



Coronary artery Disease in young



Introduction



- Cardiovascular diseases (CVD) are the most important causes of mortality and morbidity in India¹.
- Global Burden of Diseases (GBD) Study has reported that from year 1990 to 2013, IHD in India increased to become number 1 cause of death.
- This study also reported that number of patients with IHD increased from less than a million to 2 million.
- IHD in India is characterized by increasing numbers, regional variations, premature onset, poor management.



Prevalence of CAD(Coronary Artery Disease)

- Atherosclerotic cardiovascular disease (ASCVD) in young adults represents a specific and growing challenge.
- In the INTERHEART (Effect of Potentially Modifiable Risk Factors Associated With Myocardial Infarction in 52 Countries) study, risk of MI showed larger impact on younger people.
- The burden of ASCVD in young adults is an important public health issue because of potential loss of lifetime productivity and increased lifetime healthcare use.
- The 66th World Health Assembly introduced the World Health Organization Global Action Plan for the Prevention and Control of Non communicable Diseases 2013 to 2020



Prevalence of ACS in india

- Coronary artery disease (CAD) occurring in less than 45 years of age is termed as young CAD.
- Recent studies show a prevalence of 1.2% of CAD cases in this age group
- Indians are most vulnerable to have CAD in young age group with a prevalence of 5% to 10%, age limit varying from 35 years to 55 years in the spectrum of young CAD.
- The median age of presentation of CAD in young women is higher when compared to men

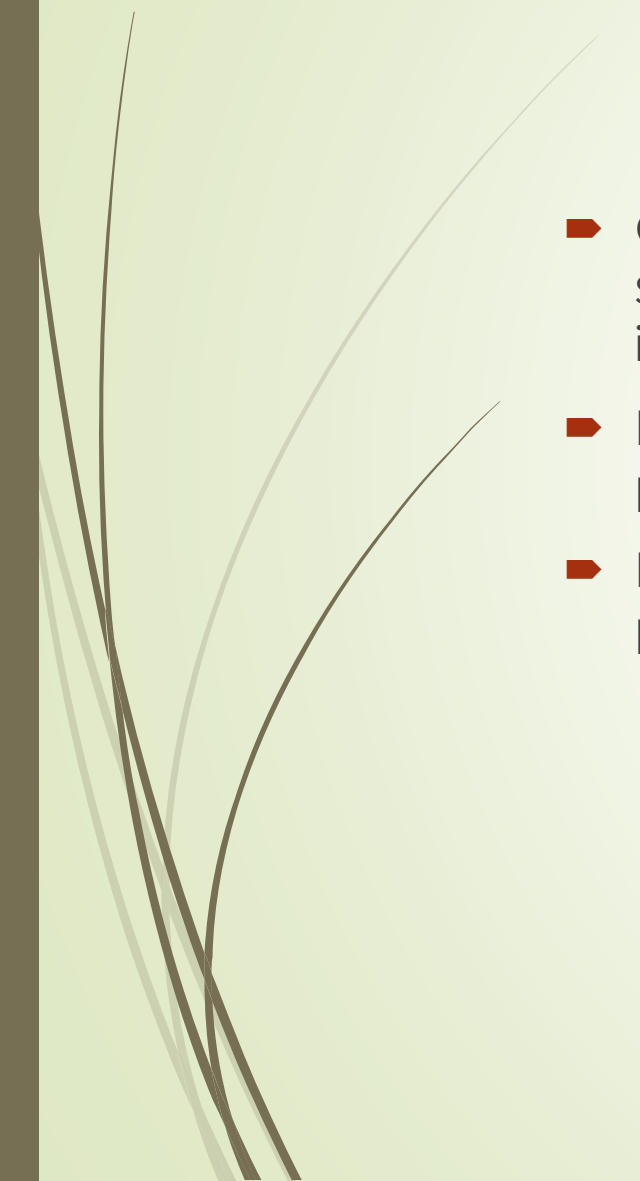


Prevalence of CAD

- About 4% of heart attacks in young adults are due to congenital abnormalities of the coronary artery anatomy
- Another 5% involves various disorders of the blood clotting system.
- 5% due to blood clots that originate elsewhere and are carried to otherwise normal coronary arteries, and block the artery.
- The remaining 6% of CAD in young adults is due to spasm or inflammation of the coronary arteries, radiation therapy for chest tumors, chest trauma, and abuse of cocaine, amphetamines, and other drugs.
- Coronary segments, with non-significant stenosis and non calcified plaque, shows positive remodeling that cause of CAD in young individuals with normal coronary artery

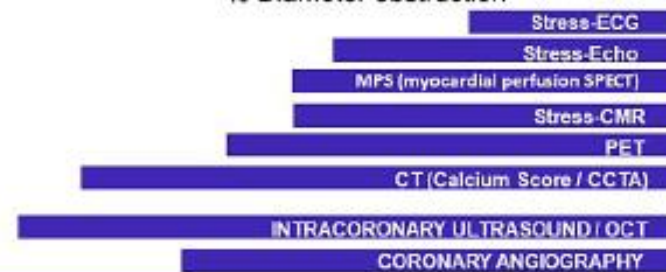
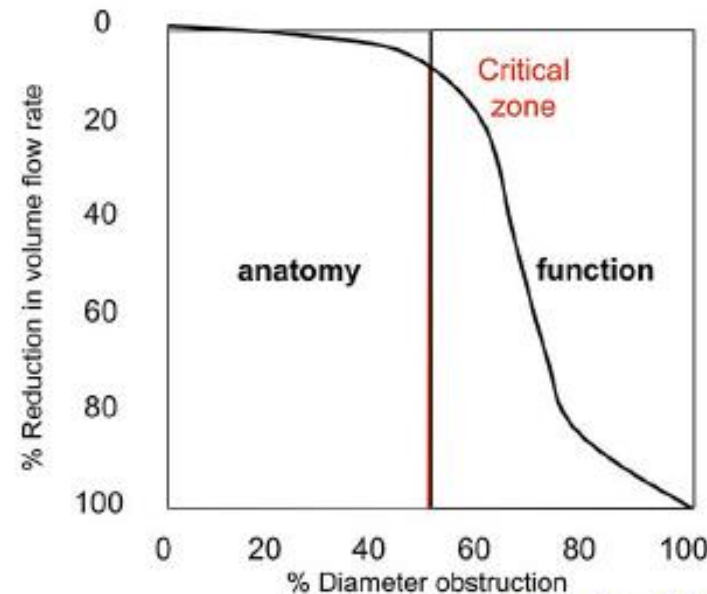


Pathophysiology



- Coronary segments, with non-significant stenosis and non calcified plaque, shows positive remodeling that might be the cause of CAD in young individuals with normal coronary artery.
- Positive remodeling is related to plaque instability, suggesting it is more prone to rupture and erosion with subsequent coronary events.
- Lipid core plaques, in contrast to the severely calcified plaques, showed positive vascular remodeling, thus early plaques are more prone for CAD

Progression of atherosclerosis



Asymptomatic
Prevention

Symptomatic
Therapy

CCTA = coronary
computed tomographic
angiography

CMR = cardiac
magnetic resonance
imaging

ECG =
electrocardiogram;

OCT = optical
coherence tomography

PET = positron emission
tomography

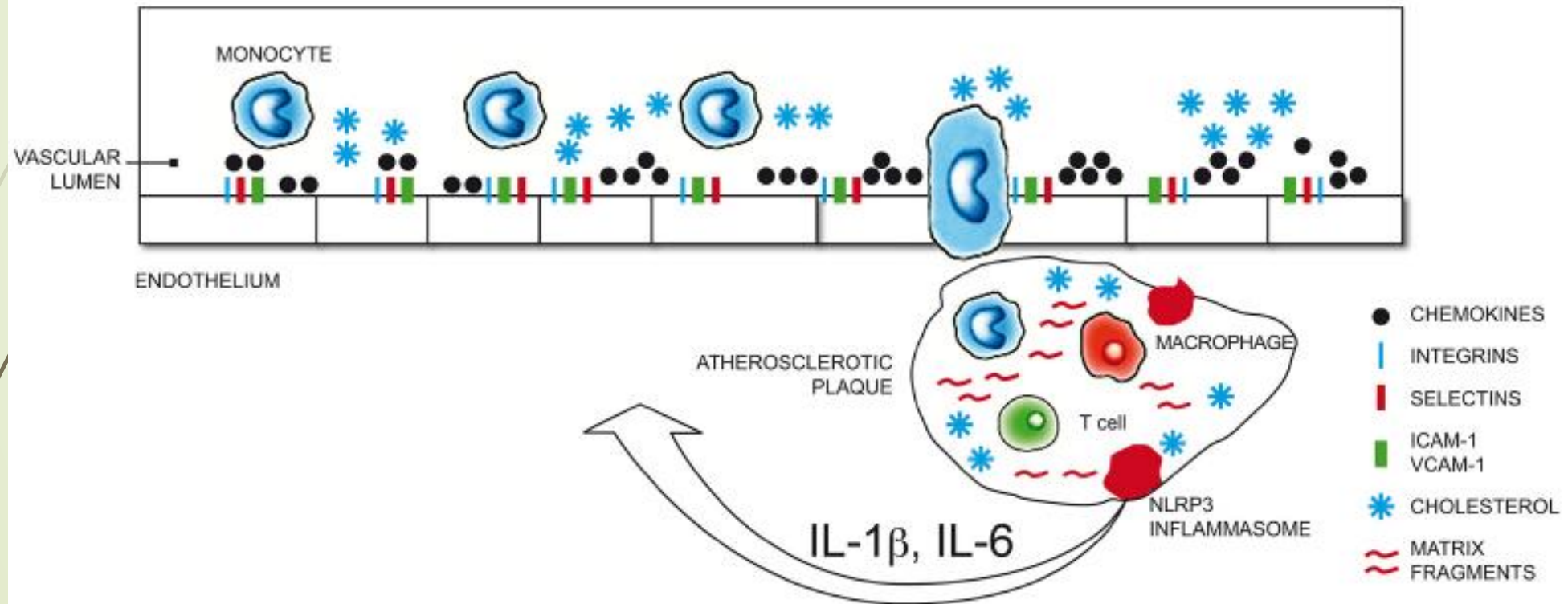
SPECT = single photon
emission

computed tomography

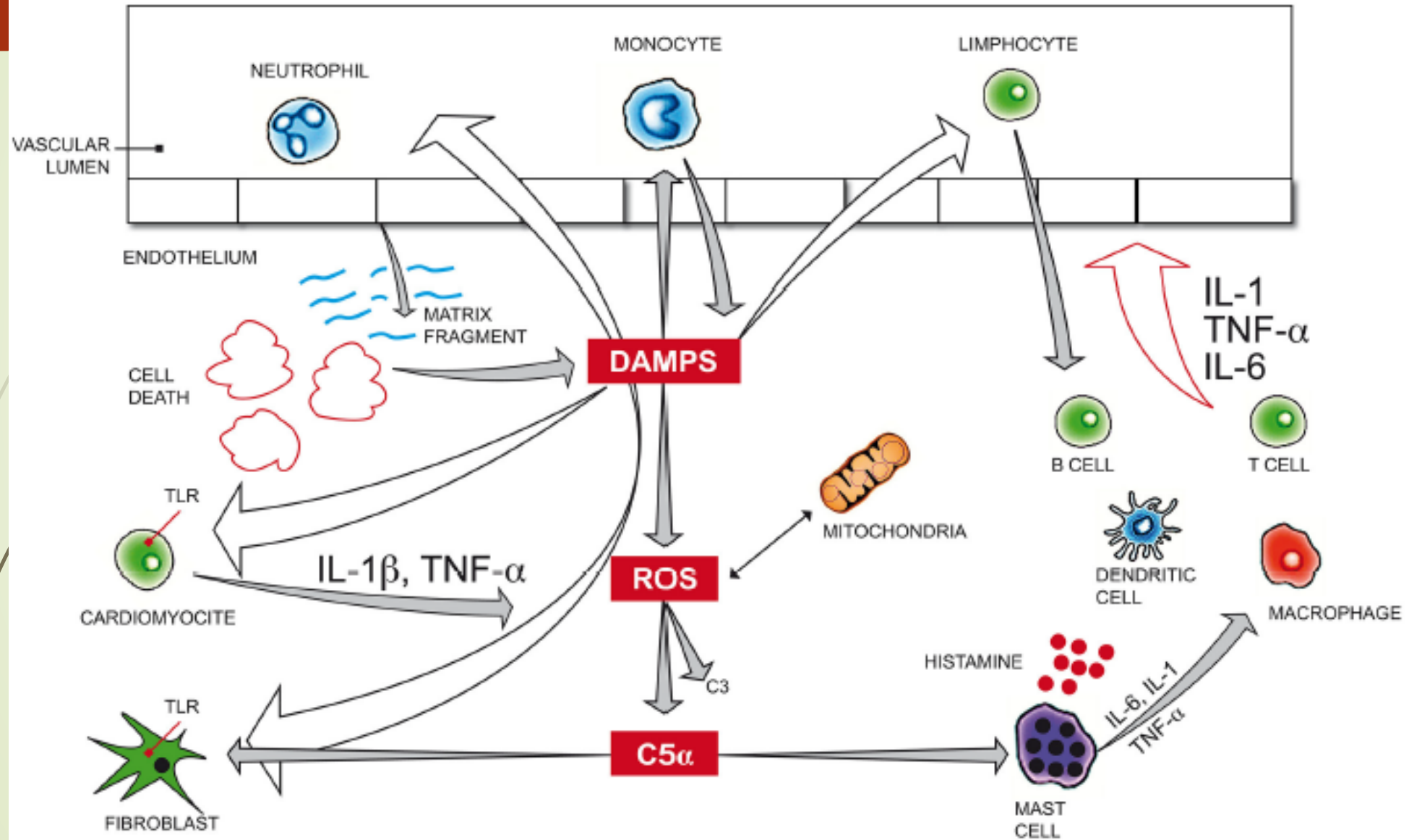
Zellweger MJ et al. Swiss Med Wkly. 2019 Feb;
119:149-150. 2019

Pathology

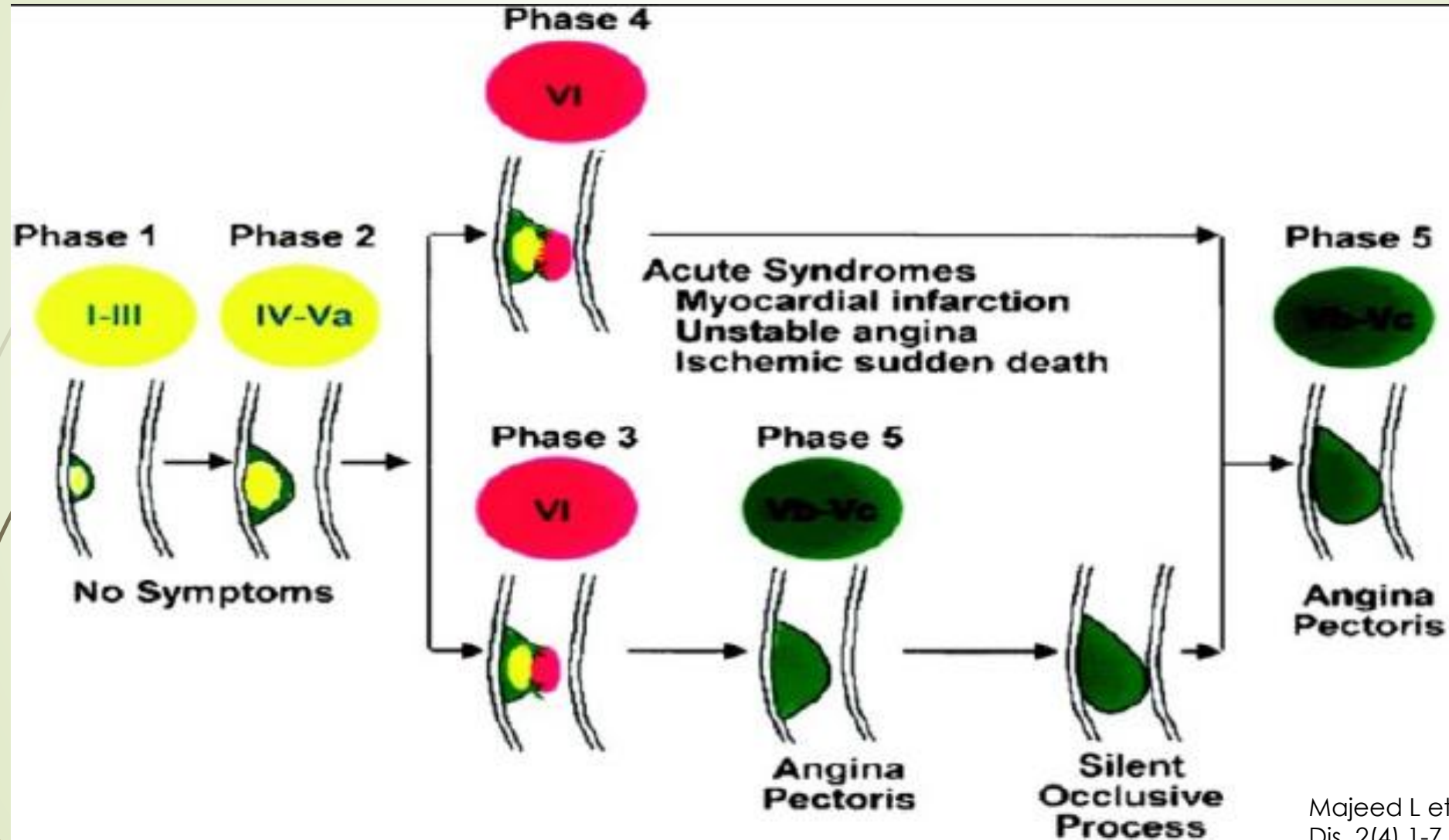
INFLAMMATION IN ATHEROSCLEROSIS



INTERPLAY BETWEEN CIRCULATING AND RESIDENT CARDIAC IMMUNE CELLS IN MYOCARDIAL ISCHAEMIA



Phases of lesion development





Risk factors for coronary artery disease in young

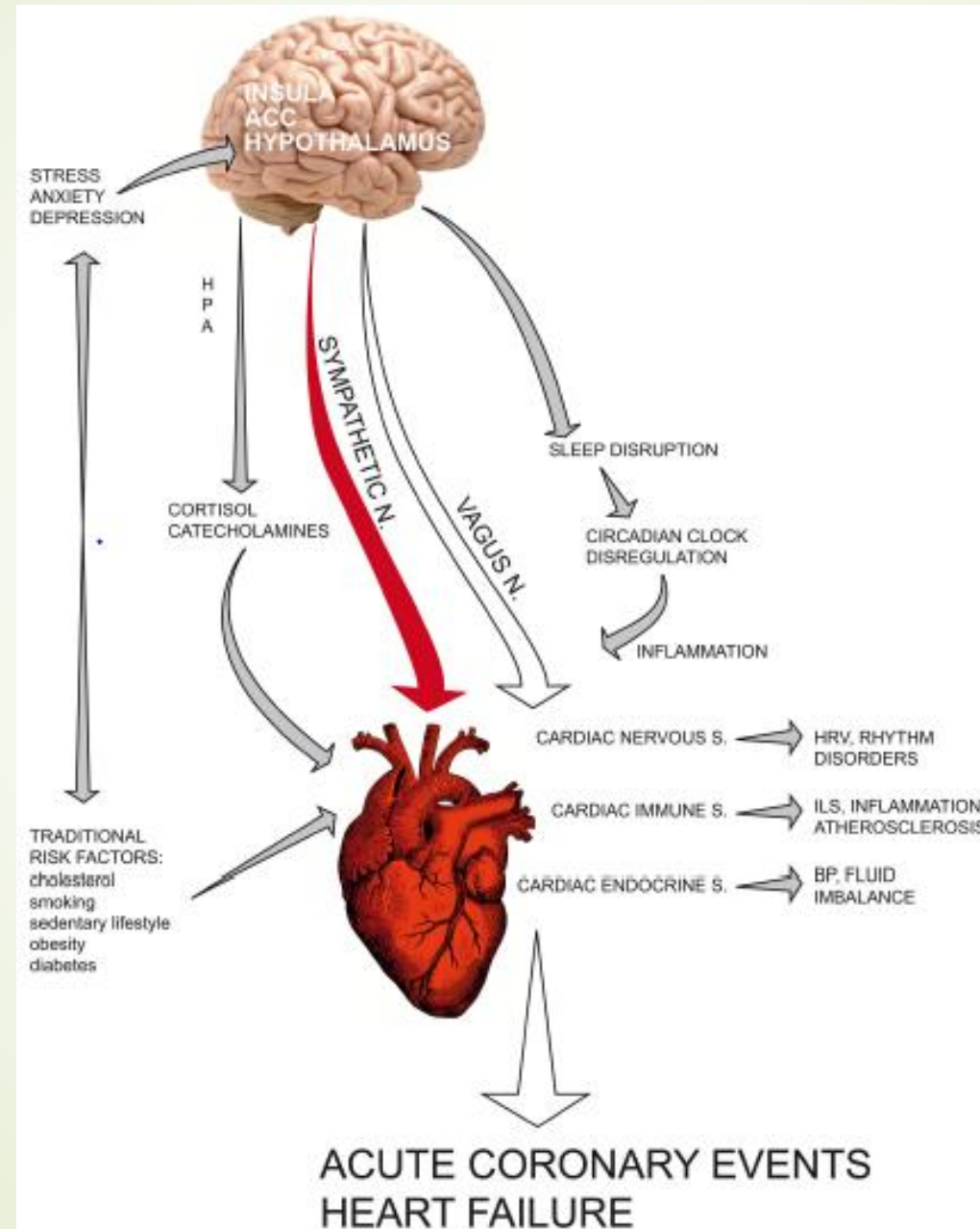
- **Smoking** — Cigarette smoking is the most common and most modifiable risk factor in young patients. It has been noted in 65 to 92 percent of young patients with MI
- Younger patients with CHD more often have a family history of premature CHD: 41 compared to 28 and 12 percent in middle aged or elderly patients, respectively.
- **Lipid abnormalities** — Hypercholesterolemia is common in young patients with CHD, but its prevalence is similar to that in older patients
- **Obesity** — Obesity appears to be an independent risk factor for coronary atherosclerosis, at least in young men
- **Paradoxical embolism** — Paradoxical embolism, primarily through a patent foramen ovale, is a rare cause of myocardial infarction in younger patients



Risk factors for coronary artery disease in young

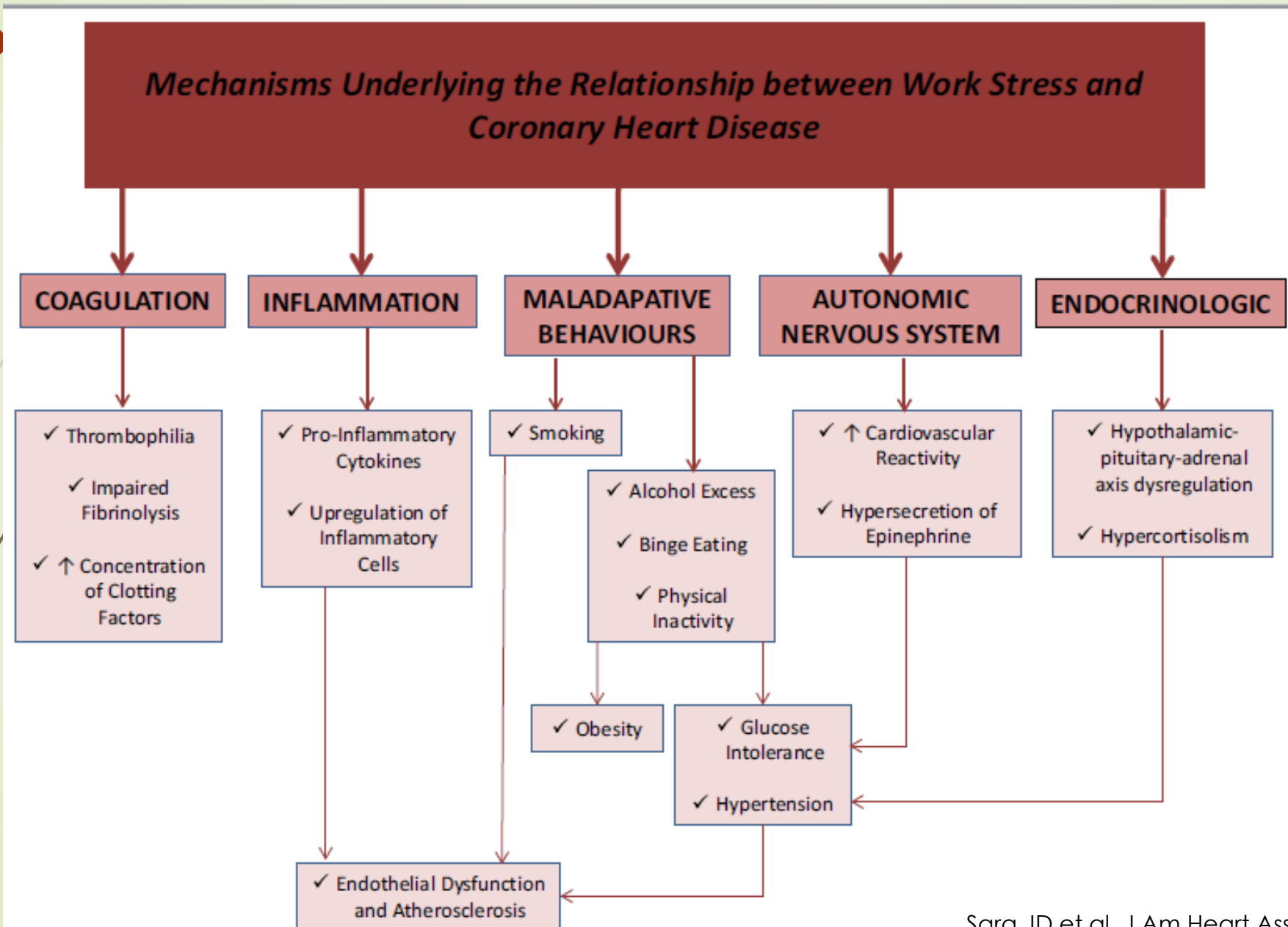
- Oral contraceptive use in young women, primarily when combined with heavy smoking.
- Frequent cocaine use, which, in the Third National Health and Nutrition Examination Survey of 10,085 adults between the ages of 18 and 45, accounted for 25 percent of MIs
- Smoking marijuana may be a rare trigger of MI
- Factor V Leiden, which is inactivated less efficiently by activated protein C than wild-type factor V, leads to a procoagulant state by increasing thrombin generation
- Children who develop Kawasaki disease (KD) in childhood (usually before the age of five) are at risk of developing coronary artery aneurysms and stenoses

Stress in Coronary Artery Disease

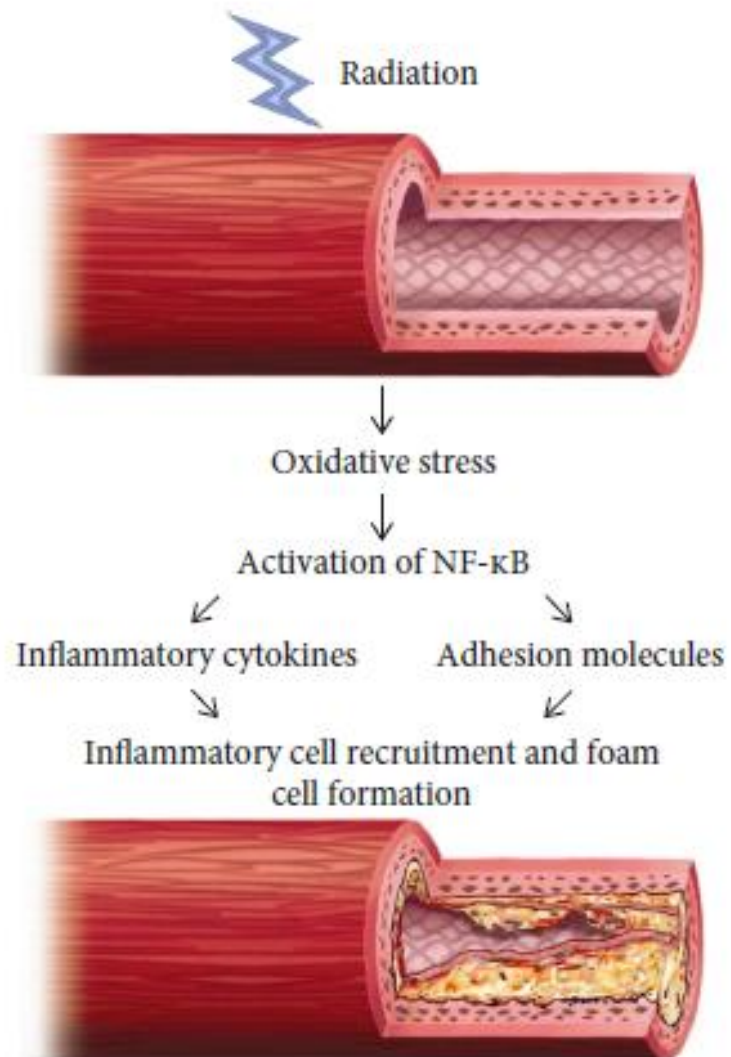


Fioranelli M et al. Front Immunol. 2018 Sep 6;9:2031.

Work related stress leading to CAD

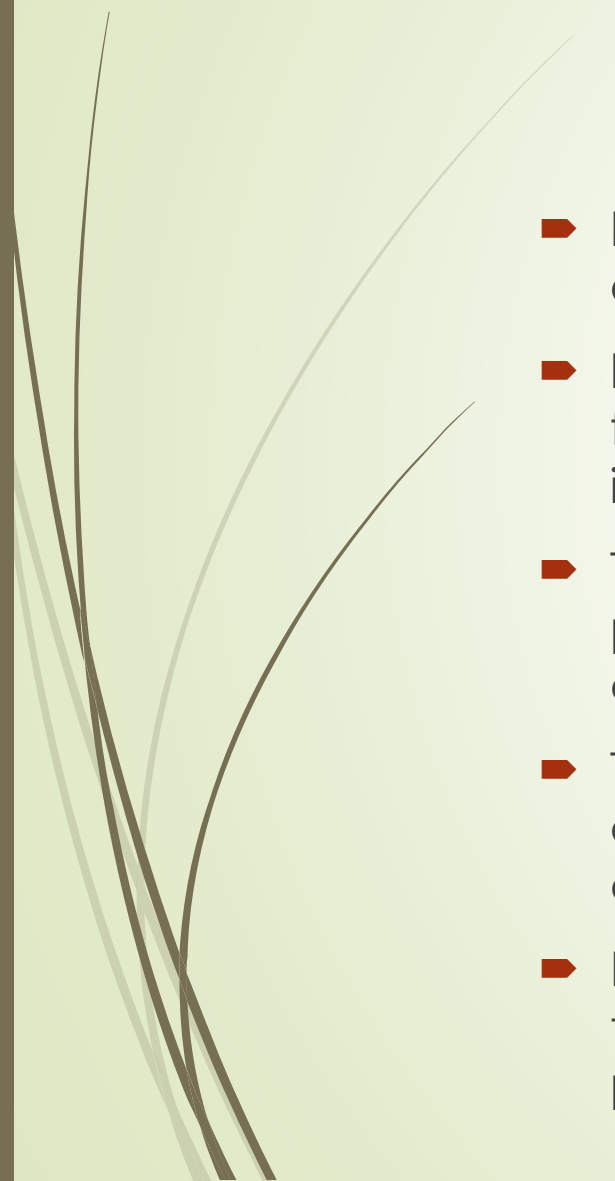


Risk factor -radiation





Kawasaki disease



- **Kawasaki disease** — Kawasaki disease (KD) is a vasculitis of infancy and early childhood.
 - It typically presents as an acute febrile illness in children under the age of five; the incidence is higher in Asian and Asian-American populations than in other groups.
 - The etiology of KD is unknown, although an inflammatory response precipitated by an infectious agent is suggested by some epidemiologic data.
 - The most important complication of KD is coronary vasculitis, leading to coronary aneurysm formation in 20 to 25 percent of untreated patients during the acute stage of the disease.
 - Nearly half of acute aneurysms regress, but approximately 20 percent lead to the development of coronary stenosis in the long term. Patients can present with MI or SCD
- Azar RR, Waters DD. Coronary heart disease and myocardial infarction in young men and women. UpToDate.(Accessed on october 11, 2019).

Table 1 List of conventional and newer risk factors in young coronary artery disease discussed in the review

Conventional risk factors	Newer risk factors
Age	Polymorphisms in <i>CETP</i> gene
Sex	Hepatic lipase gene
Hypertension	Lipoprotein lipase gene
Diabetes mellitus	C-reactive protein gene
Dyslipidaemia	<i>Apo A1</i> gene
Obesity	<i>Apo B</i> gene
Smoking	<i>Apo E</i> gene
Family history of premature CAD	<i>HIF1A</i> gene
	Factor 5 leiden
	<i>MTHFR</i> gene
	Methionine synthase gene
	Cocaine use
	Lipoprotein-a, Fibrinogen and D-dimer
	Decreased serum Wnt
	Increased gamma glutamyl transferase
	Raised vitamin D2 and D3
	Decreased osteocalcin
	Hypothyroidism
	Systemic lupus erythematosus
	Rheumatoid arthritis
	HIV patients on HAART
	Homocysteinemia
	Kawasaki disease in childhood,
	Patent foramen ovale
	Spontaneous coronary artery dissection

CETP: Cholesterol ester transfer protein
 HAART: Highly active anti retroviral therapy
MTHFR: Methylene tetrahydrofolate reductase;
HIF1A:Hypoxia inducible factor 1 alpha



Clinical presentation

- The clinical presentation of CHD in younger patients is different from that in older patients.
- A higher proportion of young patients do not experience angina, and, in the majority of cases an acute coronary syndrome that progresses rapidly to MI (ST elevation MI) if left untreated.
- In younger subjects is that myocarditis can mimic an acute MI.
- Myocarditis should be particularly considered in young patients with a clinical presentation of an acute coronary syndrome with normal coronary angiogram.
- A high rate of lifetime history of depression and depressive symptoms at the time of an AMI was observed in young AMI patients



Angiographic findings

- ▶ Younger patients have a higher incidence of normal coronary arteries, mild luminal irregularities, and single vessel coronary artery disease than do older patients.
- ▶ Spontaneous coronary artery dissection is a rare cause of acute MI that is more common in younger patients (under age 50) and in women.
- ▶ In women, the risk of spontaneous coronary dissection appears to be increased during the peripartum period.



Coronary Artery Surgery Study trial

- Normal coronary arteries were more common in the young patients (18 versus 3 percent).
- Young women had a higher frequency of angiographically normal coronary arteries than young men, despite a 10 year age difference in the definition of "young."
- Single vessel coronary disease was more common (38 versus 24 percent) and three vessel disease was less common (14 versus 39 percent) in the younger patients.
- There is a predilection for involvement of the left anterior descending artery in young patients



Investigations for MI in young adults

- Serum. Homocysteine
- Insulin level
- Serum. fibrinogen
- hsCRP (Highly sensitive C reactive protein)
- Lipoprotein (a)
- TPA or plasminogen activator inhibitor-1 (PAI-1)
- Small dense lipoprotein



Management of acute MI in young-STEMI

- ▶ **ST elevation MI** — Young patients with an acute ST elevation MI should be treated with primary PCI or, if not available, thrombolytic therapy.
- ▶ Young patients appear to respond well to thrombolytic therapy.
- ▶ Patients with high-risk features (high TIMI or GRACE risk scores, elevated cardiac biomarkers, or dynamic ECG changes), as well as those with recurrent or persistent symptoms are to be referred for early coronary angiography with percutaneous coronary revascularization when indicated.



Management of acute MI in young-NSTEMI

- ▶ Young patients with non-ST elevation acute coronary syndrome (ACS) should be promptly evaluated in the emergency department with ECG and a troponin test.
- ▶ TIMI and GRACE risk scores should be calculated, as they correlate with short- and longterm outcomes
- ▶ Patients with a non-ST elevation acute coronary syndrome (non-ST elevation (non-Q wave) MI or unstable angina) are first stabilized with medical therapy
- ▶ Should undergo early coronary angiography and revascularization, if appropriate



Management of chronic CAD

- The management of stable angina, including the indications for revascularization, is similar in younger and older patients.
- Routine coronary angiography is not recommended in young patients who have stable CHD.
- When indicated both PCI and CABG are effective and are associated with lower risks in younger compared to older patients.

Management of chronic CAD -PCI

- ▶ **Percutaneous intervention** — The long-term outcome of young patients undergoing percutaneous coronary intervention (PCI) is quite good.
- ▶ In STEMI patients receiving primary PCI, sex-related long-term outcome differences were age dependent, with younger women likely to have a worse long-term outcome when compared with younger men.
- ▶ In a study that assessed the outcome of PCI in 140 consecutive patients ≤ 40 years of age, the acute success rate was 93 percent with a 28 percent rate of angiographic restenosis
- ▶ Ten-year overall and event-free survival (without MI, elective CABG, or repeat PCI) following PCI were 96 and 58 percent, respectively.
- ▶ Among survivors, 88 percent were free of angina, 93 percent had returned to work, and 19 percent underwent a repeat revascularization procedure because of disease progression at other sites or restenosis.



Management of chronic CAD -PCI

- In a study ,the long-term prognosis in young patients was acceptable,
- A second report compared the outcome of PCI in 89 patients ≤ 40 years of age with that of 1916 patients over 40 .
- Procedural success was similar in the young and older patients (90 versus 86 percent)
- There were no periprocedural complications in the younger group, while 7 percent of patients in the older group had a cardiac event (death, MI, or urgent CABG).
- After a mean followup of 30 months, there were no deaths; however, 5 percent required elective CABG and 34 percent underwent repeat PCI for restenosis or disease progression



Management of chronic CAD -PCI

- **Bypass surgery** — Coronary artery bypass grafting (CABG) is easier to perform in young patients because they are usually in better physical condition than older patients and can better tolerate the stress of surgery and general anesthesia.
- In a study of 107 patients ≤ 35 years of age in whom the actual survival at five and ten years was 94 and 85 percent, respectively, and the actual event-free survival was 77 and 53 percent, respectively.
- The long-term patency was much higher with mammary artery grafts (93 versus 56 percent with saphenous vein grafts).



Management of chronic CAD -CABG

- In a study with Patients < 60 years of age who underwent CABG had a lower risk of adverse outcomes than older patients.
- Of particular interest is that at 5 years the <60 group reported unadjusted and adjusted significantly lower cumulative rates of all-cause death in comparison to other groups.
- Long-term mortality was considerably lower in patients < 60 years than in patients > 60.
- The long-term efficacy of CABG in patients < 60 is further confirmed by a significantly higher freedom from AMI and stroke in comparison to older patients

Characteristics of young and older patients with acute

	Young patients (<45 years)	Old patients (≥45 years)
Prevalence	-	+
Single-risk factor	-	+
Smoking	+	-
Family history	+	-
Hyperlipidemia	+	-
Hypertension	-	+
Diabetes mellitus	-	+
Single vessel disease	+	-
LAD-related infarcts	+	-
RCA related infarcts	-	+
Multiple stents	-	+
More thrombus burden and thrombectomy device used	+	-
Previous AMI	-	+
Revascularization	-	+
Left ventricular systolic impairment	-	+
Renal impairment	-	+
The 30-day MACE	-	+
Long-term follow-up MACE	-	+
In-hospital mortality	-	+
Long-term mortality	-	+

“+” was more common, “-” was uncommon. LAD: Left anterior descending, RCA: Right coronary artery, AMI: Acute myocardial infarction, MACE: Major adverse cardiac event



Prognosis



- ▶ Young CAD patients have higher rates of normal coronary vessels on angiography, mild luminal irregularities and increased prevalence of single vessel disease than older CAD patients.
- ▶ In a recent study from Nepal of young CAD less than 45 years angiography revealed 7.6% had normal or non critical disease, 6.1% had triple vessel disease, 36.9% had double vessel disease and 53.8% had single vessel disease
- ▶ Single vessel disease involving left anterior descending artery is much more common in young women when compared with young men with CAD



Prognosis

- **In-hospital mortality** — The in-hospital mortality in young patients has ranged from 0 to 4 percent, a lower than that in older patients with 9 and 21 %.
- **Long term outcome:** Young patients also have a good long-term outcome after MI
- In the large CASS trial e, survival rates at seven years after an MI were 84 versus 75 percent for young and older men and 90 versus 77 percent for young and older women



Summary



- Symptomatic coronary heart disease (CHD) is uncommon in young men and women (age less than 40 to 45 years).
- Younger patients with CHD more often have a family history of premature CHD.
- Cigarette smoking is the most common and most modifiable risk factor in young patients.
- Diabetes mellitus and hypertension appear to be less common in young patients with CHD than in older patients.
- Other risk factors such as cocaine use, factor V Leiden, and oral contraceptive use are more common in younger individuals with CHD.



Summary

- The clinical presentation of CHD in younger patients is different from that in older patients.
- A higher proportion of young patients do not experience angina, and, in the majority of cases, an acute coronary syndrome that progresses rapidly to MI if left untreated is the first manifestation of CHD.
- Younger patients have a higher incidence of normal coronary arteries, mild luminal irregularities, and single vessel coronary artery disease than do older patients.
- Rarer causes of CHD such as spontaneous coronary dissection or Kawasaki disease occur more commonly in the young.
- In general, the management of CHD in the young is similar to that in older individuals.