Coronary Atherosclerosis: Past, Present and Future

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Coronary Atherosclerosis in Time Past
Coronary Atherosclerosis in Antiquity

- Coronary artery atheroma and calcification in Egyptian mummies 1580 BC – 525 BC
- Hippocrates 460 BC – 377 BC
“And I will tell my soul, Soul, you have many goods laid up for many years. Take your ease, eat, drink, and be merry. But God said to him, Fool! This night your soul will be required of you”

- Luke 12:19-20
Life Expectancy from 1850 to 2000

(Incidence of coronary atherosclerosis was low when life expectancy was short)

[Graph showing life expectancy trends from 1850 to 2000 with notable influenza epidemics in 1918 and 1943]
Coronary Atherosclerosis in the 1950s – 1960s

• In the late fifties to mid sixties, coronary arteriography, echocardiography, IVUS, nuclear cardiology, thrombolysis, angioplasty, stents, biomarkers of inflammation or myocardial necrosis indices of left ventricular function were not available for clinical use at that time.
• Electrocardiogram and chest x-ray were the high technology at that time.
• Only nitroglycerin, morphine and bed rest were used for the management of coronary atherosclerosis at the time.
Management of AMI

- Morphine
- Heparin
- Warfarin
Selective Injection in the Right Coronary Artery in October 30, 1958 by F. Mason Sones

Cine coronary arteriography. *Modern Concepts Cardiovascular Dis* 1962; 31: 735
Chest Pain with Angiographically Normal Coronary Arteries: A New Syndrome

Myocardial lactate production in patients with angina-like chest pain and angiographically normal coronary arteries and left ventricle.

*Am J Cardiol* 1974; 30: 501
Coronary Atherosclerosis in Time Present
Genetic and environmental risk factors

- Smoking
- Sedentary Life
- Fatty Diet
- Inflammatory Process
- Stress
- Other

- Hypertension
- Inhibitory Genes
- Diabetes
- Promotor Genes
- Renal Disease
- Other

Coronary Atherosclerosis
Genetics in Coronary Atherosclerosis

- More than 55 genetic risk variants
- Chromosome 9p21 locus
- LDL receptor (discovery of statins)
- PCSK9 mutation (monoclonal, antibodies evolucubam, other)
- Variation in ANGPTL4 (lipoprotein lipase pathway)
- Blood groups A and B are risk variants for AMI compared to group 0 (higher vWF complex)
Coronary Atherosclerosis: Development and Progression

- Remodeling
- Progression
- Inflammation, neo-vessel (v-v)
- Unstable plaque-rupture - thrombosis
- Stabilization-regression
Coronary Atherosclerosis: Progression and Clinical Manifestations

- **Plaque Rupture and Thrombosis**
- **Lipid Pool**
  - **Normal**
  - **Plaque rupture**
    - **Chest Pain (Atypical)**
- **Thrombosis**
  - **Thrombosis/Progression/Angina**
  - **Occlusion**
- **AMI**
- **Myopathy, CHF/MR**
- **Asymptomatic Stable Disease (± Angina)**
- **Angina (Unstable)**
- **Death/SCD**
Prognosis is Related to Overall Disease and Not to a Specific Lesion

Coronary atherosclerosis is a systemic problem that requires systemic treatment.
Coronary Atherosclerosis: Progression and Clinical Manifestations

- Normal
- Lipid Pool
- Plaque Rupture and Thrombosis
- Thrombosis/Progression/Angina
- Myopathy, CHF/MR
- Asymptomatic Stable Disease (± Angina)
- Angina (Unstable)
- Death/SCD
- AMI
- Years
- Chest Pain (Atypical)
### Coronary Atherosclerosis: Therapy for the Plaque

<table>
<thead>
<tr>
<th>To Prevent</th>
<th>D/C Smoking</th>
<th>↓ LDL-C</th>
<th>Anti-platelet</th>
<th>β-Blocker</th>
<th>ACEI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression</td>
<td>+</td>
<td>+</td>
<td></td>
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</tr>
<tr>
<td>Rupture</td>
<td>+</td>
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<tr>
<td>Thrombosis</td>
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<td>Infarction</td>
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<tr>
<td>Death</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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</tbody>
</table>

- Moderate exercise; Mediterranean diet
- Ezetamibe
- New drugs, Evolocumab
- The role of vitamin D
- Other
Coronary Atherosclerosis: Clinical Significance of Left Ventricular (LV) Function

• LV systolic function is a stronger prognostic indicator compared to number of diseased vessels.


• CASS (Coronary Artery Surgery Study). Circulation 1983
## Coronary Atherosclerosis: Therapy to Preserve / Improve LV Function

<table>
<thead>
<tr>
<th>Goal</th>
<th>Therapy for plaque</th>
<th>β-Blocker</th>
<th>ACEI</th>
<th>Revascularization</th>
<th>Thrombolysis</th>
<th>Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stabilize Plaque Prevent Rupture, Prevent Rupture, Thrombosis, MI</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
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<tr>
<td>↓ Infract size</td>
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<td>+</td>
<td>+</td>
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<tr>
<td>Improve Function</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

- Triggers of MI
- Preconditioning, Postconditioning?
Cell Based Therapy / Biomaterial

- Intracoronary injection

- Direct injection
  - Epicardial (Surgery)
  - Endocardial (Percutaneous)
Coronary Atherosclerosis: Medical Therapy vs. Revascularization for the Individual Patient

The Superior Physician
He is skeptical toward the data of his own profession, welcomes discoveries which upset his previous hypothesis, and still animated by human sympathy and understanding.

Coronary Atherosclerosis: Medical Therapy vs. Revascularization

- Medical management improves symptoms, increases survival and in most instances is not inferior to revascularization.

- As medical therapy is getting better, revascularization looks better as well ("free ride") since all patients with coronary atherosclerosis are on optimal medical management.

- Medical therapy for most patients with chronic stable angina should be the initial approach.

- Revascularization: persistent symptoms - large area of myocardium at risk

- The greater the severity of ischemia, extent of disease and LV dysfunction the greater the benefit on survival from revascularization over medical therapy.
Coronary Atherosclerosis: PCI versus CABG
Available Information Should be Applied to the Individual Patient

<table>
<thead>
<tr>
<th>Consider CABG</th>
<th>Consider PCI</th>
</tr>
</thead>
</table>
| • Left main or equivalent  
  • 3 VD with EF < 50% or large area of ischemia  
    • 3 VD (prox. LAD), normal EF especially in diabetics  
      • 2 VD (prox. LAD), EF < 50% or large area of ischemia  
        • Proximal LAD  
        • Symptom control  
        • 2-3 VD (prox. LAD), normal LV, no diabetes  
          • Restenosis, large area of ischemia  
    • Symptom control  
    • Restenosis, large area of ischemia  
    • 1-2 VD (no prox. LAD), LV dysfunction or large area of ischemia |
| • Proximal LAD  
• Symptom control  
• Restenosis, large area of ischemia  
• 1-2 VD (no prox. LAD), LV dysfunction or large area of ischemia |
Hybrid Cardiovascular Operating Room

Operating Room  Catheterization Lab

Vanderbilt University, First Adult OR/Lab in USA
Coronary Atherosclerosis: Available Information Should be Applied to the Individual Patient

Pharmacologic Agents
Coronary Atherosclerosis in Time Future

Quo Vadis
Halfway Technology and Cost of Medicine

Medical Cost

No Therapy  |  Halfway Technology  |  Prevention/Cure
Translational research

René Magritte. *La Clairvoyance*, 1936
Certain Infections Diseases

- Rheumatic fever
- Syphilis
- Tuberculosis
- Peptic ulcer
- Other

Mortality from Cardiovascular Disease

Northwestern Europe, Australia, Canada, New Zealand, USA

"Time present and time past
Are both perhaps present in time future,
And time future contained in time past."
- T. S. Eliot, *Four Quartets*
Genome Atlas

- Coronary atherosclerosis
- Other

Immunology - Inflammation

- Developing medicines that mimic the natural successes of the human genome
- Pharmacogenetics/Pharmacogenomics
- Other

Vaccines for prevention:
- Atherosclerosis
- Other
Epigenetics

Epigenetics link genetics and environment through modification of gene expression

"πήραμε τη ζωή μας. λάθος!" - Σεφέρης

Gene

Environment A → Disease
Environment B → No Disease

Pathologic effects of tobacco
(cigarette smoke/secondhand smoke)
Coronary Atherosclerosis: Early treatment may prevent the clinical manifestations of the disease.
Coronary Atherosclerosis in Time Past, Time Present and Time Future

Developments

Pharmacologic Agents

Bypass

Stent

Prevention/Cure

1950

Time

2010
Microbiome and Chronic Disease

- Antibiotics and obesity
- Diabetes
- Coronary atherosclerosis
- Other
Mild to Moderate Coronary Artery Stenosis is Responsible for Most of the Myocardial Infarctions

Optical Coherence Tomography

Thermographic catheter

Stefanadis, Ch.
Plaque Temperature in Acute Coronary Syndromes (ACS) and Stable Angina (SA)

Opening of the Coronary Artery Stenosis Relieves Symptoms

- Gruentzig AR, Angioplasty 1977
- Sigwart U, Stents 1987
- Stefanadis Ch, Covered stents 1996
- Serruys PW, Heparin coated stents 1998

Antiplatelet Therapy
Atherosclerotic plaques as Defined by Coronary Arteriography and Intravascular Ultrasound
Progression of Coronary Atherosclerosis

- Ischemia (angina, acute coronary syndromes)
  - β-Blockers
  - Calcium blockers
  - Coronary bypass surgery
Pathologists View of Thrombosis in Acute Myocardial Infarction

“Since we did not find any thrombi without fissures or any fissures without thrombi we are forced to conclude that there was a causal association between these two findings in the cases we examined.”


*Atheroscl Res* 1966; 6: 1-7
Coronary Thrombosis in AMI Determined by Coronary Arteriography


- CCU
- PCI
- ICD
- ACE inhibitors
- β-Blockers
- Thrombolysis
- Biomarkers
- Rehabilitation
Screening of Ruptured Plaque by Intravascular Ultrasound


- Fibrous cap
- Calcification
- Rupture
- Lumen
The Shortcomings of Diagnosing Coronary Atherosclerosis Based on Stress-Induced Ischemia

“We had the experience but missed the meaning.”
- T.S. Eliot
Information Available Related to Coronary Atherosclerosis in the Late Fifties - Early Sixties

• Angina pectoris
  Heberden W. Royal College of Physicians 1768

• Coronary artery occlusion produces myocardial infarction
  Herrick JB. Association of American Physicians, Chicago 1912
  JAMA 1912; 54: 2015

Nitroglycerin
Regression of Coronary Artery Disease as a Result of Intensive Lipid-Lowering Therapy in Men with High levels of Apolipoprotein B


The Role of Statins
Therapy of Peptic Ulcer: Past and Present

Therapy of Coronary Atherosclerosis: Present and Future

PAST

PRESENT

FUTURE
(Prevention, Cure)
Imaging of the Entire Cardiovascular System / Molecular Imaging

MRI

PET/MRI

[Images showing medical imaging equipment and scans of the cardiovascular system]