

CONSENSUS STATEMENT

Indian Consensus on Optimal Treatment of Angina (OPTA)

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Introduction

Coronary artery disease or coronary heart disease (CHD) is a condition wherein the atherosclerotic plaques or vasospasm leads to narrowing of the lumen, thereby resulting in an insufficient supply of oxygenated blood to the myocardium.⁴ The reversible mismatch between the myocardial oxygen demand and supply causes myocardial ischemia or hypoxia, which is manifested as angina.

Coronary artery disease (CAD) is a major health concern today and has assumed epidemic proportions worldwide. The prevalence of CAD has been steadily increasing, and India is no exception to this.¹ In the last three decades, the prevalence of CAD has significantly increased. The prevalence of CAD in urban areas was 2.5%–12.6% and in rural areas, it was 1.4%–4.6%.² The projected data show that from 1990 to 2020, there will be a 117% and 105% rise in mortality from CAD in men and women, respectively, in India.¹ Further, CAD is known to be the leading cause of heart failure, arrhythmias, and sudden death.

Angina, the common initial manifestation of CAD, is responsible for a significant burden on Indian healthcare. Early identification of angina is important for the initiation of interventions to reduce the future risk of more serious cardiac events.³

Angina is classically described as substernal chest pain or discomfort which lasts for less than 10 minutes. Chest pain in case of stable angina is often provoked by emotional or physical stress or exercise and is relieved by rest or nitroglycerin.⁵ Stable angina consists of such transient episodes of chest pain over several weeks.⁶ The pain may be referred to the arms or jaw. Atypical presentation may include complaints of discomfort, dyspnea, and diaphoresis.

Angina may result due to different reasons listed herein (Figure 1):

- Chronic stable angina is precipitated by exercise-induced or emotional stress-induced ischemia in patients with coronary flow-limiting atherosclerotic stenosis in the large coronary arteries.
- In certain cases, the pain continues after revascularization/the coronary arteries appear normal or near normal on angiography. These cases may show a positive treadmill test. This entity is now

termed as microvascular angina and is seen in nearly 40% of the cases of angina.

- One more entity with normal coronary arteries is vasospastic angina. This is seen in a minority of the condition. This form of angina presents with specific characteristics, that is, pain is not triggered by exercise but occurs at rest.⁷

Need and Objectives of OPTA

It is well known that risk factors for CAD, such as diabetes, hypertension,

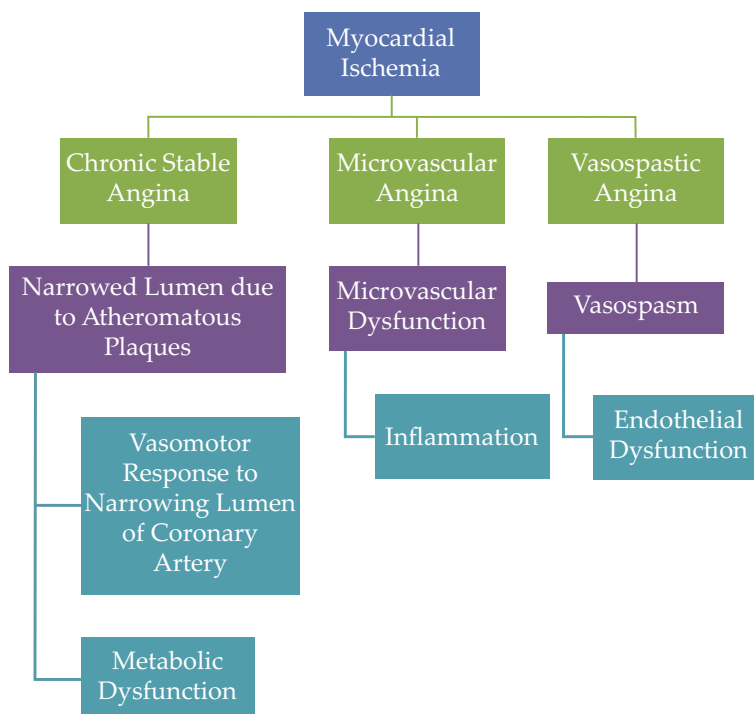


Fig.1: Different mechanisms of myocardial ischemia

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dyslipidemia, and smoking/tobacco use, have a high prevalence among the Indian population; it results in higher CAD cases in India.³ It is estimated that 60% of the global cases of heart disease will occur in India by 2020.⁸ Most of these patients develop stable ischemic heart disease and would present clinically as stable angina.

Studies have demonstrated that individuals with baseline typical angina and exertional chest pain had a worse prognosis for the long-term coronary outcome than those with no baseline chest pain did.³ In such cases, early diagnosis and intervention is necessary to reduce the morbidity and mortality due to CAD.

Further, the Indian population displays a higher trend of presenting with atypical symptoms of angina, which may result in a missed diagnosis. Due to scarce resources, healthcare affordability and delivery, and other logistical difficulties, the optimal treatment may not be available to the Indian population.⁹

Current guidelines recommend antianginal therapy even before revascularization is considered to aid in symptom control. The traditional approach has been to consider first-line and second-line therapy options, but most patients end up with multi-agent therapy and in fact, there is stronger evidence supporting the use of "second-line therapy" currently. This brings up the question of whether the first-line/second-line approach is the right approach toward optimal management of stable angina.⁷ The appropriate pharmacotherapy will ensure the optimal use of resources to reduce the risk of future cardiac events.

Thus, the combined effect of increasing the burden of CAD among Indians and concerns regarding the delivery of optimum healthcare makes it imperative that healthcare professionals are equipped with enough understanding to recognize a patient of CAD who presents with chronic stable angina and be equipped to treat the condition. This led to the conception of OPTA or "Optimal Treatment of Angina." OPTA is primarily intended to equip clinicians with the necessary expertise to ensure the following:

- To make an accurate and early diagnosis, which is the first step toward optimum management of

chronic stable angina

- To enable risk stratification of patients with angina to ensure their optimum management
- To introduce an OPTA approach that is founded on the principles of individualizing therapy which takes into consideration the presence of comorbidities and the underlying pathology responsible for angina

OPTA was created to assist healthcare professionals with tools to ensure higher standards of care for angina patients that would result in better patient outcomes. Activities of OPTA are not limited to the development of this statement but extend further to involve cardiologists, family physicians, and patients to achieve the following four important goals of optimal treatment of stable angina:

1. Disease control
2. Relief from symptoms
3. Building of exercise capacity
4. Improvement of the quality of life

The tools planned for achieving these goals are as follows:

- a. A diagnosis and treatment algorithm to manage chronic stable angina which is relevant for the Indian scenario
- b. A clinical checklist for an early and accurate diagnosis of chronic stable angina
- c. Understanding of symptoms and standard presentation of a patient with angina
- d. A questionnaire to sensitize the physicians towards important goals of stable angina management
- e. An OPTA approach toward optimal utilization of available pharmacotherapy by Indian clinicians

Methodology

With the above-mentioned objectives in mind, multiple meetings were held across India. These meetings were well attended by experts from the field of cardiology. During these meetings, there was a discussion regarding:

- a. Current burden of the disease (CAD) in India
- b. Common clinical presentation of a patient with chronic stable angina
- c. Challenges faced in the diagnosis

and management of the Indian population

- d. Various pharmacotherapies available in India and their appropriate use

Intense discussions, an extensive literature review, and feedback from experts led to the development of the following OPTA tools which were finalized in National Steering Committee attended by eminent cardiologists of India:

- I. A clinical checklist to enable the diagnosis of stable angina
- II. A questionnaire to assist in risk stratification and planning of the management
- III. An OPTA approach for the management of angina

These tools would enable clinicians in early diagnosis and appropriate management of their patients.

Outcomes of the National Steering Committee Meeting

The outcomes of the National Steering Committee Meeting can be categorized as those related to diagnosis, management, and prognosis.

Diagnosis and Assessment: The First Step of Optimal Therapy in Stable Angina

Suggestions from the expert panel on the approach toward a suspected case of angina include the following:

- A detailed history and physical examination
- Biochemical investigations, including cardiac biomarkers
- Electrocardiogram (ECG), both resting and with the treadmill test
- Echocardiography (commonly, at rest)
- Coronary angiography: CT and/or invasive
- Fractional flow reserve (FFR)/intravascular ultrasound (IVUS) [if necessary]
- Other less commonly performed procedures, including cardiac MRI, exercise echocardiography, and myocardial perfusion scintigraphy

History

History is the key to screen suspected cases of angina. The national committee of OPTA has developed a tool to screen cases of angina. This checklist provides specific questions that a clinician

Box 1: OPTA clinical checklist

If the answers to the following questions are "YES," it most likely is stable angina.

Sr. No.	Questions	Yes	No
1	Is the pain diffused and cannot be pointed by one finger?		
2	Is the chest pain or discomfort in the precordial region/ radiates to the shoulder/ back/jaw/teeth/ear or upper abdomen (above umbilicus)?		
3	Does the pain appear on exertion/is associated with a triggering factor, like climbing stairs, walking on an inclined surface, or playing with kids/ cold weather/within half an hour post meals?		
4	Does the pain relieve after stopping the activity/taking nitrate?		
5	Is the pain associated with dizziness/diaphoresis/ dyspepsia/palpitation?		
6	Is the pain lasting for less than 10 minutes?		
7	Does the pain occur at the same location always/mostly?		
8	Is age of the patient > 40 years (if male) or > 45 years (if female)?		
9	Is there a history of exertional palpitation/dyspnea/ discomfort?		
10	Compared with the previous capacity, is the patient able to do the same level of physical activity?		

If the answers to the following questions are "YES," it most likely isn't stable angina.

Sr. No.	Questions	Yes	No
1	Is the pain lasting for 20–30 seconds?		
2	Does the pain change with respiration?		
3	Does the pain change with posture?		
4	Does the pain get relieved with movements of the hand or trunk?		

can ask a patient for selecting which patients are likely to have angina and identify the cases in which other causes of angina should be looked out for.

Furthermore, a detailed history leads to the information that can identify patients who require additional testing. The history also helps in identifying the risk factors and predictors of coronary heart disease that would give a more complete picture of CSA.¹⁰

Physical examination

A systematic physical examination is a cornerstone of an accurate diagnosis. Although it is often normal in angina, it can aid in excluding other diagnoses¹¹ and in identifying the risk factors for CAD, such as hyperlipidemia

Table 1: List of investigations

Test	Look for	Indicates
CBC	Low Hemoglobin, abnormal WBC count and platelet count	Presence of Anemia/ arteritis / abnormal coagulation profile
HbA1C	Raised values	Diagnosis/ control of diabetes
Lipid profile	Deranged values	Dyslipidemia
Liver function test	Deranged values	Doses of medications may need alteration accordingly
Renal function test	High Serum creatinine value and calculate eGFR	Choice of medications and doses should be based on their safety in renal disease
Thyroid function test if clinically indicated	Deranged levels	Thyroid disease ¹³
Cardiac biomarkers		
Cardiac Troponins (Trop T and Trop I)	Elevated levels	Presence of myocardial injury in which case it is ACS and not stable angina and should be treated accordingly. ¹⁴
Creatinine kinase MB*		
NT- pro BNP**	Elevated levels	Important predictor of long-term mortality independent of age ventricular ejection fraction (EF) and conventional risk factors
Cardiac tests		
ECG	Normal/ abnormal	Previous signs of CAD and acts as a baseline ECG for the future comparison.
Treadmill Test ^f	Based on Duke's protocol	Diagnose CAD
ECHO	LVEF and structural abnormalities	Heart failure and structural abnormalities that may be causative or affect prognosis
Angiography	Coronary arterial blocks	Risk stratification rather than diagnosis
FFR/ IVUS	Measurements and cut off values	assist in decision making for treatment strategies

*Cardiac troponins are preferred to creatine kinase MB for diagnostic and prognostic; **Raised levels of natriuretic peptides are associated with an increased risk of adverse outcomes in stable disease.¹⁵ Also, a single measurement of NT-proBNP at the time of hospital admission provides the important information about the left ventricular ejection fraction (LVEF) in unselected patients.¹⁶ Yet, there is not enough evidence to recommend the routine use of these markers in all patients.¹¹ ^fFor patients who cannot exercise, Dobutamine stress test can be performed

(xanthomas) or left ventricular failure (dependent edema and third heart sound).¹²

Biochemical testing

Biochemical investigations help diagnose CAD, identify possible causes, and recognize the presence of risk factors.¹³

The Table 1 provides the list of tests which are commonly employed to provide the possible risk factors and/ cause of cardiac ischemia that has led to stable angina and also provides prognostic information.

Electrocardiogram

Mishra *et al*⁶ recommend that a resting ECG be recorded in all patients suspected of stable angina. The national committee at OPTA recommended that it is crucial to emphasize that a normal ECG does not rule out angina, while an abnormal ECG does not guarantee the presence of angina. There can be large variations in ECG reports.

Similarly, a treadmill test (stress

test) should be performed whenever possible. Treadmill or bicycle exercise is recommended for patients with a normal resting ECG.¹⁵ All physicians should be aware of the indications and contraindications of such tests. According to the available literature, the mean sensitivity and specificity of the stress test for the diagnosis of CAD is 67% and 72%, respectively.¹⁶ However, a point to remember is that the results of a stress test are largely dependent on the pretest probability, and hence should be carried out in patients with a pre-test probability of 15%–65%, wherever feasible.

Pharmacologic (Dobutamine stress test) testing can be considered wherever the patient is unable to exercise. Apart from the diagnosis of ischemia, the test provides information on several parameters that have a prognostic significance.

Echocardiography at rest

The LVEF is an important determinant for risk stratification,

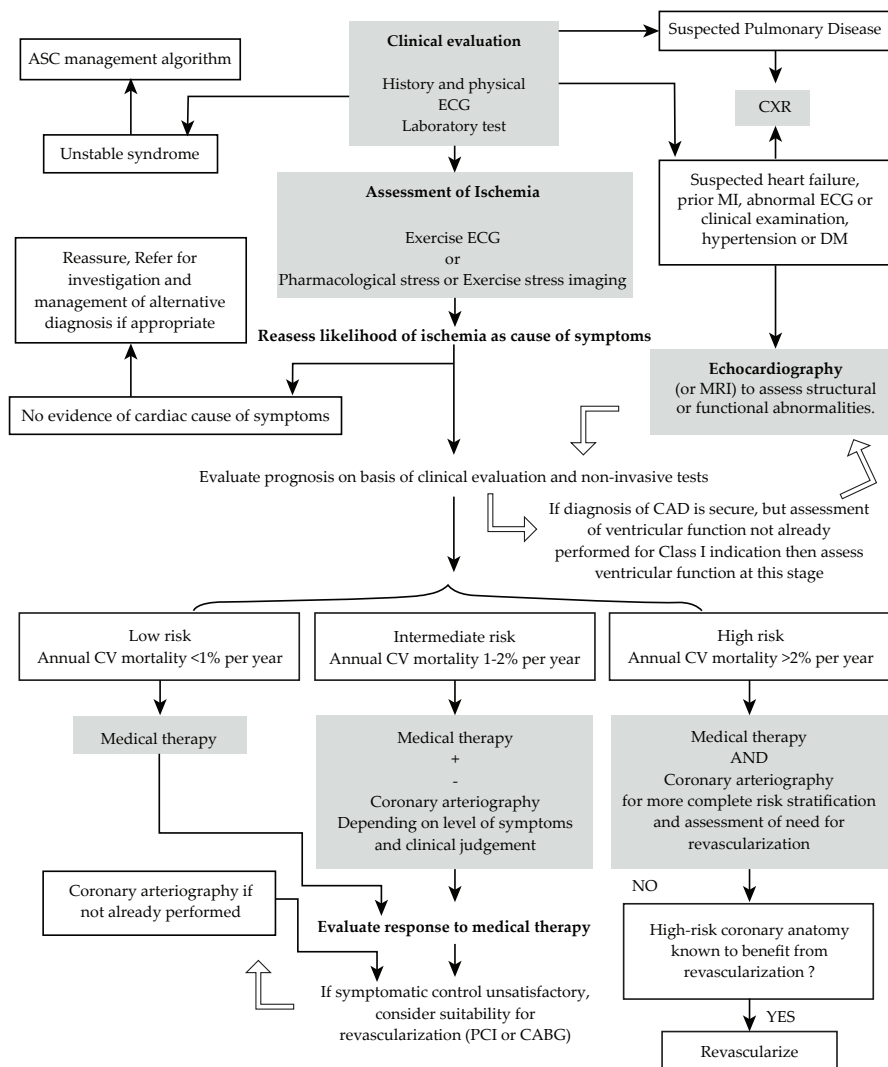


Fig.2: Management algorithm for chronic stable angina

prognosis, and management of CAD.¹⁷ The national committee recommended that apart from the diagnosis, a 2D echocardiogram aids in treatment planning and prognostication of a patient. Echocardiography measures the LVEF; a poor ejection fraction with chronic stable angina greatly increases the risk of heart failure and mortality.¹⁴ Echocardiography is also useful in determining structural abnormalities. The Experts recommend that, a 2D echocardiogram should be done as soon as possible, preferably within 24 hours of the first symptom.

Coronary angiography

In the era of coronary computed tomography angiography (coronary CTA), invasive angiography is more commonly indicated for risk stratification than for diagnosis. Coronary CTA can be considered as an alternative to stress imaging techniques

in certain patients.¹³

Fractional flow reserve: This parameter can also be calculated during coronary angiography. It carries a prognostic significance¹⁸ as well as a diagnostic value in microvascular angina where no lesions can be seen on the coronary angiogram in a suspected case of angina. It helps in decision-making for the treatment strategies in patients with stable angina.

Intravascular ultrasound: Intravascular ultrasound is an important adjunct during coronary angiography, particularly for the assessment of angiographically indeterminate left main CAD.¹⁹

Other less commonly performed procedures include cardiac MRI, exercise echocardiography, and myocardial perfusion scintigraphy.

Based on the available literature^{6,20}

and the expert recommendations from the national committee, Team OPTA has developed an algorithm for the diagnosis and management of chronic stable angina (Figure 2).

Although chest pain is a common presentation of stable angina, it is not the only possible diagnosis. It is important to know the common differential diagnoses of stable angina, so that they can be ruled out. This can aid in establishing a confirmed diagnosis with more certainty.

The common differential diagnoses include the following (Figure 3):^{7, 11}

Following the diagnosis, it is necessary to stratify the risk and accordingly plan the management. The optimal treatment of angina would aim to maintain the quality of life while preventing future adverse cardiac events. Thus, the OPTA goals of medical management of CAD were identified as follows:

- Disease control
- Relief from symptoms
- Build exercise capacity, and
- Improvement of quality of life

The expert panel of national committee developed the following OPTA questionnaire (Box 2). The objective of this questionnaire is to sensitize the clinicians toward the above mentioned four important goals of OPTA and assist in risk stratification and planning of further management in individual case.

Management

Management of chronic stable angina includes lifestyle modification, pharmacological therapy, and surgical intervention. The aim is to maintain quality of life while preventing future adverse cardiac events. Control of risk factors for coronary artery disease need lifestyle modification as well as pharmacotherapy.

Lifestyle modification

Management for event prevention includes lifestyle modification and control of risk factors which are described in Box 3.

Pharmacological management

Lifestyle management alone may not be adequate, and medical management would be necessary in most cases. The drugs that control the disease are (aspirin, statins, and angiotensin-converting-enzyme inhibitors) not

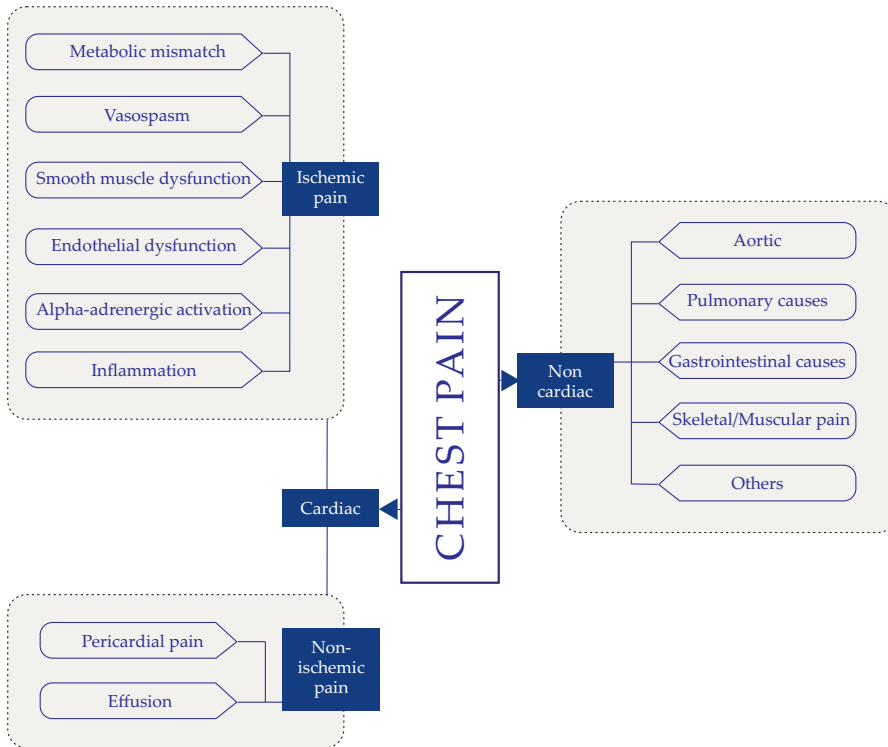


Fig. 3: Differential diagnosis for causes other than obstructive CAD^{7,11}

Box 2: OPTA questionnaire

- Over the **past 4 weeks**, my day-to-day activities have been _____.
 Extremely limited Moderately limited Not limited at all
- Over the **past 4 weeks**, I have had chest pain/tightness/discomfort/angina _____.
 Four or more times per week Three or less times per week Not at all
- Over the **past 4 weeks**, on average, how many times have you had to take short-acting nitrate for your chest pain, chest tightness, or angina? I have taken nitroglycerin...
 Four or more times per week Three or less times per week Not at all
- Over the **past 4 weeks**, how much has your chest pain, chest tightness, or angina limited your enjoyment of life?
 It has extremely limited my enjoyment of life It has moderately limited my enjoyment of life It has not limited my enjoyment of life at all
- If you had to spend the rest of your life with your chest pain, chest tightness or angina the way it is right now, how would you feel about this?
 Not satisfied at all Somewhat satisfied Mostly satisfied

capable of alleviating anginal pain and likewise the antianginals control the symptoms but not the disease.

The European Society of Cardiology explains the multi-pronged approach toward management of angina, and the optimization of medical therapy to ensure successful outcomes.²⁴

Antiplatelet drugs, statins, ACEI/ARB need to be considered for disease modulation.

Antiplatelet drugs

- They prevent the development of

thrombus by inhibiting platelet accumulation.

- Studies have shown that they reduce the recurrence of major adverse cardiac events.²⁵
- Some evidence suggests that dual antiplatelet therapy should be preferred.²⁶ However, a Cochrane review²⁷ concluded that dual therapy should be used only post-stenting.

Aspirin is the prophylactic antiplatelet drug of choice in patients with cardiovascular disease.²⁷

Box 3: Lifestyle modification for control of risk factors of CAD

Risk factor	Modification
Tobacco ^{20,21}	<ul style="list-style-type: none"> • Complete cessation of tobacco intake in any form (including chewing, passive smoking, etc.)
Deranged lipid profile / Obesity	<ul style="list-style-type: none"> • Modification of diet (diet rich in fruits and vegetables) • Diet intended for weight loss • Adequate intake of water
Sedentary lifestyle ²²	<ul style="list-style-type: none"> • Regular physical activity
Diabetes mellitus	<ul style="list-style-type: none"> • Maintenance of optimum weight • Diet modification • Pharmacological management
Hypertension ²³	<ul style="list-style-type: none"> • Systolic pressure should be maintained < 140 mmHg, and diastolic pressure < 90 mmHg • Salt restricted diet • Physical activity • Emotional state • Pharmacological therapy

Statins

- They are useful in angina due to their pleiotropic effects,²⁸ which include improvement of endothelial function, enhancement of the ischemic vasodilatory response, modulation of inflammation, and protection from ischemia-reperfusion injury.
- Several studies have independently demonstrated the major impact of statins in primary prevention of CAD.²⁹
- They have also shown to reduce the occurrence of major adverse outcomes in known patients of CAD.³⁰ It is thus recommended that irrespective of the lipid profile, statins should be prescribed to all patients with stable disease.

ACEI/ARB

Angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are known to reduce total mortality, MI, stroke, and heart failure in patients with CAD. An ACE inhibitor or ARB is recommended for patients with anterior MI or high risk diabetes/persistent hypertension, or if there is evidence of left ventricular dysfunction or heart failure. An ACE inhibitor is the first-

Table 2: Antianginal drugs with their mechanism of action, adverse effects, and special consideration points³¹

Drug group	Mechanism of action	Adverse effects	Points to consider
Nitrates	Vasodilators ³³ leading to reduction of afterload and preload	Headache, flushing, palpitations Phosphodiesterase 5 inhibitors potentiate the vasodilator effect of nitrates	Effective in microvascular and macrovascular angina Long-term use should be with caution
β -blockers	Lower heart rate and reduce myocardial work and oxygen demand	Bradycardia, hypotension, bronchospasm	First choice drugs in chronic stable angina Preferred treatment if LVEF < 40% ^{34,35} Contraindicated in vasospastic angina
Dihydropyridine calcium-channel blockers (CCBs)	Vasodilator Reduce myocardial oxygen demand	Hypotension, flushing, palpitations, and leg edema	Useful for vasospastic angina No improvement in outcome of chronic stable angina Deleterious effect in heart failure
Other CCBs	Reduce myocardial contractility and heart rate, leading to reduction in oxygen demand and in afterload	Leg edema	Useful for vasospastic angina Avoid in combination with β -blocker due to the risk of bradycardia ³⁶
Nicorandil	Increases coronary blood flow and vasodilatation	Headache, reflux, tachycardia, hypotension	No improvement seen in chronic stable angina ³⁷
Ivabradine	Reduces the heart rate Increases coronary flow reserve ³⁸	Bradycardia, phosphenes	Improvement in effort tolerance and number of angina episodes ^{39,40} Can be considered for second line therapy
Ranolazine	Improves anaerobic metabolism under ischemic conditions ⁴¹ Reduction in symptoms of chronic stable angina occurs without affecting heart rate, blood pressure, or myocardial perfusion	Prolongation of QT interval	Effective in alleviating symptoms of chronic stable angina ⁴² Contraindicated in hepatic dysfunction
Trimetazidine	Inhibits oxidation of free fatty acids and increases glucose utilization by ischemic myocardium ⁴³	Nausea, vomiting, headaches	Decreases the frequency of angina, reduces the use of nitrates, and increases exercise duration ⁴⁴ Especially useful in diabetes Contraindicated in renal dysfunction

line therapy for lower-risk patients. Hence, it is appropriate to consider ACE-I for the treatment of patients with stable chronic angina, particularly those with co-existing hypertension, LVEF \leq 40%, diabetes or CKD, unless contraindicated.^{31,32}

Antianginal medications

Antianginal therapy is recommended as the first-line management in chronic stable angina. The drugs in the antianginal class increase total exercise duration, along with a reduction in symptoms both in terms of severity and daily frequency of chronic stable angina when compared with placebo. There are several different groups that can be used in angina, each with specific

and often overlapping cardio protective roles which are described in Table 2.

Traditional approach

In several clinical guidelines, including the European clinical guidelines, medications for symptomatic angina are classified as first choice (β blockers, calcium-channel blockers, short-acting nitrates) or second choice (ivabradine, nicorandil, ranolazine, trimetazidine).

Traditionally, the recommendation was to reserve second-choice medications for patients with contraindications to first-choice agents, who do not tolerate them, or who remain symptomatic despite treatment. There haven't been studies that

directly compare the first-choice and second-choice treatments and display superiority of one group over the other. Meta-analyses support similar efficacy for all types of antianginal drugs for reduction of symptoms, but provide no evidence for improvement in survival. The newer, second-choice drugs have more evidence-based clinical data that are currently compared to the traditional first-choice drugs.³¹

'OPTA' Approach

The OPTA approach differs from this traditional approach. In most cases of angina, more than one drug may be needed for optimal control of symptoms. Also, these individuals with angina have usually several associated comorbidities. Certain agents may have properties that could be useful depending on the comorbidities present and the mechanisms of angina, but the guidelines do not provide recommendations on the optimal combinations of these drugs.

In this consensus statement, we propose an individualized approach, the OPTA approach, for the management of angina, wherein the underlying pathology responsible for angina and the associated comorbidities are taken into consideration.

Based on the presence of comorbidity, the preferable and not preferable (less attractive) antianginals have been classified in the Table 3 given below.

There have been several recent reports of additive or synergistic effects of several antianginal drugs that can be administered in combination, especially in certain conditions.⁷

The possible combinations of different classes of antianginal drugs.

The schematic diagram, shown as Figure 4, demonstrates useful combinations (green lines), combinations that are not recommended (red lines), possible combinations (blue solid lines), and drugs with similar action (blue dashed lines).

Combinations that are beneficial

- β blockers are often combined with dihydropyridine calcium-channel blockers to enhance their anti-ischemic effect.
- Combining nitrates with β blockers can be useful to block tachycardia, leading to a synergetic anti-ischemic effect.
- The synergistic effect between

Table 3: Choice of antianginals based on the presence of associated co-morbidity with angina

Comorbidity	Preferable antianginal	Less preferred choices
Based on heart rate		
High heart rate	β blockers, nonihydropyridine calcium-channel blockers (diltiazem and verapamil), and ivabradine are the preferred drugs when the heart rate is > 70 bpm.	Dihydropyridine Calcium-channel blockers and nitrates may further increase the heart rate.
Low heart rate	Dihydropyridine calcium-channel blockers, nitrates, and nicorandil help increase the heart rate by evoking sympathetic reflex. Ranolazine and trimetazidine may be considered.	
Based on blood pressure		
Hypertension	β -blockers and dihydropyridine calcium-channel blockers	
Hypotension	Ranolazine or trimetazidine Ivabradine (preferred only if associated with high HR)	Calcium-channel blockers, nitrates, and β -blockers as they would further decrease the BP
Based on the underlying pathology of angina		
Microvascular angina	β -blockers Ranolazine Trimetazidine Ivabradine	
Vasospastic angina	CCB and long-acting nitrates	β -blockers can precipitate spasm
Based on rhythm disorders		
Defects in AV conduction	Antianginals other than β -blockers and nondihydropyridine calcium-channel blockers	β -blockers and nondihydropyridine calcium-channel blockers
Atrial fibrillation	β -blockers and nondihydropyridine calcium-channel blockers	
Based on LVEF		
Heart failure and left ventricular dysfunction	β -blocker If HR remains high in spite of use of β -blocker, ivabradine may be added Trimetazidine	Diltiazem and verapamil can worsen LV dysfunction
Based on other systemic disorders		
Peripheral arterial disease	Trimetazidine Ranolazine Ivabradine	β -blockers
Diabetes	Trimetazidine Ranolazine Carvedilol/ Nebivolol	β -blockers other than vasodilating β -blockers- carvedilol/nebivolol
CKD	Other than ranolazine and trimetazidine	Ranolazine and trimetazidine not for patients with GFR < 30 ml/min/1.73 m ²
Hyperthyroidism	Nonselective β -blockers (propranolol) Diltiazem Verapamil Ivabradine	Vasodilators
COPD	Bisoprolol For reduction of heart rate, ivabradine, diltiazem or verapamil	β -blockers except bisoprolol

β -blockers and ivabradine suggests that in patients receiving treatment with β -blockers who are still symptomatic, adding ivabradine is more efficient than up-titration of β -blockers.

- Calcium-channel blockers are effective, alone or in combination with nitrates, in the treatment of vasospastic angina.

Combinations that must be avoided

- β blockers should not be combined with verapamil, and only with caution with diltiazem because of the risk of bradycardia or atrioventricular block.
- Diltiazem and verapamil should not be used in combination with ivabradine owing to the risk of severe bradycardia.
- The concomitant use of nicorandil with aspirin might increase the risk of gastrointestinal ulcers,

perforations, and hemorrhage.

- Ranolazine increases digoxin concentration and should be used with caution in patients taking digoxin.⁷

Thus, considering that the efficacy of all antianginal agents is nearly similar for symptomatic relief and without any advantage over survival, barring a few, it may now be said that the traditional approach needs a relook and the new OPTA approach may be adopted. OPTA approach is based on individualization of therapy, taking into consideration the pathophysiology of angina and the associated co morbidities. A significant number of patients with angina due to CAD will undergo revascularization procedure. But, antianginals may be needed even in these cases until the procedure actually takes place. Further, some patient may continue to be symptomatic even after the revascularization; in such cases, antianginals are needed for control of symptoms and improvement in the quality of life.⁴⁵

Revascularization

Patients of CAD with significant stenosis ($\geq 50\%$ in left main, $\geq 70\%$ in other coronary arteries) should be referred for revascularization procedures. However, the decision to revascularize should be taken after weighing in all the factors, and should be individualized.

Most of the patients with chronic stable angina can be managed with optimal medical treatment. Experts from the field recommend medical therapy for stable angina for following -

- Patients with diffuse disease
- Elderly patients (Age: ≥ 80 Yrs)
- Patients who had incomplete vascularization
- Patients who developed restenosis
- Patients who are awaiting interventions

Procedures such as PCI or CABG for revascularization are reserved for patients who have:

- Uncontrolled symptoms despite being on medical treatment
- Severe angina of class III or IV
- Large area of myocardium at jeopardy
- Left main coronary artery obstruction or proximal LAD

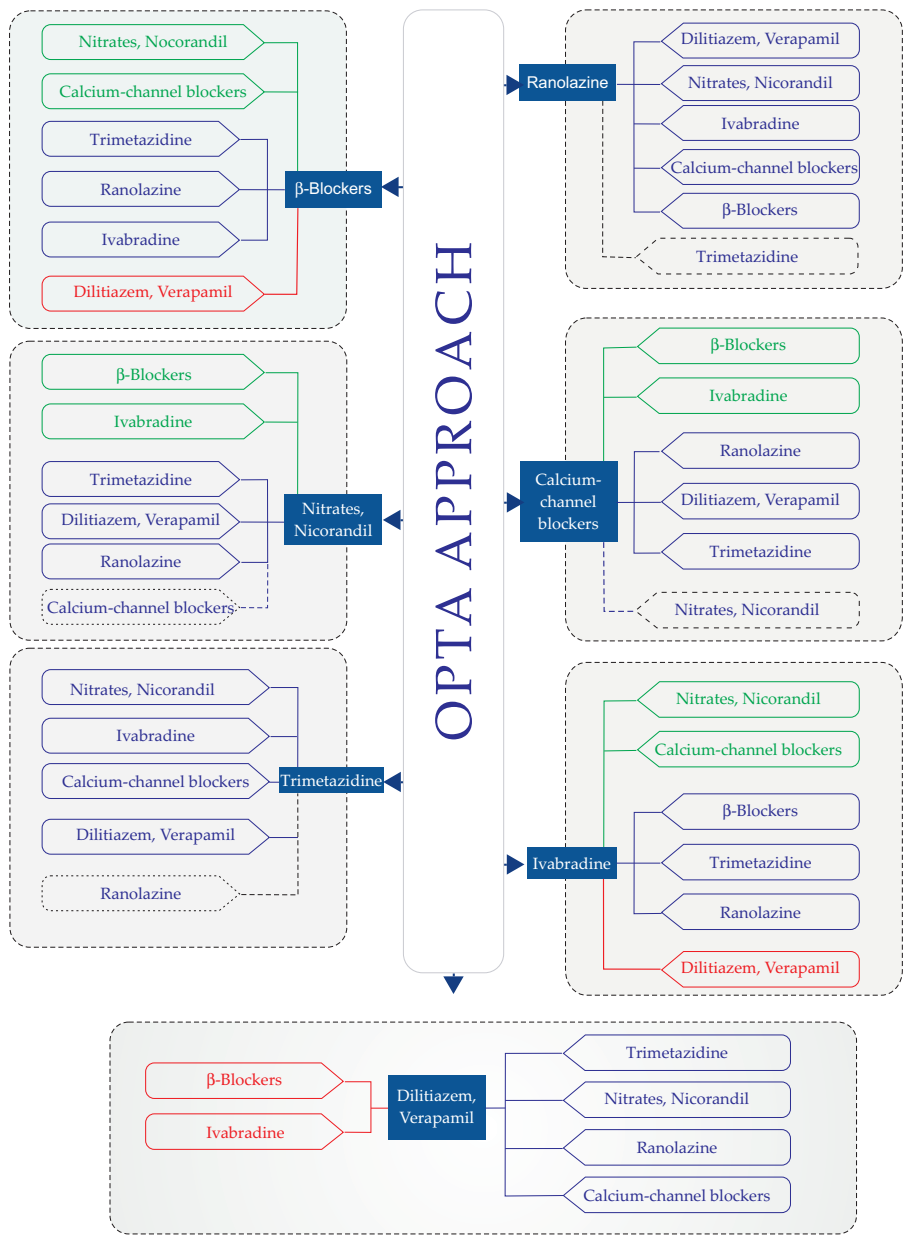


Fig. 4: OPTA approach- The schematic presentation shows useful combinations (green lines), combinations that are not recommended (red lines), possible combinations (blue solid lines), and drugs with similar actions (blue dashed lines)

lesion
 e. Microvascular disease and LV dysfunction⁴⁶
 It is beyond the scope of this document to discuss the coronary revascularization in detail.

Conclusion

Coronary artery disease has steadily increased in the Indian subcontinent, with the prevalence rising five times in the last three decades. Angina is the most common manifestation of reversible ischemia. Most cases of angina can be treated with medical management. The optimal medical

treatment of angina can control the progression of disease, relieve symptoms, and improve exercise tolerance and quality of life. This consensus statement is conceived, under the guidance of experts, for upgrading the medical management of angina in congruence to the latest available evidence.

The first step is early and accurate diagnosis. OPTA endeavoured to provide tools for screening of angina with the help of the checklist. The treatment algorithm that guides the management of the suspected cases of angina has been provided. Further, a

questionnaire for the clinicians to reach out to their patients to enable them to stratify the severity of the condition and accordingly plan the management.

The medical management of chronic stable angina was further reviewed by the experts and based on extensive literature review and discussion among experienced clinicians, a novel approach – the OPTA approach – for the optimal treatment of angina was created. The OPTA approach differs from the traditional approach of first and second line. In the OPTA approach, it is encouraged to individualize therapy taking into consideration the associated comorbidities of the patient and the specific indications and contraindications of each medication.

OPTA encompassed the entire spectrum from the diagnosis, risk stratification to optimal medical management in order to provide a more efficient use of the available armamentarium of antianginals for more successful clinical outcomes.

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