MEDICINE

432 Team

1 Acute Coronary Syndrome

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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

1. Pathophysiology of ACS
2. Classification of ACS
3. Diagnostic workup
4. Initial management
5. Common complications of ACS

What are the coronary arteries? From Davidson

The coronary arteries supply oxygenated and nutrient filled blood to the heart muscle. There are **two main** coronary arteries: right coronary artery and left coronary artery (short and important). Other arteries diverge from these two main arteries and extend to the bottom portion of the heart.

Right Coronary Artery: (Runs in the right atrioventricular groove), giving branches that supply the RA, RV (SA node and AV node) and inferoposterior aspects of the LV.

1-Posterior Descending Artery: Runs in the posterior interventricular groove and supplies the inferior part of the interventricular septum.

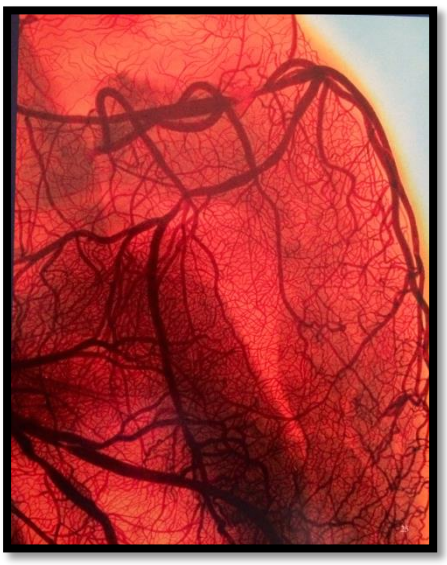
Left Main Coronary Artery: Directs oxygenated blood to the left anterior descending artery and the left circumflex.

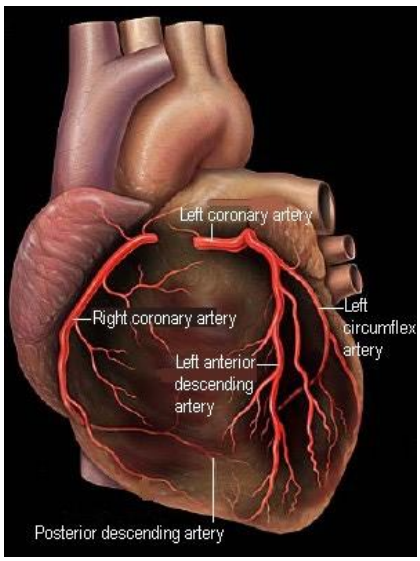
1-Left Anterior Descending Artery: Runs in the anterior interventricular groove. It gives branches to supply the anterior part of the septum (septal perforators) and the anterior, lateral and apical walls of the LV.

2-Left Circumflex Artery: Runs posteriorly in the atrioventricular groove. It gives marginal branches that supply the lateral, (sometimes posterior) and inferior segments of the LV.

When you hear about the 3 vessels disease it means a disease in one of the major epicardial vessels.

The major vessels then divide into arterioles and smaller network of capillaries.





What are the risk factors for CAD?

-Diabetes mellitus -Smoking -Hyperlipidemia Hypertensive -Obesity -Others:

1) Age: males ≥45, females ≥55 (here average age is 57)

2) Gender: (Male gender)

3) Family history of Premature CAD: males ≤55 females ≤65

Notes: *from Davidson*

These risk factors can also lead to atherosclerosis which can cause coronary artery disease.

Atherosclerosis can affect any artery in the body. When it occurs in the heart, it may cause angina, MI and sudden death. Occult coronary artery disease is common in those who present with other forms of atherosclerotic vascular disease, such as intermittent claudication or stroke and important cause of morbidity and mortality rate.

Acute coronary syndrome (an inflammatory process)

Acute coronary syndrome is a term that encompasses both unstable angina and myocardial infarction (MI). It is characterized by new-onset or rapidly worsening angina (crescendo angina), angina on minimal exertion or angina at rest in the absence of myocardial damage. In contrast, MI occurs when symptoms occur at rest and there is evidence of myocardial necrosis, as demonstrated by an elevation in (cardiac markers) cardiac troponin or creatine kinase-MB isoenzyme. ACS may present as a new phenomenon or against a background of chronic stable angina. (From Davidson)

Additional important notes:

Symptoms of angina: Chest pain is a hallmark symptom of angina. The chest pain of angina can vary in intensity from mild to severe and can be similar in to the chest pain of a heart attack. However, there generally is a key difference. The chest pain of angina is often different from the chest pain of a heart attack in that angina generally occurs with activity or exertion and goes away with rest and/or medication, such as nitroglycerin. In contrast, the chest pain of a heart attack frequently does not go away with rest or after taking nitroglycerin.

The chest pain of angina generally occurs in the center of the chest and may be experienced in a number of ways, including a pressure, pain, or squeezing sensation. These sensations may radiate to the shoulders and down the arms, especially on the left side. There may also be pain in the throat, jaw and in the back.

Symptoms that accompany the chest pain of angina can vary between individuals. They can include dizziness, sweating, and shortness of breath.

Types of angina:

-**Stable Angina**: is the most prevalent type of angina, and is usually predictable, as it exhibits a definite pattern. It is commonly induced by exercise or activities like running or walking. The pain in the chest usually resolves after taking rest for a while. The chest pain usually lasts for 3 to 5 minutes, and it can radiate to other parts of the body, such as the arms, back, and the shoulders.

-**Unstable Angina**: Unlike stable angina, it is not triggered by physical activities. Unstable angina is more severe than the stable form, and can occur even while taking rest. The chest pain can last for 10 or 15 minutes, and the pain cannot be cured by rest or medications. It does not follow a regular predictable pattern. Sometimes, it can be an indicator of an imminent heart attack.

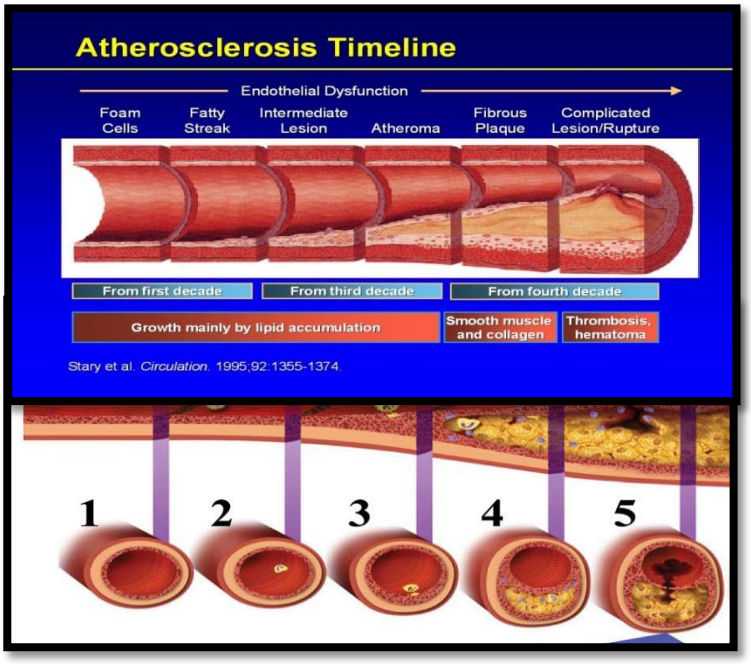
-**Variant Angina**: This condition is also known as Prinzmetal's angina. It can occur while you are resting or sleeping. The pain caused by this condition can be alleviated by taking the appropriate medications. It occurs usually between midnight and morning.

Pathophysiology of ACS from Davidson

Narrowing of the coronary arteries due to "atheroma" then development of thrombus on top of it due to endothelial wall injury causing blockage of the coronary artery causing chest pain "Angina".

The culprit lesion is usually a complex ulcerated or fissured atheromatous plaque with adherent platelet-rich thrombus and local coronary artery spasm. This is a dynamic process whereby the degree of obstruction may either increase, leading to complete vessel occlusion, or regress due to the effects of platelet disaggregation and endogenous fibrinolysis. In acute MI, occlusive thrombus is almost always present at the site of rupture or erosion of an atheromatous plaque. The thrombus may undergo spontaneous lysis over the course of the next few days, although, by this time, irreversible myocardial damage has occurred. Without treatment, the infarct-related artery remains permanently occluded in 20–30% of patients. The process of infarction progresses over several hours and most patients present when it is still possible to salvage myocardium and improve outcome.

Atherosclerosis Timeline:



-1st thing you see are the fatty streaks during the first decade lining the vessels' wall (especially if the subject has familial dyslipidemia, you can see the streaks of fat in young age (30s-40s) by noninvasive techniques like coronary CT)

-And with time endothelial injury occur because of various risk factors

-Then LDL goes from the lumen to subintimal layer of the vessel wall and become oxidized then engulfed by microphages forming foam cells. Now you have lipid core (Fat) covered by fibrous plaque (contains collagen secreted by smooth muscle cells and which is considered as the separator between the lipid core and the lumen). As the fat increases in size the lumen narrows leading to reduced blood supply to the heart causing the pain.

Cardiac demand and O2 supply

The more you work out the more your cardiac muscle demands oxygen.

When coronary arteries become narrowed by more than 50% to 70% (the cut off for having ischemia), they may no longer be able to meet the increased blood oxygen demand by the heart muscle during exercise or stress. Lack of oxygen to the heart muscle shifts the metabolism in the cardiomyocytes from aerobic to anaerobic and use the fatty cells causing production of lactic acid. The acidity activates the senses of pain and patients develop chest pain (angina).

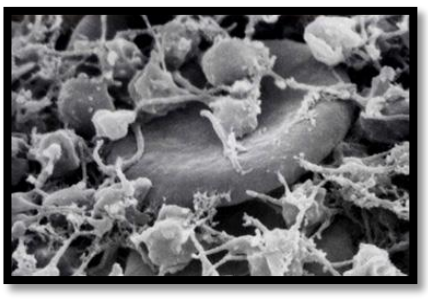
At some stage there's erosion of the plaque and blood is exposed to tissue factor, which causes thrombosis (100% occlusion) leading to a very severe angina pain at rest with basal demand of 02.

There are two types of plaques stable and vulnerable:

-**Vulnerable plaque** (معرضة)**:** plaques that are highly susceptible to rupture. Consist of thin fibrous cap, and large lipid core. In the shoulder area of atheroma we can find inflammatory cells (activated T cells), which trigger the macrophages to secrete matrix metalloproteinase that digests collagen and exposes the lipid core to the lumen and initiates thrombosis.

-**Stable plaque**: some plaques are less likely than others to rupture, so they're called stable plaques. Consist of a thick fibrous cap over a small fatty core. These plaques are rich in collagen, a protein found in connective tissue that strengthens and stabilizes the plaque and makes it unlikely to rupture.

There are some things that are still unknown about ACD and can be confusing: Some people live with atherosclerosis and tight 3 vessel disease but have never developed MI. and other young individuals have no significant disease yet they develop massive MI.



This picture shows the initial interaction of the platelets with the RBC when it first reaches the clot (it's called white clot: composes of platelets and cross linkages) then it develops to a larger red clot).

ACS classifications:

1-ST elevated Myocardial infarction (STEMI)

2-Non ST elevated Myocardial infarction (NONSTEMI)

3-Unstable angina

Each type presentations' and how to differentiate between them will be explained in the investigations.

Investigations in the Emergency room

1) ECG (First and most important thing to do with patients of ACS)
2) Markers for Myocardial infarction

1) 12 lead ECG:

1-ST elevated Myocardial infarction (STEMI): (Most dangerous type)

- Classically presented with full occlusion of the vessel.
- Davidson: The earliest ECG change is usually ST-segment deviation. With proximal occlusion of a major coronary artery, ST-segment elevation (or new bundle branch block) is seen initially, with later diminution in the size of the R wave and, in transmural (full-thickness) infarction, development of a Q wave. Subsequently, the T wave becomes inverted because of a change in ventricular repolarization; this change persists after the ST segment has returned to normal. These sequential features are sufficiently reliable for the approximate age of the infarct to be deduced.
- Once you find ST elevation in your patent's ECG, you label him ACS STEMI.
- ST elevation is a hallmark for MI.
- Some people come with full occlusion but no ST elevation (rare)

2-Non ST elevated Myocardial infarction (NSTEMI) (Cardiac enzymes PRESENT):

Davidson: In non-ST segment elevation acute coronary syndrome, there is partial occlusion of a major vessel or complete occlusion of a minor vessel, causing unstable angina or partial-thickness (subendocardial) MI. This is usually associated with ST-segment depression and T-wave changes (T inversion). In the presence of infarction, this may be accompanied by some loss of R waves in the absence of Q waves.

- If your patient has normal ECG with any presentation of this combination: No ST elevation or ST depression or T inversion + Myocardial necrosis markers (Troponin + CK-MB) = NSTEMI

3-Unstable angina (Cardiac enzymes NOT present):

- ECG findings in unstable angina are variables. It may be normal, or may found ST-segment depression or T-wave inversion but most importantly here you don't find myocardial necrosis markers (Troponin + CK-MB) in the blood and if you did it'll be in a very small amount not significant (to differentiate between unstable angina and NSTEMI).

2) Markers for myocardial necrosis:

- MI causes release of certain enzymes and proteins into the blood stream.

1- Creatine Kinase (CK) is released from multiple organs such as the myocardium, skeletal muscles, and the brain. (Still being used but the problem it's not specific this is why we use isoform CK-MB)

- The Iso-form CK-MB, is cardio-specific.
- Starts to rise 4-6 hrs after onset of ischemia, then falls within 48-72hrs (lasts up to 3 days unlike troponin around 2 weeks)

2- Cardio specific proteins Troponin I and T are the most sensitive & specific markers for myocardial necrosis.

- Released with 4-6hrs, but can last up to 2 weeks.
- When you see troponin in the blood it's coming from the heart for sure
- Both CK-MB and troponin rise at the same time but CK starts to decrease after 3 days and troponin continues for 2 weeks.

Note(s):

If the patient comes to you after only 1 hour of onset of CAS symptoms and you find that the enzymes are negative, do not exclude CAS because the enzymes aren't released until 4-6 hours after the onset.

What is Myocardial infarction?

Third universal definition of MI:

- There is a universal guideline to identify MI regardless its type whether STEMI or NSTEMI, and the guideline specifies that there has to be markers positivity therefore unstable angina doesn't consider as MI
- Typical rise in cardiac troponin T or I, CK-MB with at least one of the following:

1-Ischemic symptoms
2-Pathological Q wave on ECG(for example patient has chest pain since week ago, +ve cardiac enzymes, changes in Q wave = labeled as MI)
3-Ischemic ECG changes (e.g. ST elevation or depression , new LBBB) (a patient with ST elevation is labeled MI directly)
4-Imaging evidence of new loss of viable myocardium or a new WMA
5-Identification of an intracoronary thrombus by angiography or autopsy.

- if you have a typical cardiac marker rise (peak) then a fall with ischemic pain that's a classical MI

The Diagnosis:

The degree of arterial blockage caused by the thrombus determines the amount of myocardial damage that occurs and the type of ACS that results. The main methods used to confirm a diagnosis of ACS and identify the type of ACS include electrocardiogram (ECG) and cardiac markers. You interpret the findings and come up with diagnosis just like it was explained in the investigations.

Management of ACS:

Aims of therapy:

1. Open the artery and improve oxygen supply by:
    1. Supplemental O_2
    2. Coronary vasodilators: Nitroglycerine.
    3. Dissolve clots using:
        - Anti-platelet agents.
        - Anti-thrombotic agents. (Heparin)
    4. Reperfusion therapy: (Most important)
        - Pharmacotherapy: Fibrinolytic therapy. (Applies to STEMI only)
        - Non-pharmacotherapy: Primary percutaneous coronary intervention (PCI).

Note(s):

- *The goal of therapy is to increase the supply in order to meet the demand.*

2. Reduce O2 demand by:
    1. Beta blockers: Propranolol, Metoprolol.
    2. Analgesics: Morphine.

3. Other medications:
    1. ACE inhibitors: Enalapril, Lisinopril.
    2. Statins. (Used to reduce inflammation and stabilize the plaque. Some studies show that it also reduces infarction)

Anti-platelet therapy:

Anti-platelets work on several pathways. One agent isn't enough to do the job, that's why combination therapy is important.

1. Aspirin (ASA): ASA is Chewable 160 to 325 mg at presentation, then 75 to 325 mg daily.

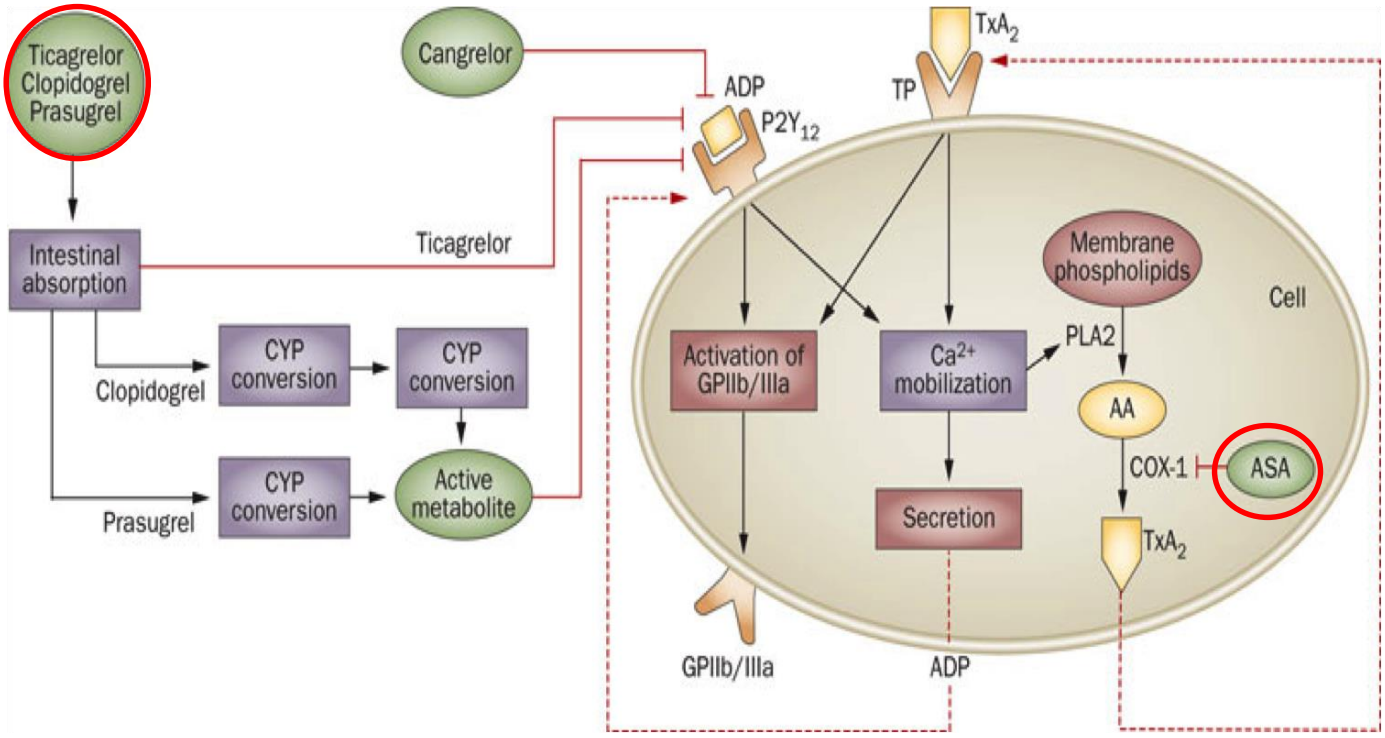
Note(s):

- *As soon as the patient arrives at the ER:*

-Give chewable aspirin 160-325 mg.
- then, you give the patient aspirin 81 mg daily for life.

2. $P2Y_{12}$ inhibitors/ADP receptor blockers:

- More potent than ASA and is combined with ASA. "We usually combine Clopidogrel with Aspirin"
- Both aspirin and $P2_{Y12}$ inhibitors are powerful adjuncts to reperfusion therapy.
- Examples:
  - Clopidogrel
  - Ticagrelor
  - Prasugrel



This picture shows the different pathways that anti-platelet agents work on.

- ASPIRIN: inhibits COX-1, which in return, will inhibit the formation of thromboxane A_2 and platelet function.
- $P2Y_{12}$ inhibitors: inhibit $P2Y_{12}$which is an ADP chemoreceptor, that's why they're also called ADP receptor blockers.

Reperfusion therapy: "only used for STEMI"

1. Fibrinolytics:

"The earlier we give the treatment, the better the effect"

> ***Note(s):***
>
> - *In strokes, fibrinolytics should be given during a 3hr window*

- Reduces short and long term mortality
- Should be given during a 12hr window, and given ASAP.
  - For the best results, fibrinolytics should be given within the first hour "the golden hour" because time is muscle, meaning the longer we wait, the more myocytes we lose and once they're lost, they do not regenerate.
- 2 types of fibrinolytics:
  1. Non-Fibrin specific (Streptokinase) "not used anymore"
  2. Fibrin specific (Tenecteplase: given as bolus injection, which is easier and has a less margin of dosage error, to dissolve clots)

Characteristic	Alteplase (t-PA)	Reteplase (rPA)	Tenecteplase (TNK)	Lanoteplase (nPA)
Immunogenicity	No	No	No	?
Plasminogen activation	Direct	Direct	Direct	Direct
Fibrin specificity	++	+	+++	+
Plasma half-life	4–6 min	18 min	20 min	37 min
Dose	15-mg bolus plus 90-min infusion up to 85 mg	10+10-MU double bolus 30 min apart	±0.5 mg/kg single bolus	120 KU/kg single bolus
PAI-1 resistance	No	?	Yes	?
Genetic alteration to native t-PA	No	Yes	Yes	Yes
	Recombinant version	Finger, EGF, and kringle-1 regions deleted	2 single amino acid substitutions in kringle-1 and substitution of 4 amino acids in catalytic domain	Finger, EGF regions deleted and glycosylation sites in kringle-1 domain modified

Contraindications of Fibrinolytics:

Absolute contraindications **"NEVER GIVE FIBRINOLYTICS"**
- Any prior intracranial hemorrhage
- Known structural cerebral vascular lesion
- Known intracranial neoplasm
- Ischemic stroke within the past 3 months (except for acute stroke within 3 hours)
- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed-head or facial trauma within 3 months

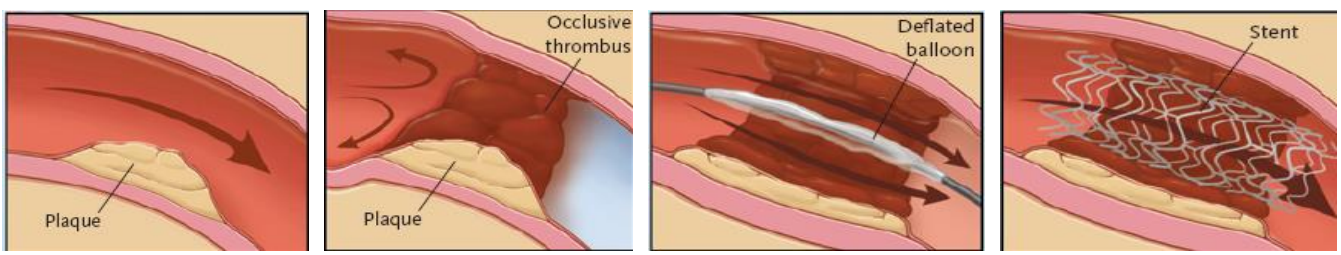
Relative contraindications **Calculate Risk vs Benefits, if the benefits are more → give therapy, if not → avoid.**
- History of chronic, sever, poorly controlled hypertension
- Systolic pressure >180 mm Hg or diastolic >110 mm Hg
- History of prior ischemic stroke >3 months previously, dementia, or known intracranial pathology not covered in absolute contraindications
- Recent (within 2–4 weeks) internal bleeding
- Noncompressible vascular punctures
- Pregnancy
- Active peptic ulcer
- Current use of anticoagulants: the higher the INR, the higher the risk of bleeding
- For streptokinase/anistreplase: prior exposure (more than 5 days previously) or prior allergic reaction to these agents

Adverse effects of Fibrinolytics:

- The main adverse effect "risk" of fibrinolytic therapy is bleeding and the worst bleeding is in the brain.
- "Older females that are thin have a high risk of bleeding, so try to avoid this type of therapy"

2. Primary Percutaneous Coronary Intervention (PCI):

Here, we open the artery mechanically by inserting a wire through the occlusion → open the occlusion using a balloon to resume the flow → remove the balloon



and insert a metal cage "stent" to keep the artery open and prevent it from recoiling and getting occluded again.

Important notes on reperfusion therapy:

- PCI is believed to be a better therapy than Fibrinolytics because fibrinolytics could be comlicated by a serious side effect which is bleeding.
- Time is important in reperfusion therapy:
  - Door to needle time "meaning from the moment the patient steps foot in the ER until he gets the needle for fibrinolytic therapy" should be less than 30 mins.
  - Door to balloon time should be less than 90 mins.

Anti-thrombotic therapy:

Heparin:

- Unfractionated
- Low molecular

- Prevents further thrombosis and aids in insuring patency of the occluded artery.
- To be used in therapy for all forms of ACS (STEMI AND NSTEMI)
- Acts as an aid to reperfusion therapy and is very important to use for:
  - Fibrinolytic therapy: "because without it, you don't get proper reperfusion"
  - PCI: "because it's important for the clot to dissolve."

Complications of MI: "specifically STEMI"

•Electrical (Arrhythmias): Ventricular fibrillation, Ventricular tachycardia and bradycardia, complete heart block "especially in inferior MI"

•Heart failure (Pulmonary Edema): most common cause of heart failure is ischemic heart disease specifically MI and is usually due to failure of therapy.

•Cardiogenic Shock: if the loss of myocytes is 40% or more →BP goes below 90 systolic → shock (carries 50% mortality rate) happens with extensive MI.

•Mechanical complications (rare and usually occur late after MI -days to weeks-): ventricular septal defect (VSD) and rupture of papillary muscle.

Clinical scenario

- Rashid, 60yr old man.
- Owns a business.
- Smoker.

On a routine medical checkup was found to have the following:

Physical Exam:

- BP of 150/90 (repeated 3 times)
- Weight 90kg, Height 170 (BMI=31)
- Waist Circumference 115 cm

Lab investigations:

- FBS (fasting blood sugar) = 9 mmol/l "high"
- TC (total cholesterol) = 6.0 mmol/l "high"
- LDL = 4.5 mmol/l "high"
- HDL = 0.7 mmol/l "low"

Note(s):

BP was repeated more than once because at first, patients might be scared/stressed, which might give false results. So, BP measurements should be repeated after the patient is more relaxed.

FBS:
-Normal: < 5.6 mmol/l
-Prediabetic: 5.6-6.9 mmol/l
-Diabetic: 7 mmol/l and above.

After that, Rashid was counseled and told he had diabetes, hypertension, dyslipidemia and that he was obese. He was strongly advised to change his lifestyle, stop smoking and undergo another checkup in 3 months after dietary changes.

Rashid forgot or was careless!
3 years later, he started feeling occasional chest heaviness while rushing on the stairs. Radiated to both shoulders, and relived with rest. "Signs of typical angina"
He decided to go to his physician again, but after finishing off some business deals.

Note(s):

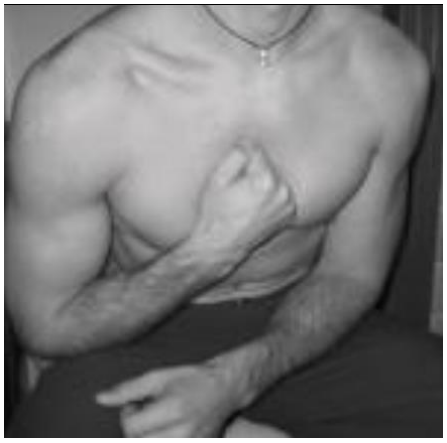
Characteristics of angina:
1) Retrosternal pain: heavy, tight, burning or crushing pain.
2) Pain increases with exertion.
3) Pain is relieved by rest or nitrates.
If three of those features are positive → Typical angina.
If 2 are positive → Atypical angina.
If 1 or non are positive → Non-cardiac chest pain.

What is happening with Rashid?

- The pathophysiological reason behind Rashid's pain is narrowing of the blood vessels due to an atheroma.
- Atheroma → narrowing of the blood vessels → ischemic changes → heart myocardium switches to anaerobic metabolism → accumulation of lactic acid → activates sensation and pain will be felt.

Rashid delayed the medical check-up for 3 months.

- Woke up at 5 AM with similar chest pain, however now at rest and severe.
- Perfuse sweating and nausea
- Called his son to take him to the ER



The clench sign "grip sign" usually indicates ischemia.

In the ER:

- HR: 110 bpm "Tachycardia"

- BP: 180/100 "hypertension"

- O2 Saturation: 95% on RA

- PE was normal

Can you explain his clinical presentation?

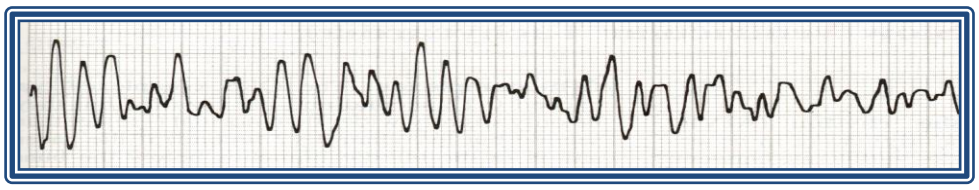
He had an acute occlusion due to the rupture/erosion of the plaque → exposes the fat core to the blood → when tissue factors are exposed → results in thrombosis → 100% occlusion.

Back in the ER, Rashid was given:

- Chewable ASA

- 3 Sublingual Nitro tablets

He had no contraindications to fibrinolytic therapy and just prior to receiving fibrinolytics, he lost consciousness. He was found to have ventricular fibrillation "most dreaded complication of STEMI and a common cause for sudden deaths"



Defibrillator paddles immediately applied and 200J delivered managed to convert him to normal sinus rhythm and then was given thrombolytic therapy.

SUMMARY

- ACS is most likely a complication of plaque buildup in the arteries in the heart (coronary atherosclerosis) causing the arteries to narrow and make it more difficult for blood to flow. Reduced blood flow means reduced O2 supply to the heart and during its demand under any physical or emotional situation it presents as chest pain (angina). Once the artery fully occludes heart attack (MI) happens.

- Acute coronary syndrome symptoms are the same as those of a heart attack

- You differentiate between ACS types by ECG and myocardial markers findings

  - STEMI (Treat immediately)- occlusive thrombus - ST elevation (and Q waves) - Cardiac Enzyme elevation - Fibrinolytics beneficial

    For the other 2 types, you can take your time and measure the cardiac enzymes to differentiate between them.
  - NSTEMI - non-occlusive thrombus - NO ST/Q - Cardiac Enzyme elevation present - Fibrinolytics not beneficial
  - UA - non-occlusive thrombus - NO ST/Q - Cardiac Enzyme elevation absent - Fibrinolytics not beneficial

- There is a universal guideline to define an MI, Markers positivity + at least one of the listed findings. If there were no markers in the blood then it's not an MI. This is why both STEMI and NSTEMI are considered MI but US isn't.

- Management of ACS includes:

  - Anti-platelet therapy.
  - Anti-thrombotic therapy.
  - Reperfusion therapy.

- Reperfusion therapy is only indicated for STEMI and includes Fibrinolytics and PCI.
- In STEMI, time to reperfusion is critical in myocardial salvage (time is muscle):
  - Door to needle time should be < 30 mins.
  - Door to balloon time should be < 90 mins.
- The effectiveness of fibrinolytic therapy is highest in the first hour "the golden hour".
- The main complications of MI include: arrhythmias (VF) and heart failure.

Questions

1) A 56-year old male presents to the ED with complaint of chest pain for the past 3 hours. He has never experienced this pain before, and it started suddenly while he was eating dinner. He describes the pain as "gripping" and radiating into his neck. Physical examination is normal. ECG shows a 1 mm ST segment depression in leads V_4 to V_6. PMH is significant for DM and HTN. Medications include insulin and a β blocker for the HTN. What does he most likely have?

a. Unstable Angina
b. NSTEMI
c. STEMI
d. Pericarditis

2) After choosing the right answer for question 1, what will your management plan be?

Continuous cardiac monitoring is indicated as well as these interventions: Heparin, aspirin, ß-Blocker, nitrates, and oxygen.

3) In which of the following patients, fibronlytics are absolutely contraindicated.

a. Pregnant lady
b. Patient with active peptic ulcer
c. Patient with a history of facial trauma from 1 week.
d. Patient with poorly controlled hypertension

432 Medicine Team Leaders

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For mistakes or feedback: *medicine341@gmail.com*

Answers:

1st Question:

A

3rd Question:

C