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Management standards for stable coronary artery disease in India

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ABSTRACT

Coronary artery disease (CAD) is one of the important causes of cardiovascular morbidity and mortality globally, giving rise to more than 7 million deaths annually. An increasing burden of CAD in India is a major cause of concern with angina being the leading manifestation. Stable coronary artery disease (SCAD) is characterised by episodes of transient central chest pain (angina pectoris), often triggered by exercise, emotion or other forms of stress, generally triggered by a reversible mismatch between myocardial oxygen demand and supply resulting in myocardial ischemia or hypoxia. A stabilised, frequently asymptomatic phase following an acute coronary syndrome (ACS) is also classified as SCAD. This definition of SCAD also encompasses vasospastic and microvascular angina under the common umbrella.

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1. Definition, prevalence and pathophysiology

Coronary artery disease (CAD) is one of the important causes of cardiovascular morbidity and mortality globally, giving rise to more than 7 million deaths annually.¹ An increasing burden of CAD in India is a major cause of concern with angina being the leading manifestation. Stable coronary artery disease (SCAD) is characterised by episodes of transient central chest pain (angina pectoris), often triggered by exercise, emotion or other forms of stress, generally triggered by a reversible mismatch between myocardial oxygen demand and supply resulting in myocardial ischaemia or hypoxia.² A stabilised, frequently asymptomatic phase following an acute coronary syndrome (ACS) is also classified as SCAD. This definition of SCAD also encompasses vasospastic and microvascular angina under the common umbrella.

The common clinical presentation of SCAD is chronic stable angina. The underlying mechanisms may include atherogenesis

and plaque formation in epicardial arteries, spasm of normal or plaque containing arteries, micro-vascular, or left ventricular dysfunction due to prior acute myocardial necrosis or ischaemic cardiomyopathy.² In addition to chest discomfort, dyspnoea, palpitations, syncope or fatigue may also be present and sometimes may be the only symptom. Classical angina and micro-vascular angina are difficult to differentiate owing to the fact that both are exercise induced. Vasospastic angina, on the other hand, occurs at rest and has preserved effort tolerance. As opposed to ACS, SCAD lesions are more fibrotic, have a small necrotic core and little or no overlying thrombus.³ Besides, they do not display erosion or rupture of endothelial lining.⁴ Vasospasm is mostly due to various vasoconstrictor stimuli acting on hyper-reactive vascular smooth muscle cells, like cellular rho-kinase activity, abnormalities in adenosine triphosphate (ATP) sensitive potassium channels and/or membrane Na⁺-H⁺ counter-current transport.⁵ The diffuse distal spastic reaction usually underlies micro-vascular angina, while focal spasm is classically observed in variant angina.

In the last three decades, the prevalence of CAD has increased from 1.1% to about 7.5% in the urban population and from 2.1% to 3.7% in the rural population.⁶ Coronary artery disease tends to

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occur at a younger age in Indians with 50% of cardiovascular mortality occurring in individuals aged <50 years.^{7,8} The younger CAD patients have more extensive angiographic involvement contributed by genetic, metabolic, conventional and nonconventional risk factors. Although several risk factors have been suggested, smoking, dyslipidemia and hypertension remain the major risk factors in the younger CAD patients.⁶

A need for developing practice standards for the management of stable CAD was perceived by experts across India. This document aims to assist physicians, particularly cardiologists, in clinical decision-making by delineating a gamut of commonly acceptable modalities for the diagnosis, management, and prevention of stable angina. The current management standards have defined practices that meet the needs of most patients in the Indian context.⁷ A modified GRADE system was used to derive quality of evidence and grades of recommendations.

2. Diagnosis

The initial and important step in the management of stable angina is the diagnosis. A detailed clinical history of angina includes assessing magnitude, location, severity, duration and precipitating factors of angina. Presence of typical nature of the discomfort, precipitating factors and relieving factors should be suggestive angina. Taking the medical history of a patient is the foremost and most vital process. Indeed in most cases a clear diagnosis can be made based on the history alone of a patient.⁹ Physical examination is required to corroborate and strengthen the diagnosis.¹⁰

Besides history and physical examination, diagnosis of stable angina needs the supporting evidence from non-invasive investigations to confirm it and sometimes provide additional prognostic information. It has been demonstrated that there is an association between low haemoglobin concentration and increased mortality in patients with stable angina.^{11,12} Similarly, fasting blood glucose has a prognostic importance in patients with stable angina.^{13,14} Furthermore, a full lipid profile, renal, liver and thyroid function tests, a 12-lead electrocardiography (ECG), resting echocardiography and chest X-ray can be helpful in evaluating stable angina.² An elevated resting heart rate is also associated with poor prognosis in patients with SCAD.¹⁵ Patients with resting heart rate ≥ 70 bpm (beats per minute) exhibit a higher risk of vascular events compared to patients with a heart rate <70 bpm.¹⁶ Therefore, it is prudent to include heart rate determination as a part of the routine cardiac assessment.

Fractional flow reserve (FFR) is an evidence-based diagnostic test gradually gaining prognostic value.¹⁷ In a meta-analysis non-invasive FFR demonstrated high diagnostic efficacy comparable with invasively measured FFR for the detection of ischaemia in stable patients with suspected or known CAD.¹⁸ Therefore, in selected patients FFR testing can be recommended if resources permit.

The diagnosis of microvascular angina can be done by a combination of various modalities. It can be diagnosed by normal coronary angiogram and the absence of epicardial coronary spasm at rest or during acetylcholine provocation. A coronary flow reserve <2.5 on adenosine-induced hyperemia,¹⁹ data from positron emission tomography²⁰ and cardiac magnetic resonance²¹ have been also used in diagnosis of micro-vascular angina. Similarly, vasospastic angina can be diagnosed by ECG and coronary arteriography showing epicardial coronary spasm at rest or during acetylcholine provocation.² Further, exercise stress test and Holter monitoring can be used to detect silent ischaemia.²²

Recommendations on diagnosis:

- Patient's history and physical examination should be considered to identify all the symptoms and signs of cardiovascular diseases (CVDs), medical history, CV risk factors, and other cardiac etiologies. [Grade A, Evidence 3]^{9,10}
- The basic first-line testing in patients with suspected SCAD includes standard laboratory biochemical testing (including haemoglobin, HbA_{1c} (glycated haemoglobin), lipid profile, liver, renal and thyroid function tests), a resting ECG, resting echocardiography and, in selected patients, a chest X-ray. [Grade A, Evidence 3]^{2,23–27}
- It is recommended to include assessment of resting heart rate in SCAD patients as a routine clinical practice. [Grade A, Evidence 2]^{15,28,29}
- Exercise ECG testing, if possible, should be preferred in patients with a pre-test probability (based on character of symptom, age and sex) of 15–65% as it is more relevant to their activities than pharmacological testing. [Grade A, Evidence 2]^{30,31}
- In patients who cannot exercise to an adequate workload, pharmacological testing with adenosine-induced vasodilator perfusion imaging or dobutamine echocardiography should be considered. [Grade A, Evidence 4]²
- An invasive coronary angiogram is indicated in significantly symptomatic patients, patients with high risk features on non-invasive testing.
- Certain specific types of angina (microvascular, vasospastic and silent angina) should be diagnosed by a combination of available diagnostic techniques and should be individualised. [Grade A, Evidence 4]²

3. Management

Diverse risk factor distribution, across various geographical locations in India mandates implementation of aggressive strategies for risk factor control and prevention. An effective usage of primary and secondary prevention strategies is another important aspect of CVD prevention and control. Developing the clinical practice algorithms translates best evidence into best practice and promotes quality by reducing healthcare variations, refining diagnostic accuracy, promoting appropriate therapy, and preventing the use of ineffective or potentially harmful interventions.

The treatment of stable angina includes anti-anginal medication, medication to modify atherosclerosis and aggressive treatment of causative risk factors. All patients with SCAD require life-long supervised treatment. Overall, management strategy includes, lifestyle changes, pharmacological management and prevention of cardiovascular events (Fig. 1), various revascularisation techniques and management considerations for special groups such as women, elderly, renal dysfunction and diabetic patients.

4. Lifestyle management and control of risk factors

4.1. Smoking

Tobacco smoking is one of the frequent causes of mortality; indeed smoking can result in at least 2.8–3.1 fold increase in the risk of CAD.³² Passive smoking or second-hand smoke has been demonstrated to exhibit a positive association with CAD (RR 1.27; 95% CI 1.10–1.48) and has displayed a crucial impact on the

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