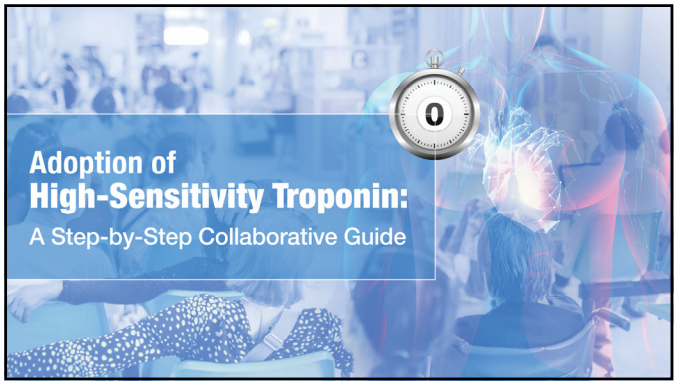


Disclosures

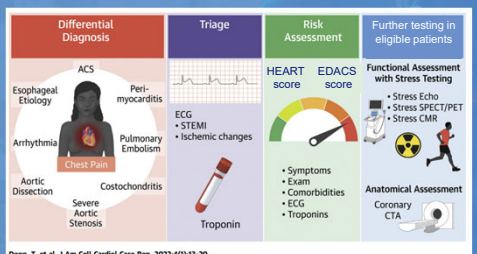
- Brian Patel, MD has no financial relationships to disclose
- Supported by an educational grant from QuidelOrtho

Learning Objectives

- Orientation – key definitions and how we got here
- The first steps – convening the right stakeholder group, advocating for the necessary resources to implement
- Pros and Cons of Integrating a risk score into the ADP
- Lab considerations for hs-cTn changeover
- ADP creation examples and go-live preparation

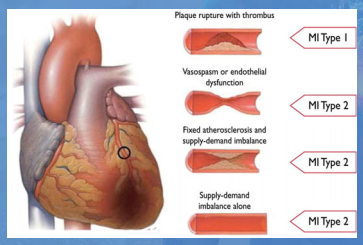
- Orientation – key definitions and how we got here

General ED approach to chest pain



Dong, T. et al. J Am Coll Cardiol Case Rep. 2022;4(1):13-20.

Type 1 and Type 2 Myocardial Infarction



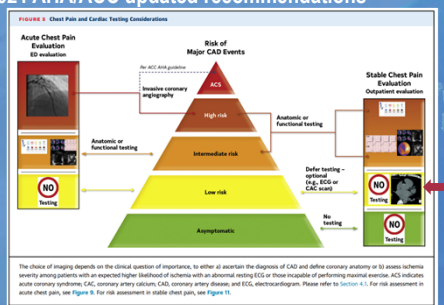
Not All Troponin Elevations are Type 1 Myocardial Infarction

Other causes of myocardial injury

Cardiac conditions	Systemic conditions
• Heart failure	• Sepsis, infectious disease
• Myocarditis	• Chronic kidney disease
• Cardiomyopathy (any type)	• Stroke, subarachnoid hemorrhage
• Takotsubo syndrome	• Pulmonary embolism, pulmonary hypertension
• Coronary revascularization procedure	• Infiltrative diseases, e.g., amyloidosis, sarcoidosis
• Cardiac procedure other than revascularization	• Chemotherapeutic agents
• Catheter ablation	• Critically ill patients
• Defibrillator shocks	• Strenuous exercise
• Cardiac contusion	

Chanana, EM Didactics, http://emdidactic.blogspot.com/2017/05/interpreting-elevated-troponins-and.html

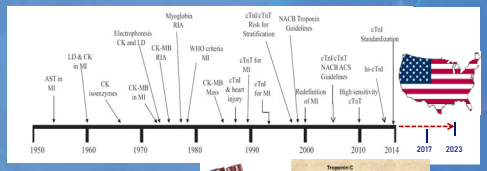
2021 AHA/ACC updated recommendations

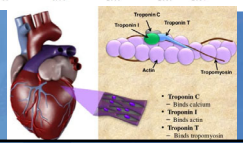


NO further testing should be considered for "low risk" patients; reassuring troponin patterns help to establish low risk

Gulati et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2021 Nov. 78 (22) 2218–2261

History of cardiac biomarkers

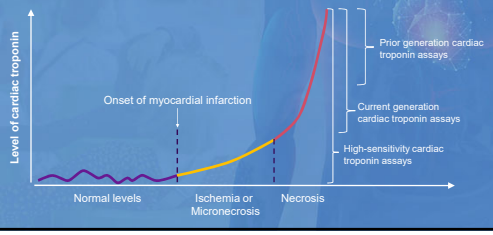




Collinson PO, Garrison L, Christenson RH. Cardiac biomarkers. A short biography. Clin Biochem 2015;48:197-200

Evolution of troponin assays

- hs-cTn is a much more sensitive marker of cardiac injury than prior cTn assays

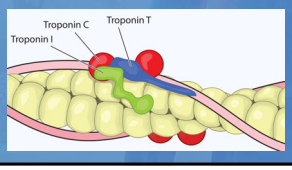


Evolution of troponin assays

	cTnI	
1st generation FY: 1994	0.5 ng/ml	AMI diagnosis
99th percentile, 2nd generation, FY: 2004	0.04 ng/ml	Minor myocardial injury
hs-cTn assays, FY: 2017	40 ng/l	
LOD	3 ng/L	

Why switch to hs-cTn

- Higher analytical sensitivity
- Higher negative predictive value
- Ability to detect smaller infarcts
- Allows use of an accelerated diagnostic protocol (ADP)
- Establishes gender specific 99th percentile upper reference limits



Where did the proof come from

Novel high-sensitivity cardiac troponin I assay in patients with suspected acute coronary syndrome

Andrew R Chapman [1], Takeshi Fujisawa [1], Kuan Ken Lee [1], Jack Patrick Andrews [1], Atul Anand [1], Dennis Sandeman [1], Amy V Ferry [1], Stacey Stewart [1], Lucy Marshall [1], Fiona E Strachan [1], Alasdair Gray [2, 3], David E Newby [1], Anoop S V Shah [1], Nicholas L Mills [1, 4]

CARDIOLOGY/ORIGINAL RESEARCH

Performance of Novel High-Sensitivity Cardiac Troponin I Assays for 0/1-Hour and 0/2- to 3-Hour Evaluations for Acute Myocardial Infarction: Results From the HIGH-US Study

Richard M. Nowak, MD*; Robert H. Christenson, PhD; Gordon Jacobsen, MS; James McCord, MD; Fred S. Apple, PhD; Adam J. Singer, MD; Alexander Limkakeng, Jr, MD; William F. Peacock, MD; Christopher R. deFilippi, MD
*Corresponding Author. E-mail: rnowak1@hfhs.org.

Definition of a high-sensitivity troponin assay

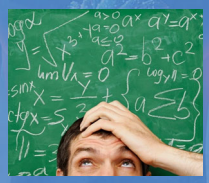
- You can detect a signal (above level of detection) in ≥50% of an underlying normal population

Corollaries:
- Extremely sensitive – measured in ng/L and not in ng/mL
- Difference is 1000x so you can use whole numbers, e.g., 0.03 ng/mL becomes 30 ng/L (or pg/mL); note there is **not** a direct conversion from one assay to another, so it would be inaccurate to simply change the units on the prior generation assay to calculate a high-sensitivity assay value
- Because the results are so sensitive, you can measure small differences in values over a time course

Comparative anchor (baseline) values Troponin T example	
hs-cTnT (new assay)	cTnT (prior assay)
30 ng/L	0.01 ng/mL
53 ng/L	0.03 ng/mL
100 ng/L	0.1 ng/mL
1,000 ng/L	1 ng/mL

Why change the units?

- Changing reporting units from ng/mL to ng/L to produce whole number results makes comparison of values much easier in whole numbers
  - Patient presents with chest pain and has initial troponin of 0.004 which increases to 0.039 within 1h
  - Is this an evolving AMI?



The First Steps

Convening the right stakeholder group and advocating for the necessary resources to implement

Who do you need?

- Multi-specialty/multi-disciplinary workgroup
  - Emergency Medicine
  - Cardiology
  - Hospitalist
  - Nursing
  - Lab
  - Information Technology
  - Project management – if available
  - Data analyst –if available
- Set go-live date
  - 6-9 months

Four primary settings to consider


Emergency


Perioperative


Inpatient


Clinic/Urgent Care

Required work: The punch list

- Which metrics will you use (collect baseline and post-launch)
- Create new pathway
  - Define 99th percentile cut points
    - Gender specific
  - Delta strategy/sampling frame
  - Guidance for renal disease
  - Risk score ADP integration
  - Use of ED observation unit
  - Role of consultants
  - Follow up guidance and resources
- IS compatibility; review order sets
- Provider education/messaging
- Go-live logistics
- Post-go-live support
- Post-go-live data monitoring and QA

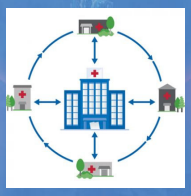
Engage with Information Technology Early and Often

Lead time needed to update test routing/naming, order sets, accommodate rapidity of serial samples, etc.

Adjust Guidance to Local Resources

Pathway may vary based on access to:

- Cardiology inpatient services
- Cardiac catheterization lab
- Cardiac stress testing
- Observation units
- Outpatient cardiology access
- Phlebotomy resources
- Turnaround time of lab



Example timeline for developing a protocol

	MONTHS				
Phase 1 AQUIRE DATA & SECURE LEADERSHIP	1-3	4	5-6	7-8	9+
Define quality & operational metrics					
Obtain baseline data					
Make a case for protocol to key leaders (e.g., Chair of EM, Chair of Cardiology, Nurse Director, CMO)					
Create charter					
Identify executive sponsors					
Develop timeline					
Obtain access to resources, (e.g., data analysts, admin. & IT support, educators)					
Consider a follow-up clinic					
Phase 2 PREPARE FOR PROTOCOL DEVELOPMENT					
Perform literature search					
Review protocols from peer institutions					
Establish a multidisciplinary workgroup and assign roles					
Identify & engage supportive key opinion leaders					
Identify & evaluate staff likely to oppose software					
Phase 3 DEVELOP PROTOCOL & KEY COMPONENTS					
Define inclusion & exclusion criteria					
Determine expected interventions					
Phase 4 VERIFY & LAUNCH PROTOCOL					
Present protocol to relevant stakeholder groups					
Revise based on feedback					
Pilot the protocol (if multiple sites available, select the most challenging)					
Revise for gaps & barriers					
Rollout protocol; publicize "go-live" event					
Phase 5 MAINTAIN PROTOCOL					
Monitor data to ensure appropriate adherence					
Report metrics to frontline staff & leadership					
Integrate protocol maintenance activities into standing meetings					
Revisit literature to ensure alignment with most recent scientific evidence					
Perform annual revisions					

Up to 9 MONTHS Needed

Pros and Cons of Integrating a Risk Score into the Accelerated Diagnostic Protocol

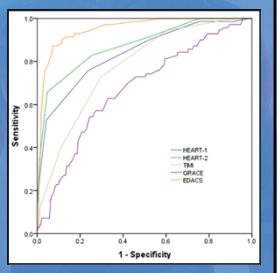
Risk stratification

Combination of:

- Symptom description
- Pre-existing risk factors
- Physical exam
- ECG
- Troponin
- Age

Comparing risk scores

- PEARL data set
  - 7 EDs
- Patient with suspected ACS
- Dr. had to document risk of MI BEFORE Tn as:
  - Low
  - Moderate
  - High Risk
- N=458



Singer A. Am J EM. 2017 Jan 5. pii: S0735-6757(17)30003-7. doi: 10.1016/j.ajem.2017.01.003.

Rapid rule-out of AMI with a single hs-cTnT measurement below the limit of detection

Purpose: Estimate the ability of a single hs-cTnT concentration <LoD (<5 ng/mL) with nonischemic ECG to rule out AMI in adult ED patients

- 9241 patients
  - 2825 (30.6%) classified as low risk
  - 14 (0.5%) low-risk patients had AMI
- Pooled sensitivity:
  - AMI = 98.7% (95% CI, 96.6% to 99.5%).
  - 30-day MACE = 98.0% (CI, 94.7% to 99.3%)
- No low-risk patients died

Pickering JW. Ann Intern Med. 2017 Oct 3;167(7):524. PMID: 28419520

Chest pain protocol VS. Accelerated Diagnostic Protocol

A CHEST PAIN PROTOCOL	AN ADP
A series of activities to identify a patient	A series of activities to identify a patient
1) Having an event	1) NOT having an event
2) Being at risk for having an event	2) Being at low risk for having an event

Lab Considerations for hs-cTn Changeover

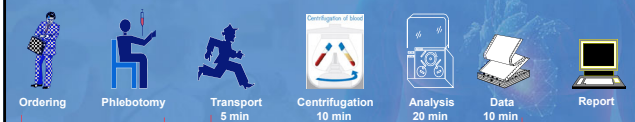
Hospital buy-in: Project the return on investment

- Work out the financials: The lab will incur more costs but the system will benefit

$$\frac{\text{Return (Benefit)}}{\text{Investment (Cost)}} = \text{ROI}$$

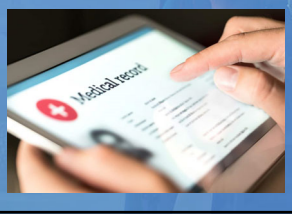
Process flow mapping your lab testing

An accelerated rule out protocol requires <1-h turnaround times for results reporting



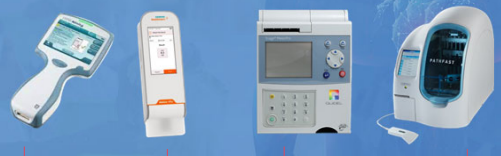
What do the orders look like in your electronic health record

- Managing nurse initiated protocols
- Identifying a 0, 1, 2, 3 hour troponin
- What will your order sets look like



POC hs-cTn: Not available yet

- When commercially available, consider hs-cTn using point-of-care



Current POCT devices are not high sensitivity and cannot be used for ADP

Let's talk values

- Absolute versus relative delta troponin values
- How to handle reporting of critical troponin results (e.g., are there any levels that will require lab staff to call the ED?)
- How to deal with hemolysis
- How to deal with interference (e.g., Biotin)
- Switchover logistics – to overlap or not?

Lab issues for implementing hs-cTn

- Review manufacturer's package insert data for the 99th percentile cutpoint
- Determine if sex specific cutpoints are warranted
- FDA recommends separate gender intervals. But does it improve clinical sensitivity for women?
- What causes gender differences?
  - Unequal heart mass
  - Different mechanisms of ischemia
  - Sex specific thrombotic activity
  - Protective role of estrogens in women

Drawing the labs

- It is essential you have the stakeholders who are actually drawing the blood involved in this discussion
  - Changing a workflow where having a timed lab draw needed can be a significant challenge for frontline staff so need to get their buy in early
  - How will the repeat labs be drawn
    - New blood draw
    - Off an IV line

Special populations: Renal disease

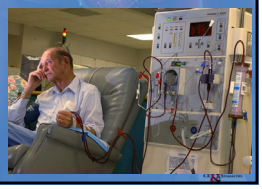
High-Sensitivity Cardiac Troponin and the Risk Stratification of Patients With Renal Impairment Presenting With Suspected Acute Coronary Syndrome

4,726 patients; 904 (19%) with renal dysfunction (GFR <60 mL/min)

17% with renal dysfunction had a hsTnI <5 ng/L vs 56% of the patients without renal dysfunction

Specificity at the 99th percentile cutoff was 70.9% versus 92.1%

Hazard ratio 2.19 at 1 year for death or MI for values >99th percentile (24% versus 10%)



Circulation. 2018;137:425–435. DOI: 10.1161/CIRCULATIONAHA. 117.030320. January 30, 2018. 425

Block 5

ADP Creation Examples and Go-Live Preparation

Build a new accelerated diagnostic protocol

- Create a new pathway/accelerated diagnostic protocol
  - Where will it live? Who will maintain it?
- Define 99th percentile for hs-cTn
  - Gender specific?
- Delta strategy/sampling frame (x1, Q1h, Q2h, Q3h, etc.)
- Which patients are excluded from ADP?

Initial publication – Implementation process

PATHWAY

Implementation of an Emergency Department High-Sensitivity Troponin Chest Pain Pathway in the United States

Christopher W. Baugh, MD, MBA, Benjamin M. Scirica, MD, MPH,† James L. Januzzi, MD,‡ David A. Morrow, MD, MPH,† Kent B. Lewandrowski, MD,§ Petr Jarolim, MD, PhD,¶ Benjamin A. White, MD,‖ Mark S. Weinfeld, MD,† Udo Hoffmann, MD, MPH,** and John T. Nagurney, MD, MPH‖*

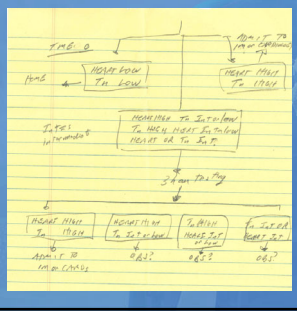
(*Crit Pathways in Cardiol* 2019;18: 1–4)

Patients frequently present to the emergency department (ED) with chest pain or other complaints concerning for an anginal equivalent. In the United States (US) each year, chest pain alone is a chief complaint encountered nearly 8–10 million times annually in the ED.[1] However, <20% of these patients will be diagnosed with an acute myocardial infarction (AMI) or unstable angina pectoris (UAP).[2,3] Chest pain pathways reduce unwarranted evaluation by leveraging evidence-based patient selection criteria, risk stratification tools, and disposition recommendations to safely and efficiently evaluate patients for AMI and UAP.

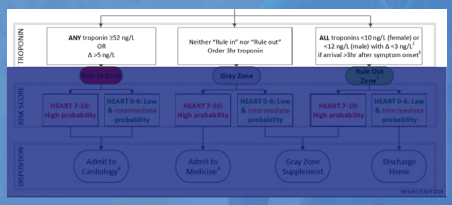
risk scores. Examples of these include the Accelerated Diagnostic Protocol, History, ECG, Age, Risk Factors, and Troponin (HEART) Score and Pathway, Troponin-only Manchester Acute Coronary Syndromes, and Emergency Department Assessment of Chest Pain Score (EDACS).

On January 19, 2017, the US Food and Drug Administration approved the first hs-cTn assay for clinical use in the US and has since approved 2 additional such assays. Years after their European colleagues adopted this assay, US clinicians now are considering how to integrate hs-cTn assays into their clinical practice. We report our institutional experience adopting one of these assays (Roche Gen 5 hs-cTnT) into our clinical practice and creating guidelines for the Partners HealthCare system.

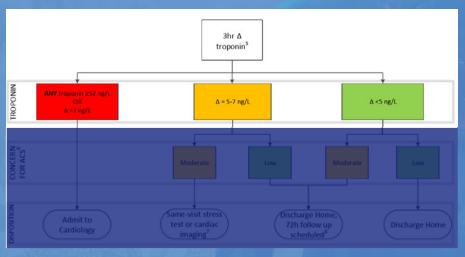
ADP genesis



ADP example: Mass General Brigham

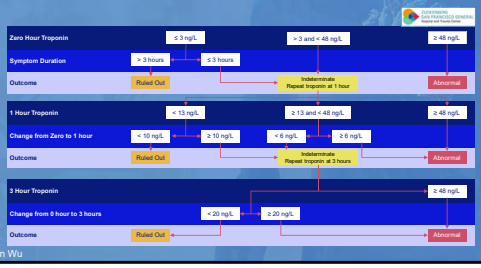


ADP example: MGB



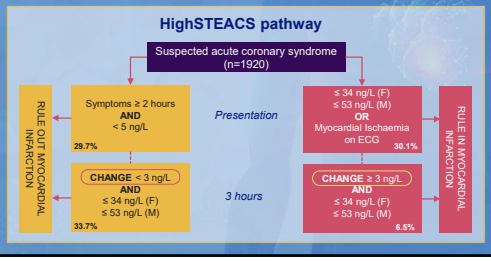
Alternative ADP example: ZSFGH

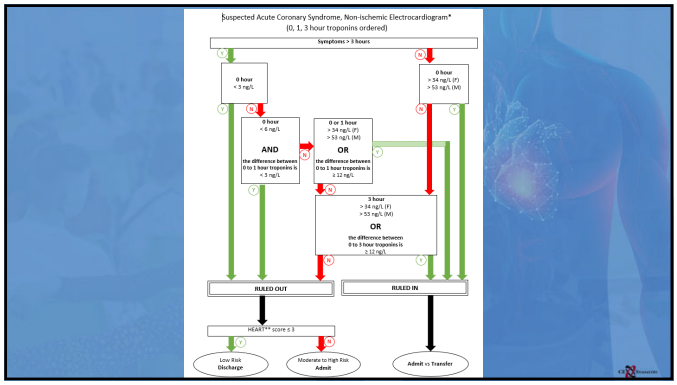
- Working with Cardiology and emergency department, determine a testing and decision algorithm



Courtesy of Dr. Alan Wu

Alternative ADP example: HighSTEACS





Impact of converting to hs-cTn on resource use

- Use of ED observation unit
- Follow-up guidance and resources: what to tell patients
- Information Systems compatibility; review order sets

Downstream impacts

- Consults
- Admissions
- Clinic Referrals

Cardiology Consult Attending

Education and messaging campaigns

- Educational efforts
  - Provider and Nursing education
  - Managed messaging/At the elbow support
  - Inservice
    - Who
    - Scheduling
- Email blasts
- Electronic and Print materials
  - Letters
  - Posters
  - Newsletters

It is a go!

- Go-live
- Post-go-live support
- Post-go-live data monitoring and QA

Summary: Putting it all together

I. CONVENE STAKEHOLDERS
- Adequate timeline

II. CREATE ADP
- Define cutpoints
- Dispo recommendations

III. INSERVICE AND SUPPORT
- Educate front line staff


bpatel2@sturdymemorial.org