POST-ACUTE CORONARY SYNDROME

IS THE MYOCARDIUM STUNNED? HIBERNATING? INFARCTED?

MILAGROS YAMAMOTO, M.D, FPCP, FPCC
SECTION OF CARDIOLOGY USTH
Atherosclerosis timeline

- Foam cells
- Fatty streak
- Intermediate lesion
- Atheroma
- Fibrous plaque
- Complicated lesion/rupture

Endothelial dysfunction

- From first decade: Growth mainly by lipid accumulation
- From third decade: Smooth muscle and collagen
- From fourth decade: Thrombosis, hematoma

Adapted from Pepine CJ. Am J Cardiol. 1998;82(suppl 10A).
Acute thrombosis occurring in the presence of pre-existing atherosclerosis producing acute ischemic strokes, acute ischemic syndromes of peripheral arteries and acute coronary syndrome including unstable angina, myocardial infarction (NSTEMI and STEMI) and sudden death.
SPECTRUM OF ACUTE CORONARY SYNDROMES (ACS)

Presentation

Working Dx

Ischemic discomfort

Acute coronary syndrome

ECG

No ST elevation

Cardiac biomarker

Unstable angina

Final Dx

NSTEMI

Myocardial infarction

NQMI

QwMI

ST elevation
TRANSMURAL DISTRIBUTION OF CORONARY RESISTANCE VESSELS

Vasodilation

- Shear stress,
- Nitrates,
- NE $\beta_2$, Ach

Vasoconstriction

- NE $\alpha_1$, TXA2
- 5-HT, ET, All

Shear stress, Nitrates

Adenosine, EDHF, NO, KATP, NE $\beta_2$

Intramural penetrating arteries

Intramyocardial Coronaries

(Modified from Duncker DJ, Baehner RJ: Regulation of coronary vasomotor tone under normal conditions and during acute myocardial hypoperfusion. Pharmacol Ther 86:87, 2000.)
Thrombotic Coronary Occlusion
- Cessation of aerobic metabolism
- Depletion of creatine phosphate
- Anaerobic glycolysis
- Accumulation of tissue lactate
- Progressive decrease in ATP level
- Accumulation of catabolites
METABOLIC AND FUNCTIONAL CONSEQUENCES OF ISCHEMIA

- Thrombotic Coronary Occlusion
  - Tissue acidosis
  - Efflux of potassium to extracellular space
  - Decrease ATP levels
  - Myocyte death
MYOCARDIAL ISCHEMIA

- Clinical syndrome manifesting a variety of tissue effects and global cardiac effects that impair cardiac function.

- When ischemia is severe and prolonged, it causes myocyte death and results in loss of contractile function and tissue infarction.

- In cases of less severe ischemia, some myocytes remain viable but have depressed contractile function.
MYOCARDIAL ISCHEMIA

Potential Outcomes of Ischemia

Atheromatous Stenosis of Coronaries Frequently With Thrombosis

Reduced perfusion

Accumulation of metabolites • Hypoxia • Formation of free radicals

Reversible injury

Platelet aggregation

Vasospasm

Increased demand

Irreversible Injury

Reperfusion

No reperfusion

Intrallesional hemorrhages

Necrosis with contraction bands

Infarction

Preservation of myocardium

Infarct

Increasing duration and severity of ischemia

Evolution and extent of irreversible tissue injury after coronary occlusion is variable and dependent on transmural location, residual coronary flow, and the hemodynamic determinants of oxygen consumption.
Irreversible myocardial injury begins after 20 minutes of coronary occlusion in the absence of significant collaterals.

Entire subendocardium is irreversibly injured within 1 hr of occlusion and the transmural progression of infarction is largely completed within 4 to 6 hrs after coronary occlusion.
WAVE FRONT OF NECROSIS IN INFARCTION IN THE ABSENCE OF COLLATERALS

Reversible injury → Irreversible injury

Area at risk → Necrosis → Area at risk

Occlusion 20 mins. 60 mins. 3 hrs. >3-6 hrs.

Reperfusion

Results
- Stunning
- Preconditioning
- No necrosis
- Subendocardial necrosis
- Necrosis extends into midmyocardium, subepicardium
- Near transmural infarction

Phenomenon in which regional myocardial function remained depressed for up to 6 hours after resolution of ischemia following a 15-minute occlusion in the absence of tissue necrosis
Clinically important to recognize because contractile function normalizes during stimulation with various inotropic agents.

Function will spontaneously normalize within 1 week.
STUNNED MYOCARDIUM

**Stunned Myocardium**

- **Normal function**
- **Regional wall motion abnormality during ischemic episode**
- **Persistent regional wall motion abnormality despite restoration of flow**
- **Return to normal function**

**Graph**

- **Percent of normal value**
- **Acute ischemic episode**
- **Restoration of coronary blood flow**

**Legend**

- **Regional function**
- **Regional flow**
Preconditioning

- Reversible ischemia is considerably more frequent than irreversible injury
- Preconditioning is an endogenous mechanism that can delay the evolution of irreversible myocardial injury
- Repetitive reversible ischemia or angina prior to an occlusion can reduce irreversible injury
EFFECTS OF ISCHEMIA ON LEFT VENTRICULAR FUNCTION AND IRREVERSIBLE INJURY (ACUTE ISCHEMIA)
Chronic contractile dysfunction and regional cellular mechanisms that downregulate contractile and metabolic function of the heart so as to protect it from irreversible injury.
SHORT-TERM HIBERNATION

- In steady-state ischemia, the close matching between perfusion and contraction leads to a reduced regional oxygen consumption and energy uptake.

- Ability to prevent necrosis is limited by the severity and duration of ischemia, with irreversible injury developing frequently after periods of more than 24 hours.
MYOCARDIAL HIBERNATION

Hibernating Myocardium

- Normal function
- Regional wall motion abnormality due to chronic hypoperfusion without acute injury
- Gradual return to normal function

Graph showing the percent of normal value over time with different phases:
- Regional function
- Regional flow

Normal coronary blood flow → Abnormal blood flow due to progressive atherosclerotic narrowing → Restoration of coronary blood flow via revascularization
EFFECTS OF ISCHEMIA ON LEFT VENTRICULAR FUNCTION AND IRREVERSIBLE INJURY (CHRONIC REPETITIVE ISCHEMIA)

- Chronically stunned myocardium
- Chronically hibernating myocardium

Repetitive ischemia

- Normal resting flow
- Cell survival Program
- ↑ Apoptosis
- ↓ β adrenergic signaling
- Inhomogeneity in innervation

Reduced resting flow

Degeneration

- Heart failure
- Progressive fibrosis

Adaptation

- Adapted to ischemia
  Vulnerable to lethal arrhythmias
Stunning and hibernation are interrelated pathophysiologic states that lead to prolonged but reversible myocardial dysfunction.
Adaptive processes that shuts down the contractile process and decreases the myocardial oxygen demand in the presence of either chronically or intermittently reduced blood flow
**REVERSIBLE ISCHEMIA**

- **Supply-induced ischemia**
  
  - arise from transient coronary occlusion resulting from coronary vasospasm or transient thrombosis in a critically stenosed coronary artery, producing transmural ischemia similar to that present at the onset of infarction
  - increases LV compliance
Demand-induced Ischemia

→ arises from an inability to increase flow in response to increases in myocardial oxygen consumption in which ischemia predominantly affects the subendocardium

→ decreases LV compliance
Describe **dysfunctional myocardium** subtended by diseased coronary arteries with limited or absent scarring that has the **potential for functional recovery**

*Camici, P. et al, Circulation, Journal of the American Heart Association, 2008*
WHAT ARE THE DIFFERENT MODALITIES THAT CAN DETECT MYOCARDIAL VIABILITY?
MODALITIES TO DETECT EPICARDIAL CORONARIES

CT CORONARY ANGIOGRAPHY

CONVENTIONAL CORONARY ANGIOGRAPHY
MODALITIES TO DETECT EPICARDIAL CORONARIES

A. CTA

B.

C. CONVENTIONAL CORONARY ANGIOGRAPHY
ECHOCardiography
EXERCISE AND PHARMACOLOGIC STRESS ECHO

ECHOCARDIOGRAPHY
CONTRAST ECHOCARDIOGRAPHY

CARDIAC MAGNETIC RESONANCE IMAGING

1. Coronary atherosclerosis/Flow limiting stenosis

2. Repetitive ischemia and stunning

3. Chronic stunning/hibernation

4. Evidence of viability by PET

5. Complete revascularization by CABG

6. Six months after CABG

Recovery of contractility and wall thickening with reverse remodelling
NUCLEAR IMAGING
SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT)
NUCLEAR IMAGING
PROGNOSTIC IMPLICATIONS

POSITRON EMISSION TOMOGRAPHY (PET SCAN)

PET

$^{13}$N-Ammonia (rest)

$^{18}$FDG

POSITRON EMISSION TOMOGRAPHY (PET SCAN)
GLOBAL LV FUNCTION RECOVERY AFTER REVASCULARIZATION AS DETECTED BY THE DIFFERENT MODALITIES

Table 1. Results of Different Imaging Modalities to Predict Recovery of Global LV Function After Revascularization

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Patients, n</th>
<th>Sensitivity, Mean (95% CI)</th>
<th>Specificity, Mean (95% CI)</th>
<th>PPV, Mean (95% CI)</th>
<th>NPV, Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional nuclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{99m}$Tc-sestamibi $^{60}$</td>
<td>19</td>
<td>71 (51–91)</td>
<td>40 (18–62)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>SPECT FDG $^{53,73}$</td>
<td>94</td>
<td>86 (79–93)</td>
<td>93 (89–98)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>$^{201}$TI rest, re-injection $^{27,29,31,35}$</td>
<td>211</td>
<td>84 (79–89)</td>
<td>70 (64–76)</td>
<td>97 (92–100)</td>
<td>93 (86–100)</td>
</tr>
<tr>
<td>$^{201}$TI rest redistribution+FDG $^{34}$</td>
<td>47</td>
<td>86 (76–96)</td>
<td>92 (84–100)</td>
<td>90 (81–99)</td>
<td>89 (80–98)</td>
</tr>
<tr>
<td>Total</td>
<td>371</td>
<td>84 (80–88)</td>
<td>77 (73–81)</td>
<td>94 (89–98)</td>
<td>91 (85–97)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSE $^{23,30,32,33,34,35,44}$</td>
<td>408</td>
<td>76 (71–80)</td>
<td>81 (77–85)</td>
<td>84 (77–91)</td>
<td>91 (85–96)</td>
</tr>
<tr>
<td>DSE + strain rate $^{36}$</td>
<td>55</td>
<td>67 (55–79)</td>
<td>89 (81–97)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>End-diastolic wall thickness $^{32}$</td>
<td>43</td>
<td>63 (49–77)</td>
<td>68 (54–82)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total</td>
<td>506</td>
<td>74 (70–77)</td>
<td>81 (77–84)</td>
<td>84 (77–91)</td>
<td>91 (85–96)</td>
</tr>
<tr>
<td>PET</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDG $^{49,70}$</td>
<td>205</td>
<td>81 (75–86)</td>
<td>65 (59–72)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total</td>
<td>205</td>
<td>81 (75–86)</td>
<td>65 (59–72)</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

PPV indicates positive predictive value; NPV, negative predictive accuracy.

IMPROVEMENT OF FUNCTION ON SEGMENTAL BASIS BY DIFFERENT MODALITIES

Table 2. Results of Studies That Evaluated the Improvement in Function on a Segmental Basis

<table>
<thead>
<tr>
<th>Method</th>
<th>Patients, n</th>
<th>Sensitivity, Mean (95% CI)</th>
<th>Specificity, Mean (95% CI)</th>
<th>PPV, Mean (95% CI)</th>
<th>NPV, Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CMR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast enhanced(^{27})</td>
<td>29</td>
<td>97 (91–100)</td>
<td>68 (51–85)</td>
<td>73 (57–89)</td>
<td>93 (84–100)</td>
</tr>
<tr>
<td>Dobutamine stress(^{73,75})</td>
<td>193</td>
<td>94 (90–97)</td>
<td>90 (86–94)</td>
<td>86 (81–91)</td>
<td>92 (88–96)</td>
</tr>
<tr>
<td>Total</td>
<td>222</td>
<td>94 (91–97)</td>
<td>87 (83–91)</td>
<td>84 (79–89)</td>
<td>87 (89–96)</td>
</tr>
<tr>
<td><strong>Conventional nuclear</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>(^{99m})Tc-sestamibi(^{76})</td>
<td>30</td>
<td>96 (89–100)</td>
<td>55 (37–73)</td>
<td>87 (75–99)</td>
<td>80 (66–94)</td>
</tr>
<tr>
<td>SPECT FDG(^{70})</td>
<td>47</td>
<td>89 (80–98)</td>
<td>86 (76–96)</td>
<td>\ldots</td>
<td>\ldots</td>
</tr>
<tr>
<td>(^{201})TI rest, reinjection(^{73,76,77})</td>
<td>104</td>
<td>86 (80–93)</td>
<td>63 (54–73)</td>
<td>69 (60–8)</td>
<td>85 (78–92)</td>
</tr>
<tr>
<td>Total</td>
<td>181</td>
<td>89 (84–93)</td>
<td>68 (61–75)</td>
<td>73 (66–81)</td>
<td>84 (78–90)</td>
</tr>
<tr>
<td><strong>Echocardiography</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSE(^{72,76,73,73,74,76})</td>
<td>424</td>
<td>76 (72–80)</td>
<td>81 (77–84)</td>
<td>66 (61–71)</td>
<td>89 (86–93)</td>
</tr>
<tr>
<td>DSE SRI(^{76})</td>
<td>55</td>
<td>82 (72–92)</td>
<td>80 (69–91)</td>
<td>\ldots</td>
<td>\ldots</td>
</tr>
<tr>
<td>End-diastolic wall thickness(^{72})</td>
<td>43</td>
<td>94 (87–100)</td>
<td>48 (33–63)</td>
<td>53 (38–68)</td>
<td>93 (85–100)</td>
</tr>
<tr>
<td>Total</td>
<td>522</td>
<td>78 (74–81)</td>
<td>78 (74–81)</td>
<td>64 (59–70)</td>
<td>90 (86–93)</td>
</tr>
<tr>
<td><strong>PET</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PET-FDG(^{77,73,75,75,73,81})</td>
<td>280</td>
<td>89 (85–93)</td>
<td>57 (51–63)</td>
<td>73 (66–80)</td>
<td>90 (86–95)</td>
</tr>
<tr>
<td>Total</td>
<td>280</td>
<td>89 (85–93)</td>
<td>57 (51–63)</td>
<td>73 (66–80)</td>
<td>90 (86–95)</td>
</tr>
</tbody>
</table>

PPV indicates positive predictive accuracy; NPV, negative predictive accuracy; CMR, cardiovascular magnetic resonance; and SRI, strain rate index.

WHICH MODALITY TO USE???

... IT’S UP FOR DISCUSSION!
THANK YOU!!!