor,
³Professor (Jr), ⁴Professor
⁵Associate Professor
⁶Senior Resident, Dept. of
Cardiology, Dr. Ram Manohar
Lohia Institute of Medical
Sciences, Lucknow, Uttar
Pradesh 226010, India.

Corresponding Author:

Naveen Jamwal,
Assistant Professor,
Dept. of Cardiology,
Dr. Ram Manohar Lohia
Institute of Medical Sciences,
Lucknow, Uttar Pradesh
226010, India.
E-mail: drjamwal@yahoo.com

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Introduction

Chest pain is one of the commonest reasons for presentation to emergency medicine and cardiology departments. Although only a small fraction of these patients actually turn out to be having serious cardiac disease, missing correct diagnosis in this subset of patients may have life threatening consequences for them.

Such patients who have typical cardiac pain often are subjected to coronary angiography for further evaluation. Usually CT coronary angiography is preferred where there is intermediate probability of having the coronary artery disease (CAD), whereas in patients with

high probability of having CAD a conventional coronary angiography is done.

In some of these patients the severity of a borderline coronary stenosis might have been misjudged or coronary spasm could have been demonstrated, if provocative tests were used in all patients, but in majority of such patients, chest pain is not due to epicardial artery disease. There may be other operative mechanism leading to myocardial ischemia in such patients such as coronary bridging, congenital coronary anomalies, coronary slow-flow, Tako-tsubo cardiomyopathy and coronary micro-vascular dysfunction.

There is a paucity of Indian data on this subgroup of patients with non obstructive coronary artery disease on coronary angiogram.

Aims and Objectives

- To evaluate the frequency of normal coronary arteries in patients with suspected cardiac chest pain
- To look for clinical presentation and mortality at 1 yr follow up in these patients with normal coronary arteries

Material and Methods

This is a registry based retrospective study conducted at a tertiary care hospital in all the patients presenting with suspected cardiac origin chest pain who underwent coronary angiogram from Nov 2013 to Feb 2017. Patients were assessed for clinical features at presentation; angiographic parameters and mortality at 1 yr follow up.

Statistical Analysis

The results are presented in mean±SD and percentages or as median+/-IQR. The angiographic findings were presented in number and percentage of total. All the analysis was carried out by using SPSS 20.0 version (Chicago, Inc., USA).

Observations and Results

During the study period 3975 patients underwent invasive coronary angiography, out of which 573 patients (14.41%) were found to have no significant obstructive coronary artery disease (coronary artery stenosis <50%).

Baseline characteristics of these patients revealed that nearly 60% were males. Pre-existing Hypertension was present in 41% and Diabetes in 25% patients (Table 1).

These patients presented most often with the diagnosis of unstable angina (73.8%). Stable angina was seen in 14.8% patients, whereas a minority of these patients presented with Non-ST Elevation MI (5.6%) or ST Elevation MI (4.4%) (**Figure 1**). Thrombolytic therapy was used in 25% of the patients presenting with STEMI.

Majority of these patients who had normal or near normal coronary angiograms were hemodynamically stable. Hypotension was seen in 1.4% and cardiogenic shock in 0.2% of patients.

On echocardiography their mean LVEF was 56.6±8.4%. RWMA was seen in 9.6% and global hypokinesia in 4.9% of patients. Some degree of

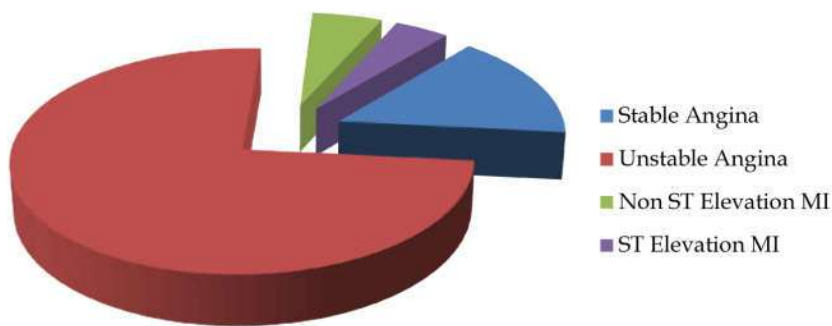


Fig. 1: Presenting Diagnosis of chest pain patients undergoing coronary angiography.

Table 1: Baseline characteristics and clinical presentation.

Variables	N (%) (N=573)	Mean	Std deviation	Median (IQR)
Age (yrs)		53.52	10.68	54 (45-61)
Gender(M/F)	224 (39.1)/349 (60.9)			
Risk Factors:				
Diabetes	146 (25.5)			
Hypertension	238 (41.5)			
Diagnosis:				
Stable Angina	85 (14.8)			
USA	423 (73.8)			
NSTEMI	32 (5.6)			
STEMI	25 (4.4)			
Clinical Presentation:				
Hypotension	7 (1.4)			
CHF	1 (0.2)			

CHB	0 (0)			
VT/VF	5 (0.9)			
AF	17 (3)			
SBP		132.1	8.1	130 (126-140)
DBP		80.9	5.7	80 (80-84)
Pulse rate		78.9	10.2	78 (74-82)
Cardiogenic Shock	1 (0.2)			
Echo Findings:				
LVEF		56.6	8.4	60 (60-60)
RWMA	55 (9.6)			
Global dysfunction	28 (4.9)			
MR (Mild/Mod)	229 (40)			
MR (severe)	10 (1.7)			
Pericardial effusion	3 (0.5)			
Death at 1 yr f/up	1 (0.2)			
DAPT use	57 (9.9)			

MR was seen in 40% of these patients whereas severe MR was seen in only 1.7% of patients (Table 1).

Radial access was used for coronary angiogram in 55% and femoral access in 45% of these patients. Coronary angiogram was found to be completely normal in 82% of these patients. Slow flow and other evidences of endothelial dysfunction were seen in 14.8 % of patients (Table 2). Coronary ectasia or aneurysmal disease was seen in 0.9% and recanalized artery with no significant residual coronary stenosis was seen in 0.3% of patients (Figure 2). One patient had ulcerated coronary artery lesion with thrombus which needed stenting with a DES.

Specific provocative tests for coronary vasospasm in these patients who had no evidence of obstructive coronary artery disease were not done in this study.

Majority of these patients were discharged within 1 day of catheterization and were found to be alive at 1 yr follow up with only 1 death among these patients over the period of 1 yr. This patient had presented with cardiogenic shock and severe LV systolic dysfunction and had recanalized LAD coronary artery. He died 2 days after the catheterization due to progressive cardiogenic shock (Table 1).

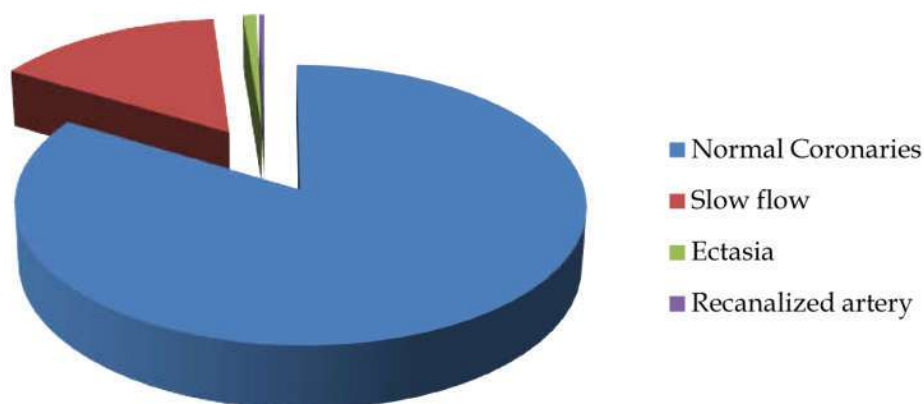


Fig. 2: Findings of CAG in patients with no significant epicardial coronary artery obstruction.

Table 2: Angiographic Parameters.

Angiographic parameter	Number of Pt (N=573)	Percentage of total (%)
Vascular Access:		
Radial	315	55
Femoral	258	45
CAG findings:		
Normal Coronaries	470	82
Slow Flow	84	14.8
Ectasia/Aneurysm	5	0.9
Recanalized Non critical Obstruction	2	0.3
PCI	1	0.2

Discussion

The combination of typical angina and an abnormal stress test in the presence of normal epicardial coronary arteries is seen in nearly 20% of patients undergoing coronary angiography [1,2]. These patients may present with stable angina with evidence of exercise inducible ischemia on non invasive stress tests or may present with resting chest pain with or without elevated cardiac biomarkers and occasionally ST segment elevation MI.

There may be several possible explanations for this scenario. Firstly chest pain may be non-cardiac and the non invasive tests like ECG, stress tests and cardiac biomarkers being falsely positive. Myocardial ischemia in the absence of coronary artery stenosis may be because of increase in myocardial oxygen demand (e.g. in patients with marked LVH, marked tachycardia, severe aortic stenosis) or decrease in oxygen carrying capacity of blood (e.g. with severe anemia, profound hypotension). Neurological diseases like CVA and extreme mental stress may also mimic ACS by producing ECG changes, hemodynamic changes and causing elevation of cardiac biomarkers [2]. Clear-cut alternative diagnoses like gastro-esophageal diseases, musculoskeletal chest pain or pleuro-pericardial diseases may be present in some patients.

When there is a typical exertional chest pain and unequivocal evidence of stress inducible ischemia in spite of normal epicardial coronary arteries the diagnosis is most commonly Microvascular Angina or Syndrome X. These patients have classical risk factors for atherosclerotic CAD and are more likely to be females. They have normal or borderline elevated resting coronary blood flow but reduced coronary flow reserve (CFR < 2.5). This finding of coronary microvascular dysfunction has been seen in 30-65% of patients with chest pain with normal coronary arteries [3,4]. These patients usually have good long term prognosis with one large study showing 7 yr survival of 96% in patients with normal coronary arteries and 92% in those with mild CAD [5].

Approximately 20% to 30% of patients with stable microvascular angina may experience progressive worsening of symptoms, leading to impaired quality of life [6].

Both obstructive CAD and Microvascular angina patient have similar risk factor, but the reason why some subjects develop epicardial artery disease whereas others develop microcirculation disease is not clear. Differentiation based on

clinical features is impossible, but some clues suggesting microvascular angina include: chest pain persisting for several minutes after effort interruption, chest pain showing poor response to nitroglycerin, stress tests induce angina and ST-segment depression but no left ventricular contractile abnormalities during stress echocardiography.

There are several other causes for typical cardiac chest pain and apparently normal epicardial coronary arteries. There may be an element of large vessel spasm for example in Prinzmetal's angina, which may present as variable threshold angina with near normal coronary artery and inducible spasm on provocative invasive test. Some patients have diffuse coronary artery narrowing which could be picked on intravascular ultrasound only and otherwise appears as a small caliber vessel with no focal disease on conventional coronary angiography.

Some patients have congenital coronary artery abnormalities including coronary AV fistula and anomalous origin or course of coronary arteries. Patients with hypertrophic cardiomyopathy and some patients with dilated cardiomyopathy may also present with typical chest pain with normal coronary arteries. Patients with aortic dissection and aneurysm may also have similar presentation. Stress cardiomyopathy which is also known as Tako-tsubo cardiomyopathy may also have presentation typically like an acute coronary syndrome with typical apical hypokinesia or dyskinesia and basal hyperkinesis on echocardiogram but have normal coronary arteries. These patients frequently give a history of recent severe emotional stress as a precipitating factor. They have usually a good recovery with medical treatment.

There is a paucity of data on patients of chest pain with normal coronary arteries from India. This study is a large retrospective study which included all the patients undergoing coronary angiography at a tertiary care teaching hospital in north India during a period of 3 years. The study revealed that nearly 1/7th (14%) of all patients undergoing coronary angiograms had normal coronary arteries. Among these patients 82% had completely normal coronary arteries and 15% had slow flow or other markers of endothelial dysfunction. A small fraction of patients had coronary ectasia or aneurysm without any significant obstruction.

Limitations

There are several limitations of this study. First of all it is a retrospective study and thus has all the limitations associated with this kind of studies. In this study IVUS was not used routinely to study

the actual extent of atherosclerotic burden and to look for atherosclerotic disease with positive remodeling. FFR was not used routinely to assess borderline lesions (30 to <50% stenosis) or to assess coronary flow reserves. Mortality at the end of 1 yr was found to be very low in this study (0.2%).

Conclusions

Despite these limitations this study is one of the largest one to tell us about the incidence of normal coronary arteries in patients with typical cardiac chest pain from India. There is a need for doing prospective studies in these patients looking for coronary flow reserve, IVUS data and vaso-reactivity in these patients.

The finding of normal coronary arteries on angiography does not mean that epicardial arteries have no atherosclerosis. These patients may be having non flow-limiting soft plaques which may rupture and cause acute coronary syndrome and these lesions may be actually more dangerous than stable stenotic lesions. Such patients have risk for future cardiovascular events. If arteries show luminal irregularities or if risk assessment shows presence of risk factors for ASCVD, Statins should be initiated and preventative measures, including smoking cessation, weight management, regular exercise, optimal blood pressure and diabetes management should be emphasized upon.

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None

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