CORONARY CIRCULATION
AND ACUTE CORONARY
SYNDROMES

LeRoy E. Rabbani, MD
Director, Cardiac Inpatient Services
Director, Cardiac Intensive Care Unit
Professor of Clinical Medicine

MYOCARDIAL OXYGEN DEMAND

1. Wall Tension
2. Heart Rate
3. Contractility (Inotropic State)

WALL TENSION

Wall Tension $\propto \frac{P \cdot r}{h}$ Formula of Laplace

$P = LV$ Systolic Pressure
$r = LV$ Radius
$h = LV$ Wall Thickness
MYOCARDIAL OXYGEN SUPPLY

1. Diastolic Perfusion Pressure
2. Coronary Vascular Resistance
3. Oxygen Carrying Capacity

INTRINSIC CONTROL OF CORONARY TONE

1. Heart in basal state consumes as much oxygen as it can (3-5 times as much as most organs)
2. Heart cannot increase oxygen extraction on demand
3. Any additional oxygen requirement must be provided by an increase in blood flow (autoregulation of coronary vascular tone)

CORONARY BLOOD FLOW REGULATION

\[ Q \propto \frac{P}{R} \]

\[ Q = \text{Coronary Artery Blood Flow} \]
\[ P = \text{Perfusion Pressure} \]
\[ R = \text{Coronary Vascular Resistance} \]
CORONARY VASCULAR RESISTANCE

1. External Compression
2. Intrinsic Regulation
   a) Local Metabolites
   b) Endothelial Factors
   c) Neural Innervation

EXTERNAL COMPRESSION OF CORONARIES

1. Greatest in systole
2. Directly related to intramyocardial pressure
3. Subendocardium, adjacent to high intraventricular pressure, is most vulnerable to ischemic damage
AUTOREGULATION OF CORONARY VASCULAR TONE

I. Local Metabolites
   a) Oxygen - Vasconstrictor
   b) Adenosine - Vasodilator
   c) Lactate
   d) Prostaglandins
   e) Hydrogen ions

II. Endothelial Factors
   1. Endothelial-dependent vasodilators:
      (ATP, ADP, bradykinin, histamine, acetylcholine)
   2. EDHF (nitric oxide free radical) stimulates SMC guanylate
      cyclase activity.
   3. Increased cGMP mediates vasodilatation through inhibition
      of calcium release.
<table>
<thead>
<tr>
<th>Table 1. Unstable Angina Presentations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest angina within 1 week of presentation</td>
</tr>
<tr>
<td>New onset angina of Canadian Cardiovascular Society Classification (CCSC) class III or IV within 2 months of presentation (see Table 4)</td>
</tr>
<tr>
<td>Angina increasing in CCSC class to at least CCSC III or IV</td>
</tr>
<tr>
<td>Variant angina</td>
</tr>
<tr>
<td>Non-Q-wave myocardial infarction</td>
</tr>
<tr>
<td>Post-myocardial infarction angina (&gt;24 hours)</td>
</tr>
</tbody>
</table>

![Image of plaque, thrombus, and lumen]

**Fissured plaque with overlying thrombus**

![Image of fissured plaque with overlying thrombus]
Table 1. Biochemical Analysis of Protein and Extracellular Lipid Content of Ulcerated and Intact Human Aortic Plaque Caps

<table>
<thead>
<tr>
<th></th>
<th>Ulcerated Plaques (n = 20)</th>
<th>Nonulcerated Plaques (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein (%) dry weight</td>
<td>54.8 ± 1.2</td>
<td>57.2 ± 2.2</td>
</tr>
<tr>
<td>Collagen</td>
<td>52.4 ± 8.4</td>
<td>56.8 ± 1.4*</td>
</tr>
<tr>
<td>Elastin</td>
<td>0.27 ± 0.37</td>
<td>1.37 ± 0.31</td>
</tr>
<tr>
<td>Glycosaminoglycan</td>
<td>0.9 ± 0.20</td>
<td>1.9 ± 0.2*</td>
</tr>
<tr>
<td>Extracellular lipid (% plaque volume)</td>
<td>54.9 ± 3.8</td>
<td>22.1 ± 2.4*</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.001. Values presented as mean value ± SEM. Modified, with permission, from Davies et al. (80).

Table 2. Cellular Content of Ulcerated and Intact Human Aortic Plaque Caps

<table>
<thead>
<tr>
<th></th>
<th>Ulcerated Plaques (n = 20)</th>
<th>Nonulcerated Plaques (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density of SMC</td>
<td>65.2 ± 13.2</td>
<td>74.0 ± 13.9*</td>
</tr>
<tr>
<td>Density of MO</td>
<td>122.1 ± 13.3</td>
<td>62.2 ± 8.8*</td>
</tr>
<tr>
<td>SMC/MO ratio</td>
<td>1.2</td>
<td>5.9*</td>
</tr>
</tbody>
</table>

*p < 0.001. Values presented as mean value (SEM). MO = monocytes; SMC = smooth muscle cells. Modified, with permission, from Davies et al. (80).

Figure 4. Circumferential tension on the fibrous cap of an atherosclerotic plaque containing a lipid pool (hatched area) is determined by the law of Laplace. This relates tension (T) to the intraluminal pressure (p) and the inner radius (r). The mean circumferential stress (σ) on the fibrous cap is related to circumferential tension and cap thickness (t).
Pathological View of Plaque Rupture

- Plaques with increased lipid content appear more prone to rupture, particularly when the lipid pool is localized eccentrically within the intima.

Plaque Rupture of Lipid-Rich Plaques

Mild-to-Moderate Lesions that Rupture are the Most Common Cause of Cardiac Events

Dynamics of Atherosclerotic Plaque Stability

Factors increasing stress
- Large lipid pool
- Less atherosclerotic lesions
- Y (esterified) cholesterol

Factors weakening the cap
- Collagen synthesis
- Collagen degradation
- Macrophages, T cells
- Smooth muscle cells
Macrophage Foam Cells

- Matrix Metalloproteinases
  - Collagenase
  - Stromelysin
  - Gelatinase
  - Elastase
- Tissue Factor
- CRP
- Myeloperoxidase

Platelet
Active Platelets
RESPONSES & CONSEQUENCES OF PLATELET ACTIVATION

<table>
<thead>
<tr>
<th>FACTOR RELEASED</th>
<th>PHYSIOLOGICAL RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADP, THROMBOXANE A2</td>
<td>PLATELET AGGREGATION</td>
</tr>
<tr>
<td>PLATELET FACTOR 4</td>
<td>HUMORAL CLOTTING</td>
</tr>
<tr>
<td>SNOOTON, THROMBOXANE A2</td>
<td>VASOCONSTRICTION</td>
</tr>
<tr>
<td>PLATELET DERIVED GROWTH FACTOR</td>
<td>SMOOTH MUSCLE CELL PROLIFERATION</td>
</tr>
</tbody>
</table>

Platelet Aggregate (5000x)

Platelet deposition on injured endothelial surface
TIMI Risk Score for UA/NSTEMI: 7 Independent Predictors

1. Age ≥ 65 y
2. ≥ 3 CAD Risk Factors (↑ chol, FHx, HTN, DM, smoking)
3. Prior CAD (cath stenosis >50%)
4. ASA in last 7 days
5. ≥ 2 anginal events ≤ 24 hours
6. ST deviation
7. Elevated cardiac markers (CK-MB or troponin)

TIMI = Thrombolysis in Myocardial Infarction.

ACC/AHA Guidelines Recommendations:
NSTE ACS Patients at High Risk of Death or MI

At least one of the following features must be present:
- Prolonged ongoing rest pain > 20 minutes
- Elevated cardiac troponin (TnT or TnI > 0.1 ng/mL)
- New or presumably new ST-segment depression
- Sustained ventricular tachycardia
- Pulmonary edema, most likely due to ischemia
- New or worsening mitral regurgitation (MR) murmur
- S3 or new/worsening rales
- Hypotension, bradycardia, tachycardia
- Age > 75 years

Figure 2: The “weight of the evidence” showing benefit of an invasive vs. conservative strategy in patients with UA/NSTEMI. The size of the boxes for each of the 9 randomized trials corresponds to the number of patients enrolled.

Figure 4: Benefit of invasive strategy by troponin and ST.A.s

Management Strategies in NSTE ACS
Death, MI, Rehospitalization with GP IIb-IIIa inhibitors at 6 Months

O.R. 0.78
95% CI (0.62, 0.97)
P = 0.029

CONSERVATIVE
INVASIVE
**Table 2. Localizing Myocardial Infarction**

<table>
<thead>
<tr>
<th>LOCATION</th>
<th>ECG LEADS INVOLVED</th>
<th>PROBABLE ARTERY INVOLVED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anteroseptal</td>
<td>V1-V4</td>
<td>Proximal left anterior descending (LAD), anterior branches</td>
</tr>
<tr>
<td>Anterolateral</td>
<td>V1-V4, L, AVL</td>
<td>LAD or its branches</td>
</tr>
<tr>
<td>Anterior</td>
<td>V1-V3, L, AVL</td>
<td>Medial LAD or circumflex</td>
</tr>
<tr>
<td>High anterior</td>
<td>V1-V3</td>
<td>Proximal LAD</td>
</tr>
<tr>
<td>Inferior</td>
<td>II, III, AVF</td>
<td>Inferior wall less often circumflex or posterior LAD</td>
</tr>
<tr>
<td>Posterior</td>
<td>Meno image in V1 and V4 (ST depression, osseous T, tall R, loss of S waves)</td>
<td></td>
</tr>
<tr>
<td>Right ventricle</td>
<td>V1 and reversed chest leads</td>
<td>Right coronary</td>
</tr>
</tbody>
</table>

**Lateral: Circumflex / Anterior: LAD**

**Vessel: RCA, Circumflex**
Vessel: RCA

Acute Posterior Infarction

<table>
<thead>
<tr>
<th>Location</th>
<th>Leads</th>
<th>Vessel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>V3-V4</td>
<td>LAD</td>
</tr>
<tr>
<td>Anterolateral</td>
<td>V1-V2</td>
<td>LAD, Circumflex</td>
</tr>
<tr>
<td>Anterior</td>
<td>V3-V4</td>
<td>LAD</td>
</tr>
<tr>
<td>Inferior</td>
<td>V3-V4</td>
<td>RCA, Circumflex</td>
</tr>
<tr>
<td>Right Ventr.</td>
<td>V1-V3</td>
<td>RCA</td>
</tr>
<tr>
<td>Lateral</td>
<td>V4-V6</td>
<td>Circumflex, Diagonal</td>
</tr>
<tr>
<td>Posterior</td>
<td>V1-V3, Large R + ST Depression</td>
<td>RCA</td>
</tr>
</tbody>
</table>
PROGNOSIS IN ACUTE MYOCARDIAL INFARCTION

1. LVEF - mechanical (pump failure)
2. Arrhythmias - electrical

PRINCIPAL OBJECTIVES IN MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION

1. Salvage myocardium - minimize the mass of infarcted tissue.
2. Prevent death from arrhythmias.

REPERFUSION IN ACUTE MYOCARDIAL INFARCTION

Early reperfusion (pharmacologic with thrombolytic treatment or mechanical with PTCA) of ischemic myocardium can salvage tissue before it becomes irreversibly injured.
Goal

“Door-to-lytic”
30 minutes

“Door-to-balloon”
90 minutes

Pharmacological Reperfusion for STEMI
Fibrinolysis Background/Limitations

- Initial occluded artery remains (TFG 0/1), in ~20% of patients → 2-fold ↑ in mortality\(^1,2\)
- Reocclusion occurs in 5-10% of patients → 3-fold ↑ in mortality\(^3,4\)
- Reinfarction occurs in ~5% of patients → 3-fold ↑ in mortality\(^5\)

1. TIMI 1, Am J Cardiol 1986;58:1179 2. GUSTO I, NEJM 1993;329:1615 3. Ohman et al., Circulation
Percutaneous Coronary Intervention (PCI)

The advantages of Primary PCI
- High 85-95% infarct vessel patency rate
- Low rates of recurrent ischemia, reinfarction, death, and stroke
- Avoidance of ICH
- Shortened LOS
- Ability to treat lytic-ineligible patients

Transfer for PCI in STEMI:
NRMI (1999–2002), 4278 Patients

<table>
<thead>
<tr>
<th>Door-to-Balloon Time</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;90 min</td>
<td>4.2</td>
</tr>
<tr>
<td>&lt;2 h</td>
<td>16.2</td>
</tr>
<tr>
<td>2–4 h</td>
<td>55.4</td>
</tr>
<tr>
<td>&gt;4 h</td>
<td>28.4</td>
</tr>
</tbody>
</table>

**D2B: Strategies Associated With a Significant Reduction in Door-to-Balloon Time (“Code 90”)**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Mean reduction in door-to-balloon time (min)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Having emergency medicine physicians activate the cath lab</td>
<td>8.2</td>
</tr>
<tr>
<td>Having a single call to a central page operator activate the cath lab</td>
<td>13.8</td>
</tr>
<tr>
<td>*Having the ED activate the cath lab while patient is still en route</td>
<td>15.4</td>
</tr>
<tr>
<td>Expecting staff to arrive at the cath lab within 20 minutes after page</td>
<td>19.3</td>
</tr>
<tr>
<td>Having an attending cardiologist always on site</td>
<td>14.6</td>
</tr>
<tr>
<td>Having staff in the ED and cath lab use and receive real-time feedback</td>
<td>8.6</td>
</tr>
</tbody>
</table>

*P<.05 for all.

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**Evidence-Based Strategy for Patients WithRecent Myocardial Infarction**

- **Myocardial Injury**
  - **Measure EF**
  - **Antiplatelet, β-blocker, ACE inhibitor, statin**
  - **If within 24 hr**
    - ASA/Dipyridamole
    - IV nitroglycerin or amiodarone
    - PCI/Coronary angioplasty
    - ACE inhibitor (12 to 24 hrs) Statin (first 24 hrs)
  - **EF ≤ 40%**
    - Antiplatelet, carvedilol, ACE inhibitor, statin
    - Asymptomatic
    - Antiplatelet, carvedilol, ACE inhibitor, eplerenone, statin
    - Symptomatic

---

**Table 2: Risk factor modification**

<table>
<thead>
<tr>
<th>Class I</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Smoking cessation</td>
</tr>
<tr>
<td>• Achieve optimal weight</td>
</tr>
<tr>
<td>• Daily exercise</td>
</tr>
<tr>
<td>• AHA Diet</td>
</tr>
<tr>
<td>• Hypertension control to a BP &lt;130/80 mm Hg</td>
</tr>
<tr>
<td>• Tight control of hyperglycemia in diabetics</td>
</tr>
<tr>
<td>• HMG-CoA reductase inhibitor for LDL</td>
</tr>
<tr>
<td>cholesterol &gt;160 mg/dL</td>
</tr>
<tr>
<td>• Lipid-lowering agent if LDL cholesterol after</td>
</tr>
<tr>
<td>diet is &gt;100 mg/dL</td>
</tr>
<tr>
<td>• A fibria or nisom if HDL &lt;10 mg/dL</td>
</tr>
</tbody>
</table>
POSTINFARCTION RISK STRATIFICATION

1. Submaximal ETT prior to discharge to detect residual ischemia and ventricular ectopy
2. Maximal (symptom-limited) ETT 4-6 weeks post infarction
3. Assessment of LVEF:
   - 2-D Echo
   - Radionuclide Ventriculography
4. High risk findings:
   - Angina at low workload
   - Lags reversible defect on perfusion imaging
   - Depressed LVEF with ischemia
   - ETT-induced symptomatic ventricular arrhythmias
5. Proceed with cardiac catheterization and/or invasive electrophysiologic study as needed

VENTRICULAR FIBRILLATION AND ACUTE MYOCARDIAL INFARCTION

1. Most common form of arrhythmic death in acute MI.
2. Vast majority of deaths due to V fib occur within the first 24 hrs. of the advent of symptoms; of these deaths, over half occur in the first hour.
3. Most out-of-hospital deaths from MI are due to V fib.
4. May occur without warning symptoms or warning arrhythmias.
5. In-hospital mortality from acute MI has decreased from 30% to 10-15%; death from in-hospital ventricular arrhythmia is now unusual.

VENTRICULAR FIBRILLATION POSTINfarction

1. Primary V fib (owing to acute ischemia; not associated with CHF, shock, BBB, or LV aneurysm) has a good long-term survival (>90% at one year).
2. Secondary V fib (owing to severe pump failure) occurring late in the hospital course has an extremely poor prognosis (85% mortality at one year); consider EFS.
### Atrioventricular and Intraventricular Conduction Disturbances Postinfarction

1. Anterior MI and CHB: 60-70% mortality
   Inferior MI and CHB: 25-40% mortality

2. Anterior MI and heart block - ischemic malfunction of all 3 fascicles of conduction system - extensive myocardial necrosis

3. Inferior MI and heart block - AV nodal ischemia - small amount of myocardium

4. Anterior MI: Mobitz type II block
   Inferior MI: First-degree AV block
   Mobitz type I block

### Management of CHF Postinfarction

1. Cautious use of Lasix
2. Nitrites - reduce preload; help LV remodeling
3. ACE inhibitors to attenuate LV dilatation - SAVE study
4. Avoid digoxin
5. Optimize PCWP to 18-20 mmHg

### Cardiogenic Shock

1. Infarct of >40% of LV; days 1-6
2. Marked hypotension (<80 mmHg), marked reduction in cardiac index (<1.8 L/min/m²) with PCWP >18 mmHg
3. Mortality of 60%
4. Risk Factors for Cardiogenic Shock:
   - Advanced age
   - Depressed LV EF
   - large MI
   - previous MI
   - diabetes mellitus
5. Treatment:
   - Hemodynamic Monitoring
   - Vasopressors
   - IABP
   - thrombolytic therapy/PTCA
### IABP

1. Inflates during early diastole, enhancing coronary blood flow and peripheral perfusion.
2. Deflates in early systole, reducing afterload.
3. Indications: intractable ischemia, cardiogenic shock, VSD, MR.
5. Morbidity of 10%.

### POSTINFARCTION MITRAL REGURGITATION

1. MR murmur in up to 50% of post MI patients; hemodynamically significant MI in only a minority.
2. Papillary muscle dysfunction secondary to ischemia or infarction > MR due to change in LV size or shape from asynergy or impaired contractility.
3. Involvement of Posteroventricular muscle (circumflex artery) > Anterolateral muscle (circumflex and LAD arteries).
4. 2-D Echo.
5. Papillary muscle dysfunction is frequently compatible with long-term survival.

### PAPILLARY MUSCLE RUPTURE

1. Occurs in 1% of MIs and accounts for 1-5% of MI deaths.
2. Days 2-7 post MI: sudden onset of pulmonary edema with murmur in patients with inferior and/or lateral MI.
3. Posteroventricular papillary muscle is 6-12 x’s more likely to rupture than anterolateral papillary muscle.
4. Diagnosis: 2-D Echo and Swan-Ganz catheter.
5. Treatment: IABP with vasodilator and inotropic therapy for stabilization → surgery.
VSD POSTINFARCTION

1. Occurs in 1-3% of MIs and accounts for 6% of MI deaths
2. Equal frequency between anterior and inferior MIs
3. Majority occur during first week post MI
4. New murmur, CHP, hypotension
5. Diagnosis: Doppler-Echo and Swan-Ganz catheter
6. Treatment: IABP, inotropes, vasopressors → rapid surgery (high risk)
7. Surgical results are worse if VSD complicates an inferior MI and if there is concomitant RV dysfunction

MYOCARDIAL RUPTURE

1. 24% of fatal MIs
2. Free wall of LV ruptures
3. Characteristics: first week post MI
   - first MI
   - age > 70
   - history of hypertension; no LVH
   - no history of angina
   - large Q wave infarct
   - women
4. Prevented by intravenous beta-blockade
5. EMD - almost universally fatal

LV ANEURYSM

1. Dyskinesis - local expansile paradoxical wall motion
2. Scar tissue - not associated with cardiac rupture
3. Complications occur weeks-months after MI: CHF, arterial embolism, ventricular arrhythmia.
4. Apical aneurysms - double, diffuse, or displaced apical impulse
5. EKG finding of ST segment elevation at rest in precordial leads in 25% of patients with apical or anterior aneurysms
6. 2-D Echo: detect mural thrombus
7. Pseudoaneurysm - limited myocardial rupture - needs surgical repair
RIGHT VENTRICULAR INFARCTION

1. 1/3 of patients with inferoposterior MI have some degree of LV ejection.
2. Severe RV failure (JVD, Kussmanl's sign, hepatomegaly with or without hyperechocardiog; low cardiac output if severe, lungs are clear.
3. ST-segment elevations of right-sided precordial leads, particularly lead V4R.
4. Diagnosis: 2-D Echo, Swan-Ganz catheterization reveals equalization of diastolic pressures.
5. Treatment: volume expansion, - Swan-Ganz catheter avoid nitrites, vasodilators, diuretics and LBBB, dopamine, dobutamine as needed.
If needed anticoagulation therapy, PTCA.
Dual chamber AV sequential pacing if CHF.
6. Mortality: 20%

PERICARDITIS POSTINFARCTION

1. Pericardial friction rub with pericarditic pain.
2. Manage with high dose aspirin (650 mg p.o. q.i.d.)
3. Avoid NSAIDs and steroids.
4. Must be careful in using heparin or Coumadin because of danger of tamponade.

THROMBOEMBOLISM POSTINFARCTION

1. Clinically apparent in 10% of MI cases.
2. Embolic lesions in 45% at autopsy.
3. Contributes to death in 25% of MI patients.
4. LV mural thrombi on 2-D Echo, 20% spontaneous regression; treat with Coumadin for 3-6 months, particularly if large anterior wall MI with CHF, akinesis, or dyskinesis.
5. SQ heparin to prevent pulmonary emboli arising from leg veins.