

## Chapter V: Asymptomatic Coronary Artery Disease

### Risk Factors

- Smoking
- Hypertension
- Diabetes mellitus
- Physical inactivity (Sedentary life style)
- High cholesterol, high triglycerides and other dyslipidemias
- Family history of heart disease
- Obesity and overweight

### Burden

- Atherosclerotic coronary artery disease (CAD) is the underlying cause of most ischemic cardiac events and can result in:
  - Stable angina pectoris
  - Acute coronary syndrome (ACS)
  - Acute myocardial infarction (AMI)
  - Cardiomyopathy and Congestive heart failure
  - Cardiac arrhythmias
  - Sudden cardiac death

### Screening tests

- **The principal tests include:**
  - Resting ECG.
  - Exercise ECG (Stress test).
- **The less commonly used tests for screening purposes:**
  - Thallium-201 scintigraphy (Thalium scan)
  - Exercise echocardiography
  - Ambulatory ECG (Holter monitoring)

## Recommendations for prevention

- There is insufficient evidence to recommend for or against screening middle-aged and older men and women for asymptomatic coronary artery disease, using resting electrocardiography (ECG), ambulatory ECG, or exercise ECG.
- Recommendations against routine screening can be made on other grounds for individuals who are not at high risk of developing clinical heart disease (see clinical intervention).
- Routine screening is not recommended as part of the periodic health visit or pre-participation sports examination for children, adolescents, or young adults.
- Clinicians should emphasize proven measures for the primary prevention of coronary disease (see clinical intervention).

## **Burden of suffering**

- o Ischemic heart disease is one of the leading causes of death in Egypt.
- o Atherosclerotic coronary artery disease (CAD) is the underlying cause of most ischemic cardiac events and can result in:
  - Stable angina pectoris,
  - Acute coronary syndrome (ACS),
  - Myocardial infarction,
  - Congestive heart failure,
  - Cardiac arrhythmias, and
  - Sudden cardiac death.
- o Clinically significant CAD is uncommon in men under 40 and premenopausal women, but risk increases with advancing age and in the presence of risk factors such as:
  - Smoking,
  - Hypertension,
  - Diabetes,
  - High cholesterol, high triglycerides and other dyslipidemias,
  - Family history of heart disease, and
  - Obesity.
- o The total burden of coronary disease is predicted to increase substantially over the next years due to the increasing size of the elderly population.<sup>1</sup>
- o Angina is the most common presenting symptom of myocardial ischemia and underlying CAD, but in many persons the first evidence of CAD may be myocardial infarction or sudden death.<sup>2</sup>
- o Great number of men has asymptomatic but physiologically significant coronary disease, also referred to as silent myocardial ischemia.<sup>2,3</sup>

## **Accuracy of screening tests**

There are two screening strategies to reduce morbidity and mortality from CAD:

### ***The first strategy***

- o It involves screening for modifiable cardiac risk factors, such as:
  - Diabetes,
  - Hypertension,
  - Elevated serum cholesterol and triglycerides,
  - Cigarette smoking,
  - Physical inactivity, and
  - Diet.

### ***The second strategy***

- o It is the early detection of asymptomatic CAD.
- o The principal tests for detecting asymptomatic CAD which can provide evidence of previous silent myocardial infarctions and silent or inducible myocardial ischemia include:
  - Resting ECG, and

- Exercise ECG (Stress test).
- o The less commonly used tests for screening purposes are:
  - Thallium-201 scintigraphy (Thallium scan),
  - Exercise echocardiography, and
  - Ambulatory ECG (Holter monitoring).
- o The efficacy of each of these tests may be evaluated by:
  - Its ability to detect atherosclerotic plaque, and significant narrowing of coronaries.
  - Its ability to predict the occurrence of a serious clinical event in the future (acute coronary syndrome, acute myocardial infarction, sudden cardiac death).

### Resting ECG

- o An electrocardiogram is a test that records the electrical activity of the heart.
- o ECG is used to assess:<sup>65</sup>
  - The rate and rhythm regularity of heartbeats,
  - The size and position of the chambers,
  - The presence of any damage to the heart (ischemia and infarction),
  - The effects of drugs and electrolytes, and
  - Effect of devices used to regulate the heart (such as a pacemaker).
- o Regular periodic resting ECG increases the likelihood of early detection of coronary atherosclerosis and of future coronary events. Significant findings include:
  - ST depression or elevation ( $\geq 1$  mm).
  - T-wave inversion.
  - "Q" or "QS" waves.
  - Left axis deviation and left bundle branch block (LBBB).
- o However, these findings are uncommon in asymptomatic persons, occurring in only 1-4% of middle-aged men without clinical evidence of CAD.<sup>4,5</sup>
- o One third to one half of patients with angiographically normal coronary arteries have Q waves, T-wave inversion, or ST-T changes on their resting ECG.<sup>6-8</sup>
- o Conversely, a normal ECG does not rule out CAD, as some of patients with symptomatic, angiographically proven CAD demonstrate a normal resting ECG.<sup>9</sup>
- o Asymptomatic persons with the following baseline ECG abnormalities have a higher risk of future coronary events:<sup>4,10-17</sup>
  - "Q" or "QS" waves,
  - ST-segment depression or elevation,
  - T-wave inversion,
  - Left ventricular hypertrophy & strain, and
  - Ventricular premature beats (significant/serious criteria).
- o However, symptomatic CAD develops in only 3-15% of persons with the previous ECG findings.<sup>4,11,16,18</sup>
- o Furthermore, most coronary events occur in persons without resting ECG abnormalities.<sup>4,5,16,19,20</sup>

- o Thus, routine ECG testing in asymptomatic persons, in whom the pretest probability of having CAD is relatively low, is not an efficient process for detecting CAD or for predicting future coronary events.

### Exercise ECG (Stress test)

- o It is a recording of the electrical activity of the heart during physical stress to test the heart's reaction to increased demand for oxygen:<sup>66</sup>
  - An electrocardiogram (ECG) is used to record the activity of the heart, and blood pressure readings are taken while the patient walks on a treadmill or pedal a stationary bicycle.
  - The response of the heart to this increased workload is monitored.
  - The test continues until the patient reaches a target heart rate, unless complications such as chest pain or an exaggerated rise in blood pressure develop with activity.
  - Monitoring continues after exercise for 10 to 15 minutes or until the heart rate returns to baseline.
- o The exercise ECG is more accurate than the resting ECG for detecting clinically significant CAD.
- o Most patients with asymptomatic CAD do not have a positive exercise ECG.<sup>21-24</sup>
- o ECG changes often do not become apparent until an atherosclerotic plaque has progressed to the point that it significantly impedes coronary blood flow.<sup>22,25</sup>
- o In addition, most asymptomatic persons with an abnormal exercise ECG result (usually defined by a specific magnitude of ST-segment depression) do not have underlying CAD.<sup>25,26</sup>
- o The exercise ECG is also more accurate than the resting ECG in predicting future coronary events.
- o While asymptomatic persons with a positive exercise ECG are more likely to experience an event than those with negative tests,<sup>23,27,32</sup> studies have shown that only 1-11% will suffer an acute coronary syndrome, acute myocardial infarction or sudden death.<sup>23,31,33,34</sup>
- o The majority of critical events will occur in those with a negative exercise test result,<sup>22,24,33-36</sup> and the majority of less serious events occur in those with positive stress test.
- o The pathophysiology of acute coronary syndromes may explain the insensitivity of exercise ECG for subsequent coronary events. Unstable angina, acute myocardial infarction (AMI), and sudden death often result from an acute, occluding thrombus precipitated by the rupture of a mild, non-flow-limiting plaque.<sup>37-39</sup>
- o Among healthy men who subsequently developed symptomatic CAD after a negative screening test, 73% experienced an AMI or sudden death as their initial manifestation.<sup>22,34</sup>
- o In contrast, the majority of asymptomatic persons with a positive exercise ECG develop angina as their initial event.<sup>3,22,34,40</sup>
- o Thus, while exercise ECG may predict the presence of more severe coronary stenosis and risk of angina in asymptomatic persons, it does not accurately predict risk of acute coronary events with serious outcome.

### Thallium-201 scintigraphy (Thallium scan)

- o Imaging with radiopharmaceuticals that localize in either the myocardium or in the blood pool is a sensitive means of detecting and quantitatively assessing numerous conditions involving the heart.<sup>67</sup>
- o The goal of cardiac scintigraphy is to evaluate myocardial perfusion and/or function to detect physiologic and anatomic abnormalities of the heart.<sup>67</sup>
- o The addition of thallium-201 scintigraphy to conventional exercise testing improves its accuracy in detecting CAD, making it a useful diagnostic test in persons with symptoms of CAD.<sup>41,42</sup>
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- o There are five major classes of cardiac scintigraphy:<sup>67</sup>
  - Myocardial Perfusion Imaging (single-photon emission computed tomography [SPECT] or planar, stress and/or resting, gated or ungated):
    - Detecting the presence, location, and extent of coronary artery disease.
    - Evaluating the physiologic significance or sequelae of known or suspected coronary artery stenoses.
    - Monitoring the effects of treatment of coronary artery disease, including revascularization and medical therapy.
    - Detecting acute myocardial infarction.
    - Evaluating the viability of dysfunctional myocardium.
    - Stratifying risk of myocardial events.
    - Evaluating ventricular function (using gated images).
    - Determining prognosis after myocardial infarction.
  - Gated Cardiac Blood-Pool Imaging (resting and/or stress):
    - Quantifying parameters of ventricular function (e.g., ejection fraction, wall motion, ventricular volume, cardiac output, and diastolic function);
    - Detecting the presence, location, and extent of coronary artery disease;
    - Assessing whether congestive heart failure is due to ischemic or nonischemic causes;
    - Evaluating potential cardiotoxic effects of chemotherapy; and
    - Evaluating the effects of valvular abnormalities.
  - First-Pass Cardiac Imaging:
    - Calculating left and right ventricular ejection fractions;
    - Assessing wall motion abnormalities;
    - Quantifying left-to-right cardiac shunts; and
    - Measuring cardiac output and absolute ventricular chamber volumes.
  - Myocardial Infarction Imaging:
    - Diagnosing and assessing the location and extent of acutely infarcted myocardium.

- Right-to-Left Shunt Evaluation:
  - Detecting and quantifying right-to-left shunts using radiolabeled particles.
- o However, the probability of CAD after a positive scan is low in asymptomatic persons, and most coronary events occur in those with a negative test result.<sup>21,33</sup>
- o Because of these limitations and its expense, thallium-201 scintigraphy is not a practical screening test for asymptomatic persons.<sup>21,33,41,43</sup>

### Ambulatory ECG (Holter monitoring)

- o Holter monitoring provides a continuous recording of heart rhythm during normal activity.<sup>68</sup>
  - The monitor is usually worn for 24 hours at least to obtain a recording of a complete day.
  - Electrodes (small conducting patches) are placed on the patient's chest and attached to a small recording monitor that the patient can carry in a pocket or in a small pouch worn around the neck. The monitor is battery operated.
  - Electrical activity of the heart is recorded (much like the recording of an ECG), usually for a 24-hour period while the patient keeps a diary of his/her activities.
  - The recording is then analyzed, a report of the heart's activity is tabulated, and irregular heart activity is correlated with the patient's activity at the time.
  - It is very important that the patient accurately record his/her symptoms and activities so that the doctor can correlate them with his/her Holter monitor findings.
- o The ambulatory ECG can detect episodes of ST-segment depression which may indicate silent ischemia in asymptomatic persons with CAD.
- o These episodes, however, also occur commonly in healthy volunteers<sup>44,46</sup> and are not reliable predictors of future coronary events, even in asymptomatic or mildly symptomatic patients with documented CAD.<sup>47,48</sup>

### Exercise echocardiography<sup>69</sup>

- o The rationale behind exercise testing is to increase myocardial oxygen demand by increasing heart rate, blood pressure and contractility.
- o Exercise echocardiography is used to diagnose myocardial ischemia by detecting regional abnormalities in wall motion during or immediately following exercise.
- o Exercise echocardiography is useful in:
  - Evaluating patients with chest pain that is atypical for myocardial ischemia.
  - Determining the prognosis in patients with known coronary artery disease, such as following myocardial infarction or in patients with chronic angina.
- o The exercise electrocardiogram alone is usually of little clinical value when the pretest likelihood of coronary artery disease is low or when the electrocardiogram is inaccurate in detecting myocardial ischemia, as in patients with bundle branch blocks, left ventricular hypertrophy, pre-excitation or in patients taking digoxin. In these patients, the predictive value of exercise echocardiography in detecting coronary artery disease is high.
- o However, there have been no studies of exercise echocardiography in screening asymptomatic populations for CAD.

### False-positive screening

- o False-positive screening test results are undesirable for several reasons:
  - Persons with abnormal results frequently undergo invasive diagnostic procedures such as coronary angiography.
  - Abnormal test results may produce considerable anxiety.
  - An abnormal ECG tracing may disqualify some patients from jobs, insurance eligibility, and other opportunities, although the extent of these problems is not known.
- o Proposed strategies for reducing false-positive results include:
  - Performing workups in accordance with a Bayesian model,<sup>59</sup>
  - Using discriminant functions to interpret the stress ECG,<sup>30</sup> and
  - Targeting testing to high-risk groups.

### **Effectiveness of Early Detection**

- o Asymptomatic persons with selected ECG findings are at increased risk of myocardial infarction and cardiac death,<sup>3,5,20,23,27-32</sup> but there is little evidence that routine screening is an effective means to reduce the incidence of acute coronary events in asymptomatic persons.

### ***Antianginal drugs***

- o Antianginal drugs such as nitroglycerine,  $\beta$ -adrenergic blockers, and calcium channel blockers reduce the frequency and the duration of silent ischemia.<sup>50-52</sup>
- o In a recent study, atenolol reduced the incidence of cardiac events (MI, cardiac arrest, or worsening angina) in patients who had both silent ischemia and CAD documented by angiography or prior myocardial infarction;<sup>53,54</sup> extrapolating these benefits to completely asymptomatic patients with silent ischemia on routine screening may not be justified, given their much lower risk of acute events.<sup>35</sup>
- o Both aspirin therapy and drug treatment for high cholesterol reduce the incidence of MI and cardiac mortality in patients with symptomatic coronary disease, but the balance of risks and benefits of these therapies in asymptomatic patients is not resolved.
- o Benefits are more likely to exceed risks in asymptomatic patients with underlying coronary disease, however, due to their higher absolute risk of MI and sudden death.

### ***New diagnostic techniques***

- o New diagnostic techniques may prove more sensitive than angiography in identifying the mild-to-moderate plaques that are a risk factor for developing an acute occlusive thrombus.<sup>55,56</sup>
- o Their utility will remain in question, however, until appropriate trials demonstrate that early detection and treatment of small coronary plaques is more effective than treatment based on identifiable risk factors (e.g., high blood pressure or high cholesterol) in asymptomatic patients.<sup>37,38</sup>

- o Among patients with symptomatic coronary disease, coronary artery by-pass grafting prolongs life compared with medical therapy in patients with left main coronary or three-vessel disease with poor left ventricular function.<sup>9</sup>
- o The prevalence of high-risk coronary disease among asymptomatic persons, however, is very low; while some patients may suffer a MI or sudden cardiac death as their initial manifestation of CAD, most patients with severe coronary disease initially develop angina.<sup>3,34</sup>
- o As a result, it is not clear that the benefit of identifying a small number of individuals with severe coronary disease before they develop symptoms is sufficient to justify routine screening of large populations of asymptomatic persons.
- o Percutaneous transluminal coronary angioplasty (PTCA) reduces the frequency of angina in patients with symptomatic CAD, but it does not reduce the incidence of MI or cardiac death.<sup>57,58</sup>
- o The value of coronary angioplasty for asymptomatic coronary stenosis is not known.

### ***Screening ECG***

#### Baseline ECG

- o A screening ECG has been recommended to provide a “baseline” to help interpret changes in subsequent ECGs.<sup>59</sup>
- o Even when important differences are noted between the baseline ECG and a subsequent tracing, these do not necessarily reflect ongoing or recent ischemia.
- o Baseline ECGs are often not available when needed for comparison, nor do they significantly contribute to decision making for patients being evaluated for chest pain,<sup>60-63</sup> especially in those with no history of cardiovascular disease.<sup>64</sup>
- o The availability of a prior ECG is associated with small but significant reduction in hospitalization rates for those patients who had chest pain not due to acute MI.<sup>61</sup>
- o Only a small subset of the asymptomatic population is likely to benefit from having a baseline ECG, however: those with baseline ECG abnormalities suggestive of ischemia who subsequently develop acute noncardiac chest pain.
- o Savings from preventing a few unnecessary hospitalizations among these patients must be weighed against the high costs of routine ECG screening in the large population of asymptomatic persons.
- o The early identification of persons at increased risk for CAD on the basis of ECG findings may help to modify other important cardiac risk factors such as cigarette smoking, hypertension, and elevated serum cholesterol.<sup>59</sup>

#### Periodic ECG

- o Periodic ECG screening is often recommended for persons who might endanger public safety were they to experience an acute cardiac event at work (e.g., airline pilots, bus and truck drivers, railroad engineers).
- o Cardiac events in such individuals are more likely to affect the safety of a large number of persons, and clinical intervention, either through medical treatment or work restrictions, might prevent such catastrophes.

- o No studies have addressed the efficacy of ECG screening in these persons, however.

### Preliminary exercise ECG

- o Preliminary exercise ECG testing has also been recommended for sedentary persons planning to begin vigorous exercise programs, based on evidence that strenuous exertion may increase the risk of sudden cardiac death.
- o The usual underlying cause of sudden cardiac death during exercise is hypertrophic cardiomyopathy or congenital coronary anomalies in young persons and CAD in older persons.
- o Cardiac events during exercise in persons without symptomatic heart disease are uncommon, however, and exercise ECG may not accurately predict those who are at risk.
- o Given the low incidence of activity-related events in middle-aged men, and the uncertain benefit of restricting activity in those with abnormal exercise tests, the potential benefits of pre-exercise testing appear small.
- o In populations at low risk for heart disease, any benefits of detecting the rare individual with asymptomatic CAD may be offset by adverse effects of labeling and exercise restrictions for the larger number of persons with false-positive ECG results.

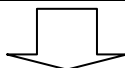
## **Clinical Intervention**

### ***Screening***

- o There is insufficient evidence to recommend for or against screening middle-aged and older men and women for asymptomatic coronary artery disease with resting electrocardiography ECG, ambulatory ECG, or exercise ECG.
- o Recommendations against routine screening may be made on other grounds for persons who are not at high risk of developing symptomatic CAD; these grounds include:
  - The limited sensitivity and low predictive value of an abnormal resting ECG in asymptomatic persons, and
  - The high cost of screening and follow-up.
- o Screening selected high-risk asymptomatic persons (e.g., those with multiple cardiac risk factors) is indicated only where results will influence treatment decisions (e.g., use of aspirin or lipid-lowering drugs in asymptomatic persons).
- o Screening individuals in certain occupations (pilots, truck drivers, etc.) can be recommended on other grounds, including possible benefits to public safety.
- o The choice of specific screening test for asymptomatic CAD is left to clinical discretion: exercise ECG is more accurate than resting ECG but is more expensive.
- o Routine ECG screening as part of the periodic health visit or preparticipation in physical sports is not recommended for asymptomatic children, adolescents, or young adults.
- o Clinicians should emphasize proven measures for the primary prevention of coronary disease in all patients.

## Management of Stable Angina<sup>70</sup>

### SUSPECTED ANGINA



### HISTORY

### CLINICAL EXAMINATION

- CBC to identify underlying anaemia.
- Fasting and postprandial blood glucose to identify previously undiagnosed diabetes mellitus.
- Full lipid profile.

- Resting 12-lead ECG.  
*(A normal ECG does not exclude the possibility of CHD)*

- Patients may be referred to a cardiologist at any point if symptoms or test results indicate.
- The following should be specifically referred:
  1. Patients who appear to have had a previous MI on their initial ECG or other abnormality that the general practitioner considers significant.
  2. Patients who fail to respond to medical treatment having already had an exercise tolerance test (ETT).
  3. Patients who have an ejection systolic murmur suggesting aortic stenosis or hypertrophic obstructive cardiomyopathy (HOCM).

- Patients with the following conditions may have unstable angina and should be considered for immediate referral:
  1. Pain on minimal exertion,
  2. Pain at rest (which may occur at night), or
  3. Angina which appears to be progressing rapidly despite increasing medical treatment.

- Exercise tolerance test (ETT) for risk stratification.  
*(Myocardial perfusion imaging where ETT is not possible)*

- ETT should be performed whilst patients are taking their normal medication.

- Cardiac assessment of 2D echodoppler study should be done before ETT is performed.

- Patients should not be referred for ETT if:
  1. They are physically incapable of performing the test,
  2. They may have aortic stenosis,
  3. They may have cardiomyopathy, or
  4. The results of stress testing would not affect management.

## RISK FACTOR MANAGEMENT

### • Smoking

- All patients with angina who smoke should be advised to stop
- Brief advice from a health professional, tailored self-help materials, individual and group counselling and antidepressants (with behavioural support) can increase chances of smoking cessation

### • Hypertension

- All patients with angina should have blood pressure assessed and managed if elevated ( $\geq 140/90$ )

### • Diet

- Patients with angina should modify their diet in line with healthy eating habits

### • Exercise

- All those with CHD should be encouraged to increase their exercise levels within the limits set by their disease state

### • Overweight

- All patients with CHD should be actively encouraged to lose weight towards body mass index (BMI)  $<25$

### • Lipids

- All patients with angina should have a cholesterol and triglycerides measurement

### If total cholesterol (TC) is $\geq 5.0$ mmol/l

- Appropriate dietary measures should be recommended and a random non-fasting cholesterol measurement repeated after 6-12 weeks

- If required, drug therapy should then be initiated to reduce TC to  $< 5.0$  mmol/l

## DRUG THERAPY

### • Secondary prophylactic treatment

- Patients with stable angina should be treated with aspirin 75 to 150 mg daily (unless contraindicated)

### • Short term control of angina symptoms

- All patients with symptomatic coronary heart disease should be prescribed sublingual glyceryl trinitrate (GTN) and should be educated in its use

### • Long term prevention of angina symptoms

- Patients who require regular symptomatic treatment should be treated initially with a  $\beta$ -blocker (unless specifically contraindicated)
- Patients should be warned not to stop  $\beta$ -blockers suddenly or allow them to run out
- Patients intolerant of  $\beta$ -blockers and who show no LVSD should be treated with:
  1. A rate limiting calcium channel blocker,
  2. A long-acting dihydropyridine,
  3. A nitrate,
  4. A potassium channel opening agent,
  5. Or a drug improving cardiac metabolism.

- If symptoms are not controlled in patients taking  $\beta$ -blockers, add:
  1. Isosorbide mononitrate,
  2. A long-acting dihydropyridine
  3. Calcium channel blocker with rate limiting property (but observe the cautions),
  4. Or drugs improving cardiac metabolism and oxygen utilization by myocardial cells (Trimetazidines).

### • Referral

- Consideration should be given to referral to a cardiologist:
  1. On initiation of treatment,
  2. If the patient is perceived to be at increased risk,
  3. If at any stage medical treatment fails to control symptoms,
  4. Or if these symptoms limit the patients' desired activities.

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