Cardiac Bio-Marker Testing in Acute Coronary Syndromes

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Objectives

1. Describe current limitations of traditional cardiac biomarker testing.

2. Examine the utilization of a rapid algorithm to aid in ACS.

3. Discuss evidence based indications of use for Point-of-Care through review of current literature.

Challenges in Healthcare

Highest Quality of Care

Patient Satisfaction

Minimizing ED Overcrowding

Enhancing Operational Efficiency

Ideal Marker

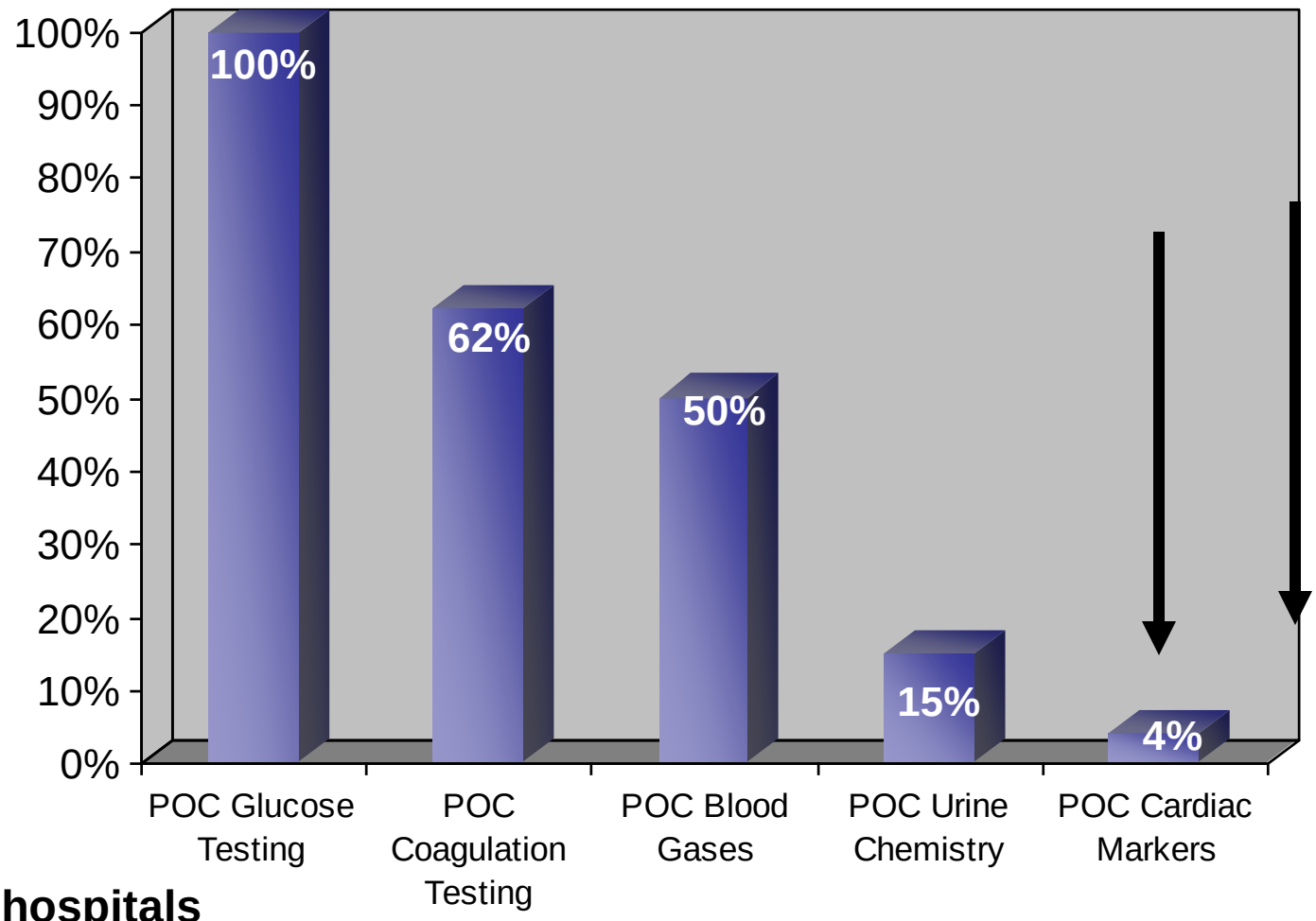
- Found in high concentration in the heart
- Not found in other tissues
- Low molecular weight and thus released early in the course of AMI
- Remains elevated for several days

Currently, no single marker meets these ideal requirements

Professional Guidelines* Have Been Established for AMI Management

- Turn around Time (TAT) for cardiac markers should be 30 minutes

High Percentage of Hospitals Perform POC Testing



N = 584 hospitals

Enterprise Analysis Corporation Hospital point-of-care survey report 2001

Turnaround Times for Common Laboratory Tests

Test	Turn around time before POCT (min)	Turn around time during POC (min)	Change in Turnaround time after Initiating POCT
Urinalysis	40	4	90%
Pregnancy Testing	78	5	94%
Glucose testing	10	6	60%
Cardiac markers	110	17	84.5%
Average	59.5	8	86.6%

IVD Technology June 2003 Study published; Archives of Pathology and Laboratory Medicine 2003 Study done at Massachusetts General Hospital (Boston)

Biomarkers of Choice

ADVANTAGES

CK-MB

- Cost-efficient
- Prior Standard

Myoglobin

- High sensitivity
- Useful in early detection of AMI
- Useful in ruling out AMI (must use a more specific marker)

Troponins

- Risk Stratification
- Greater specificity then CK-MB
- Detection of recent AMI up to 2 weeks after onset

ACC/AHA Pocket Guideline Update, 2002

Biomarkers of Choice

DISADVANTAGES

CK-MB

Lacks specificity with skeletal muscle disease/injury

- Low sensitivity during early AMI (<6h) or late (>36h) after symptom onset and for minor myocardial damage

Myoglobin

Very low specificity with skeletal muscle injury

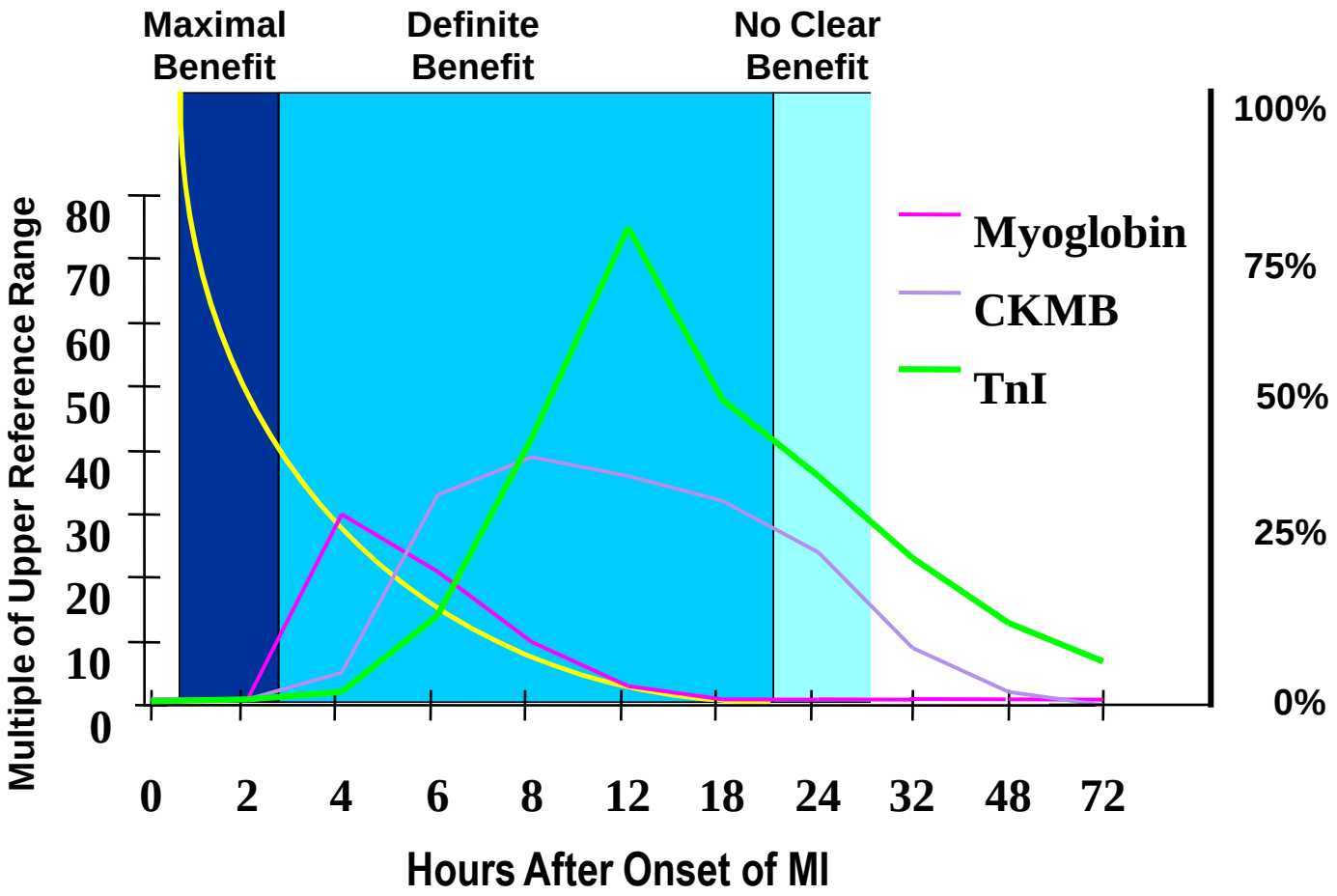
- Rapid return to normal

Troponins

- Low sensitivity in early phase of AMI (<6 h after symptom onset)
- Limited ability to detect late minor reinfarction

ACC/AHA Pocket Guideline Update, 2002

Biomarker Release Kinetics Demonstrate “real time” Value



Your door to treatment is too long, Where Is the problem??????????

- For emergency department physicians, timely triage and risk stratification of chest pain patients remains a challenge.
- clinicians are seeking more effective ways to diagnose acute coronary syndromes rapidly and accurately.

Your door to treatment is too long, Where Is the problem??????????

- Clinical algorithm based on these cardiac markers— myoglobin, cardiac troponin (cTnI), creatine kinase-MB, and B-type natriuretic peptide (BNP)—

provides the sensitivity and specificity required for confirmatory diagnosis and rapid rule-out method.

Your door to treatment is too long,
Where Is the problem?????????

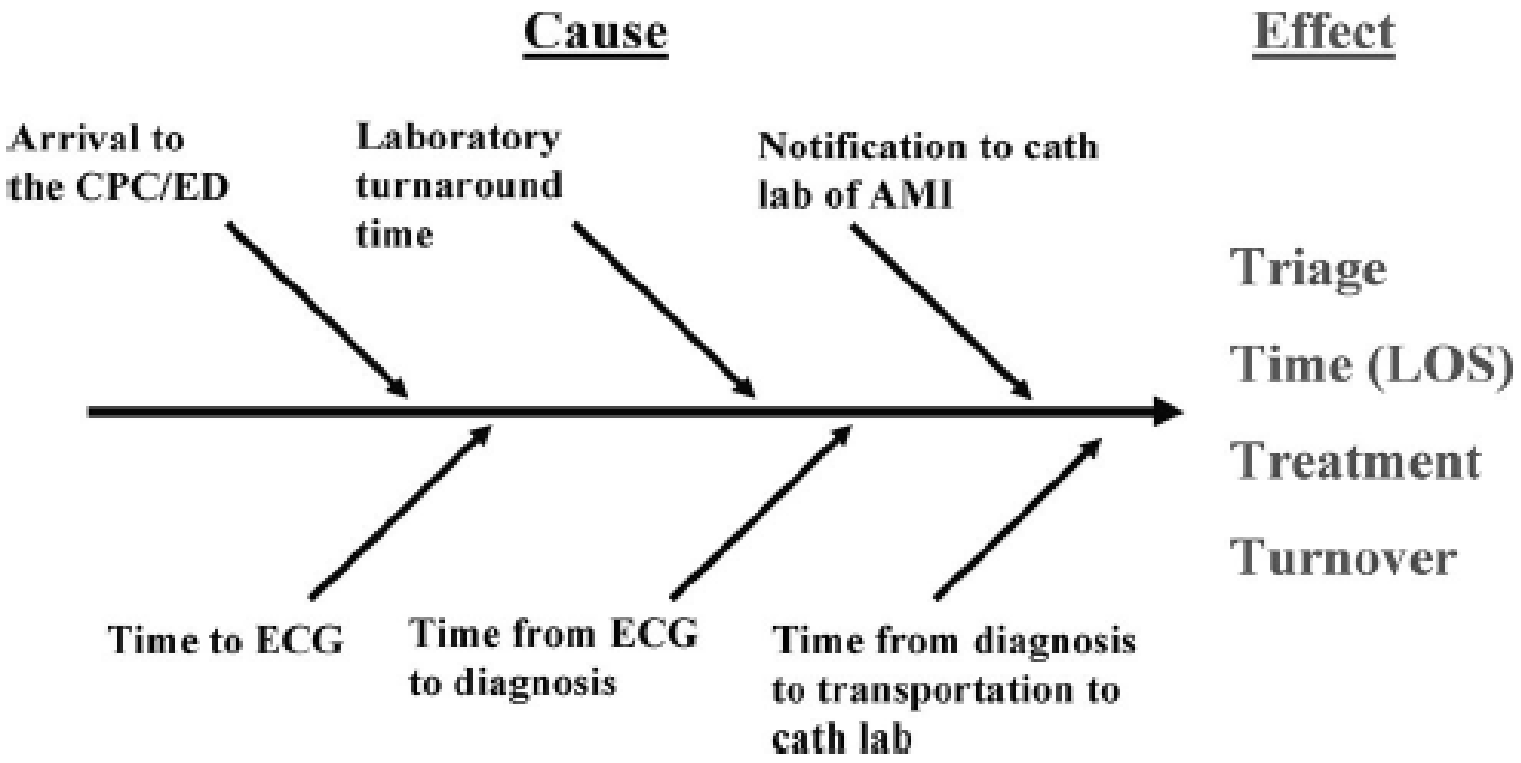


FIGURE 5. Reducing interval between chest pain onset and intervention (wire) "P2W."

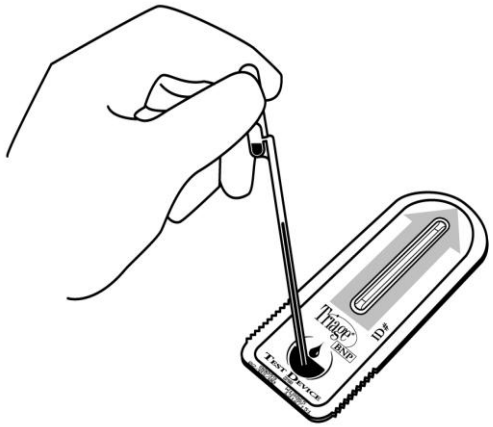
Your door to treatment is too long, Where Is the problem??????????

- The second most common cause of treatment delay is delayed test results
- TAT, the interval between ordering a test and the availability of a definitive report or interpretation.

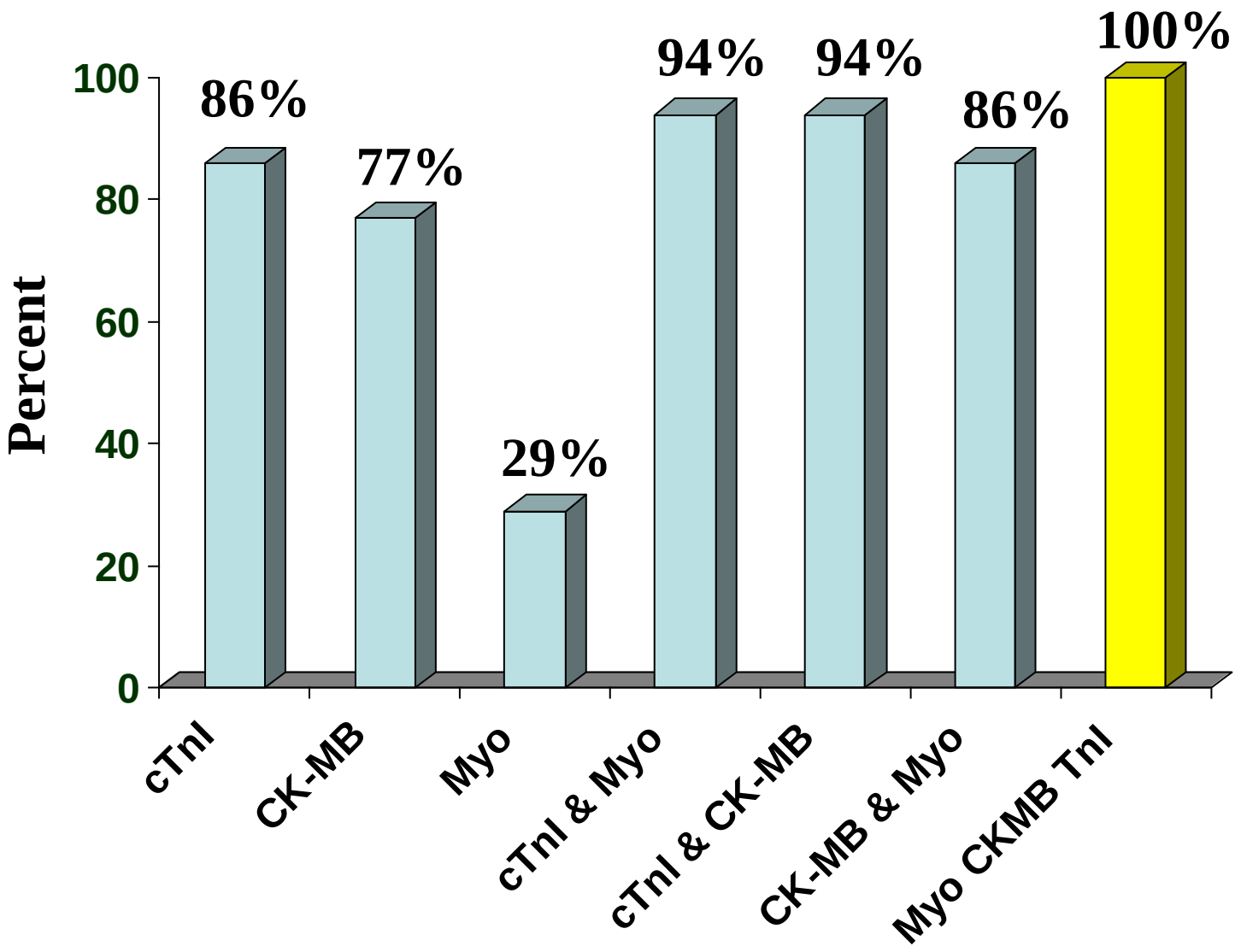
Your door to treatment is too long, Where Is the problem??????????

- According to the ACC/AHA guidelines, the suggested TAT for cardiac biomarkers is 60 minutes or less, with a preferred time of 30 minutes.

Assay Procedure



Sensitivity of Algorithm at 90 Minutes Following Patient Arrival



CHECKMATE The Chest pain Evaluation by Creatine Kinase-MB, Myoglobin and Troponin I Study

Purpose: Evaluate the ability of quantitative bedside markers to risk stratify patients with chest pain and non-diagnostic ECG

Newby, K. MD et al

Circulation

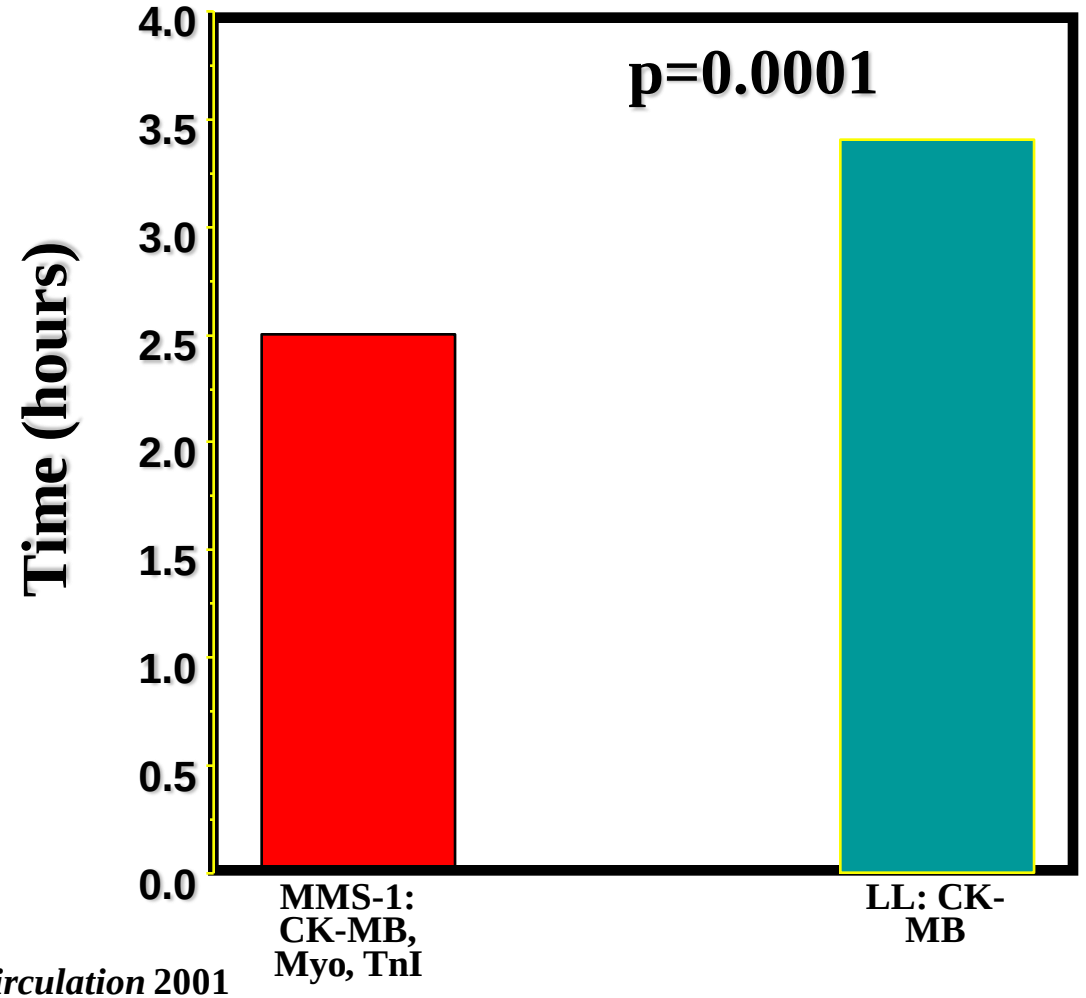
2001

Design / Methods

- 1,005 chest pain patients, non-diagnostic ECG
- Prospective, multi-center trial 6 CPUs in US
- Compared local lab (LL) testing with near patient multiple marker strategies (MMS).
  - MMS-1 = Myoglobin, CK-MB, TnI
  - MM-2 = CK-MB, TnI
  - Testing frequency
    - Baseline, 3 hours and 6 hours
    - 9-12 hours and 16-24 hours if patient still under observation

Newby, K. MD et al *Circulation* 2001

CHECKMATE Trial: Median Time to Positivity



Newby, K. MD et al *Circulation* 2001

Conclusions

- Quantitative, multi-marker strategies identifies positive patients earlier and provides better risk stratification for mortality than a local laboratory single-marker approach.
- Myoglobin helped reduce time to positive result
- Myoglobin has excellent sensitivity and negative predictive value

Newby, K. MD et al *Circulation* 2001

Ninety-Minute Exclusion of Acute Myocardial Infarction By Use of Quantitative Point-of-Care Testing of Myoglobin and Troponin I

Purpose: Determine if a combination of a biomarker that rises early (Myo) with one that rises later (CK-MB or TnI) could exclude AMI in either 90 or 180 minutes

McCord, J. MD et al

Circulation

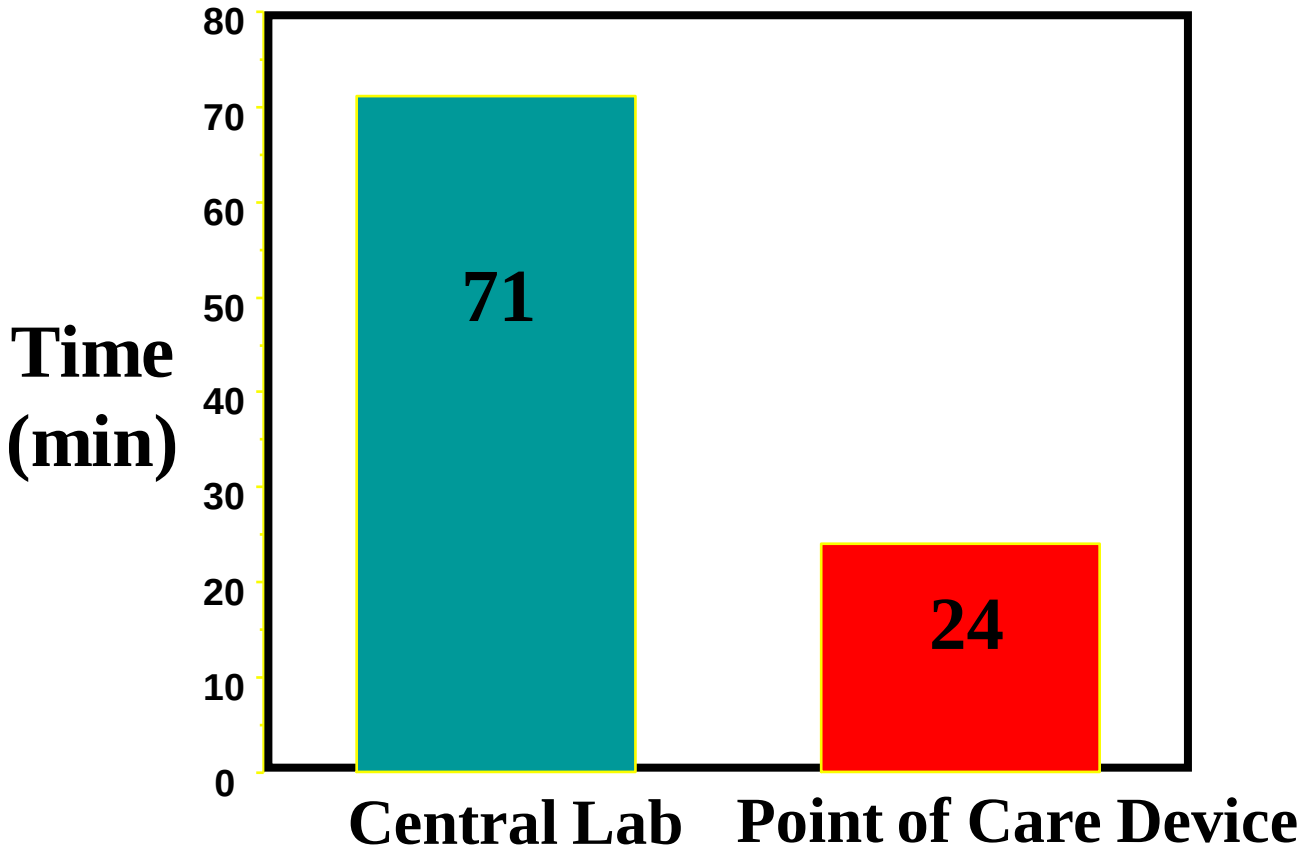
September 2001

Study Design / Methods

- Study looked at 817 patients with nondiagnostic ECGs
- Measurements of Myo, TnI, and CK-MB were obtained at baseline, 90 minutes, 3 hours and 9 hours.
- Triage decisions were made by ED physicians who were unaware of the point-of-care results.

Circulation, McCord, J Vol. 104 no. 13 September 2001

Henry Ford Trial: Time to Laboratory Reporting



Circulation, McCord, J. Vol. 104 no. 13 September 2001

Conclusions

- Myoglobin and Troponin I at 0 and 90 minutes is a rapid and effective strategy to exclude AMI in pts presenting to the Emergency Department
- More rapid turnaround time of cardiac marker results was achieved with POC technology
- This may lead to more rapid patient triage and treatment

Circulation, McCord, J. Vol. 104 no. 13 September 2001

Improving Care of ACS Patients

3- Marker Panel
Accelerated Algorithm

Risk Stratification

- More positives identified with 3 markers
- Earlier and more accurate diagnosis allows for speedier, targeted use of medicines

CHECKMATE, *Circulation* 2001

Appropriate Disposition

- 100% Sensitivity within 90 minutes
- NPV 99.7%
- Decreased CCU admissions 40%

90 Minute Accelerated Pathway, *Am J Cardiol* 2001

Rapid Rule-Out

- Effective in rule out of AMI
- 99.6% NPV at 90 minutes
- Reduce length of stay in ED

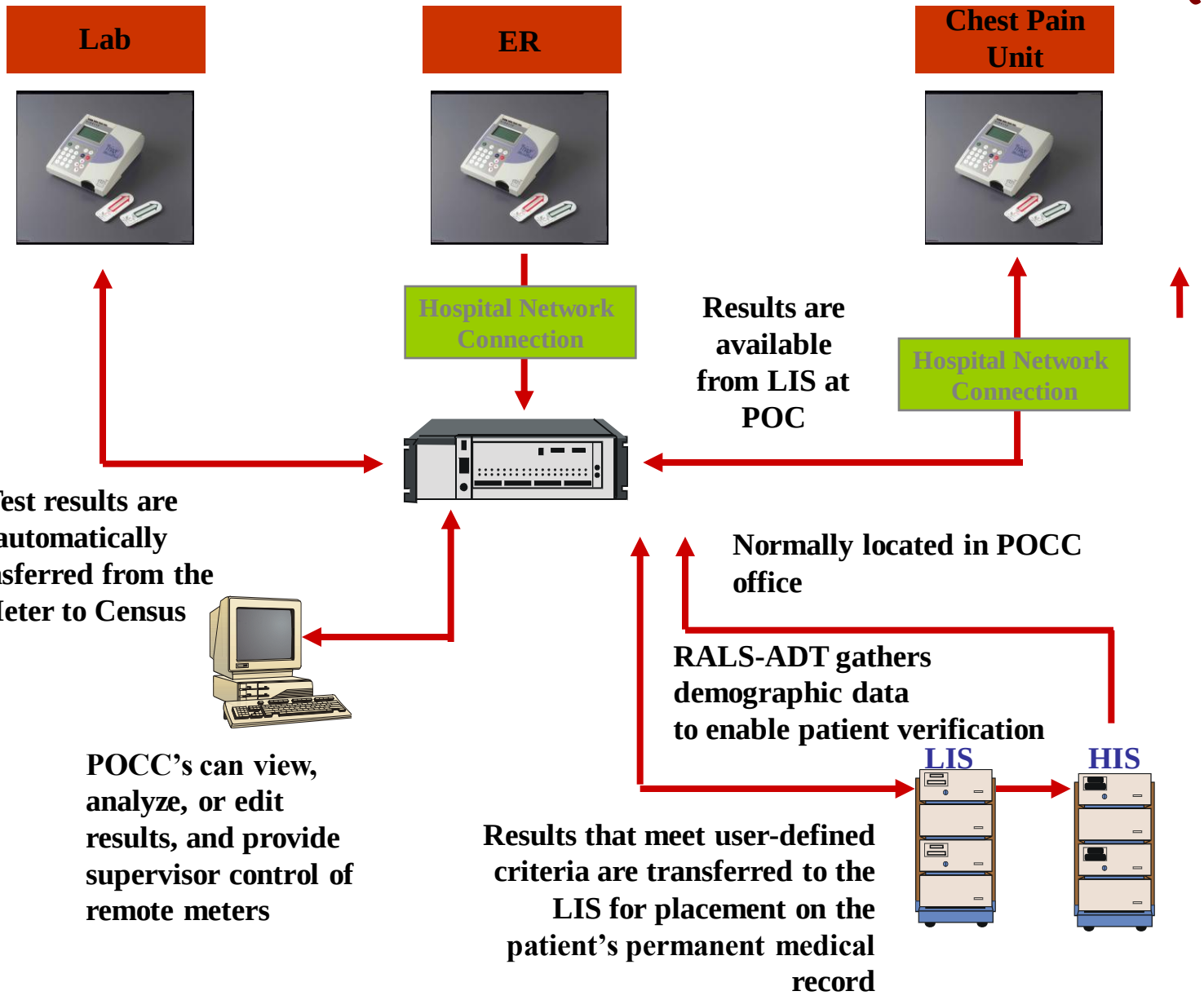
90 Minute Rule-out, *Circulation* 2001

Triage Cardiac Panel Highlights

- **Triage Cardiac is a fluorescence immunoassay used for the quantitative determination of Creatine Kinase MB, Myoglobin and Troponin I in whole blood or plasma**
- **No interference with typically prescribed heart related drugs**

Triage cardiac package insert. Data on File at Biosite Diagnostics Inc.

Census Connectivity



Impact of point-of-care testing in the emergency department evaluation and treatment of patients with suspected acute coronary syndromes.

- OBJECTIVES: To assess the impact of point-of-care testing (POCT) for troponin I (cTnI) measurement on the time to anti-ischemic therapy (TAIT) for patients with suspected (NSTE-ACS) presenting to the emergency department (ED).

Acad Emerg Med. 2008 Mar;15(3):216-24

Renaud B, Maison P, Ngako A, Cunin P, Santin A, Hervé J, Salloum M, Calmettes MJ, Boraud C, Lemiale V, Grégo JC, Debacker M, Hémery F, Roupie E.

Impact of point-of-care testing in the emergency department evaluation and treatment of patients with suspected acute coronary syndromes.

- METHODS: This was an open-label, randomized, single-center trial conducted in a university-affiliated hospital.
- cTnI measurement of patients with suspicion of NSTE-ACS coming to the ED was randomly allocated to POCT or central hospital laboratory testing

Impact of point-of-care testing in the emergency department evaluation and treatment of patients with suspected acute coronary syndromes.

RESULTS:

- Of the 860 patients enrolled, 113 were high-risk NSTE-ACS patients, including 53 (46.9%) allocated to POCT and 60 (53.1%) to CHLT.
- POCT was associated with decreased time to anti-ischemic therapy of about three-quarters of an hour, which was due to a shorter time to physician notification of cTnI level, in both all and subgroup participants.

Impact of point-of-care testing in the emergency department evaluation and treatment of patients with suspected acute coronary syndromes.

CONCLUSIONS:

Point-of-care testing for cTnI measurement might be clinically relevant for ED patients with a suspicion of NSTE-ACS, particularly for high-risk patients with a low suspicion of ACS.

The Value of Bedside Cardiac Multibiomarker Assay in Rapid and Accurate Diagnosis of Acute Coronary Syndromes

Shahriar Dadkhah, MD, Korosh Sharain, BS, Roza Sharain, BS, Hamid Kiabayan, MD, Alberto Foschi, MD, Carolynn Zonia, DO, Brian Huettl, MD, Scott French, MD, Elizabeth Gray, BA, Sridhar Venkatachalam, MD, Housam Hegazy, MD, and Glenn Aldinger, MD

(*Crit Pathways in Cardiol* 2007;6: 76–84)

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- SFH has focused on the critical steps that impact time to intervention, including
  - the reduction of patient delay time to the ED
  - improving the time to (ECG)
  - minimizing laboratory TAT.

- they implemented a 4-hour rule-out protocol in the ED, testing cardiac multimarkers

0,2 and 4h

- The rapid diagnostic protocol has enabled SFH to triage patients quickly and get them on the appropriate care pathway.

Myoglobin

- is the first biomarker to become elevated after an ischemic event, increasing at approximately 1 to 2 hours post-MI.
- has a low specificity
- it is an early ischemic marker
- a sensitivity and negative predictive value of 100% when considered 2 hours apart, at admission 2 hours post admission.

Montague C, Kircher T. Myoglobin in the early evaluation of chest pain. *Am J Clin Pathol*. 1995;104:472– 476.

Myoglobin & Troponin

	Time 0		0, 90 min		0, 90 min, 3 h	
Point of Care	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Myo	70.8 (58–81)	75.6 (72–79)	84.6 (74–92)	73.0 (70–76)	84.6 (74–92)	71.1 (68–74)
CK-MB	75.4 (63–85)	84.7 (82–87)	83.1 (72–91)	83.0 (80–86)	89.2 (79–96)	81.6 (79–84)
cTnI	64.6 (52–76)	87.6 (85–90)	76.9 (65–86)	79.0 (76–82)	87.7 (77–94)	69.8 (66–73)
Myo, CK-MB	83.1 (72–91)	70.2 (67–73)	92.3 (83–98)	67.5 (64–71)	92.3 (83–98)	65.7 (62–69)
Myo, cTnI	84.6 (74–92)	66.8 (63–70)	96.9 (89–100)	59.7 (56–63)	96.9 (89–100)	53.1 (49–57)
	Negative Predictive Value	Positive Predictive Value	Negative Predictive Value	Positive Predictive Value	Negative Predictive Value	Positive Predictive Value
Myo	96.8 (95–98)	20.1 (15–26)	98.2 (97–99)	21.4 (16–27)	98.3 (97–99)	20.4 (16–26)
CK-MB	97.5 (96–99)	29.9 (23–38)	98.3 (97–99)	29.8 (23–37)	98.9 (98–100)	29.9 (24–38)
cTnI	96.6 (95–98)	31.1 (23–40)	97.5 (96–99)	24.2 (18–31)	98.5 (97–99)	20.2 (16–25)
Myo, CK-MB	98.0 (96–99)	19.4 (15–25)	99.0 (98–100)	19.7 (15–25)	99.0 (98–100)	19.0 (15–24)
Myo, cTnI	98.0 (96–99)	18.1 (14–23)	99.6 (98–100)	17.3 (14–22)	99.5 (98–100)	15.2 (12–19)

Myo indicates myoglobin. Values are all % (95% CI). If any value of a combination of markers was positive, the combination was considered positive. All values had to be negative for the combination to be considered negative.

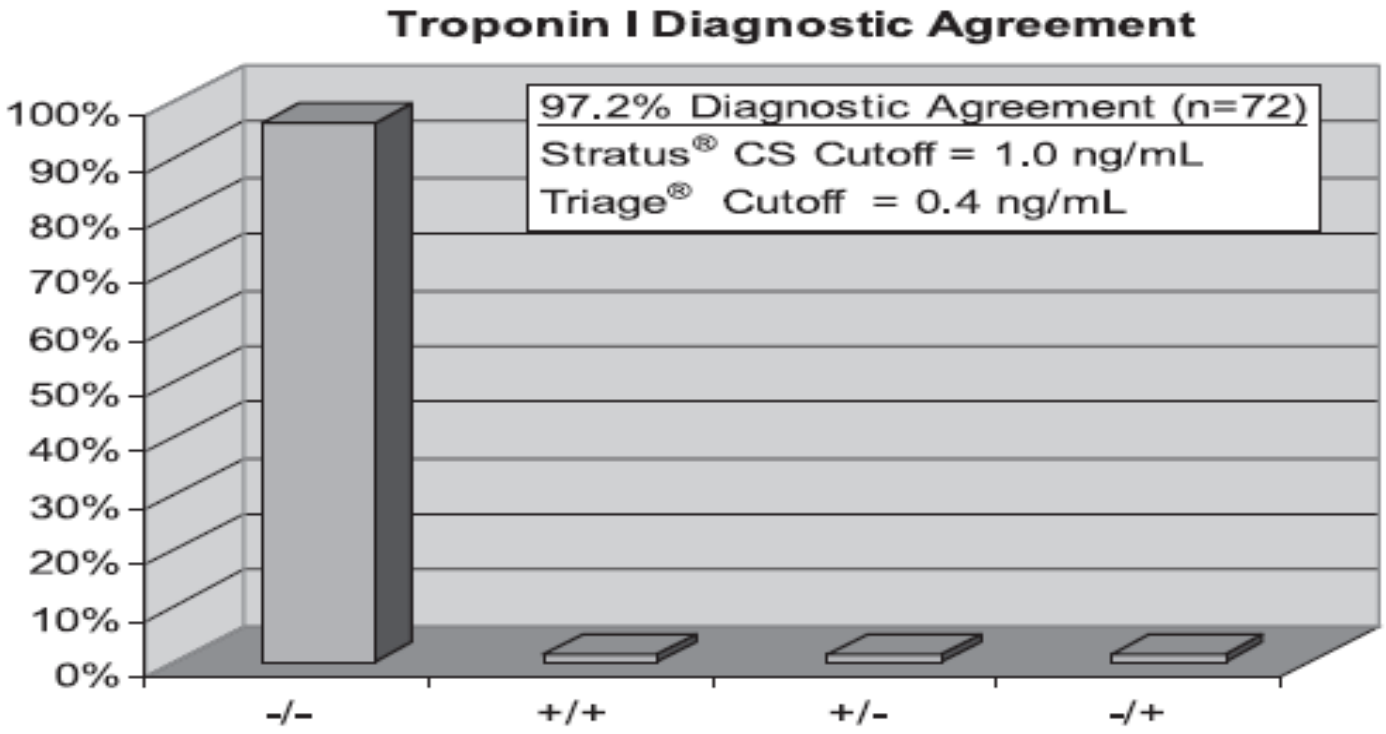
TABLE 2. Turnaround Time (Min)

Reference	POCT	Central Laboratory	% Reduction
Caragher et al	38	87	76
Lee-Lewandrowski et al	17	110	87
Collinson et al	20	79	80
McCord et al	24	71	75
Singer et al	15	83	85
Mean	23	89	79

Adapted from Wu.[8]

- Bedside testing implementation for cardiac biomarkers reduced TATs by approximately 79% over central laboratory methods.

Wu AHB. Point-of-care testing for conventional cardiac markers. *Point Care*. 2006;5:20 –24.



Ghani SN, Dadkhah S, Bishop DRN. Rapid quantitative bedside test of troponin I and myoglobin in patients with acute coronary syndrome. *Crit Pathways Cardiol*. 2004;3:136.

in a historically controlled study of 4 hospitals

- mortality rate of 8.9% for ACS patients (n = 1092) for central lab
- and only 6.7% (n = 1156) (*P* = 0.049) when cardiac markers were measured by a point-of-care device

Kugelmass AD, Anderson A, Katz M, et al. Point-of-care biomarkers: does it make a difference in acute myocardial infarction outcomes? *Circulation Online*. May 25, 2004

- In 773 consecutive patients who had had acute chest pain for less than 12 hours without ST-segment elevation on their ECGs, troponin T and troponin I status (positive or negative)

Emergency Room Triage of Patients with Acute Chest Pain by Means of Rapid Testing for Cardiac Troponin T or Troponin I.
Hamm, Christian W.; Goldmann, Britta U.; Heeschen, Christopher; Kreymann, Georg; Berger, Jurgen; Meinertz, Thomas **New England Journal of Medicine**. 337(23):1648-1653, December 4, 1997

- Troponin T and troponin I proved to be strong, independent predictors of cardiac events.
- The event rates in patients with negative tests were only 1.1 percent for troponin T and 0.3 percent for troponin I.

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- 151 patients
- There was no difference in diagnostic performance
- For exclusion of damage, the two tests have similar and reliable diagnostic capacities 12 hours after the onset of symptoms.

- The bedside diagnosis or exclusion of acute myocardial infarction was carried out rapidly (within 20 minutes) and reliably by the CCU nurses.

Excellent reliability of nurse-based bedside diagnosis of acute myocardial infarction by rapid dry-strip creatine kinase MB, myoglobin, and troponin T. Sylven, Christer, MD, PhD, FACC, FESC, Lindahl, Susanne, Hellkvist, Karin, Nyquist, Olof, MD, PhD, Rasmanis, Gundars, MD, PhDAmerican Heart Journal. 135(4):677-683, April 1998.

The Benefits of Bedside Testing

- do not require centrifugation or anticoagulation
- do not require laboratory personnel to conduct testing.
- nurses and patient care technicians can easily be trained to perform

- This allows nurses to be more involved with their patient's condition, because they are the medium between blood draw and test analysis.

Thank you

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