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Non Interventional Management of Coronary Artery Disease

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In India, among adults over the age of 20 the prevalence of Coronary Artery Disease (CAD) is about 3 - 4 percent in rural areas and 8 - 10 percent in the urban areas [1]. Indian migrants in various parts of the world also have shown an increase in susceptibility to CAD when compared to the native population [2]. The management of Coronary Artery Disease has seen a sea change over the years. The management of the condition is mainly interventional in most centers now where the facilities are available. But the non-interventional management is also of equal importance, especially in a few subsets of patients as we shall see subsequently.

Presentation of coronary artery disease [3]

The presentation of coronary artery disease (CAD) varies from patient to patient and from time to time in the same patient. There are many presentations and combinations of two or more clinical presentations are also possible. The main presentations of CAD are as follows:

1. Asymptomatic Ischemia
2. Chronic Stable Angina Pectoris
3. Acute Coronary Syndrome (ACS)
 - a. Unstable Angina Pectoris
 - b. ST elevation myocardial infarction - STEMI
 - c. Non-ST elevation myocardial infarction – NSTEMI
4. Cardiac Failure - Ischemic Cardiomyopathy
5. Arrhythmias
6. Sudden Cardiac Death

Chronic stable angina

The symptoms of chronic stable angina (CSA) are only too well known. In the medical management of CSA the main emphasis is on goal directed therapy aiming at preventing death and myocardial infarction and also controlling the signs and symptoms of myocardial ischemia to give the patient a reasonably good quality of life. It is with these aims that the therapy of CSA is planned.

Non Invasive Risk Stratification of CAD [4]

In the management of CSA, patients can be divided into three categories according to the risk. They are as follows:

1. High Risk with and Annual Mortality Rate more than 3% :

Severe resting left ventricular (LV) dysfunction (EF < 35%)
 High Risk Treadmill stress test
 Severe Exercise LV dysfunction (Ex. LVEF < 35%)
 Stress induced single large perfusion defect on myocardial perfusion studies
 Stress induced multiple perfusion defects
 Echo wall motion abnormality in more than two segments with low dose dobutamine
 Stress echo evidence of severe ischemia
 Large perfusion defect with LV dilatation

2. Intermediate Risk with Annual Mortality Rate of 1% - 3% :

Mild to moderate resting LV dysfunction (EF = 35 – 49%)
 Intermediate risk Treadmill stress test
 Stress induced moderate perfusion defect without LV dilatation
 Limited stress echo ischemia with a wall motion abnormality of < 2 segments with high dose dobutamine

3. Low Risk with Annual Mortality Rate of < 1% :

Low risk treadmill stress test
 Normal or small myocardial perfusion defect at rest or with stress
 Normal stress echo wall motion or no change in a preexisting limited resting wall motion on stress

Management of Chronic Stable Angina [5]

The management of chronic stable angina is mainly to relieve symptoms and to prevent adverse events and complications. Antiplatelet therapy with aspirin, clopidogrel, prasugrel or ticagrelor is mandatory if there are no contraindications. Even if the lipid levels are normal, lipid lowering drugs are indicated in the management. By convention, the LDL-c is targeted to below 70 mg / dL. Beta blockers are the mainstay in the management of CSA and are ideally titrated to achieve a resting heart rate of 60 bpm and an exercise heart rate of 75 bpm. Alternatively, calcium channel blockers like diltiazem, verapamil or amlodipine may be used. Angiotensin Converting Enzyme Inhibitors (ACEI) like Ramipril (HOPE study) and Perindopril (EUROPA study) have been shown to have salutary effects in CSA. For the relief of symptoms and improving the quality of life, nitrates like Nitroglycerine, Isosorbide mononitrate or Isosorbide dinitrate are indicated though there are no studies to show that they improve survival or prevent adverse events. Of late a new drug, Ranolazine has been found beneficial in reducing the symptoms of CSA especially when used in conjunction with beta blockers or calcium channel blockers.

Acute coronary syndromes (ACS)

Acute coronary syndromes constitute Unstable angina pectoris, ST elevation myocardial infarction (STEMI) and Non ST elevation myocardial infarction (NSTEMI). All these are medical emergencies and need to be treated in the acute coronary care setting with either interventional or non-interventional means. Often treatment in ACS is delayed due to various factors and some of the factors are outlined below.

The time for the patient to recognize the seriousness of the problem and seek medical attention. Awareness of ACS is often the most important factor in our setting. Most people do not give importance to the symptoms especially when they are atypical, thus losing precious time in the management of the condition. Also there may be a bias between males and females where the symptoms of a female with ACS are often underplayed or ignored and hence females may seek medical help later than males.

The other cause of delay may be the time taken for a pre hospital evaluation, initial treatment or transportation of the patient to a hospital. This may be due to various factors like availability of Emergency medical services, lack of adequate transportation facilities or delay in the transportation due to traffic issues and other causes.

Once the patient is in the hospital, there may be a delay in the diagnosis and initiation of treatment.

Finally, the time taken from the initiation of treatment to the restoration of flow in the coronary artery determines the outcome of treatment.

Delay can occur in any of these components and the shorter the delay in getting the patient to the hospital and initiating treatment, the better the prognosis and salvage of myocardium.

Reasons for delay - Patient related factors

Just as there are factors common to all causing a delay in the treatment of patients, there are also factors related to patients which are equally important in making timely help available to patients with ACS.

Age is an important factor especially in our setting. Younger patients seek medical help sooner than the elderly. A breadwinner of the family gets to the hospital quickly even if his symptoms are minor compared to an old dependent retiree. Females are also slow in getting medical aid compared to males. More so if they are unemployed homemakers. This has been observed universally and is not confined to the Asian population alone. In the West, it has been observed that the black races seek aid later than the white races. Also the socio economic status of the individual counts. Patients belonging to the lower socio economic status seek medical help later compared to those in the upper strata. Other important factors noted are the low emotional or somatic awareness of some individuals, or the presence of angina where a prolonged pain is also dismissed as angina and timely medical help is not sought. Patients with diabetes mellitus who have atypical or no symptoms due to ACS also have a delay in seeking help.

Risk stratification in ACS – TIMI Risk Score [6]

In acute coronary syndrome, stratification of risk is done using the TIMI risk scoring which gives us an idea as to the seriousness of the condition and the urgency of treatment. There are seven criteria and each is given a score of one. It was noted that when the score was 0 - 1, the risk was 4.7%, for a score of 4 it was 19.9% and for a score of 6/7 it was 40.9% showing thereby that the risk exponentially increases with the number of risk factors. The criteria for the risk stratification are as follows:

1. Age > 65 years
2. Three or more coronary risk factors
3. Known CAD - more than 50% stenosis
4. Current aspirin use
5. Two or more episodes of chest pain in the last 24 hours

6. Elevated cardiac biomarkers
7. ST elevation of 0.5 mm or more

Acute Coronary Syndromes - Treatment – Medical

The mainstay of treatment is the relief of symptoms and restoration of coronary flow at the earliest. General measures like monitoring in the intensive coronary unit, relief of pain, oxygen inhalation, comfortable position and anxiolytics are needed in all patients. A loading dose of aspirin 300 mg and a loading dose of clopidogrel 300 mg are given immediately on diagnosis. High dose atorvastatin - 40 - 80 mg is started. Beta blockers are given intravenously or orally, if not contraindicated. An infusion of nitroglycerine is helpful in relieving pain and also controlling the blood pressure, if elevated. It is also of help in reducing the pre load of the left ventricle especially if there is evidence of LV dysfunction. Angiotensin converting enzyme inhibitors and angiotensin receptor blockers are of importance in those patients with LV dysfunction. Intravenous heparin or low molecular weight heparin is given after thrombolysis.

Thrombolysis in ACS – When and in Whom [7]

Thrombolysis using a thrombolytic agent is considered in the medical management on acute coronary syndrome in the setting of STEMI only. In unstable angina and NSTEMI, thrombolysis is contraindicated and appropriate interventional management is considered. Thrombolysis is considered in patients who present early especially within 3 hours of onset of symptoms and if there is a delay in invasive management. The delay in intervention could be due to the location of the patient or the primary care center, transportation problems or a delay in decision making by the patient or his relatives, as is common in our set up.

In certain circumstances, the invasive strategy, though indicated, is not possible and in them thrombolysis has to be offered unless there is an absolute contraindication. A cardiac catheterization laboratory may not be available readily in some cases or the undue delay in reaching an invasive set up. There may be prolonged transportation time from the primary care center to an invasive cardiac facility or there may be a patient or physician preference for invasive versus noninvasive management. Also in cases where the door to balloon time would take more than 1 hour, it is justified in thrombolysing the patient. Patients with difficult vascular access or those with low TIMI Risk scores may be subject to thrombolysis rather than persist with invasive strategy.

Fibrinolytic Agents

The commonest fibrinolytic agent used is Streptokinase in a dose of 1.5 million units given in 100 ml of normal saline over 30 minutes. It is comparatively cheap and has been used extensively and is rather predictable, though the vessel patency after thrombolysis with streptokinase may be only about 50%.

Tenecteplase is another thrombolytic agent which has the advantage of being given as a single intravenous bolus dose. It is given as 0.5 mg / kg as a single rapid bolus dose and has the advantage of being ideal for pro-hospital thrombolysis.

Retepase in a dose of 10 units intravenously over a period of two minutes followed by another 10 units after 30 minutes is also available and used frequently. Alteplase is given in a total dose of 100 mg.

Following thrombolysis the patient is given unfractionated heparin- 60 units/kg bolus (upto 4000 units) followed by and infusion of 14 units/kg/hour. Alternatively, low molecular weight heparin like Enoxaparin may be given in two doses of 0.4 to 0.6 ml subcutaneously daily.

NSTEMI – Management

The non invasive management of NSTEMI is mainly after stratifying the risk. Invasive strategy is planned for patients who need the same. Patients who cannot be taken for invasive management due to the various reasons cited above are decided on medical management. Thrombolysis is contraindicated in NSTEMI. Other general measures, beta blockers, antiplatelets, statins and heparin are given as in the management of STEMI.

Addressing Co-morbidities and Complications

In addition to the noninvasive management of the cardiac condition, stress is also given to the adequate management of the co morbidities in patients with CAD. All risk factors should be evaluated and appropriate advice given on their management. Smoking should be strictly proscribed and obesity is to be appropriately controlled with diet, exercise and other measures. Diabetes mellitus which is one of the most important co morbidities needs to be well controlled with insulin during the acute phase and later with appropriate drugs. Systemic hypertension needs to be controlled with drugs, one or more as needed. Infections, especially respiratory infection may be important co morbidity in most patients and needs to be effectively addressed with antibiotics dictated by microbiological studies. The presence of left ventricular dysfunction or frank failure would necessitate the use of diuretics in adequate doses and where needed, assisted ventilation may have to be employed. Any fall of blood pressure has to be treated with pressor agents after ascertaining the cause for the hypotension. Any arrhythmias noted during the acute phase have to be treated with the appropriate anti arrhythmic drug.

In conclusion, the medical management of CAD assumes importance in our prevailing conditions as the invasive strategy is not available in all hospitals and due to the logistical problems in patient transportation and accessing medical facilities. Though in most patients, the invasive strategy would be ideal given the proper circumstances, one has to follow a middle path to identify the patients needing urgent intervention and those that will benefit with medical management alone.

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