

Non-invasive Investigation of Chronic Stable Angina – A Practical overview for Medical Practitioners

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SUMMARY

How does one decide on the best non-invasive test to investigate stable coronary ischaemia? This is a very common question faced by many medical practitioners. Chronic stable angina is a common presentation encountered in general practice. Upon clinical assessment and risk stratification the patient needs to be investigated further to confirm the diagnosis. The first investigational modality involves a non-invasive test. It is important that practitioners possess a practical knowledge of the array of different tests that are available so that the best suited one for each patient can be chosen. This article aims to compare the efficacy and accuracy and the practical utility of the different non-invasive tests for coronary ischaemia and aid the practitioner in making sound decisions in this regard.

KEY WORDS:

Angina, Stress testing, Angiography

INTRODUCTION

Coronary Artery Disease (CAD) remains a major cause of morbidity and mortality in our community. Advances in research and technology have enabled clinicians with a selection of available non-invasive tests to investigate not only the presence of coronary artery disease but also its severity which is important for prognostic purposes.

The use of these tests varies significantly between clinicians. There are several likely explanations for this, such as accessibility, availability, cost, experience with its use, pre-conceived bias, patient characteristics, local protocols and guidelines.

The majority of patients with symptomatic CAD present to the general practice or the hospital outpatient clinic with chest pain on exertion. It is important that the doctor is able to identify the salient features that may suggest angina as the cause of the presenting complaint and estimate the clinical urgency to investigate and/or intervene. The first investigation in the stable CAD patient is a non-invasive test for reversible coronary ischaemia. In addition to investigation it is important to assess patient's coronary risk factor profile and manage the same appropriately. Angina may also require anti-anginal therapy to be decided upon based on its severity, frequency and the patient's haemodynamic parameters.

Oral or topical glyceryl trinitrate, beta-blockers and calcium channel blockers are the first line agents for angina management. Ivabradine, perhexiline and nicorandil can be used as additional agents. Upon further investigation some may be treated with percutaneous coronary intervention (PCI) or coronary artery bypass surgery.

The purpose of this article is to outline the major non-invasive tests (exercise ECG test, myocardial perfusion scan, and stress echocardiography), their diagnostic accuracy, limitations and clinical situations for their appropriate use.

Chronic stable angina

Chronic stable angina is chest discomfort caused by myocardial ischemia on exertion without necrosis. Chronic stable angina includes predictable and reproducible chest discomfort after physical activity, emotional stress, or both: symptoms are typically worse in cold weather or after meals and are relieved by rest or sublingual nitroglycerin¹. Approximately 1% of the patients presenting to general practitioners are due to symptoms of angina².

Chronic stable angina results from the imbalance between myocardial oxygen demand and supply due to impaired myocardial perfusion as a consequence of coronary stenosis. CAD is a result of the formation of mural atherosclerotic plaques due to several highly interrelated processes including lipid disturbances, platelet activation, thrombus formation, endothelial dysfunction, inflammation, oxidative stress, vascular smooth cell activation, altered matrix metabolism, remodelling and genetic factors³.

People with angina are at increased risk of serious cardiovascular events and mortality compared to those without angina. The annual mortality is 1-2 % and annual risk of myocardial infarction is 2-3%. Features that indicate a poorer prognosis include more severe symptoms, male sex, abnormal resting ECG, previous MI, left ventricular dysfunction, easily provoked or widespread coronary ischemia on stress testing, and significant stenoses of all three major coronary arteries or the left main coronary artery. In addition, the standard coronary risk factors continue to exert a detrimental and additive effect on prognosis in people with CAD².

The goals in treatment of chronic stable angina are to 1) relieve symptoms 2) to prevent progression of the

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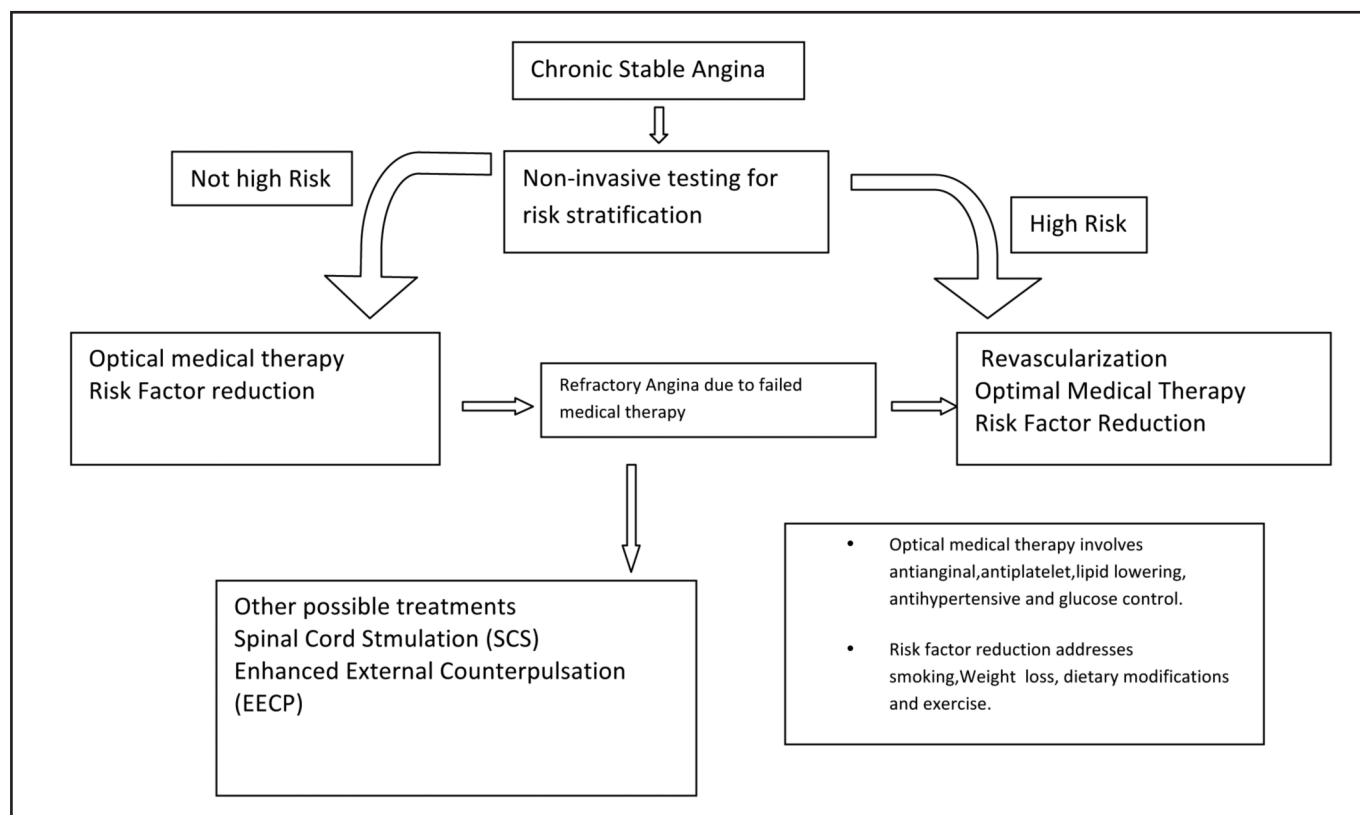


Fig. 1: Algorithm on Management of Chronic Stable Angina

atherosclerotic process and reduce risk of myocardial infarction (MI) or sudden cardiac death 3) to control complicating factors which trigger or worsen ischemia. Figure 1 gives a broad outline of management of chronic stable angina. The COURAGE trial demonstrated that outcomes in patients treated for chronic angina did not differ significantly between the medical therapy group and the group undergoing PCI⁴. This reaffirms the importance of optimal medical therapy and risk factor management – therapeutic strategy that can be initiated by the primary care practitioner.

How do you select the most appropriate test for your patient?

The important determinants for choice of test include:

- Pre-test probability of coronary artery disease
- Patient's ability to exercise to the required level
- Patient's baseline ECG characteristics
- Previous history of myocardial infarction, revascularization

Exercise Stress Test

Exercise stress test (EST) is often the first line test used in the diagnosis of CAD. It is the most studied, widely available and least expensive of all the non-invasive tests. Data pooled from 132 studies calculated a sensitivity of 68% and specificity of 77%⁵. It is also useful for the assessment of prognosis in known CAD with the objective assessment of exercise capacity and exercise tolerance. Duke nomogram and Duke treadmill score are validated tools for the risk stratification of patients referred for EST. The Duke treadmill

score is a composite index that was designed to provide survival estimates based on results from the exercise test, including ST-segment depression, chest pain, and exercise duration⁶.

This test is not suitable for patients who are unable to exercise sufficiently due to various reasons such as arthritis, leg claudication, deconditioning or pulmonary disease. It is not suitable in those with ECG changes at rest that would interfere with the interpretation of the result⁷. These are complete left bundle branch block (LBBB), paced ventricular rhythm, more than 1mm of ST-segment depression at rest, pre-excitation (Wolff-Parkinson-White) syndrome, or other similar ECG conduction abnormalities.

The result of the test can be influenced by several drugs including Digoxin, beta blockers, anti-anginals and some anti-hypertensives such as non-dihydropyridine calcium channel blockers. It is recommended whenever feasible to withhold these medications up to 2 days (4-5 half-lives) before the test^{5,8}.

Myocardial Perfusion Scan - MPS (Radionuclide Imaging)

This test relies on the uptake of tracers labelled with radio isotopes (Thallium TI 201 or Technetium Tc 99m) by myocardial cells, which is determined by its perfusion from the territorial coronary vessel. SPECT scanners detect emission from the tracer and reconstruct anatomical slices of the heart. Reversible defects indicate ischemia.

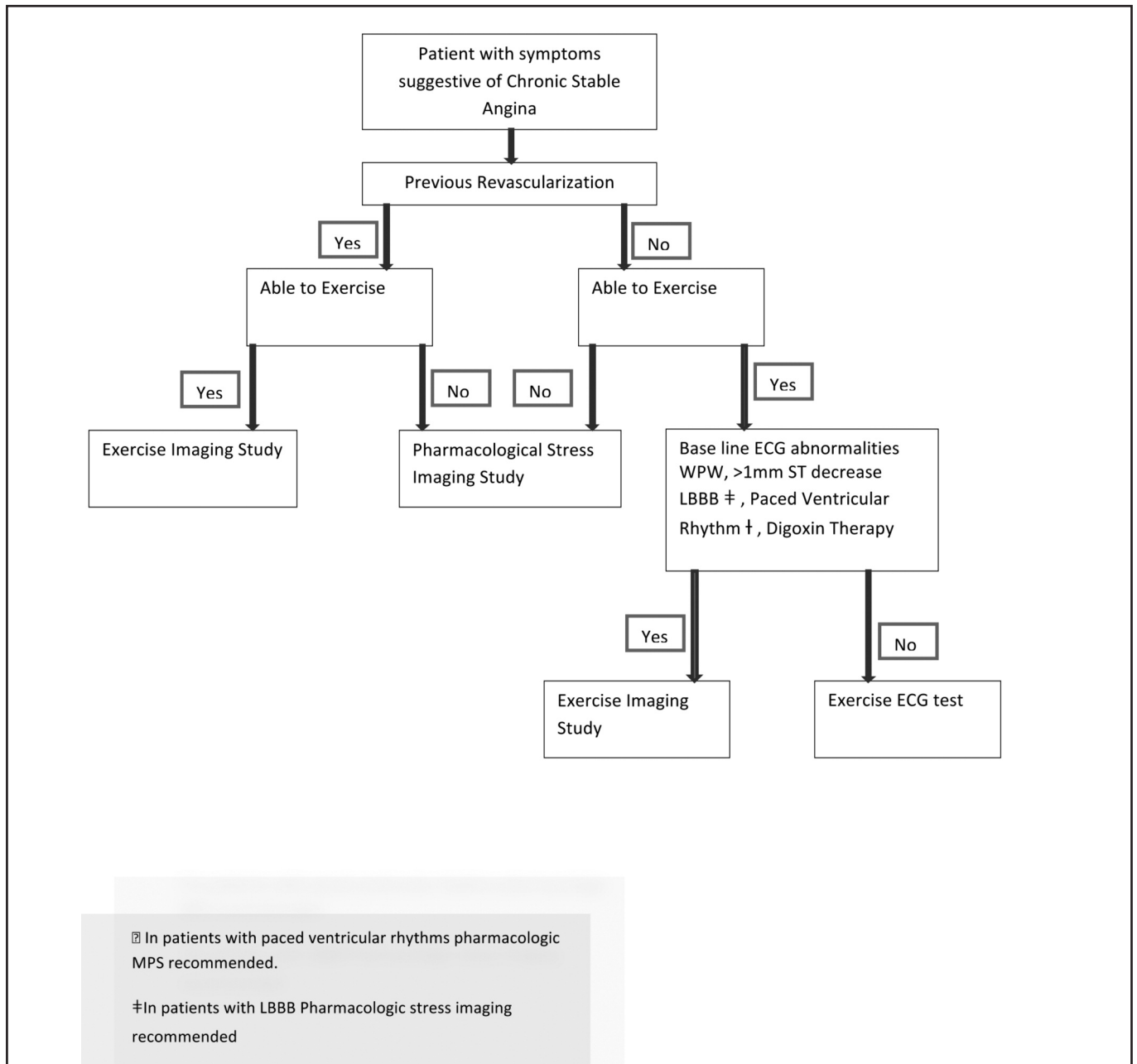


Fig. 2: The Choice of Exercise Testing Modality in Different Clinical Settings

Ischemia can be induced with physical exercise or via pharmacological means (dobutamine, adenosine, or dipyridamole). It has a better sensitivity (70-94%) but variable specificity (43-97%) compared to EST and is able to assess myocardial viability⁵.

The disadvantages of MPS include cost, time consumption, radiation exposure and compromised accuracy of the results that can be affected by artefacts due to soft tissue (breast) or the diaphragm. It also has lower specificity in LBBB because of false positive results⁸.

Stress Echocardiography

This test can be performed with exercise or pharmacological agents (dobutamine, dipyridamole). Echocardiographic images are obtained at rest and during or immediately after stress. These are then compared to look for wall-motion abnormalities during exercise. A positive test is usually indicated by new or worsening wall-motion abnormalities.

It has excellent sensitivity (85%) and specificity (90%). McCully et al. concluded that a negative exercise stress echo is associated with rates of survival without cardiac event of 99.2% (1 year) and 97.4% (3 years)⁹.

The other advantages apart from relative low cost and portability are the ability to assess global and regional ventricular function, chamber size, wall thickness and valvular function.

The disadvantage includes interpretation of results which can be subjective and non-standardized. Image quality can also be affected by patient factors such as obesity, structural abnormalities of the thorax and lung pathology.

Computed Tomography Coronary Angiography (CTCA)

Compared with other imaging techniques, CTCA provides anatomic rather than functional information regarding coronary patency. The advent of multi-slice CT has led to the wider acceptance of CTCA as an imaging tool for coronary vascular disease.

CTCA involves injection of contrast and breath holding by the patient, but requires very little time to scan the whole heart. CTCA has been shown to have good negative predictive value and therefore may be considered in low to intermediate-risk patient groups as a non-invasive of practical utility to rule out obstructive coronary disease¹⁰. Its sensitivity is 96-99% and specificity 85-88%. This is superior to that of stress testing modalities¹¹.

The disadvantages are that patient needs to have a slower heart rate for the procedure and most patients will require beta blockade or ivabradine for this reason. Irregular heart rhythms such as atrial fibrillation and inability to breath-hold for about 15-20 seconds may prevent patients from having this test. There is a small but appreciable amount of radiation exposure to the patient. Well known complications related to contrast (hypersensitivity, nephropathy) need to be assessed with each individual patient. Extensive coronary calcification can reduce the ability to interpret the test results accurately. If the non invasive test suggests the presence of underlying possible significant coronary artery disease the patient should be referred for coronary angiography. Coronary angiography is an invasive investigation.

Coronary angiography

Although the non-invasive tests provide useful diagnostic and prognostic information in patients suspected of having CAD, Coronary angiography has been regarded as the gold standard in establishing the diagnosis of coronary artery disease, and in overall assessment of the patient.

In addition to anatomical information on the coronary vasculature, intervention (balloon and stent angioplasty) can be performed in selected patients at the same time.

Although the cardiac catheterisation is done under local anaesthetic with a skin puncture, it's not without risks.

The procedure carries a small risk (<1%) of mortality, myocardial infarction and cerebrovascular accident. In addition to that vascular complications such as local haematoma that may occasionally require evacuation need to be discussed with the patient. Contrast related complications are not uncommon. Contrast induced nephropathy is

particularly seen in patients with prior renal impairment. In addition certain patients may be hypersensitive to contrast agent which could occasionally lead to bronchospasm and shock.

CONCLUSION

The role of non- invasive investigations especially in suspected Chronic Stable Angina is to risk stratify and ascertain the likelihood of significant coronary artery disease. This information in turn helps the clinician decide which patient needs further invasive investigation and treatment (coronary angiography and revascularization) in addition to appropriate medical therapy.

The evidence (BARI-2D study, COURAGE study) supports the adoption of a conservative strategy in the stable patient with CAD, with optimal medical therapy^{12,13}. The high-risk patients require early invasive investigation for prognostic benefit. The patient population where the non- invasive investigations are most likely to influence and clarify clinical decisions is the intermediate risk group.

The provided algorithm (Figure 2) is only a guide to test selection in different clinical settings. A normal test result should never be taken as an absolute guarantee against the presence of coronary artery disease or the risk of cardiovascular events. If there is still clinical suspicion of significant coronary artery disease, further testing should be pursued. There is no substitute for good clinical judgement.

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(True/False)

1. The important determinants for the choice of preliminary tests for coronary ischaemia include:

- A. Pre-test probability of coronary artery disease
- B. Previous history of heart failure
- C. Patient's ability to exercise to the required level
- D. Patient's baseline ECG characteristics
- E. Previous history of myocardial infarction

2. Which of the following are factors that indicate a poor prognosis in coronary artery disease?

- A. Severe symptoms
- B. Female sex
- C. Left ventricular dysfunction
- D. Male sex
- E. Previous MI

3. Results of the exercise stress test may not be influenced by:

- A. Digoxin
- B. Beta blocker
- C. Aspirin
- D. Calcium channel blocker
- E. Metformin

4. Sensitivity of stress echocardiography at detecting coronary ischaemia is:

- A. 75%
- B. 65%
- C. 55%
- D. 85%
- E. 95%

5. Which test has the highest sensitivity when performed in the appropriate patient?

- A. Exercise stress test
- B. Stress echo
- C. Myocardial perfusion scan
- D. Six minute walk test
- E. CT coronary angiogram