



# Coronary Microvascular Disease: A hidden cause of Angina



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## Abstract

In cardiology practice, we often come across patients presenting with anginal pain who undergo coronary angiogram which reveals either normal or non-obstructive epicardial coronaries. Importance is given to epicardial coronaries and the coronary microvasculature which could be the cause of angina is often overlooked. These patients are then labeled to have non-cardiac chest pain and musculoskeletal or psychogenic etiology is suggested. However, with growing interest in coronary microvasculature which are the tiny blood vessels at the tissue level in myocardium, diagnostic modalities and treatment options for coronary microvascular disease are being explored.

**Keywords:** Microvascular disease; Cardiac syndrome X; Angina with normal coronaries; TIMI perfusion grade; TIMI frame count; Coronary flow reserve

**Abbreviations:** MI: Myocardial Infarction; STEMI: ST Segment Elevation Myocardial Infarction; CMVD: Coronary Microvascular Disease; CAD: Coronary Artery Disease

## Introduction

Coronary artery disease is atherosclerotic plaque deposition on the inner walls of epicardial coronary arteries and can cause obstruction to blood flow through them. This limits the nutrition and oxygen supply to myocardium. These patients present with angina or myocardial infarction (MI) depending on acuity and the severity of blockage. Primary percutaneous coronary intervention is critical in case of ST segment elevation MI (STEMI) and non-STEMI to restore normal epicardial coronary flow. However, perfusion at tissue level in the myocardium by coronary microvasculature may be persistently impaired. It has been demonstrated that decreased myocardial perfusion from coronary microvascular disease (CMVD) carries just as high morbidity and mortality as not opening the epicardial coronaries in the setting of MI [1]. On many occasions, patient presenting with angina may have normal epicardial coronaries on angiogram but have CMVD and this is also known as Cardiac Syndrome X.

## Epidemiology

CAD is often associated with CMVD. However, CMVD may be present even in the absence of CAD as mentioned above and this is more frequent in young females [2]. The risk factors for CMVD are same as those for CAD such as smoking, diabetes, hypertension, hyperlipidemia, family history, illicit drug abuse such as cocaine.

In a study by Gibson et al. [3] which assessed for epicardial coronary blood flow and CMVD in the setting of acute MI in cocaine abusers, CMVD was noted to be significantly higher despite restoration of epicardial coronary flow. In another study comparing 202 cocaine abusers with 210 non-cocaine abusers presenting with chest pain and who had normal or non-significant CAD, cocaine abusers had significantly higher incidence of CMVD [4]. Non-cocaine group had significantly less CMVD despite having higher prevalence of hyperlipidemia and older age.

## Diagnosis

Diagnosing CMVD is often challenging as routine cardiac tests may not reveal CMVD. Following may be used for diagnosis:

1. Stress test: When a nuclear perfusion stress test using adenosine or analogues demonstrates ischemia and patient has normal or non-significant disease in epicardial coronaries, it is suggestive of CMVD.
2. Coronary angiogram: assessment of flow through the epicardial coronaries and the myocardial perfusion can be assess as follows:
  - a. TIMI flow grade: grading of velocity of blood flow through the epicardial coronaries. Grade 2 or lower is suggestive of CMVD.

b. TIMI frame count [5]: quantitating the velocity of blood flow through the epicardial coronaries by counting the number of cine frames required by the contrast to reach the standardized distal landmark of the epicardial coronary artery. Higher frame count suggests slow flow which could indicate resistance in distal coronary microvasculature.

c. TIMI perfusion grade [1]: where the myocardial perfusion is assessed by “blush”. Depending on the severity of CMVD, there is either absence (Grade 0), stain or delay (Grade 1) in clearance of the myocardial blush after injection of contrast into the epicardial coronary artery.

3. Coronary flow reserve: ratio of epicardial coronary blood flow after inducing hyperemia to basal coronary blood flow. Ratio less than 2.5 is suggestive of distal microvascular resistance.

a. It can be measured invasively by passing a doppler wire into the coronary artery, and measuring pre- and post-intravenous or intracoronary infusion of adenosine [6].

b. Flow reserve can also be measured noninvasively using high-resolution transthoracic color doppler echocardiogram [7] or positron emission tomography [8].

4. Cardiac Magnetic Resonance Imaging [9]: can be used to assess for differences in regional myocardial perfusion after administration of adenosine. This non-invasive modality is useful only after ruling out significant CAD.

## Treatment

There is limited data regarding treatment of patients with CMVD. Although risk factor modification is the corner stone, pharmacotherapy needs further robust research. Antiplatelets to prevent clot formation and statins to decrease lipid burden for prevention of progression of CMVD to CAD may be advocated.

Several antianginal medications can be used to manage angina from CMVD.

1. Nitrates: have mixed results. Sublingual nitrates have shown to relieve angina as demonstrated in 42% of patients in a study by Kaski et al. [10]. However, long acting nitrates have demonstrated no benefit [11].

2. Beta-blocker: in particular atenolol and propranolol have shown to be effective in CMVD [11,12].

3. Calcium channel blockers: can be used if beta-blockers are contraindicated such as in patients who are cocaine abusers.

4. Ranolazine: has shown to be beneficial in symptom control and improvement in quality of life. This was based on a study where 31 patients were administered questionnaires regarding their angina and quality of life after 6 weeks of treatment with ranolazine [13].

The 2013 European Society of Cardiology guidelines recommend that all patients with stable coronary heart disease should be treated with aspirin and statin with beta blocker [14].

## Conclusion

Demonstration of normal or non-obstructive epicardial coronary arteries by coronary angiogram among patient presenting with angina is an incomplete management. Suspicion of CMVD should be high in the presence of risk factors. It is reasonable to manage these patients along the lines of CAD, by using antiplatelets, statins and beta-blockers. Continued research aimed at cost effective and reliable method to diagnose and clinical trials in treatment of these patients with CMVD is necessary.

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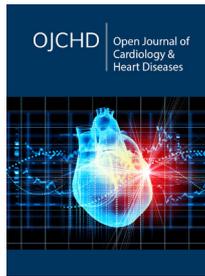
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