Coronary Syndromes: are we Still at the Take off Point? REVIEW ARTICLE
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Ischaemic heart disease [IHD] is one of the leading causes of mortality and morbidity worldwide despite the developments in diagnostic and treatment techniques. The aim of this editorial is to give an updated over view of the current diagnostic and treatment strategies for patients with IHD

Key Words: Stable angina, acute coronary syndromes [ACS], revascularization

Although coronary artery disease [CAD] may present in other forms e.g. heart failure or arrhythmias, the ischaemic presentation, which may be looked at from symptomatic or prognostic perspectives is the most common.

The story of the atherosclerotic plaque and the schematic presentation of this article are summarized in Fig 1.

Risk Factors
The Framingham study stratified the risks for CAD and used a projection of 10-year CAD risk to:
- Identify patients with > 20% risk for more intensive treatment and control of cholesterol level [Table 1].
- Raise patients with diabetes without CAD to the level of CAD risk equivalent.
- Identify persons with metabolic syndrome for therapeutic life style changes [TLC]. [Table 2]

The importance of risk factor control and TLC in both primary and secondary prevention cannot be over emphasized 1, 2.

Stable Angina
The anginal symptoms usually begin when the resultant stenosis from the atherosclerotic plaque reaches 70%. The symptoms are graded according to the Canadian Cardiac Society [CCS] classes 3
Class I: Ordinary activity will not cause angina.
Class II: Slight limitation of ordinary physical activity.
Class III: Marked limitation of ordinary physical activity.
Class IV: Inability to carry on any physical activity.

The ECG, radio nucleotide imaging and echocardiography at rest and during exercise are the corner stone of the diagnosis and are of prognostic significance. These investigations together with the clinical picture are used for risk stratification and selection of patients for coronary angiography with prospects for revascularization. The modern techniques e.g. Multi Detector CT scanning [MDCT] and MRI are of high negative predictive value for CAD and may be used to rule out atypical patients or those with equivocal stress tests and may be of value to determine myocardial perfusion, viability and function 4-6

Drugs used for symptomatic and prognostic treatment for stable angina are shown in table 3 4

Although stable angina quotes with symptoms, certain subgroups of patients have poor prognosis and may benefit more from revascularization (those who show evidence of large ischaemia by non invasive tests or who had bad coronary involvement on coronary angiography (left main coronary artery disease [LMCA], proximal left anterior descending artery [LAD] or three vessel disease [3VD].

Revascularization is achieved by coronary artery by pass graft (CABG) or percutaneous coronary intervention [PCI] 4. Still some patients who are not eligible for either procedure or those with refractory angina may benefit from some of the new modalities of treatment e.g. transmyocardial laser revascularization, enhanced external counter pulsation [EECP] or neuromodulation techniques (transcutaneous electric nerve stimulation and spinal cord stimulation ) 7.

The Vulnerable Plaque
This is the most challenging part as vulnerable plaques are usually hemodynamically insignificant but are related to prognosis and accounts for about 80% of myocardial infarction (MI) cases, and may be defined as a plaque that thromboses leading to ACS. Four pathological types may be encountered:
1. Plaque rupture [60-75%].
2- Erosion [25-40%] - in special subgroups women, young and smokers-
3- Calcification [5%]
4- Recently, after stent implantation especially DES, the delayed healing may lead to in stent thrombosis [IST] 8-10.

Screening for vulnerable plaques is not an indication for coronary angiography. However, they may be discovered during coronary angiography done for another indication. Testing
Table 1: National Cholesterol Educational Program [NCEP], adult treatment panel [ATP] 111 Guidelines.

<table>
<thead>
<tr>
<th>Patients with</th>
<th>Initiate TLC if LDL-C</th>
<th>Drug therapy Considered if LDL-C</th>
<th>LDL-C treatment goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>0=1 risk factor</td>
<td>&gt; 160 mg/dL</td>
<td>&gt;190 mg/dL</td>
<td>&lt;160 mg/dL</td>
</tr>
<tr>
<td>&gt;-risk factors (10 yr risk&lt;20%) CHD or CHD risk equivalent (10 yr risk&gt;20%)</td>
<td>&gt;130 mg/dL</td>
<td>-10-yr risk&lt;10%: &gt;160 mg/dL -10-yr risk 10-20%: &gt;130 mg/dL</td>
<td>&lt;130 mg/dL</td>
</tr>
<tr>
<td></td>
<td>&gt;100 mg/dL</td>
<td>&gt;130 mg/dL</td>
<td>&lt;100 mg/dL</td>
</tr>
<tr>
<td></td>
<td>[drug optional]</td>
<td>100-130 mg/dL</td>
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for instability of these plaques requires special techniques such as intravascular ultrasound [IVUS], direct angioscopy [rarely used now], thermography, optical coherence tomography etc... but the role of these techniques in routine clinical practice is not established.

Some authorities advocate plaque sealing of such lesions if they are proximal with balloon angioplasty without stenting but this is not recommended as part of the routine guidelines11, 12.

Vulnerable plaques may also be detected non-invasively by MDCT scanning and MRI, again there are many open questions like whom to screen? and what to do if such insignificant hemodynamic lesions are discovered?. So the current policy of giving an antiplatelet and statin to reduce plaque activity and fragility seems to be the most practical one 5,6, 11, 12.

Acute coronary syndromes [ACS]

ACS quote with prognosis as they are associated with increased mortality and morbidity and they are used to be classified from prognostic point of view, according to myocardial damage as:

- Full wall thickness MI, with ST elevation [STE], Q waves and raised cardiac markers [STEMI].
- Subendocardial MI, with symmetrical T wave inversion and raised cardiac markers.
- Unstable angina with other ECG changes and normal cardiac markers.

During the thrombolysis era, patients with STEMI or new left bundle branch block [LBBB] are recommended for immediate thrombolysis if there is no contraindication.

The current classification is primarily related to the timing for PCI:

a- STEMI or new LBBB for immediate primary PCI

The non ST elevation acute coronary syndrome [NSTE-ACS] is classified as:

b- High risk for early revascularization.

c- Low risk for reassessment and delayed intervention if indicated11-13

STEMI

The best contextual approach to patients with STEMI may be chronological which conforms to the ECS Guidelines14.

A- Evolving MI [within the first 12 hrs after on set of chest pain] where the priorities are:

1- Pain relief
2- Immediate revascularization:

Within the first three hours after the onset of chest pain, both primary PCI and thrombolysis seems to be equally effective in reducing infarct size and mortality but PCI may be preferred because of stroke prevention, while between 3 and 12 hours PCI is superior to salvage the myocardium and reduce Major Adverse Cardiac Events [MACE]. However PCI is not widely available, so many patients may still receive thrombolytic therapy [if they have no contraindication].

3- Guard against serious complications

a- arrhythmias

- Ventricular Tachycardia (VT) and Ventricular Fibrillation (VF) [more common with anterior MI]
- Brady rhythm and heart block [more common with inferior MI]

b- Hemodynamic compromise Killip classification [four grades according to pulmonary oedema, [no oedema, <50%, >50% and cardiogenic shock]

B- Completed MI [after the first 12 hrs till pre discharge i.e. about 7 days]

Points A (1&3) may still happen in addition to the mechanical complications of papillary muscle rupture with acute mitral regurgitation [MR] or interventricular septal rupture leading to Ventricular Septal Defect [VSD], both conditions may lead to acute severe pulmonary edema, thrombotic and embolic complications and the inflammatory response e.g. pericarditis.

C- Convalescent MI [from discharge till the end of the first 2months]

- To look for post MI angina, heart failure or arrhythmia
- TLC and control of risk factors 14
- Risk stratification and assessment for referral for invasive treatment

NSTE-ACS

Risk stratification to identify high risk patients should be specific, reliable and simple. The following methods are recommended:

A- Markers for thrombotic risk i.e. acute risk

1- Recurrence of chest pain
2- Hemodynamic instability
3- Major arrhythmias
4- ST-segment depression, pronounced or in multiple leads
5- Dynamic ST-segment changes
6- Elevated level of cardiac Troponins
Table 2: The Metabolic Syndrome [Diagnosis is established when three or more of these risk factors are present]

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
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<tbody>
<tr>
<td>Abdominal obesity [waist circumference]</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&gt;102 cm</td>
</tr>
<tr>
<td>Women</td>
<td>&gt;88 cm</td>
</tr>
<tr>
<td>Triglycerides TG</td>
<td>&gt;150 mg/dL</td>
</tr>
<tr>
<td>HDL-C</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&lt;40 mg/dL</td>
</tr>
<tr>
<td>Women</td>
<td>&lt;50 mg/dL</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>&gt;135/85 mm Hg</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>&gt;110 mg/dL</td>
</tr>
</tbody>
</table>

Table 3: Recommendations for pharmacological therapy inpatients with stable angina
* a drug is recommended provided there is no major contraindication

<table>
<thead>
<tr>
<th>DRUG*</th>
<th>Class of Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>a- For PROGNOSIS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Aspirin [ASA] for all patients</td>
<td></td>
<td></td>
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<tr>
<td>- Statin therapy for all patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ACE inhibitors in patients with coincident indication</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td>- Beta blockers in patients post MI or with heart failure ACE inhibitors in all patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Clopidogrel in patients who cannot take aspirin</td>
<td>11a</td>
<td>B</td>
</tr>
<tr>
<td>- High dose Statin in high risk patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b- To improve Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Short acting Nitroglycerin for acute symptom relief</td>
<td>1</td>
<td>B</td>
</tr>
<tr>
<td>- Beta blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- In case of beta blockers intolerance or poor efficacy Attempt monotherapy with:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Calcium channel blocker [CCB]</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td>- Long acting Nitrate</td>
<td>1</td>
<td>C</td>
</tr>
<tr>
<td>- Nicorandil [K channel opener]</td>
<td>1</td>
<td>C</td>
</tr>
<tr>
<td>- Sinus node inhibitors</td>
<td>11a</td>
<td>B</td>
</tr>
<tr>
<td>If the effect of Beta blocker is insufficient add:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- dihydropyridine CCB</td>
<td>1</td>
<td>B</td>
</tr>
<tr>
<td>- long acting nitrate</td>
<td>11a</td>
<td>C</td>
</tr>
<tr>
<td>- Nicorandil</td>
<td>11a</td>
<td>C</td>
</tr>
</tbody>
</table>
Clinical suspicion of ACS
Physical examination, ECG, Blood samples for markers

- Persistent STE
  - Thrombolysis / PCI
    - High Risk

- Non persistent TSE
  - ASA, LMW Heparin, Clopidogrel, Betablockers, Nitrates
    - Second Treponin sample
      - Gp2b/3a-
        - Positive
          - PCI*
          - CABG*
      - Twice negative
        - Non invasive tests
          - +ve for Coronary Angio
          - -ve for medical treatment
    - Low Risk

- Undetermined diagnosis
  - ASA

*The choice between PCI and CABG will follow the same lines as for patients with stable angina.
B- Markers for underlying disease i.e. long term risk:
   B1: Clinical markers
   1- Age
2- History of pervious MI, prior CABG, diabetes, congestive heart failure or >3 risk factors
   B2: Biological markers
   1- Renal dysfunction [elevated creatinine level]
   2- Inflammatory markers [e.g. elevated CRP level] Level evidence of all markers; A

The strategy of managing patients with NSTE-ACS is shown in Fig 2. 13

Conclusion

Stable angina may quote with prognosis in patients with evidence of large ischaemia or bad coronary anatomy but their prognosis may be improved with revascularization, on the other hand thrombosis of a vulnerable plaque which is unpredictable is the crucial prognostic step as it leads to ACS and myocardial damage. The current diagnostic and management modalities for vulnerable plaques are far to be an applied clinical guidelines on daily practice. Till then control of risk factors, the daily use of aspirin, public awareness, trained crash ambulatory service and the provision of a readily accessible and widely available service for primary PCI may be the available means to lessen the impact of IHD. Nevertheless the rapid developments in the diagnostic modalities, PCI, CABG and medications make any recommendations and guidelines on the move and alert the practicing clinicians to remain abreast of current literature and to conspire for the change.

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