

Clinical Application of Cardiac Biomarkers in an Accredited Chest Pain Center

Laboratory's Best Practices

Noemi Melendres-Wozny, BSN., RN
Accreditation Review Specialist
National Client Relations Manager



Collaboration

SCPC shares with its facilities the goal of early diagnosis of myocardial infarction (MI) and improvement in patient outcomes through education, accreditation and process improvement.

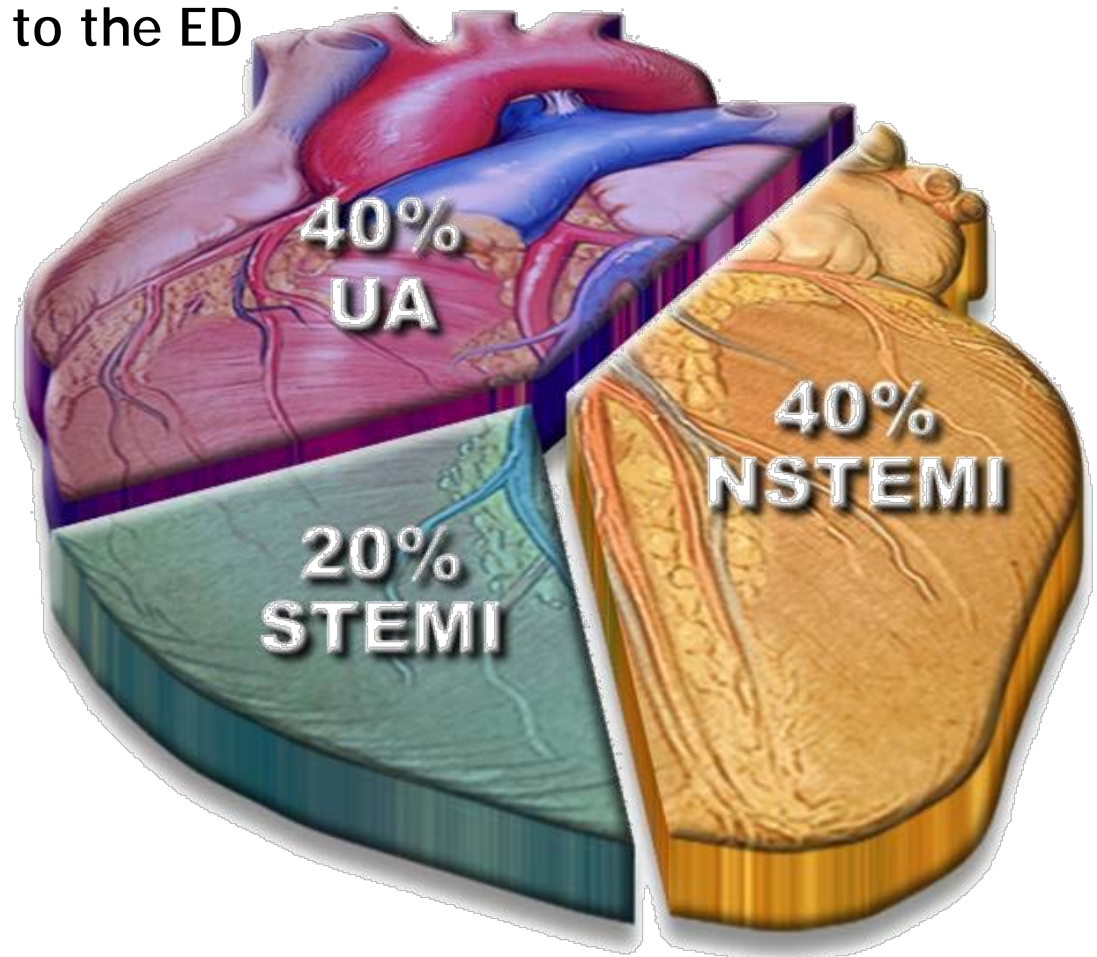
Through the *process of accreditation* we help break down barriers and facilitate communication to achieve successful continuum of care.


Acute Coronary Syndrome (ACS)



5-8 million patients present to the ED annually for chest pain

- ▶ 20-25% diagnosed with some form of ACS

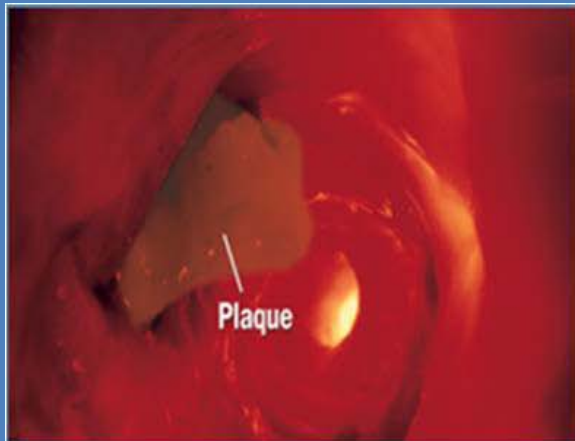


Source: **American Heart Association** 
Learn and Live

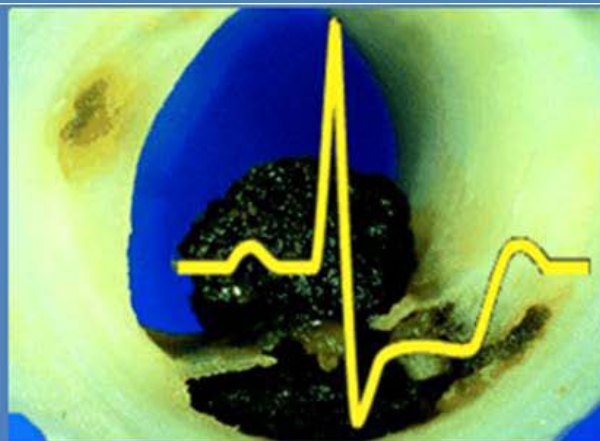
New Definition of MI: *New Focus*



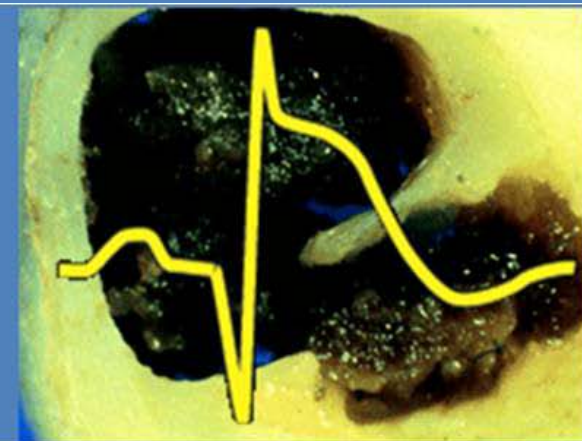
Today's guidelines are less focused on a separate decision limit for AMI, but more focused on early detection of myocardial *injury* along with symptoms of ischemia.



Diagnosis: UA
Troponin - EKG -



Diagnosis: NSTEMI
Troponin + EKG -

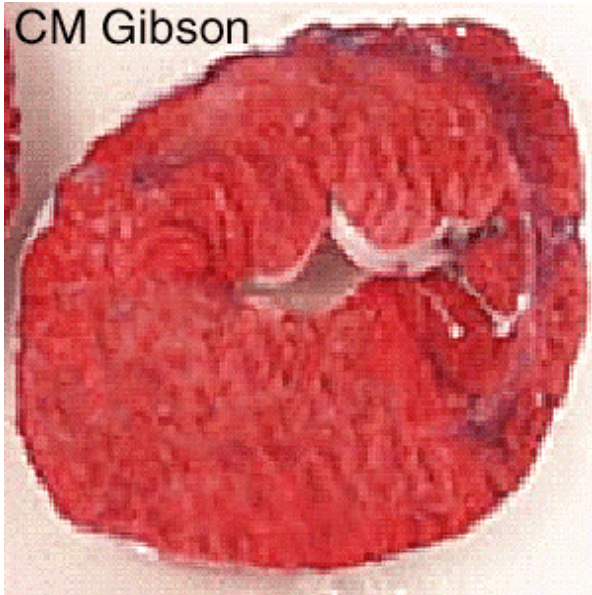


Diagnosis: STEMI
EKG + Troponin +

Estimated In-hospital Mortality by Door-to-balloon Times



| Time (min) | Adjusted mortality* |
|------------|---------------------|
| 15 | 2.9 (2.8–3.1) |
| 30 | 3.0 (2.9–3.2) |
| 60 | 3.5 (3.4–3.6) |
| 90 | 4.3 (4.2--4.4) |
| 120 | 5.6 (5.4–5.7) |
| 180 | 8.4 (8.2–8.7) |
| 240 | 10.3 (10.0–10.7) |



**There is no “floor”
to the mortality
reduction that can
be achieved by
reducing time to
treatment.**

***Adjusted for age, sex, race, findings on presentation, medical history, procedural characteristics, angiographic findings, and hospital factors**

Any delay in D2B time associated with increased in-hospital mortality
Rathore SS, et al. *BMJ* 2009; 339:b1807. Yale University School of Medicine; ACC-NCDR

A background image showing several medical professionals in white coats and scrubs, focused on a patient. One person is using a stethoscope, and another is holding a patient's arm. The scene is brightly lit, suggesting a hospital or clinic environment.

Guidelines

Cardiac Biomarkers in Acute Coronary Syndrome Care

Third Universal Definition of Myocardial Infarction

published online August 24, 2012



- TROPONIN (I or T) = preferred biomarker overall and for each specific category of MI
- Diagnosis of acute MI=detection of a rise and/or fall of the measurements.
- Increased cTn concentration is defined as a value exceeding the 99th percentile of a normal reference population [URL]

→ This discriminatory 99th percentile is *designated* as the decision level for the diagnosis of MI and must be determined for each specific assay with appropriate quality control in each laboratory

Third Universal Definition of Myocardial Infarction

Kristian Thygesen, Joseph S. Alpert, Allan S. Jaffe, Maarten L. Simoons, Bernard R. Chaitman and Harvey D. White

Dec. 2012 IFCC Table : Analytical characteristics of commercial and research Cardiac Troponin I and T assays



| Commercially available assays - Company/ platform(s)/ assay | LoB _a (µg/L) | LoD _b (µg/L) | 99 th % (µg/L) | %CV at 99 th % | 10% CV (µg/L) | Reference population N: age range (y) | Epitopes recognised by Antibodies | Detection Antibody Tag |
|---|-------------------------|-------------------------|---------------------------|---------------------------|---------------|---------------------------------------|------------------------------------|------------------------|
| Abbott AxSYM ADV | 0.02 | | 0.04 | 14.0 | 0.16 | | C 87-91, 41-49; D 24-40 | ALP |
| Abbott Architect | <0.01 | | 0.028 | 14.0 | 0.032 | | C 87-91, 24-40; D: 41-49 | Acridinium |
| Abbott i-STAT | 0.02 | | 0.08 | 16.5 | 0.10 | | C: 41-49, 88-91; D: 28-39, 62-78 | ALP |
| Alere Triage SOB | 0.05 | | NAD | NA | NA | | C: NA; D: 27-40 | Fluorophor |
| Alere Triage Cardio 3 | 0.002 | 0.01 | 0.02 | 17.0 | 0.04 | | C: 27-39; D: 83-93, 190-196 | Fluorophor |
| Beckman Coulter Access Accu | 0.01 | | 0.04 | 14.0 | 0.06 | | C: 41-49; D: 24-40 | ALP |
| bioMerieux Vidas Ultra | <0.01 | <0.01 | 0.01 | 27.7 | 0.11 | 747: 20 - 81 | C: 41-49, 22-29; D: 87-91, 7B9 | ALP |
| Mitsubishi Chemical PATHFAST | 0.002 | 0.008 | 0.029 | 5.0 | 0.014 | 490: 18 - 78 | C: 41-49; D: 71-116, 163-209 | ALP |
| Ortho VITROS Troponin I ES | 0.007 | 0.012 | 0.034 | 10.0 | 0.034 | | C: 24-40, 41-49; D: 87-91 | HRP |
| Radiometer AQT90 FLEX TnI | | 0.0095 | 0.023 | 17.7 | 0.039 | | C: 41-49, 190-196; D: 137-149 | Europium |
| Radiometer AQT90 FLEX TnT | | 0.0080 | 0.017 | 15.2 | 0.026 | | C: 125-131; D: 136-147 | Europium |
| Response Biomedical RAMP | 0.03 | | NAD | 18.5 (at 0.05) | 0.21 | | C: 85-92; D: 26-38 | Fluorophor |
| Roche Cardiac Reader cTnT | 0.03 | | NAD | NA | NA | | C: 125-131; D:136-147 | Gold particles |
| Roche cobas h 232 TnT | 0.05 | | NAD | NA | NA | | C: 125-131; D:136-147 | Gold particles |
| Roche E 2010 /cobas e 411 / E 170 / cobas e 601 / 602 TnT (4 th gen) | 0.01 | | NAD | NA | 0.03 | 533: 20 - 71 (M: 268; F: 265) | C: 125-131; D:136-147 | Ruthenium |
| Roche E 2010/cobas e 411 / E 170 / cobas e 601 / 602 hs-TnT | | 0.005 | 0.014 | 10.0 | 0.013 | | C: 125-131; D: 136-147 | Ruthenium |
| Roche E 2010/cobas e 411 / Roche E 170/cobas e 601 / 602 cTnI | | 0.16 | 0.16 _c | NA | 0.3 | | C: 87-91, 190-196; D: 23-29, 27-43 | Ruthenium |
| Siemens ADVIA Centaur [®] TnI-Ultra [™] | 0.006 | | 0.04 | 8.8 | 0.03 | 684: 17 - 91 | C: 41-49, 87-91; D: 27-40 | Acridinium |
| Siemens Dimension [®] EXL [™] TNI | 0.010 | 0.017 | 0.056 | 10.0 | 0.05 | 241 | C: 27-32; D: 41-56 | Chemiluminescence |
| Siemens Dimension [®] RxL CTNI | 0.04 _d | | 0.07 | 15 - 22 | 0.14 | 342: 18 - 83 | C: 27-32; D: 41-56 | ALP |
| Siemens Dimension VISTA [®] CTNI | 0.015 | | 0.045 | 10.0 | 0.04 | 199 | C: 27-32; D: 41-56 | Chemiluminescence |
| Siemens IMMULITE [®] 1000 Turbo _c | 0.15 | | 0.30 | 14 | 0.59 | 300 | C: 87-91; D: 27-40 | ALP |
| Siemens IMMULITE [®] 1000 _c | 0.1 | | 0.19 | 11 | 0.22 | 300 | C: 87-91; D: 27-40 | ALP |
| Siemens IMMULITE [®] 2000 XPi _c | 0.2 | | 0.29 | 10.3 | 0.32 | 300 | C: 87-91; D: 27-40 | ALP |
| Siemens IMMULITE [®] 2500 STAT _r | 0.1 | | 0.2 | NA | 0.42 | 255 | C: 87-91; D: 27-40 | ALP |
| Siemens IMMULITE [®] 1000 Turbo _r | 0.15 | | NA | NA | 0.64 | | C: 87-91; D: 27-40 | ALP |
| Siemens Stratus [®] CS cTnI | 0.03 _d | | 0.07 | 10.0 | 0.06 | 101 | C: 27-32; D: 41-56 | ALP |
| Tosoh ST AIA-PACK | 0.06 | | 0.06 _c | 8.5 | NA | | C: 41-49; D: 87-91 | ALP |

Third Universal Definition of Myocardial Infarction

published online August 24, 2012



- Optimal precision= coefficient of variation (CV) at the 99th percentile URL for each assay, should be defined as **<10%**.
- Better precision (CV<10%) allows for more sensitive assays and facilitates the detection of changing values.
- Use of assays that do not have optimal precision (CV<10% at the 99th percentile URL) makes determination of a significant change difficult but *does not cause false positive results*
- Assays with CV **>20%** at the 99th percentile URL *should not be used*

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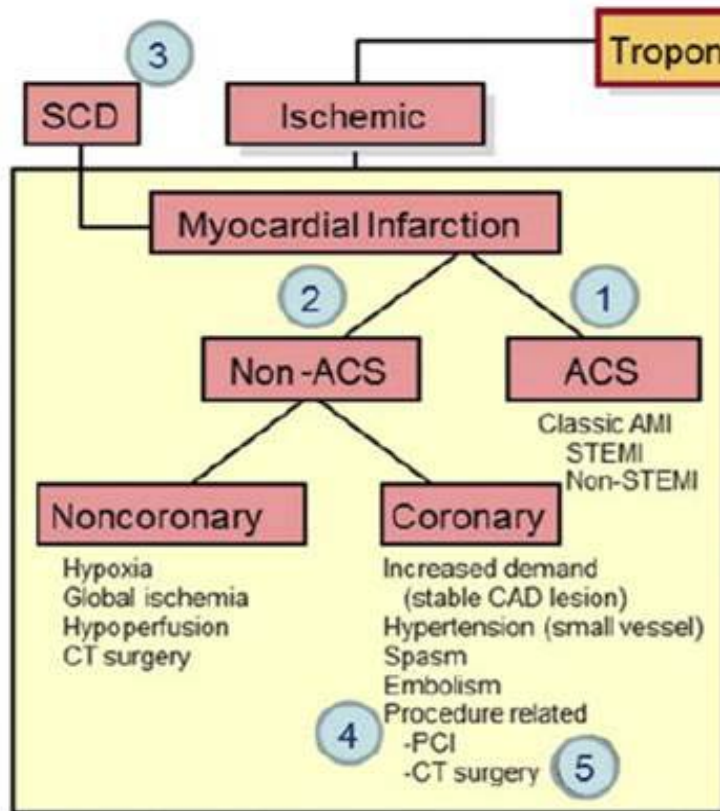
- Troponin samples should be drawn on first assessment and repeated 3 to 6 hours later.
- To establish the diagnosis of MI, a rise and/or fall in values with at least one value above the decision level is required, coupled with a strong pre-test likelihood.
- Renal Failure or Heart Failure patients can have significant chronic elevations in cTn. These elevations can be marked as seen in patients with MI but they do not change acutely.
- Troponin values may remain elevated for 2 weeks or more following the onset of myocyte necrosis.

Third Universal Definition of Myocardial Infarction

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Troponin Positivity and Universal Definition of MI

Classification of MI Type



Type 1: Ischemic myocardial necrosis secondary to plaque rupture (ACS)

Type 2: Ischemic myocardial necrosis not due to ACS (e.g., supply/demand mismatch, coronary spasm, embolism, \uparrow or \downarrow BP, anemia, arrhythmia)

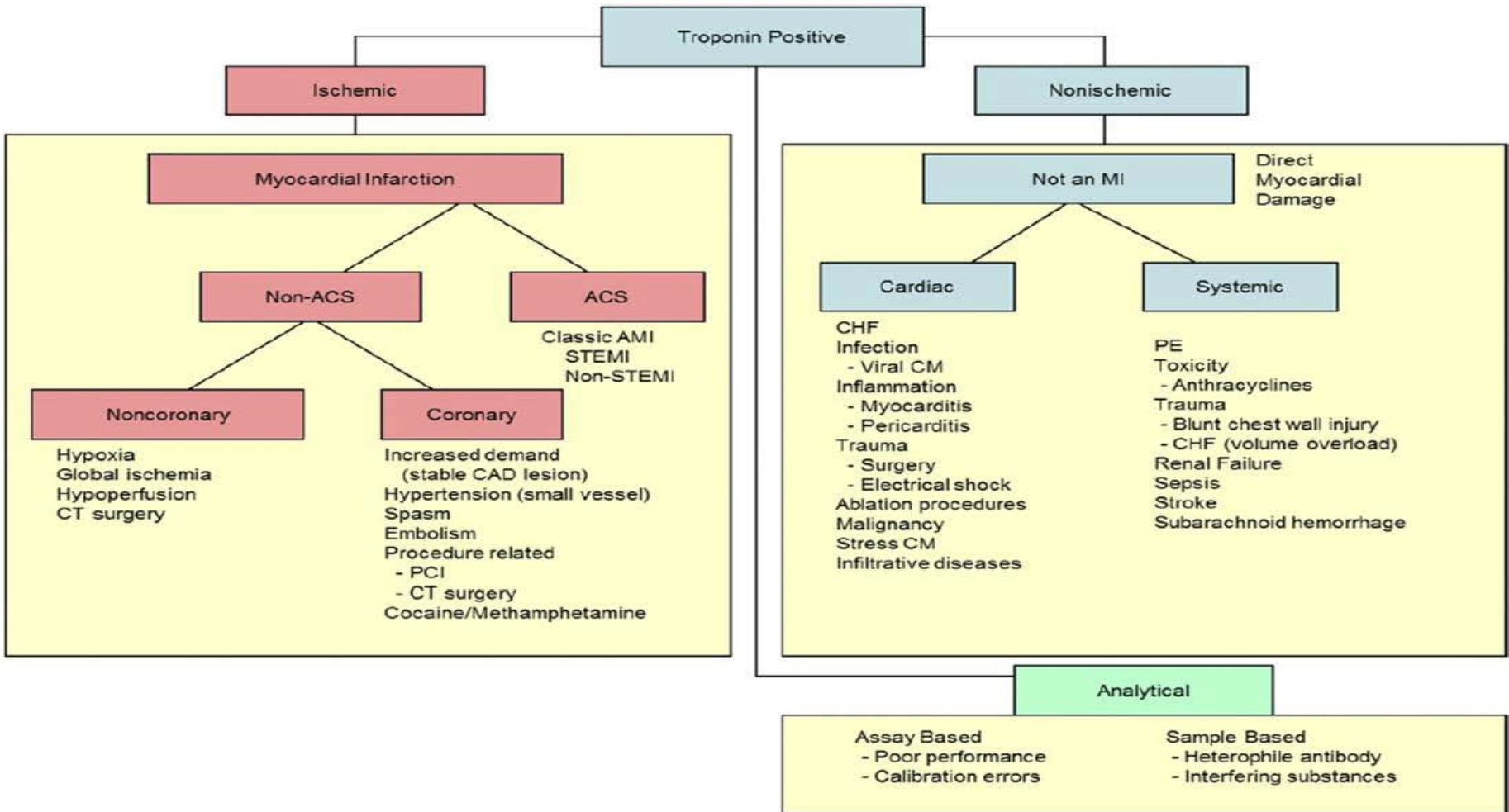
Type 3: Sudden cardiac death

Type 4: Procedure related
a) Secondary to PCI
b) From stent thrombosis

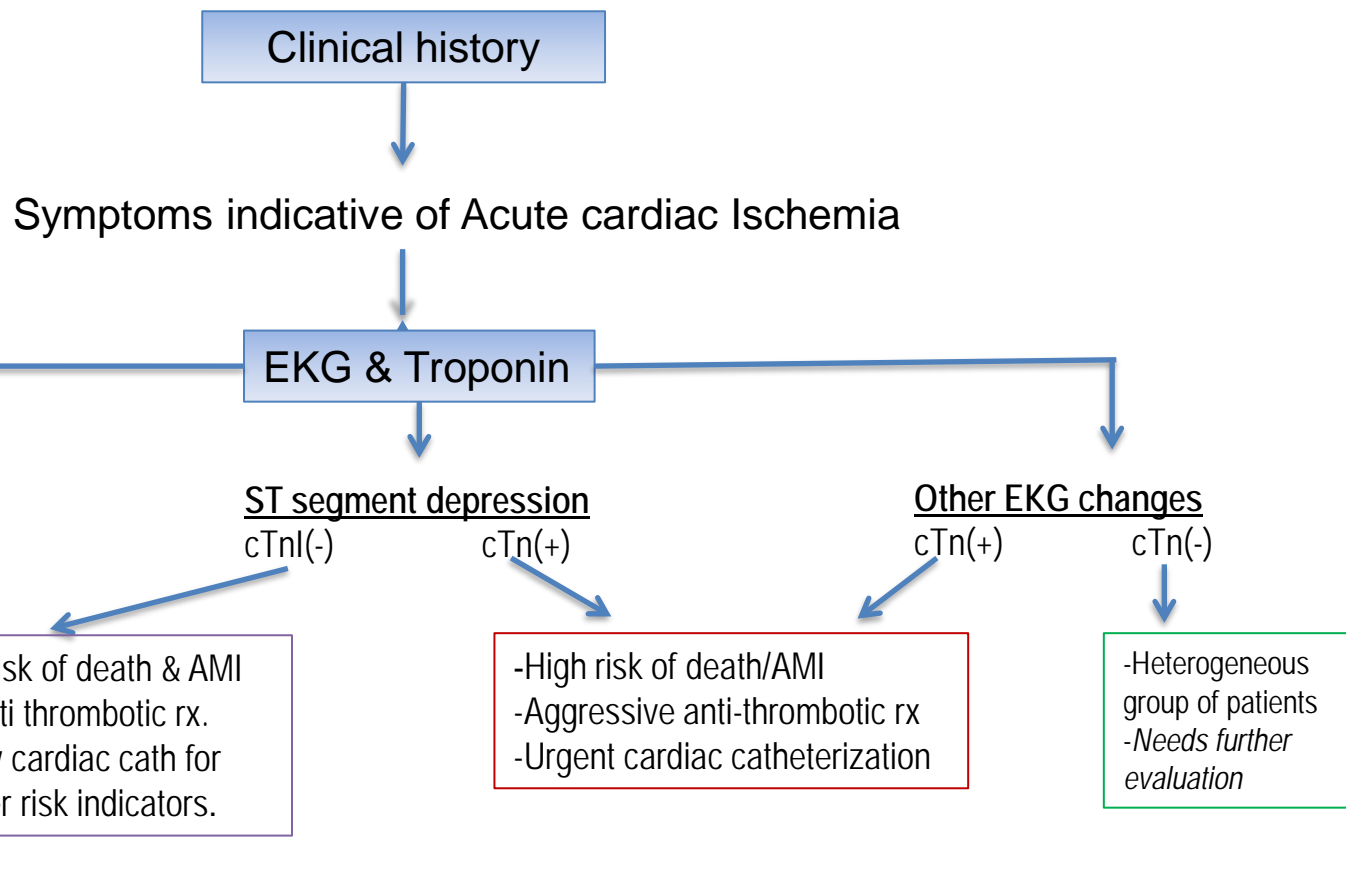
Type 5: CABG related



Clinical Distribution of Elevated Troponin



Risk Prediction and Treatment on Patients with clinical suspicion of NSTEMI/ACS



Reference: Cardiovascular Biomarkers, Pathophysiology and Disease Management; David A. Morrow, MD, MPH, Humana Press Inc. 2006

Considering Single Marker strategy?



- Preferred marker for myocardial injury/necrosis = Troponin I or T
- Troponin elevations are nearly totally specific for Cardiac Injury
- Troponin is substantially more sensitive than CKMB
- Elevations of CKMB indicative of myocardial injury
- Troponin levels rise **2-3 hours** after the onset of chest discomfort
- High sensitive troponin= definitive rule in diagnosis can be made in 2-3 hours
- CKMB less diagnostically sensitive compared with troponin I or T.
- Myoglobin has low diagnostic specificity for myocardial injury

*Cardiovascular Biomarkers: Pathophysiology and Disease Management; 2006.Humana Press: C. Cannon, MD, A. Armani, D. Morrow
Circulation 2008: Requiem for a Heavyweight, The Demise of Creatine Kinase-MB; Amy Saenger, PhD; Allan Jaffe, MD*



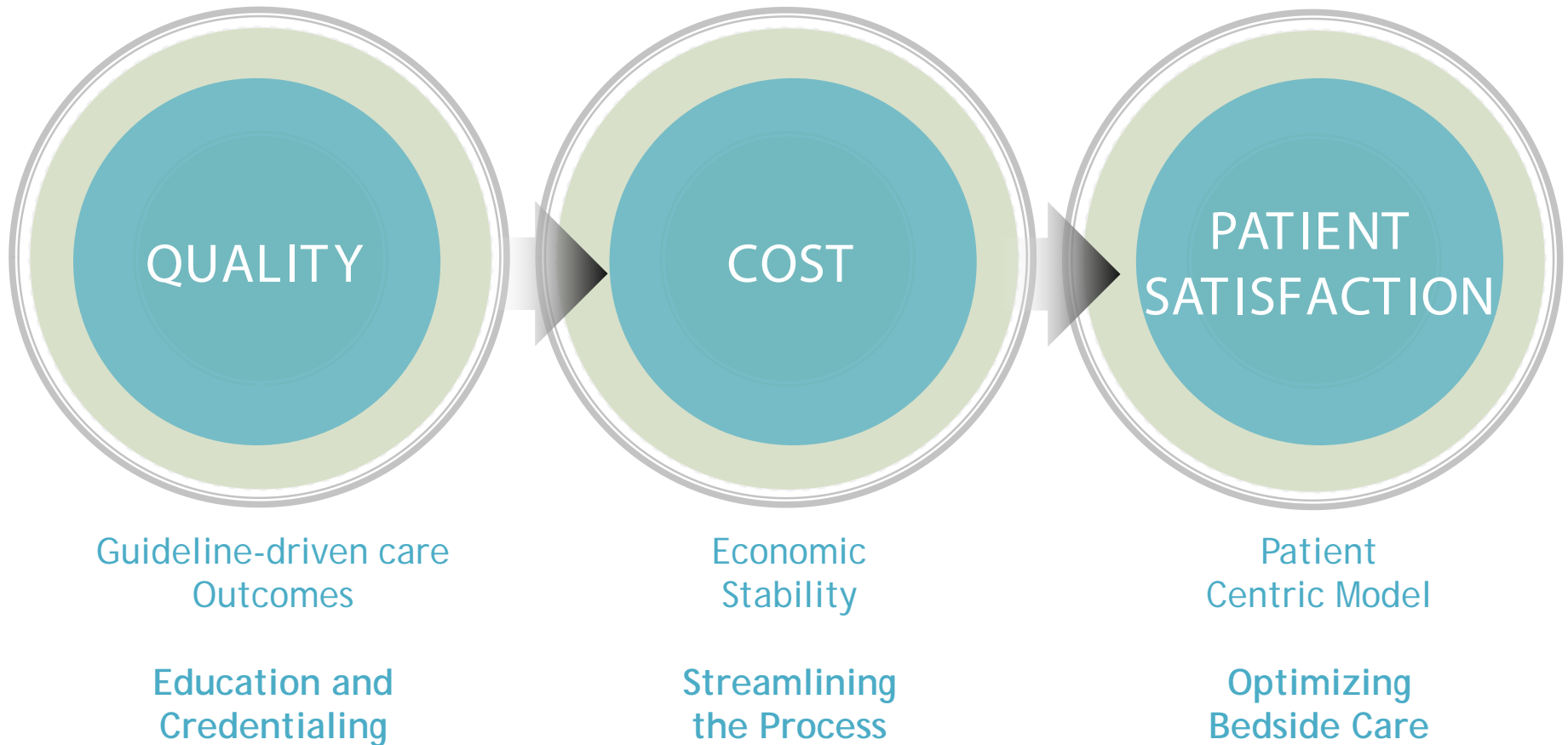
Questions for you...



CPC Accreditation Cycle IV

- Lab requirements
- Identified Vulnerabilities
- Opportunities for Improvement

Accreditation Process *focus*



CPC Accreditation Cycle IV

Lab participation required

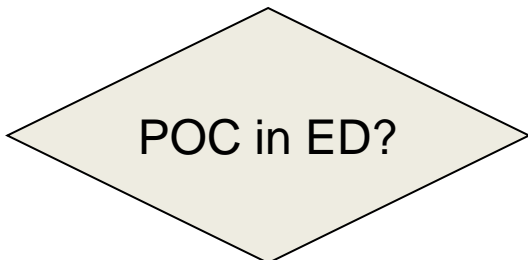


- The NSTEMI/UA process clearly defines a method of risk stratification that demonstrates evidence-based practice
- The process for the ACS patient includes baseline troponin , at a minimum, throughout the facility
- The facility has a process in place to monitor the TAT of serial draws for troponin. (minimum 6 months metrics)

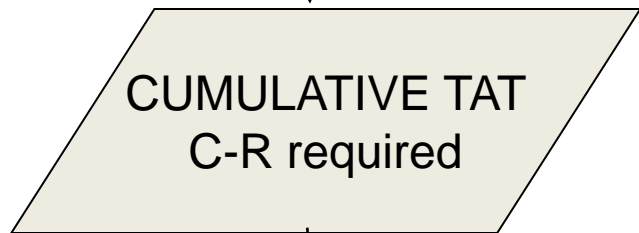
SCPC ACCREDITATION & BIOMARKER TESTING: Key Element 4



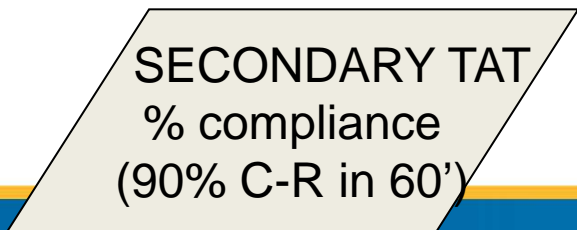
KE 4.4.0.0



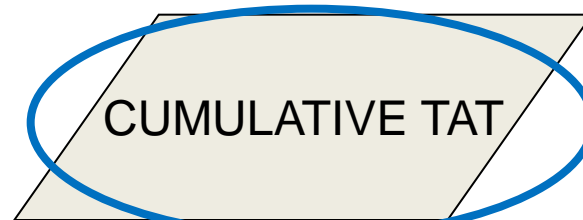
IF YES



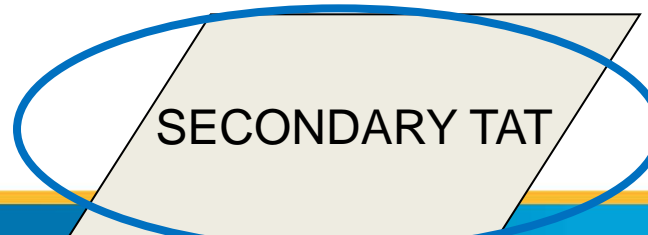
AND



IF NO



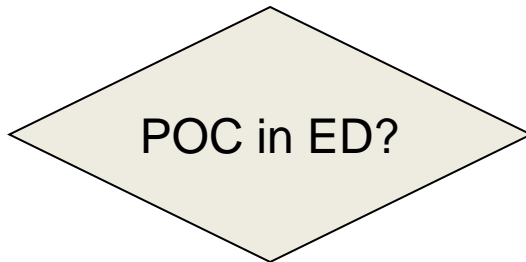
AND



SCPC ACCREDITATION & BIOMARKER TESTING: Key Element 4



KE 4.4.0.0



IF YES

IF NO

CUMULATIVE TAT
C-R required

CUMULATIVE TAT

AND

AND

SECONDARY TAT
% compliance
(90% C-R in 60')

SECONDARY TAT

CPC Accreditation Cycle IV

Lab participation required

- The cardiac biomarker protocol includes a serial troponin from **ED arrival up to 6 hours**. The protocol may last less than 6 hours if provocative testing or imaging takes place
- The facility demonstrates a process change that results in improvement in door to biomarker results. (minimum 6 months metrics)
- 90% of baseline troponin TAT of Order to Result or Collect to Result is within 30 min.

Team Process Improvement

Beyond TAT



ED [Order to Receive]

1. Nurse-First: recognition ACS s/s?
2. Pre-Approved Orders (CBM)
3. Protocol-driven care
4. Phlebotomy
5. E order initiation (US/RN/Tech)
6. Transport (sneaker/PTS)



Lab [Received to Result]

1. Receiving station –process
2. Centrifugation –Stat spin ?
3. Analysis :
 - POC
 - Lab
4. Resulting
 - Auto Verify/ Release
 - Auto reflex on +
5. Reporting
 - Reference range
 - Cutpoint for positive
 - No gray zone or indeterminate

Process Improvement: LEAN, PDCA, RCA

(Quality of care, Cost, Patient Satisfaction)

CPC Accreditation Cycle IV

Lab participation required

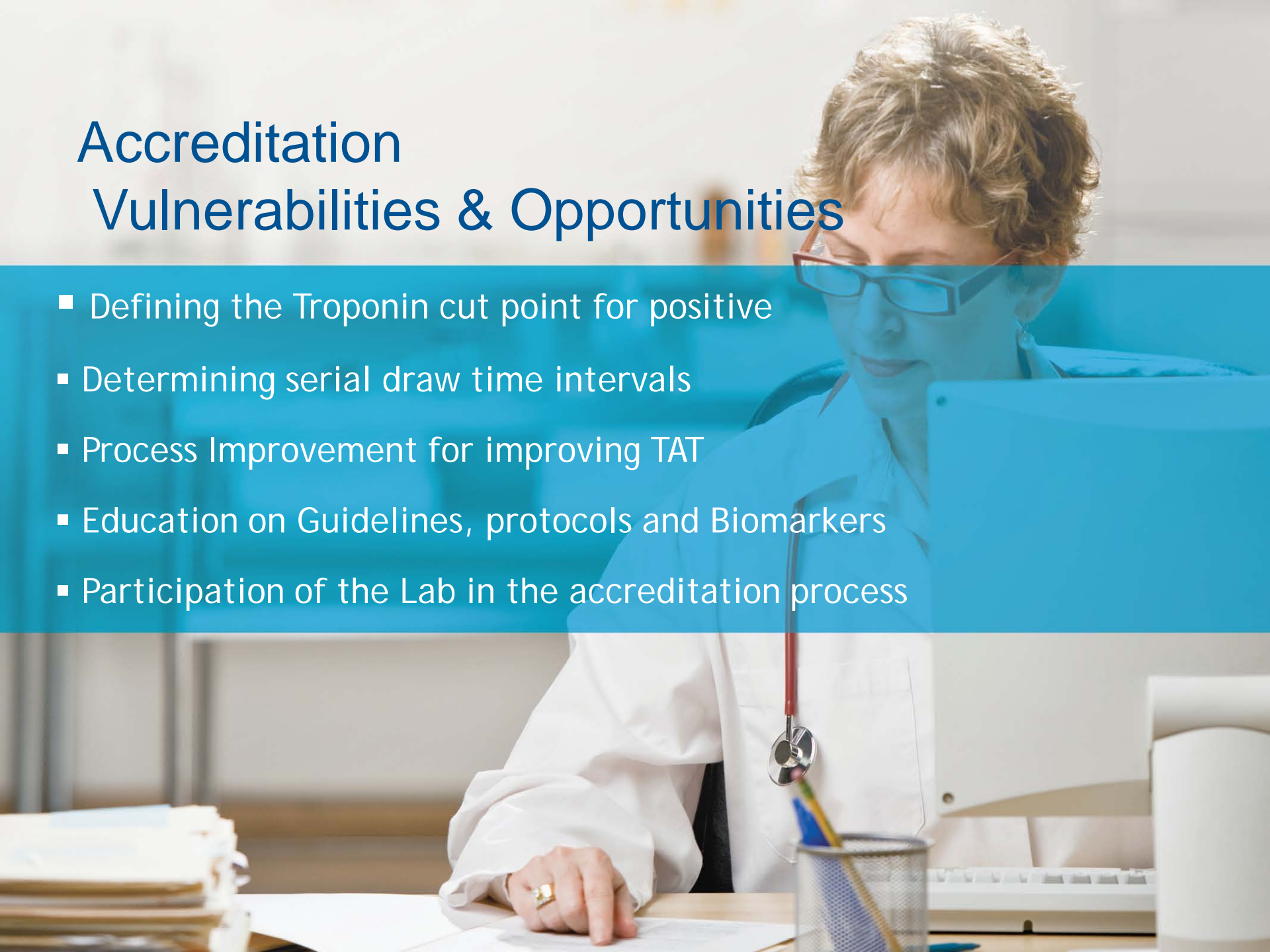
- All nurses caring for ACS patients complete annual education, competencies, or training related to ACS that includes: **Education on current ACC/AHA ACS guidelines and Education on cardiac biomarkers.**
- The facility has in place a membership roster for the chest pain center committee who is *multidisciplinary* with functional areas defined



Questions for you...

Accreditation Vulnerabilities & Opportunities

- Defining the Troponin cut point for positive
- Determining serial draw time intervals
- Process Improvement for improving TAT
- Education on Guidelines, protocols and Biomarkers
- Participation of the Lab in the accreditation process



Facility 1

Lab Troponin I serial protocol: 0, 8, 16 hrs

Cut-point used for negative result: ≤ 0.034 (99th %)

~~Intermediate or gray-zone: 0.035 to 0.120~~

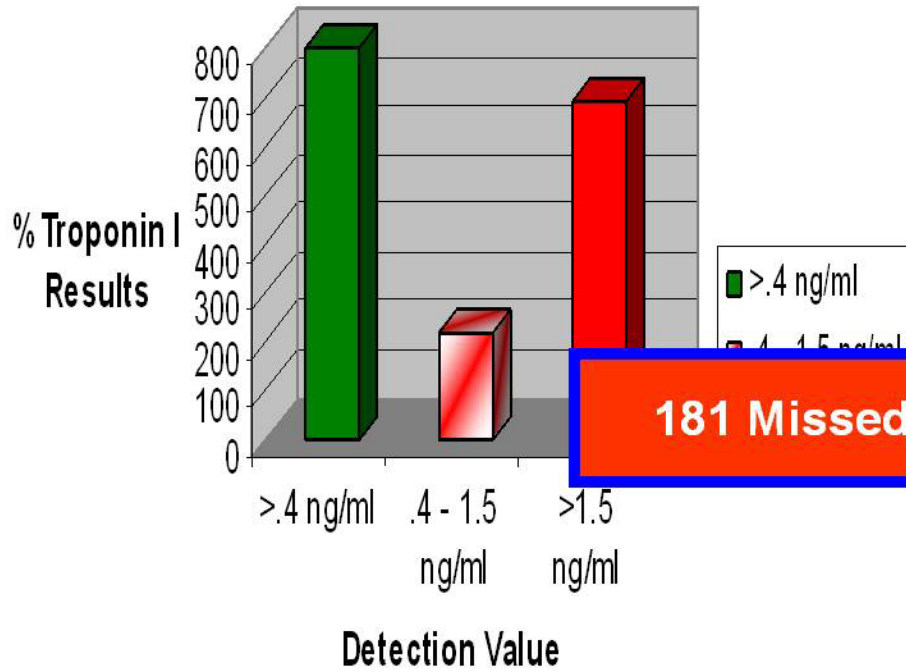
Decision point used for positive: > 0.120

OPPORTUNITY :

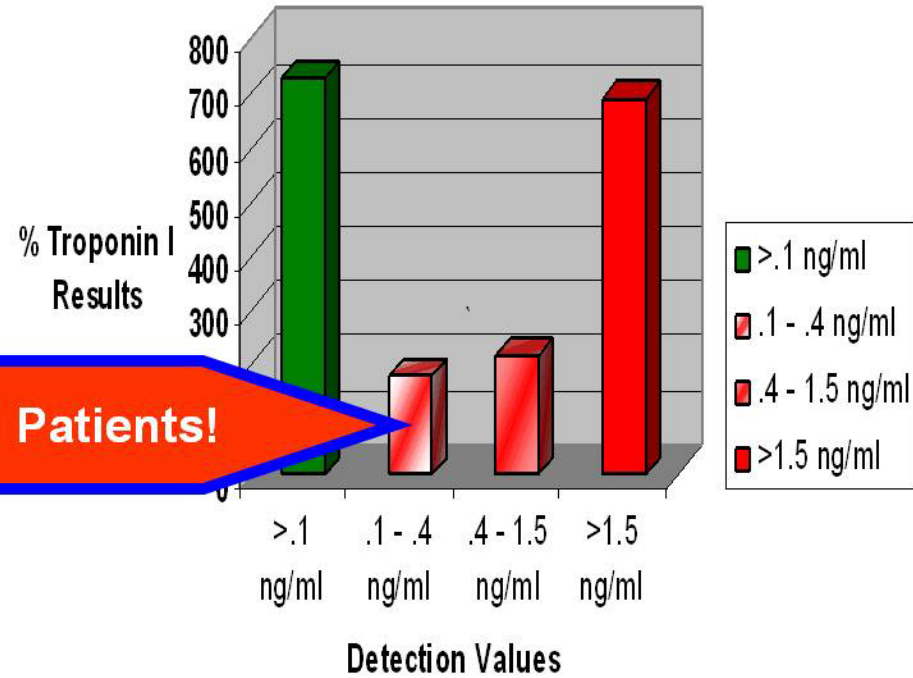
- Serial sample Protocol: 0, 3, 6 Hours
- **One decision limit**, the **99th percentile (0.034)**, the optimum cutoff
- Results **above** the decision limit = **myocardial injury**



Troponin I Patient Population



Troponin I Patient Population



Source: Ability of Minor Elevations of Troponin I and Troponin T to Predict Benefit From an Early Invasive Strategy in Patients with UA and NSTEMI; Morrow, Cannon, Rifai, Frey, Vicari, Lakkis, Robertson, Hille, DeLucca, DiBattiste, Demopoulos, Weintraub, Braunwald for the TACTICS - TIMI 18 Investigators

Facility 2

50 yr old Female presents with chest pressure & shortness of breath

Hx of HTN, High cholesterol, smoker, obese

Initial EKG : normal

ED POCT cTnI @ presentation: 0.02 Decision point for positive: 0.5

Lab cTnI @ 3 hours: 0.2 Decision point for positive : 0.05

OPPORTUNITY:

- Establish decision limits
- The 99th percentile of the reference population should be the decision limit for myocardial injury

high sensitive Troponin

Impact on Process of Care Outcomes (VBP)



2007 Study at Brigham and Women's Hospital (Boston)

Comparison of a high Sensitive Troponin (hsTnl) assay to a standard assay (Tnl)

Specimens where initially negative, then positive on serial testing

Serial markers drawn at presentation, 6-9 hrs & 12-24 hrs.

hsTnl showed positive results before Tnl in 64% of samples

"Time Is Muscle"

Conclusion: *"...reporting (hsTnl) results would allow the diagnosis to be made an average of 9 hours sooner"...*

"The ability to provide earlier detection for 50% of confirmed ACS patients has the potential to substantially enhance early triage in the emergency setting and treat high-risk patients as early as possible."

American Society of Clinical Pathology 2007: 128,282-286



Outcomes

The Impact of Cardiac Biomarkers in
Value-Based Purchasing
Quality of Care, Cost, Patient Satisfaction

ACS Patient Risk Stratification

Impact on Quality, Cost and Patient Satisfaction



| Criteria | 2002 Pre-POCT | 2004 Post POCT hs CTNI | Impact |
|--|----------------------------------|---------------------------------|------------------|
| TAT(Vein to Brain Time) | 90 minutes | <20 minutes | 450% |
| ED Volume | 32,945 patients | 36,832 patients | 11.8% |
| CDU Volume | No CDU | 2,366 | New added volume |
| ALOS DRG 143 (pts) | 2.35days (n=294) | 2.16days (n=132) | (8%) |
| ALOS APC 0339(pts) | ---- | 18 hours (n=712) | ---- |
| ED STEMI Volume | 47 | 38 | (19%) |
| ED NSTEMI Volume | 21 | 105 | 500% |
| ED Patient Satisfaction HCA ranking | # 123 (out of 167HCA hosp)Q2, | #26 (out of 179HCA hosp) Q2, | 59% |

| 2004 CP Admission Classification | Variable Facility Cost | Average Reimbursement | % Margin | Difference | Patient Volume | Financial Outcome |
|--|------------------------------|--------------------------|-------------|------------|-------------------|----------------------|
| APC 0339 Chest Pain | \$862. | \$1,553.00 | 56% | \$ 691.00 | 712 | \$491,992.00 |
| DRG 313 Chest Pain NOS | \$1,322. | \$2,471.00 | 54% | \$1,149.00 | 132 | \$151,668.00 |

Cardiac Biomarkers impact on Outcomes

Health system process improvement using LEAN



| By APR DRG 190 | <u>Before Improvements:</u> January 2002 - June 2004 | <u>Post Control:</u> October 2004 - July 2007 | Rate Percent Improvement |
|-----------------|---|--|--------------------------|
| # of Discharges | 508 | 447 | |
| # of Deaths | 86 | 60 | |
| Mortality Rate | 0.169 | 0.134 | 20.61% |
| ALOS | 6.20 | 5.55 | 10.48% |

| By APR DRG 190 | <u>Baseline:</u> January 2002 - March 2005 | <u>Post Control:</u> April 2005 - September 2007 | Rate Percent Improvement |
|-----------------|--|--|--------------------------|
| # of Discharges | 459 | 363 | |
| # of Deaths | 74 | 34 | |
| Mortality Rate | 0.161 | 0.095 | 40.99% |
| ALOS | 7.30 | 6.70 | 8.22% |

The “Other Cost” of Failure to Diagnose Myocardial Infarction



Recent Jury Verdicts:

- I. Case #1 65 yr old male died of “Heart Attack”
failed to perform proper diagnostic testing
Diagnosis: Sepsis
Total Verdict: **\$ 1,538,000 + \$10,000** funeral expenses

- II. Case # 2 38 yr old woman presented with Chest Pain,
pain in left arm and difficulty of breathing
Diagnosis: ??? (failed to diagnose correctly)
Total verdict: **\$ 1,225,000**

- III. Case # 3 Patient presented with CP, SOB, pain in right elbow
Diagnosis: GERD, Hyperlipidemia, Hypertension
Total Verdict: **\$ 1,534,369.00**

Summary and Conclusions



- Cardiac troponin is the cornerstone of MI diagnosis.
- Cardiac troponin is a heart specific biomarker, not a disease specific marker.
- Use of a sensitive cTn assay allows earlier reliable patient assessment.
- Use of 99th percentile cutoff leads to better outcomes.
- Use of an '**Absolute**' increase (ng/mL) more effective than 'Relative' increase (%)
- Not all troponin are created equal. Refer to IFCC chart as resource/Package Insert
- Avoid patient misclassification, determine the 99th percentile of each analyzer used for troponin.
- Accuracy and quality of troponin result to better outcome.

Lab can help impact Outcomes!

~ *Lab's Best Practices*



- Leadership in guidelines applied to practice
- Drive quality at all Levels
- Be patient centered and outcome-oriented
- Communicate and collaborate with all disciplines
- Partner with your vendor as a resource to drive best practice

Technologies:

Emergency cardiac care app can save lives



thebesthearthospital app
(free download)

- Enter your location
- Find the closest accredited chest pain center
- choose to call 9-1-1

Resources:

SCPC

www.scpcp.org

info@scpcp.org

Subject line: SCPC Laboratory Subject-Matter-Expert



SOCIETY OF CARDIOVASCULAR PATIENT CARE

Contacts:



Ruth Cantu
rcantu@scpcp.org



Noemi Melendres-Wozny
Nmelendres-wozny@scpcp.org



SOCIETY OF CARDIOVASCULAR PATIENT CARE