Cardiovascular Disease

Risk Factors and Laboratory Markers

Cardiovascular disease (CVD) affects the majority of people over 60

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Major types of CVD:

Coronary Heart Disease (CHD)	aortic atherosclerotic disease	cerebrovascular disease peripheral arterial disease
 <u>myocardial infarction (MI)</u> angina pectoris heart failure 	 aneurysms dissection 	stroke intermittent claudication transient ischemic attack
sudden cardiac death	What do Sulaf Farhar	these have in common?

Atherosclerosis

"response-to-injury hypothesis"

Definition

- Atherosclerosis is an abnormal thickening and loss of elasticity in the walls of arteries
- The response-to-injury hypothesis views atherosclerosis as a chronic inflammatory response of the arterial wall to endothelial injury



Endothelium – Intima — Media — Adventitia —

1. Chronic

endothelial "injury".

- Hyperlipidemia
- Hypertension
- Smoking
- Homocysteine
- Hemodynamic factors
- Toxins
- Viruses
- Immune reactions

Response to injury

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Inflammation

2. Endothelial dysfunction (e.g., increased permeability, leukocyte adhesion), monocyte adhesion, and migration

Platelet

Monocyte

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Inflammation

3. Macrophage activation, smooth muscle recruitment, accumulation of lipids in vessel wall

Smooth muscle cell

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4. Macrophages and smooth muscle cells engulf lipid

Lymphocyte

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Foam cell

Fatty streak



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Clinicopathologic Consequences

- Large elastic arteries (aorta, carotid, and iliac) and largeand medium-sized muscular arteries (coronary, renal, and popliteal) are the most commonly involved
- Rupture, ulceration, or erosion of the luminal surface of plaques induces thrombus formation
- Outcome varies depending on the size of the affected vessel, the size and stability of the plaques, and the degree to which plaques disrupt the vessel wall

Risk Factors



Constitutional

• genetics + family history

• age

gender

Modifiable

- hyperlipidemia
- hypertension + diabetes
- smoking

Additional

- inflammation
- metabolic syndrome
- hyperhomocysteinemia + elevated procoagulants

Difficult to Quantify

- obesity
- lack of exercise
- stressful lifestyle

Lipids

- Cholesterol and its esters, triglycerides and phospholipids are all transported in plasma as <u>lipoprotein particles:</u>
 - <u>Chylomicrons:</u> principal form in which dietary triglycerides are carried to tissues
 - VLDL: triglyceride-rich particles carrying endogenous triglycerides tissues from the liver or the small intestines
 - LDL: cholesterol-rich particles formed by the removal of triglycerides from VLDLs
 - HDL: transport cholesterol from peripheral cells to the liver for excretion



- Risk of cardiovascular disease <u>disproportionately</u> <u>increases</u> with:
 - \bullet \uparrow total cholesterol
 - V 🛧 LDL
 - ♥ ♥ HDL
 - ♥ **↑** TG?



TABLE 34.15 ATP III Classification of LDL, Total, and HDL Cholesterol, mg/dL[×]

LDL cholesterol	<100	Optimum		
	100–129	Near or above optimum		
	130–159	Borderline high		
	160–189	High		
	≥190	Very high		
Total cholesterol	<200	Desirable		
	200–239 Borderline high			
	≥240	High		
HDL cholesterol	<40	Low		
	≥60	High		



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 - \bullet \uparrow total cholesterol
 - V 🛧 LDL
 - ♥ ♥ HDL
 - **▼ ↑** TG?
- Also, non-HDL cholesterol

 Many studies have suggested that small, dense LDL subfractions may be better correlated with CHD risk than large, less dense LDL subfractions

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♥ C-reactive protein is an <u>acute phase reactant</u> that is

For CHD risk assessment high-sensitivity CRP (hsCRP) should be used (detection limits less than 0.3 mg/L)

 Increased serum CRP concentrations are positively associated with the risk of future CHD

Homocysteine

- A sulfur-containing amino acid and an intermediate compound in the metabolism of methionine to cysteine
- ★ A deficiency of folic acid or vitamins B₆ and B₁₂
 can result in increased concentrations of it (Why?)
- Studies suggest an association between elevated homocysteine and cardiovascular disorders
- But measurement of tHcy in the general population to screen for CVD risk is <u>not recommended</u>

Myocardial Infarction

"acute coronary syndromes"

Definition

- The term acute <u>myocardial infarction</u> (AMI) refers to the death of myocytes due to an imbalance between myocardial oxygen supply and demand
- When the blood supply to the heart is interrupted, gross necrosis of the myocardium results. In addition, a substantial number of cells die as the result of apoptosis
- Such damage is most often associated with a thrombotic occlusion superimposed on <u>coronary</u> <u>atherosclerosis</u>



Clinical Signs & Symptoms

- ♥ Acute chest pain
- ♥ Sweating
- ♥ Nausea or vomiting
- ♥ Shortness of breath and fatigue
- Abnormalities in heart rate and/or blood pressure
- ♥ Loss of consciousness
- Changes on an electrocardiogram (ECG)
- Changes in the motion of the heart wall on imaging

Laboratory Markers

Troponins

Biochemical Tests in MI

Enzymes

Myoglobin

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Troponin I

Troponin T

CK &

CK-MB

AST

LDH



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Troponins

- The troponin complex is exclusively present in striated muscle fibers
- It regulates the calcium mediated interactions of actin and myosin
- Troponin T (TnT) binds tropomyosin, troponin I
 (TnI) is an inhibitory protein and troponin C (TnC) is responsible for binding calcium
- Three distinct isoforms of TnT and TnI exist, one of which is <u>cardiac-specific</u>

Troponins

- Cardiac-specific isoforms of these troponins makes them the <u>most specific</u> of all the biochemical markers for cardiac damage
- Under normal circumstances there is no cardiac troponin T or I detectable in the circulation by conventional troponin assays
- Any detectable rise is of significance,
 contributing to the high sensitivity of these tests

Taken together, the characteristics of specific, sensitive, and rapid detection propelled cardiac troponins **cTnT & cTnI** to the center of MI diagnosis

CK & CK-MB

- Skeletal muscle has a very high total CK content; over 98% CK-MM and less than 2% CK-MB
- Cardiac muscle also has a high CK content. It comprises 70–80% CK-MM and 20–30% CK-MB

It used to be used in the diagnosis of MI, but this is <u>no longer recommended</u> because of its <u>lack of specificity</u>

If troponin assays are not available, the next best alternative is **CK-MB**, and measurement of total CK is <u>no longer recommended</u> for the diagnosis of MI

Myoglobin

- Myoglobin is an iron- and oxygen-binding protein found exclusively in the muscle and is normally absent from the circulation
- Because myoglobin is released so quickly, it has been proposed as an adjunct marker for troponin or CK-MB in the <u>early diagnosis of MI</u>

Not specific for the heart, being elevated with any cause of skeletal muscle damage

Conclusion

points to remember

Many types of cardiovascular disease

In common: Atherosclerosis (inflammatory response to vascular injury)

Many factors can help assess risk of CHD

Myocardial infarction (MI): damage to heart muscle cells

Cardiac Troponins are the best lab markers for cardiac damage

March 9, 2020			36
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