What is atherosclerosis?

Arteries are the blood vessels that carry blood away from the heart out to the body.

Atherosclerosis is a condition in which fatty deposits called “plaques” build up inside the arteries in the body.

There are different names for atherosclerosis depending on which arteries it affects: carotid artery disease, coronary artery disease, peripheral arterial disease, etc.
Inflammation is a Risk Factor for Atherosclerosis

- Increased levels of hs-CRP and IL-6 have been shown to predict future cardiovascular events in women.

Plaque Composition

- The risk of an acute cardiac event is affected by the plaque composition i.e. calcified (hard), mixed or noncalcified (soft) (rather than the severity of stenosis).

- In a study of 40 patients with heart disease, significantly more noncalcified (soft) plaques were found in patients with acute coronary syndrome than in stable angina pectoris patients.

Noncalcified (soft) Plaque

- A calcified (hard) plaque is a more stable plaque and therefore unlikely to be the best measure of the risk of a clinical event.

- By administering an intravenous contrast agent, noncalcified (soft) plaque can now be detected by CT Angiogram.

- CT Angiogram can evaluate both the coronary lumen and determine calcified (hard)/noncalcified (soft) coronary plaques.
### Risk factors

<table>
<thead>
<tr>
<th>Nonmodifiable</th>
<th>Modifiable</th>
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<tbody>
<tr>
<td>Increasing age</td>
<td>Hypertension</td>
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<tr>
<td>Family history</td>
<td>Diabetes</td>
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<tr>
<td>Male Gender</td>
<td>Hyperlipidemia</td>
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<tr>
<td>Genetic predisposition</td>
<td>Obesity</td>
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<td></td>
<td>Cigarette smoking</td>
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<td>Homocysteine</td>
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**SLE specific risk factors**

<table>
<thead>
<tr>
<th>Disease activity and duration</th>
<th>Renal disease</th>
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<td>Glucocorticoids</td>
<td>NSAIDs</td>
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### Cardiovascular risk in Lupus

- **Accelerated atherosclerosis is a major cause of morbidity and mortality in SLE**
- **Patients with SLE have a 2.66 times higher risk of cardiovascular events compared to the general population**  
- **Traditional cardiovascular risk factors do not account for the entire risk**  

### Smoking

- Leading preventable cause of death in the United States—400,000 deaths annually.
- 8% of deaths attributable to *second-hand* smoke exposure
- Smoking one to four cigarettes daily still increases coronary artery disease risk
- Directly related to increased rates of: myocardial infarction, sudden death, aortic aneurysm formation, peripheral vascular disease, and stroke


- Inhibits the efficacy of hydroxychloroquine


### Hypertension

- Normal blood pressure — Less than 120 over less than 80
- Only a minority of SLE patients reach the goal of well controlled hypertension
- **Risk in SLE:**
  a) 2.66 increase in cardiovascular events
  b) Increased risk of coronary artery disease and stroke
  c) Increased risk of poor renal outcomes
Hyperlipidemia

- Hyperlipidemia refers to increased levels of lipids (fats) in the blood, including cholesterol and triglycerides.
- High cholesterol levels correlate with cardiovascular death.
- Lowering LDL cholesterol levels with statins reduced coronary events by up to one third over a 5-year period in the general population.

Diabetes mellitus

- Presence of diabetes confers an equivalent risk to aging 15 years, an impact higher than that of smoking
  Booth et al. Lancet 2006; 368:29
- Two- to eightfold higher rates of future cardiovascular events compared to nondiabetic individuals
- 75% of all deaths in diabetic patients result from CHD.

Obesity

- Obesity is associated with more morbidity than smoking, alcoholism, and poverty
- It may soon overtake cigarette abuse as the leading cause of preventable death in the U.S.
- Increases risk of developing type 2 diabetes mellitus, hypertension, dyslipidemia, heart failure, coronary heart disease, atrial fibrillation, obstructive sleep apnea/sleep-disordered breathing, proteinuria, and osteoarthritis

Homocysteine

- Amino acid derived from the demethylation of dietary methionine
- Elevated homocysteine may result due to dietary or genetic factors
- Is an independent risk factor for stroke and thrombotic events in patients with SLE
- It may also be a risk factor for the later development of coronary artery disease in SLE
SLE-specific risk factors

Disease activity and duration
- Incidence of cardiovascular events is significantly higher in patients with high SLE disease activity
- Inverse relationship between SLE activity and plaque size
- Disease duration is significantly associated with coronary calcium scores
- Longer disease duration and higher SLICC damage index are independent predictors of carotid plaque

Renal disease
- Patients with proteinuria have an increased risk of thrombosis
- Elevated serum creatinine is associated with early atherosclerosis in patients with SLE
- History of lupus nephritis is associated with subclinical atherosclerosis

Prednisone
- Glucocorticoid use has been associated with atherosclerosis in SLE
- Taking prednisone at a dose of 10mg/day or more leads to significantly higher rates of CVE.
- A cumulative dose equivalent to >10 mg/day for 10 years is associated with a higher risk of atherosclerosis
Nonsteroidal antiinflammatory drugs

- NSAID treatment predisposes to non-fatal and fatal cardiovascular events
- Rofecoxib is associated with the highest risk of myocardial infarction,
- Ibuprofen with the highest risk of stroke, and
- Diclofenac with the highest risk of cardiovascular death.
- Naproxen seems least harmful.
  Trelle et al. BMJ. 2011 Jan 11;342:c7086

Prevention and treatment

STOP SMOKING!

- THE single most important intervention in preventive cardiology
- Reduces CHD mortality by 36% as compared with mortality in subjects who continue smoking
- Low-yield cigarettes do not appear to reduce the risks of myocardial infarction.
- REMEMBER- smoking cessation by a spouse decreases a person’s chance of smoking by 67%

General

- Recommendations for therapy are based on prevention guidelines for the general population.
- SLE should be considered a coronary heart disease equivalent
Hypertension therapy
- Reduce the amount of salt in your diet
- Lose weight if you are overweight or obese
- Avoid drinking too much alcohol
- Stop smoking
- Exercise at least 30 minutes per day most days of the week
- Be compliant with anti hypertensive therapy
- Hydroxychloroquine use is associated with better control of hypertension in SLE
- Increase in Vitamin D improves systolic blood pressure in SLE

Hydroxychloroquine
- Hydroxychloroquine is cardioprotective
- Lowsers total cholesterol in patients receiving steroids
- Lowsers fasting blood glucose concentration
  Petri. Lupus 9(Suppl. 1), S6–S22 (1996).
- Reduces incidence of thrombotic events
- Improves overall survival in patients with SLE

Hyperlipidemia treatment
- Goal LDL in SLE is <100
- Lifestyle changes: reduce total and saturated fat in the diet, lose weight (if overweight or obese), perform aerobic exercise, and eat a diet rich in fruits and vegetables
- Statins are the most effective drug for prevention of coronary heart disease, heart attack, stroke, and death BUT
- LAPS trial- NO benefit in the primary (coronary artery calcium) and secondary (carotid IMT, carotid plaque) atherosclerosis outcomes of SLE patients.

Elevated homocysteine treatment
- Combination therapy of folic acid, vitamin B6 and B12 (folbic)
- Lack of evidence that homocysteine reduction lowers risk of atherosclerosis in general population
- Treatment in specific patient populations may be appropriate, including in SLE
Conclusions

- Patients with systemic lupus erythematosus (SLE) have a significantly increased risk for developing cardiovascular disease (CVD) at a younger age.
- The increased incidence of CVD in SLE is due to a combination of traditional and SLE-specific risk factors.
- The longer a patient has had SLE, the higher the risk of developing CVD.
- Current therapeutic approaches to prevent CVD in SLE include following recommended national guidelines to target modifiable traditional cardiac risk factors such as hypertension, dyslipidemia, BMI, diabetes and tobacco use.