



Referral pathway for chronic stable angina: OPTA approach

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Abstract

Rapid globalization associated with a paradigm shift in the lifestyle behaviour has made a deep impact on the cardiovascular health and disease in India, which is evidenced by a steep rise in the Coronary Artery Disease (CAD) cases past few years. This calls for a timely implementation of aggressive strategies to contain the morbidity and mortality associated with the same. Angina is the classical presenting clinical symptom in CAD, often known to worsen the patient's Quality of Life (QoL) due to its uniqueness of the absence of a standard yardstick to detect the same for appropriate referral and treatment. So, the therapeutic optimization lies in the fact of early and accurate diagnosis. Considering the wide range of diversity in India in terms of its geographical distribution, risk factors across the sections of population and the healthcare delivery spectrum ranging from primary health physicians to the cardiologists, there is a requirement of a standard consensus which would aid the clinician in prompt identification of the angina case and stratify the risk in the same so as to deploy further investigations to assess its severity for further treatment or for appropriate referral to the next level of healthcare.

Keywords: coronary artery disease, risk stratification, angina, optimal medical therapy, revascularization

1. Introduction

Globally, an annual estimate of over 7 million deaths occurs due to Coronary Artery Disease (CAD) - the leading cause of Cardiovascular (CV) morbidity and mortality. By 2015, it was estimated that the number of CAD cases in India would rise to 615 lakhs, which is a major concern especially drawing attention for implementation of aggressive strategies for its prevention and control. It is noteworthy to state that Indians are more susceptible to CAD than their western counterparts in terms of a higher CV mortality rate, which may be attributed to distribution of diverse risk factors and control across various geographical locations in India. Hence, one of the key strategies in the primary prevention of CAD is achievement of the risk factors control, which has been stressed even in recent clinical practice guidelines ^[1].

Classically, angina, which constitutes recurrent transient episodes of chest pain, is considered to be due to flow-limiting CAD, which results in a supply-demand mismatch in myocardial perfusion ^[2]. It is commonly known to worsen the patient's Quality of Life (QoL) as it is the patient-reported symptoms that drive healthcare utilization. Furthermore, the symptom of angina stands unique because of the absence of a standard yardstick like laboratory or imaging tests to detect the same. Despite the limitations in the anginal evaluation, still an effective history taking by the physician stands the cornerstone for an optimal

quantification of the anginal burden, which further cascades to the deployment of appropriate tests to take therapeutic decisions.³ Most cases of angina can be medically managed. The optimal medical treatment of angina is desirable to: Delay in disease progression, achieve symptomatic relief and improve exercise tolerance and thereby the QoL ^[4]. The first step for therapeutic optimization is an early and accurate diagnosis for which the recent Indian consensus for optimal treatment of angina has facilitated by providing: Simple tool for screening of angina in the form of a checklist, treatment algorithm for managing a suspected case of angina, patient outreach questionnaire for the clinicians to assist them in risk stratification for further management planning ^[4].

In a country like India, the complete infrastructure of Indian healthcare delivery system is diverse with a wide range of doctors spanning across the system, starting from primary health care practitioners, physicians up to the speciality personnel like cardiologists. So, weighing the population: doctor ratio, it is practically challenging for every patient with suspected angina to get a cardiologist's access. Further, the severity and the nature of angina are highly detrimental for further diagnostic or therapeutic planning. In other words, an increase in the severity of the case may primarily require a cardiological intervention and a less

severe one could be efficiently managed by the physicians themselves.

Optimal Treatment of Angina (OPTA) consensus gives us the clarity on anginal identification and measures that could be administered in such episodes, but the questions on "when to administer" and "whom to administer" still require a clearance. So, the call of the hour necessitates the requirement of a "streamlined approach to categorize the risk or magnitude of the CV burden in an anginal patient" for prompt referral up across the clinician's spectrum which paves way for proper management [i.e., management based on risk stratification].

Currently, there are no definite guidelines (Indian) at the national level to combat this problem and thus, the need for clinical management guidelines for referral was considered [5].

2. Methodology

With the aforesaid objective, multiple meetings were held across India with experts from the field of cardiology. During these meetings, there was a discussion regarding the anginal risk stratification for appropriate referral. As an outcome, expert consensus has laid down a path of recommendations for risk stratification considering the prevailing healthcare service infrastructure, local evidence-based studies as well as major international guidelines

3. Risk stratification and referral pathway

The very purpose of risk stratification helps in identifying a patient at a higher risk of getting a CV event like risk of CV death or Myocardial Infarction (MI), who would benefit from optimizing the medical therapy or revascularization beyond the symptom amelioration.

The current risk classification of patients with annual CV mortality risk is trichotomized as: [6].

- **Low-risk group:** Low event risk patients are those with an annual mortality of 1% per year
- **Intermediate-risk group:** Intermediate event risk group has an annual mortality of $\geq 1\%$ but $\leq 3\%$ per year
- **High-risk group:** High event risk patients are those with an annual mortality of $>3\%$

The sequential assessment of risk involves an integrated approach to stratify the same based on:

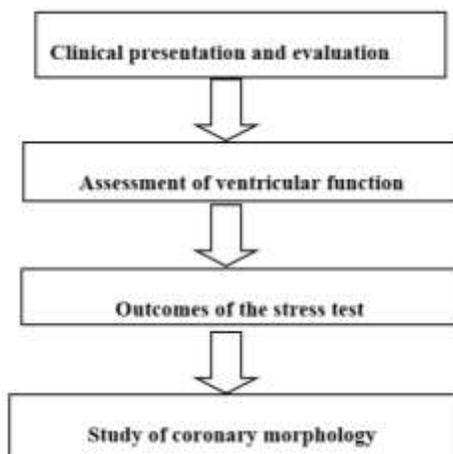


Fig 1

A good clinical history to understand the pattern of occurrence (recent onset or progressive) and severity of angina, particularly if unresponsive to therapy (OPTA Questionnaire) [4]. And clinical examination can provide important prognostic information. Increasing age is an important factor to consider, as it is directly proportional to the disease downhill dynamics. Additionally, it would be worthwhile to elicit a robust history related to diabetes, hypertension, dyslipidemia (untreated or elevated despite treatment), presence of Chronic Kidney Disease (CKD), peripheral vascular disease, prior MI, heart failure and smoking which all are known to be predictive of adverse outcome in patients with CAD or other populations with established CV disease [6].

3.1. Risk stratification based on presentation

3.1.1. Risk stratification based on age and gender

Hubbard's score is considered among risk stratification scoring system, which includes both male and female of age between 40 years and greater than 80 years in addition to a history of angina/MI, diabetes mellitus, and exercise testing (i.e., stress ECG) result (positive or negative).

Table 1: Risk stratification scoring system - age and gender-based (Adapted from Hubbard's 5point scoring system)

Variables	Score
Sex	
Female	1
Male	0
Age group	
<40 years	0
40 to 49 years	1
50 to 59 years	2
60 to 69 years	3
70 to 79 years	4
At or older than 80 years	5

The male and female gender and the age are given a score (as indicated in the above table); higher age is associated with a profile of higher CV risk.

The male gender itself is an additional score, which is self-explanatory of a higher score in men. Additionally, MI is more common in men, but women have a worse prognosis due to higher rates of death and re-infarction.

As for angina pectoris, despite its higher frequency in women, the prevalence of significant CAD is lower, causing a lower predictive value for non-invasive testing. Hence, the significance of risk stratification (for a prompt, timely referral) based on age and gender may not be completely based on the same said parameters but also to be taken in light of comorbidities and investigative modalities [7].

In a nutshell, the shortcomings of considering age and gender alone for risk stratification could be summarized as in the below mentioned table:

- Clinical presentation of CAD and the interpretation of noninvasive diagnostic testing are less reliable in women compared with men, especially in the age group below 55 years
- Chest pain syndromes are more common in women than in men and are less related to the presence of atherosclerosis in

the large epicardial coronary arteries

- Women who are diagnosed with non-cardiac chest pain have a two-fold increased risk to develop a Coronary Heart Disease (CHD) event in the next 5–7 years and have 4x higher risk for re-hospitalizations and recurrent angiograms in the next 180 days [8].

This implies that the traditional diagnostic methods are not optimal for women and that they should be treated more aggressively for their risk factors.

3.1.2. Risk stratification based on clinical presentation and severity

Angina pectoris by nature has a myriad of presentations which may sometimes pose a problem to the general practitioner in identifying the same and more, so the burden becomes manifold if the patient has comorbid conditions like diabetes, hypertension, dyslipidemia, etc. So, chest pain scoring may improve the quality of understanding the nature and severity of angina in patients which will pave way for appropriate identification and referral. The components of the same and the comorbidities have been described in Tables 2 and 3 below [9].

Table 2: Risk scoring for stratification by clinical presentation and severity (with or without co-morbidities) [10].

Factors		Score
Precipitating factor	Always on exertion, relieved by rest	3
	Emotional stress/exposure to cold/after meal	1
	Nothing in particular/unpredictable	0
	Breathing in/out	-1
Position of pain	Front of chest/ Neck/ Shoulders/ Jaw/ Arms/	1
	Epigastric Right-side/ Sub-mammary/ very localized	0
Type of pain	Constricting/cramping/heavy/tight/burning/dull ache	1
	Stabbing/Sharp	0
	Reproducible by manual pressure on chest wall	-1
Duration of pain	<15 minutes	1
	Few seconds only	0
	>15 minutes or hour	-1
	Total chest pain score	

Table 3: Risk factors and co-morbidities [10].

Risk Factors	
Diabetes mellitus	Yes/No
Cholesterol >6.47 mmol/L	Yes/No
Current smoker or recent ex-smoker	Yes/No
Family history of a first-degree relative with coronary disease <60 years	Yes/No
Hypertension	Yes/No
Past history of IHD#?	Yes/No

#If Yes, refer to cardiology clinic if suspected of a cardiac origin

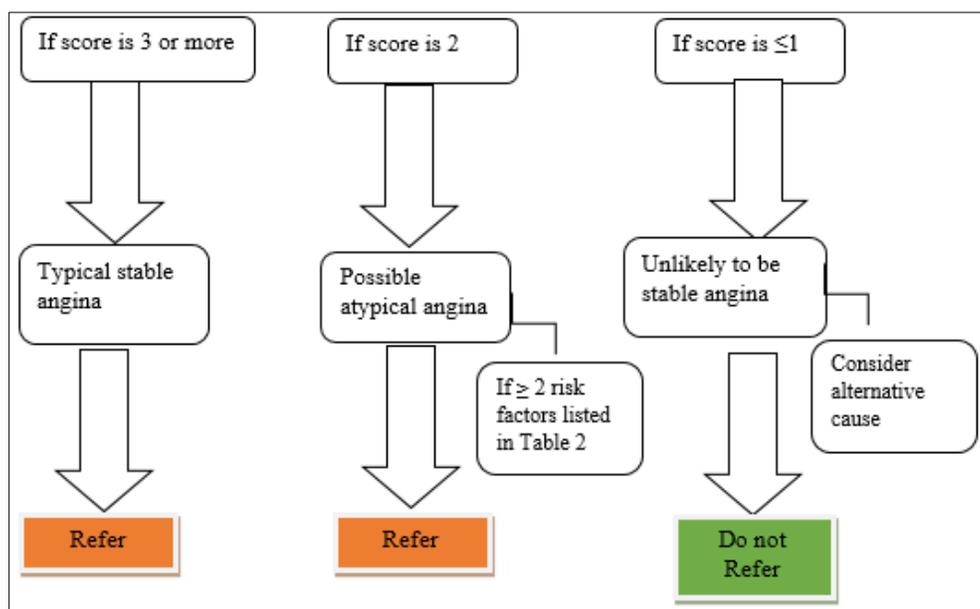


Fig 1: Pain symptom score scoring based cardiological referral (for general practitioners) [10].

A low total chest pain symptom score (i.e., ≤ 1) indicates that stable angina is very unlikely and General Practitioners (GPs) should refrain from referring such cases to a cardiologist and are advised to investigate for an alternative cause of the chest pain, for which the GPs need to be trained. An intermediate total score of 2 equates to possible atypical angina and requires the presence of at least one conventional CV risk factor to meet the threshold for referral for assessment. A total score of 3 or more indicates typical angina symptoms and automatically fulfils referral

criteria. The chest pain symptom score offers doctors working in the peripheral regions, an objective and quantitative diagnostic tool to guide the likelihood of angina and appropriateness of referral to the next level of healthcare. The clinician has to also take into consideration the other co-morbidities like diabetes mellitus, hypertension etc., which will make the assessment more comprehensive [10].

3.1.3. Risk stratification based on grading of angina

Table 4: Classification of angina severity according to the Canadian Cardiovascular Society

Class	Level of Symptoms
Class I	Ordinary activity does not cause angina Angina with strenuous or rapid or prolonged exertion only
Class II	Slight limitation of ordinary activity Angina on walking or climbing stairs rapidly Walking uphill or exertion after meals in cold weather, when under emotional stress or only during the first few hours after awakening
Class III	Marked limitation of ordinary physical activity Angina on walking one or two blocks on the level or one flight of stairs at a normal pace under normal conditions
Class IV	Inability to carry out any physical activity without discomfort or 'angina at rest'

For patients with stable angina, it is also useful to classify the severity of symptoms using a grading system such as that of the Canadian Cardiovascular Society Classification. Severity of the angina increments across the grades, which may also be used in determining the functional impairment of the patient and quantifying response to therapy, may offer superior prognostic capability. Grading could be further ascertained by performing a baseline Electrocardiogram (ECG), and if positive and the patient is suitable, could further be subjected to a stress ECG or a treadmill test [9].

3.2. Risk stratification based on ventricular function

Left Ventricular (LV) function is obtained by doing a resting echocardiogram and is the strongest predictor of long-term survival. A decline in the LV function is associated with increased chances of mortality in a Stable CAD (SCAD) patient. Based on the ventricular ejection fraction, the Coronary Artery Surgery Study (CASS) registry reported the 12-year survival of SCAD patients (Table 5) [6].

Table 5: Risk stratification based on Resting Echocardiography (LVEF - Left Ventricular Ejection Fraction) [6].

Ejection fraction (%)	12-year survival rate (%)
≥ 50	73
35-49	54
< 35	21

Hence, a patient with a Left Ventricular Ejection Fraction (LVEF) $< 50\%$ is already at high risk for CV death (annual mortality $> 3\%$), even without accounting for additional event risk factors, such as the extent of ischemia. As a reduced LVEF $< 50\%$ confers such an important increase in event risk, it may be important not to miss obstructed vessels causing ischemia in such patients [6].

Guidelines recommend a mandatory resting echocardiography in following patients with stable angina, the quantification of which helps in risk stratification [6].

1. Those with abnormal auscultatory findings suggestive of valvular heart disease or hypertrophic cardiomyopathy
2. Those with suspicion of heart failure

3. History of prior MI
4. Those with Left Bundle-branch Block (LBBB), Q waves, or other significant pathological changes on ECG, including electrocardiographic left anterior hemiblock (LVH) [9].

3.3. Risk stratification based on stress testing

Patients with suspected or known CAD with anginal symptoms should undergo stress testing to perform event risk stratification which becomes the basis for therapeutic decisions to see if they are the candidates suited for coronary revascularization. As most patients would have undergone some form of diagnostic testing anyway, these results can also be used for event risk stratification. The common modes of stress testing are stress ECG or stress ECHO.

3.3.1. Risk stratification based on stress ECG

Considering its simplicity and widespread availability, treadmill or bicycle exercise testing with a 12-lead ECG monitoring remains a good option in anginal patient with suspected CAD. The chief diagnostic abnormality during the testing consists of a horizontal or downsloping ST-segment depression ≥ 0.1 mV, persisting for at least 0.06–0.08s after the J-point, in one or more ECG leads. It is of significance that in approximately 15% of the patients, diagnostic ST-segment changes appear only during the recovery phase.

Additional information such as heart rate response, Blood Pressure (BP) response, symptoms, and workload achieved, which has both diagnostic and prognostic relevance, also can be obtained by this test. An optimal diagnostic information is got from ECG stress testing if performed when the patient is having limited symptoms or signs and not being administered or under the effect of antianginal agents.

Based on the stress ECG findings, the risk stratification (based on CV mortality) of the anginal patients could be as low, intermediate and high-risk group [6,11].

[Stress testing can also be useful to evaluate the efficacy of medical treatment or after revascularization, or to assist prescription of exercise after control of symptoms. For these indications, it should be performed on treatment to evaluate control of ischemia or effort performance.] Stress ECG testing is

not of any diagnostic value in the presence of Left Bundle-branch Block (LBBB), paced rhythm and Wolff-Parkinson-White syndrome, in which cases the electrical changes may not be interpretable. Additionally, false positive results are seen as an abnormal resting ECG in patients with Left Ventricular Hypertrophy (LVH), women with hyperventilation, in hypertensives, diabetics [12, 13], electrolyte imbalance, intra ventricular conduction abnormalities, atrial fibrillation and use of digitalis. Also, this test is less sensitive and specific in women. Noteworthy would it be to mention that this test may be inconclusive in patients whose heart rate is not achievable up to 85% in absence of ischemic symptomatology, with exercise limitation due to orthopaedic and non-cardiac problems and those with equivocal ECG. In these patients, an alternative non-invasive imaging test with pharmacologic stress should be selected [6].

3.3.2. Risk stratification based on stress ECHO

Stress (exercise or pharmacological) echocardiography can be employed to demonstrate the presence of CAD by the induction of wall motion abnormalities. Stress echocardiography enhances our interpretation of the exercise stress test by sub-classifying the

risk in all grades of Duke Treadmill Score (DTS) and has been utilized for the evaluation of the functional importance of CAD and for risk stratification in patients with known or suspected SCAD.

Choosing the type of a stress test is based upon the patient’s ability to perform the exercise protocol, presence of baseline electrocardiographic abnormalities that could interfere with the interpretation of the exercise ECG, preoperative risk stratification prior to non-cardiac surgery, and whether we want to localize ischemia or assess myocardial viability. Still, many patients are unable to exercise maximally for stress testing because of varied conditions, including arthritis, severe lung and cardiac disease, orthopedic conditions and diseases of the nervous system. In such patients, pharmacological stress testing is often performed [12, 13]. Exercise echocardiography provides a more physiological environment than pharmacological tests and provides additional physiological data such as exercise time and workload as well as information about changes in heart rate, BP, and ECG. Whereas, pharmacological test is preferred when there is already a significant resting wall motion abnormality (dobutamine for viability assessment) and/or if the patient is unable to exercise adequately [6].

Table 6: Summary findings of risk stratification based on stress electrocardiography and echocardiography [6,11,12,13]

Modality used	Parameter/s indicative of Risk			Score	Risk group
	Stenosis $\geq 75\%$	Multi-vessel disease	1-year mortality		
Stress ECG	40.1%	23.7%	0.25%	≥ 5	Low
	67.3%	55.0%	1.25%	-10 to 4	Intermediate
	99.6%	93.7%	5.25%	≤ -11	High
	Wall Abnormalities			Area of Ischemia	Risk Group
Stress ECHO (17-segment LV model)	No Ischemia			-	Low
	Any Ischemia < 3 segments			1-10%	Intermediate
	New perfusion defects of $\geq 3/17$ segments			$> 10\%$	High

The 17-segment LV model is used, and a 4-point scale used to assess wall thickening score at rest and at stress. The locations of the segments follow the territory of the coronary arteries to accelerate the evaluation of ischemia [13]. Inducible ischemia is defined as new or worsening wall thickening abnormality during stress in two or more contiguous LV segments. [12] Patients with inducible wall motion abnormalities in ≥ 3 of the 17 segments of the standard LV model are to be considered as being at high-event risk (corresponding to an annual mortality $> 3\%$) and coronary angiography should be considered [6]. The ECG and ECHO based risk stratification are summarized in the below-mentioned table 6.

3.3.3. Risk stratification based on stress perfusion scintigraphy

Myocardial perfusion imaging using Single Photon Emission Computed Tomography (SPECT) is a useful method of non-invasive risk stratification, readily identifies those patients at greatest risk for subsequent death and MI. Patients with stress-

induced reversible perfusion deficits $> 10\%$ of the total LV myocardium (≥ 2 of the 17 segments) represent a high-risk subset who might require an early coronary angiography.

The extent and severity of ischemia and scar on PET MPI in patients with known or suspected CAD also provides incremental event risk estimates of cardiac death and all-cause death, compared with conventional coronary risk factors [6].

3.3.4. Risk stratification based on stress cardiac magnetic resonance

There is an independent association between adverse cardiac outcomes for patients with an abnormal dobutamine stress CMR and $> 99\%$ event-free survival in patients with no evidence of ischemia over a 36-month follow-up. Similar to stress echocardiography and stress SPECT, new wall motion abnormalities (≥ 3 segments in the 17-segment model) induced by stress or stress-induced reversible perfusion deficits $> 10\%$ (≥ 2 segments) of the LV myocardium should be regarded as indicating a high-event risk situation [6].

3.4. Risk stratification based on coronary angiography

3.4.1. Risk stratification based on coronary computed tomography angiography

Table 7: ESC 2013 Recommendations for the use of CCTA for the diagnosis of stable CAD⁶

Recommendations	Class ^a	Level ^b
Coronary CTA should be considered as an alternative to stress imaging techniques for ruling out SCAD in patients within the lower range of intermediate PTP for SCAD in whom good image quality can be expected	IIa	C
Coronary CTA should be considered in patients with lower range of intermediate PTP for SCAD after a non-conclusive exercise ECG or stress imaging test or who have contraindications to stress testing in order to avoid otherwise necessary invasive coronary angiography if fully diagnostic image quality of coronary CTA can be expected	IIa	C

The evolution of Coronary Computed Tomography Angiography (CCTA) has seen improved temporal and spatial resolution and has raised the promise of providing such an accurate non-invasive anatomical evaluation of the coronary arteries. More recently, questions have focused, not only on the diagnostic accuracy of CCTA but also its clinical application in planning for appropriate therapeutic intervention like Optimal Medical Therapy (OMT) or revascularization (PCI or CABG) therapies and thereby adding value in improving patient outcomes in terms of reduction in the futuristic

Risk of MI ^[14] Development of a standard 16-segment anatomic segmental analysis for image interpretation forms the basis for CCTA. All the segments are coded for the presence and severity of coronary arterial stenosis. Extent of obstructive CAD is defined by $\geq 50\%$ stenosis in 0, 1, 2, or 3 coronary artery vessels. Left main CAD is grouped with three-vessel obstructive CAD. Noteworthy would it be to mention that CCTA has an added established prognostic value in detecting a non-obstructive coronary atherosclerotic plaque too.¹⁵The CCTA based risk stratification is as follows:

Table 8: CCTA-based risk stratification ^[15]

Group	No. of vascular segments involved	Stenosis %	Risk Group Stratification
0	-	-	Low Risk
1	≥ 1 segment	1-49%	
2	≥ 2 segments ≥ 1 proximal segment	1-49% with any stenosis	
3	≥ 1 segment	50-69%	Intermediate Risk
4	≥ 2 segments (or) ≥ 1 segment	50-69% (or) $\geq 70\%$	
5	≥ 3 segments (or) ≥ 2 segments	50-69% (or) $\geq 70\%$	High Risk
6	≥ 3 segments (or) ≥ 2 segments	$\geq 70\%$ (or) $\geq 70\%$ AND proximal LAD with $\geq 70\%$ stenosis	
7	Left main	$\geq 50\%$	

Studies point out that CCTA demonstrated a negative predictive value of 83% and positive predictive value of 91% when used in symptomatic patients with suspected CHD, implying that CCTA can provide robust diagnostic information in higher risk groups.¹³ But, the specificity of CCTA decreases with increasing amounts of coronary calcium, and the prevalence of coronary artery stenosis is found to be high in symptomatic individuals with a calcium score of >400 . Hence, it would be reasonable not to proceed with CCTA if the calcium score exceeds 400 ^[6].

3.4.2. Risk stratification based on Invasive Coronary Angiography (ICA)

Non-invasive testing can establish the likelihood of the presence of obstructive coronary disease with an acceptable degree of certainty. Thus, ICA will only rarely be necessary in- stable patients with suspected CAD, for establishing or excluding the diagnosis, situations arising where the patients may be ineligible to undergo stress imaging techniques, patients with reduced LVEF ($<50\%$) and typical anginal symptomatology.

ICA may, however, be indicated following non-invasive risk stratification for determination of options for revascularization. Despite the identified limitations of ICA to recognize vulnerable

plaques, the extent and severity of luminal obstruction and location of coronary disease on coronary arteriography have been credibly shown to be vital prognostic indicators in angina patients ^[6, 16].

Although ICA remains the standard for the detection of CAD, it is reserved for patients whose clinical risk is assessed as high or when stress testing indicates considerable ischemic burden. Despite this known algorithm in our guidelines, there are two major concerns for the intermediate-risk patient:

- Coronary angiography is over-used and of low yield
- Stress imaging has improved diagnostic accuracy compared with history alone and can avoid invasive procedures

Appropriate utilization of non-invasive diagnostic testing is crucial to ensure that patients with CAD are referred to angiography for diagnosis and that patients who do not have CAD can avoid unnecessary invasive testing.¹⁷

4. Discussion

The long-term prognosis of SCAD depends upon a number of factors like clinical and demographic variables, LV function, the result of stress testing and coronary anatomy as determined by

Angiographic techniques. When discussing risk stratification in patients with SCAD, event risk refers principally to the risk of CV death and MI although in some studies even wider combinations of CV endpoints are employed. As all-cause death is more specifically defined than other weaker endpoints, including MI, these guidelines stratify event risk according to this hard endpoint. The process of risk stratification serves to identify patients at high-event risk who will benefit from revascularization beyond the amelioration of symptoms, as a guide for the medical practitioners/physicians for understanding the disease burden paving way for an appropriate/timely referral to the cardiologist,

As a good guidance in which group of patients OMT could be initiated instead of revascularization.

As per the key experts opinion across India, the process generally follows a sequential order, of risk stratification by: Clinical evaluation as the first premise; resting ECG and/or echocardiography to document the ischemic and ventricular functional changes if the baseline ECG/ECHO are normal, then subjecting to stress exercise and imaging tests to document the inducible ischemia; non-invasive assessment of ischemia/coronary anatomy which is usually obtained in the process of making a diagnosis of SCAD; ICA for required only in a selected subgroup of patients [6].

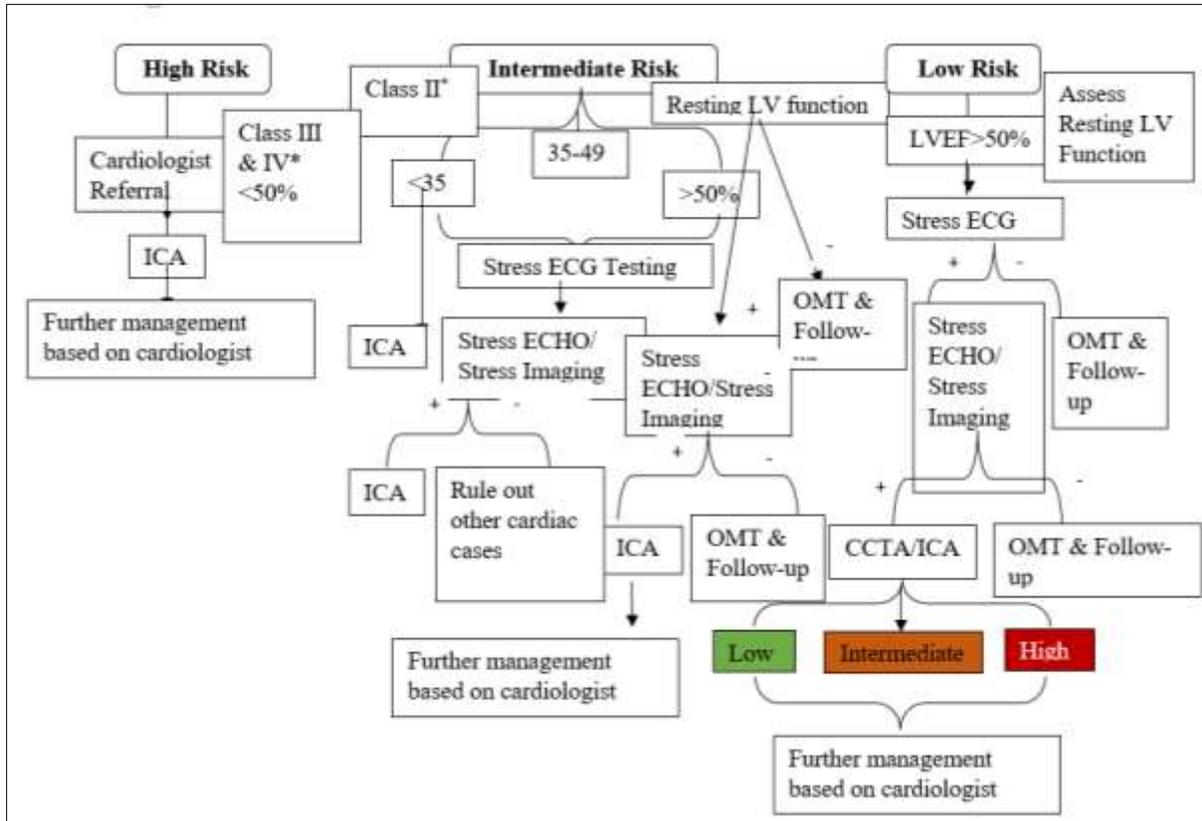


Fig 2: Algorithm for the most probable referral and management of the risk groups [The "+" or "-" signs indicates a positive or a negative test, based on which the further step of investigation/therapy could be considered. * - Canadian Cardiovascular Society grading of angina pectoris, ICA-Invasive coronary angiography, OMT-Optimal medical therapy

Before concluding, it is to be accepted that every yardstick of assessment has its own advantages and disadvantages (as mentioned in the table below). Successful risk stratification lies in the physician's discretion of applying the appropriate test for optimal outcomes in terms of therapy and patient's well-being.

5. Conclusion

"Risk stratification of angina patients" is a dynamic process which begins with clinical evaluation of the anginal symptoms (new or recurrent) and grades the risk accordingly while conducting aggressive lifestyle modification and medical therapy. In developing countries like India where there is cardiologist reach to the peripheral areas are minimal, there is a strong need to understand the importance of risk stratification of patients and thus appropriate management. OMT could be a safe option instead of invasive revascularization in patients with minimal or acceptable symptoms and determined to be at low risk where symptom relief and quality of life form a chief aspect. Higher risk

patients may benefit from early revascularization in addition to OMT to improve long-term prognosis; however, absolute risk, and thus the prognostic benefits of revascularization may be overestimated in data based on historical studies. Further studies are currently underway aiming to clarify this.

6. Acknowledgement

Authors gratefully acknowledge the following experts across India who gave their expert opinion in the advisory board meetings; Dr. Sunil Lhila, Dr. S S Chatterjee, Dr. Pankaj Singh, Dr. Sunil Baran Roy, Dr. Debabrata Mitra, Dr. Ranjan Srivastava, Dr. Satrajit Samanta, Dr. Soumik Basu, Dr. Gautam Sarkar, Dr. Louie Fischer, Dr. Anil Kumar, Dr. Saji Subramaniam, Dr. Himal Raj, Dr. C Jaya Rama Reedy, Dr. Anil Balachandran, Dr. Jimmy George, Dr. Ranju Kumar, Dr. Cibi Issac, Dr. Blessan Varghese, Dr. S S Binu, Dr. Mangalanandan, Dr. Pradeep P, Dr. Jayapal V, Dr. Thomas Mathew, Dr. Arshad, Dr. Praveen.G.K, Dr. Sajith, Dr. Harihara Sharma, Dr. K Suresh, Dr. Sheeba George, Dr.

Ramesh Natarajan, Dr Abhijit Vaidya, Dr Abhijeet Joshi, Dr Amit Sinkar, Dr Gaurav Ganeshwala, Dr M Durairaj, Dr Satish Kolekar, Dr Manoj Bhise, Dr Shailesh Patil, Dr Satyajeet Suryawanshi, Dr Rahul Sawant, Dr Abhay Khode, Dr B K Singh, Dr Manoj Gupta, Dr Vikas Agrawal, Dr Ashish Jaiswal, Dr Alok Kumar Singh, Dr Rajiv Gupta, Dr.Ram Murti Singh, Dr Anand Singh, Dr Birendra Kumar, Dr J Kannan, Dr Narayana Murthy, Dr Anand Shenoy, Dr Pradeep Deokate, Dr G Sridhar, Dr Srinivas Prasad, Dr Vikram Kolhari, Dr Ashutosh Vashistha, Dr Vijay Sai, Dr Naushad Ahmed Peeran, Dr B Vinod Kumar, Dr M. Kathiresan, Dr K.P Shamsuddeen, Dr J. V Balasubramaniam, Dr P Balaji, Dr C.Arumugam, Dr A Krishnamurthy, Dr G. Ashok, Dr S. Ramesh, Dr U. Kalaichelvan, Dr S.U Thillai Vallal
The authors would like to thank Dr Durga Prasad from Magna Health Solutions for providing support in manuscript writing.

7. Disclosure

Funding for writing support was provided by Abbott Healthcare Pvt Ltd. The authors have declared and confirmed that there is no conflict of interest with respect to this authored publication. The views expressed and stated in this article are the independent views of the authors and not of Abbott Healthcare Pvt. Ltd.

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