Cardiac Markers in Acute Coronary Syndromes

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Scope

- Acute coronary syndrome
- WHO criteria
- Ideal cardiac markers
- Cardiac markers
- Clinical uses of cardiac markers
- New criteria for diagnosis ACS
- Summary
ACS

❤ Unstable angina pectoris (UAP)
❤ Acute myocardial infarction (AMI): Non-Q wave MI, Q-wave MI
❤ Cardiac (coronary) sudden death
WHO criteria 1979

- History of chest pain consistent with myocardial ischemia
- Electrocardiographic (ECG) changes consistent with AMI
- Typical myocardial infarction plasma or serum enzyme changes
Ideal Cardiac Markers

- High sensitivity: abundant in cardiac tissue
- High specificity: absent from non-cardiac tissue
- Release pattern: rapid, long blood half life
- Clinical usefulness: influence therapy
- Analytical performance: automation
Cytosolic marker

Contractile protein
Cardiac Markers

♥ Cytosolic markers: AST, LDH, CK, myoglobin
♥ Isoenzyme of CK: CK-MB, isoenzyme of LDH
♥ Contractile proteins: myosin, troponin
AST
Aspartate aminotransferase
First cardiac marker
Aspartate aminotransferase = ASAT
Marked increase in

> 10 times

♥ Viral hepatitis
♥ Carbon tetrachloride poisoning
♥ Shock and circulation failure
Mild to moderate increase in

- Myocardial infarction, pericarditis
- Pulmonary infarction
- Hepatic diseases: cirrhosis, obstructive jaundice, neoplasm
- Skeletal muscle diseases: progressive muscular dystrophy, dematomyositis, trauma
- Hemolytic anemia
LDH

Lactate dehydrogenase
Pyruvate $\xrightarrow{\text{NADH} + H^+} {\text{Lactate dehydrogenase}} \xrightarrow{\text{NAD}^+} \text{Lactate}$. 
LDH

♥ Increase in: megaloblastic anemia, metastatic carcinoma, CML, pulmonary infarction, hepatic disease, skeletal muscle disease, hemolytic anemia
Creatine phosphokinase
Creatine phosphate + ADP → Creatine + ATP
Marked increase in

> 10 times

♥ Progressive muscular dystrophy
♥ Rhabdomyolysis
♥ Shock and circulation failure
Mild to moderate increase in

- Myocardial infarction
- Exercise, intramuscular injection, major surgery
- Alcoholic myopathy, delirium tremens, acute psychotic reaction
- Strokes, brain trauma
- Hypothyroidism
CK isoenzyme

- B (brain) subunit
- M (muscle) subunit
- CK-BB (CK₁): brain, fast
- CK-MB (CK₂): cardiac muscle, skeletal muscle
- CK-MM (CK₃): skeletal muscle, cardiac muscle, slow
CK-MB

- Cardiac muscle > skeletal muscle
- Increase in cardiac disease: After cardioversion, cardiac surgery, Pericarditis, myocarditis, after PTCA, AMI
CK-MB: increase in non cardiac disease

- Skeletal muscle injury
- Skeletal muscle disease: dermatomyositis, polymyositis, rhabdomyositis, Duchene’s muscular dystrophy
- Reye’s syndrome
- Hypothyroidism
- Chronic renal failure
- Labor and peripartum period
CK-MB: increase in non cardiac disease

- Laboratory artifact: hemolysis, hyperbilirubinemia, drugs, macro-CK
- Tumor: lung cancer
**CK-MB**: ลักษณะที่บอกว่ามาจากกล้ามเนื้อสาขา

- Appropriate clinical setting (History: trauma, skeletal muscle disease)
- No rise and fall pattern
- %CK-MB < 10-15% of total CK
- Total CK increase > 20-30 times
Myoglobin

♥ Heme protein
♥ Muscle cell
♥ Storage and transport $O_2$
♥ ขึ้นเร็ว ลงเร็ว
Troponin

- Contractile protein
- Contraction of muscle
- Skeletal and cardiac troponin
- Cardiac troponin T and cardiac troponin I
(a) Myosin binding sites blocked; muscle cannot contract

(b) Myosin binding sites exposed; muscle can contract
cTn: increase in cardiac disease

♥ Primary ischemic cardiac injury: ACS

♥ Secondary ischemic cardiac injury: coronary intervention, pulmonary embolus, coronary artery spasm, vasculitides, end state renal failure, acute heart failure, exercise

♥ Myocarditis, cardiac trauma
cTn: increase in non cardiac disease

- Metabolic toxic
- Rhabdomyolysis
- Hypertensive emergency
- Acute neurologic disease
- Sepsis
- Hematologic malignancies
- Endocrine disease
- Intubated patients
Clinical Use of Cardiac Markers
<table>
<thead>
<tr>
<th>Marker</th>
<th>Rise (xULN)</th>
<th>Start (Hr)</th>
<th>Peak (Hr)</th>
<th>Return (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK</td>
<td>5-8</td>
<td>3-8</td>
<td>10-24</td>
<td>3-4</td>
</tr>
<tr>
<td>CK-MB</td>
<td>5-15</td>
<td>3-8</td>
<td>10-24</td>
<td>2-3</td>
</tr>
<tr>
<td>LDH</td>
<td>2-4</td>
<td>8-12</td>
<td>72-144 (3-6 days)</td>
<td>8-14</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>1-3</td>
<td>6-9</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>cTn</td>
<td>3-8</td>
<td></td>
<td>24-48 (1&lt;sup&gt;st&lt;/sup&gt;) 72-100 (2&lt;sup&gt;nd&lt;/sup&gt;)</td>
<td>4-10</td>
</tr>
</tbody>
</table>
## Diagnostic Performance

<table>
<thead>
<tr>
<th>Markers</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK</td>
<td>94</td>
<td>57</td>
</tr>
<tr>
<td>CK MB</td>
<td>90.7</td>
<td>99.6</td>
</tr>
<tr>
<td>LDH/AST</td>
<td>64</td>
<td>92</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>86.5 (97)</td>
<td>90.2 (57)</td>
</tr>
<tr>
<td>cTn</td>
<td>86.5</td>
<td>96.4</td>
</tr>
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AST/LDH

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Limitation</th>
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</thead>
<tbody>
<tr>
<td>Low cost, available in developing country</td>
<td>Low specificity</td>
</tr>
<tr>
<td>Rapid</td>
<td>Low sensitivity</td>
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</table>
## CK-MB

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Limitation</th>
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<tbody>
<tr>
<td>1. Rapid, cost efficient, accurate assay</td>
<td>1. Low specificity</td>
</tr>
<tr>
<td>2. Ability to detect early reinfarction</td>
<td>2. Low sensitivity during early (&lt;6 hr after symptom onset) or later after symptom onset (&gt;36 hr) and for minor myocardial damage</td>
</tr>
<tr>
<td>Advantage</td>
<td>Limitation</td>
</tr>
<tr>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td>1. High sensitivity</td>
<td>1. Very low specificity in setting of skeletal muscle injury or disease</td>
</tr>
<tr>
<td>2. Useful in early detection of MI</td>
<td>2. Rapid return to normal range limits sensitivity for later presentations</td>
</tr>
<tr>
<td>3. Detection of reperfusion</td>
<td></td>
</tr>
<tr>
<td>4. Most useful in ruling out MI</td>
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## Cardiac troponin

<table>
<thead>
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<th>Advantage</th>
<th>Limitation</th>
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</thead>
<tbody>
<tr>
<td>1. Powerful tool for risk stratification</td>
<td>1. Low sensitivity in very early phase of MI and requires repeat measuremen at 8-12 hr, if negative</td>
</tr>
<tr>
<td>2. Greater sensitivity and specificity than CK-MB</td>
<td>2. Limited ability to detect late minor reinfarction</td>
</tr>
<tr>
<td>3. Detection of recent MI up to 2 weeks after onset</td>
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<tr>
<td>4. Useful for selection of therapy</td>
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<tr>
<td>5. Detection of reperfusion</td>
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New criteria: ACC/ESC 2000

- Rise and flow pattern of cTn or CK-MB: รวมกับความผิดปกติต่อไปนี้อย่างน้อย 1 ข้อ:
  - Symptom of AMI
  - ECG: pathologic Q waves
  - ECG: ischemia
  - Coronary intervention
  - Pathologic finding: AMI
New criteria: British Cardiac Society 2004

♥ Increase TnT and/or CK-MB or Accu TnI
♥ ECG: ST elevation or ST depression or T inversion
Patient with suspected ACS

- **ECG-ST elevation MI**
  - **Q wave MI**
    - Immediate consideration of reperfusion therapy
  - **Non-Q wave MI**
    - Evidence of myonecrosis (Non-Q wave MI)
      - Anti-plt therapy
      - Anti-thrombotic
      - Early invasive therapy
    - Tn+
  - Tn-

- **No ECG-ST elevation MI**
  - Tn+
  - Tn-
  - Evaluation for myonecrosis (CK-MB or troponin)
    - Tn+
    - Tn-
    - No myonecrosis
    - Consideration alternate diagnosis: No ACS
  - Unstable Angina
Frequency

❤ AHA: First: admit, Second 6-12 hr after onset
❤ ESC/ACC: first admit, Second 6-9 hr after onset, Third 12-24 hr after onset of chest pain
Summary

- Acute coronary syndrome
- WHO criteria
- Ideal cardiac markers
- Cardiac markers
- Clinical uses of cardiac markers
- New criteria for diagnosis ACS
Thank You for Your Attention