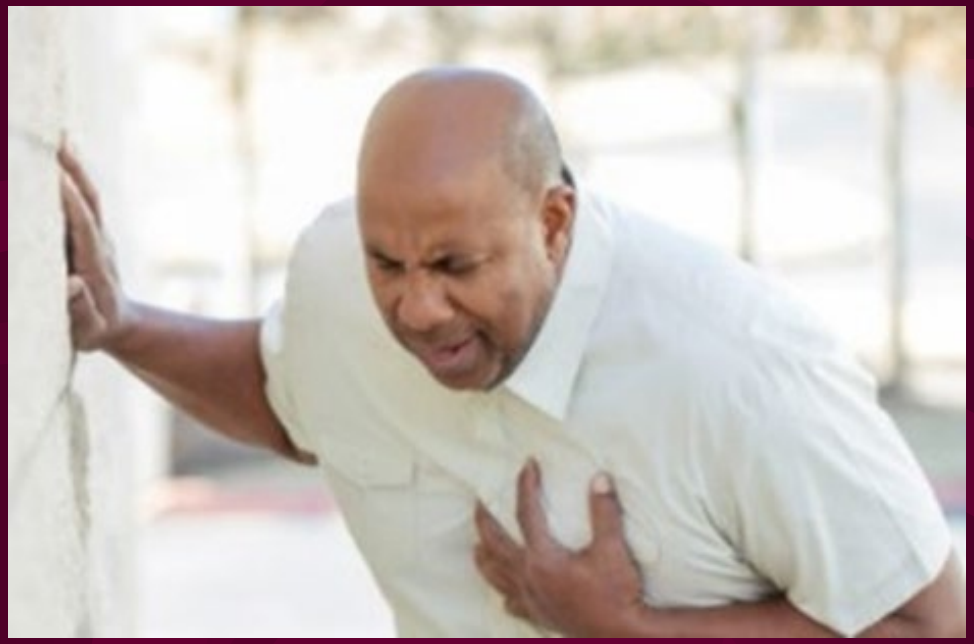
Troponin Leaks, Myocardial Injury, Type 2 MI, & Unstable Angina



Jeffrey Tabas MD

Take Home Points

- Emergency Physicians deal more in “risk” rather than underlying pathology
- Pts w negative hsTrop pathways have very low risk of 30 day MACE (Major Adverse Cardiac Events) = 1 in 500 - 1000
- Pts w mildly elevated, non-rising hsTrops have moderate risk of 30 day MACE = 1 in 20 - 50
- Pts w markedly elevated or rising hsTrops have high risk for 30 day death or AMI = 1 in 10

Case Study: Severe Hypertension with Chest Pain and Headache

- 55 M c/o's HA and CP for a day or two off Htn meds x several weeks
- Exam
  - BP = 220/110, otherwise nonfocal
- EKG
  - High voltage, peaked T waves
- Labs
  - hsTnI 72 and 68 at 0, 1 hrs (ULN <47)

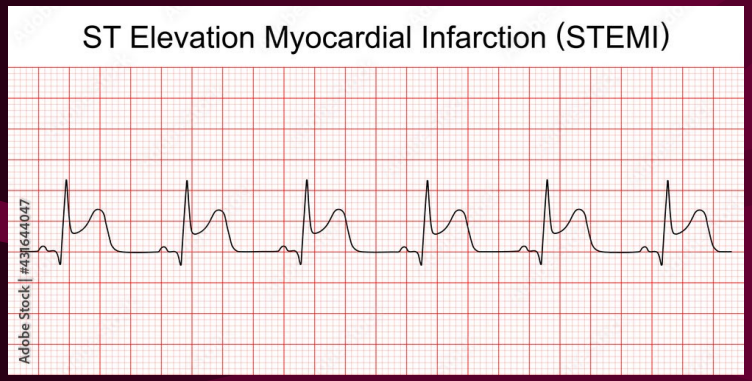
Case Study: Severe Hypertension with Chest Pain and Headache

- Diagnosis - Severe Htn (Htn emergency?) elevated non-rising troponins

- You call for admission
  - R2 asks if you can just treat him in ED and see if he improves
  - They explain that the troponin elevation is likely just some myocardial injury & they wouldn't do further workup even if admitted

AMI Diagnosis

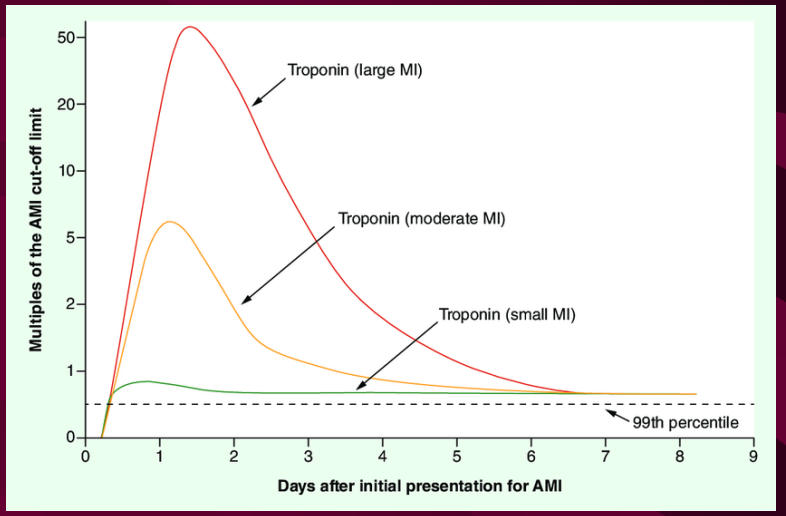
STEMI



Diagnosis:

EKG + Symptoms

NSTEMI



Diagnosis:

Troponin Rise and Fall + Symptoms or EKG

AMI Treatment

- PCI for STEMI:
  - Symptoms < 12 hours
  - Or Any symptom duration IF ongoing ischemia, severe CHF, or life-threatening arrhythmia
- Thrombolysis for STEMI
  - Symptoms < 12 hours and delay to PCI > 2 hours
- PCI for NSTEMI:
  - Hemodynamic instability = hypotension
  - Electrical instability = Vtach
  - Pain refractory to medical (non-opioid) management

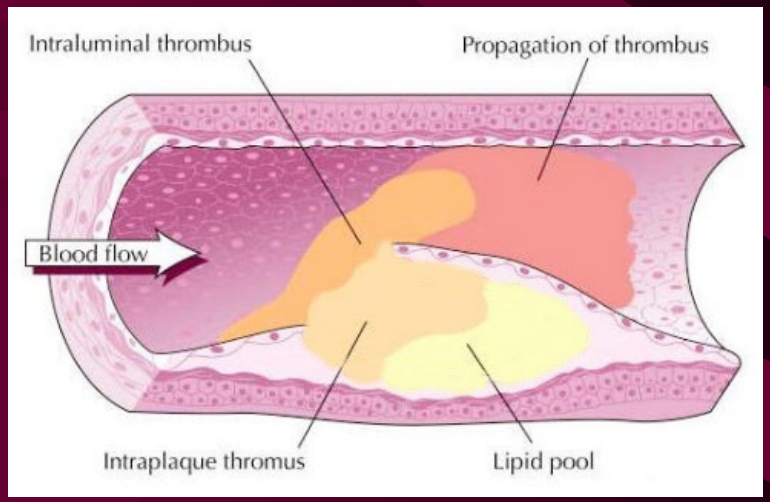
AMI Type 1

Cause: Plaque Rupture

Frequency: 85-90% of AMI (600,00 / year)

Dx: Trop Rise and Fall with either:

- **Symptoms**
- **EKG evolution**
- **Evidence of thrombus (imaging or response to reperfusion**



- **Can result in STEMI or NSTEMI**

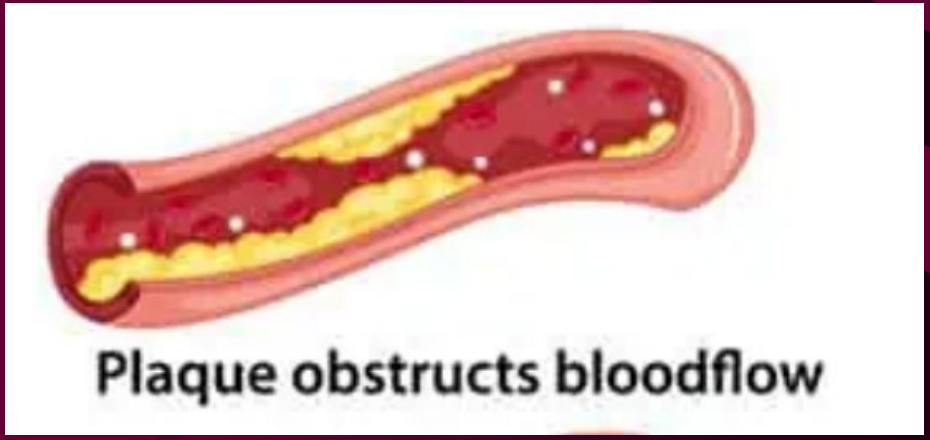
AMI Type 2

Cause: Supply/Demand Mismatch

Frequency: 10-15% of AMI (120,000 / year)

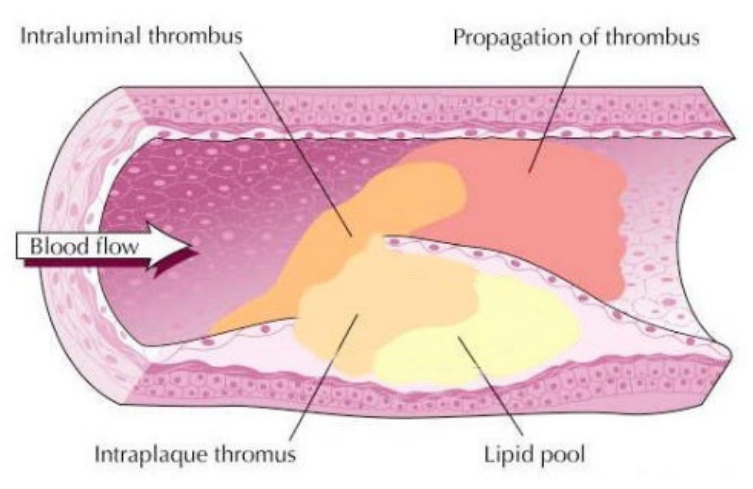
Dx: Trop Rise and Fall with either:

- **Clean Cath or "Expert" Opinion**
- **Typically diagnosed as NSTEMI**



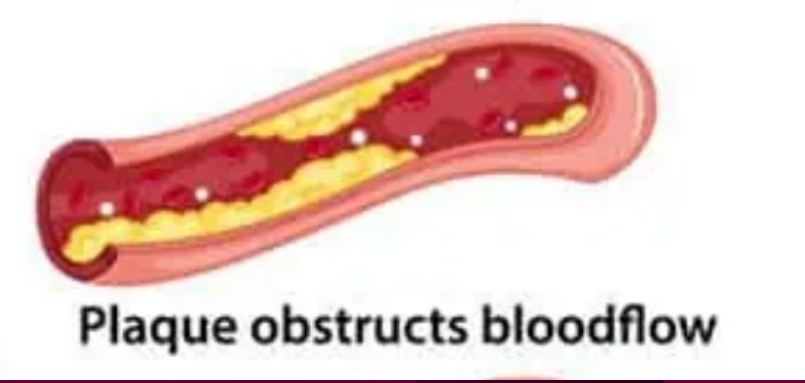
Outcome: AMI Type 1 vs Type 2

Type 1



VS

Type 2



Outcome: In-hospital mortality is the SAME for Type 1 and Type 2 AMI = 9%!

McCarthy, JACC, 2021

Myocardial Injury (aka "troponin leak")

Definition of Normal Troponins

- **Levels below the 99th percentile of the population**
- **Also called the ULN (upper limit normal)**
- **Depends on assay type (Trop I vs Trop T) and the manufacturer**

Definition of Myocardial Injury

- **Troponin results above the ULN**

Myocardial Injury (aka “troponin leak”)

Cause: Supply/Demand Mismatch (+/- impaired clearance from renal failure) resulting in minor myocardial damage

Frequency: A lot

Diagnosis: Elevated non-rising troponins. Sometimes diagnosed as “Type 2 AMI” depending on degree of elevation

Outcome: 30 day MACE is 2-5%

Unstable Angina

- Cause: Critical stenosis resulting in Supply/Demand mismatch = “pre-infarction” condition
- Frequency: Usually have elevated non-rising troponins.
- Diagnosis: Non-invasive testing, cardiac cath, or subsequent MACE. Often diagnosed as myocardial injury/NSTEMI
-

Prognosis for Mildly Elevated, Non-Rising Troponins

Bjurman et al. Biomarkers. 2021

- **Swedish pts w CP/SOB evaluated in ED and discharged home.**
  - **99^{th} percentile (ULN) for hsTnT <14ng/L**
- **<u>90 day mortality</u> (1480 pts)**
  - **hsTn 14-22 = 4.1%**

Prognosis for Mildly Elevated, Non-Rising Troponins

Neumann NEJM 2019:

- **Meta-analysis of 15 studies and 22,000 ED pts who had hsTrop testing**
- **A Troponin minimally above the ULN (14-18 ng/L) resulted in a 4 fold increased risk of death/MI**

Summary: Troponin Elevations

- Rising or Significantly Elevated Troponins
  - Type 1 vs Type 2 AMI
  - NOT an ED distinction!
  - Equivalent high risk
- Mild, non-rising Troponin elevations
  - Myocardial Injury (Troponin Leak)
  - Unstable Angina
  - Still with elevated risk

Rapid Atrial Fibrillation

- One thing my cardiologists have clearly taught me:
  - Tachyarrhythmias are not associated with AMI
  - Therefore no need to order troponins on these patients
  - **The literature suggests otherwise!**

Atrial Fibrillation: Mortality Mildly Elevated, Non-Rising Troponins

- **Aristotle – Hijazi, Circulation, 2014**
  - **14,821 Afib pts w CP or SOB & hsTnT**
  - **9% with elevations over 99th percentile (>14 ng/L)**
  - **10 fold increase of cardiac death from group with elevation vs no elevation**

Atrial Fibrillation: CAD Dx Mildly Elevated, Non-Rising Troponins

- **Butts, CAD, 2023**
  - **281 pts w new AF & subsequent cardiac w/u**
  - **Mild Trop Elevations Vs Negative Trops**
  - **Critical CAD found in:**
    - **34.5% in pts with troponin elevation**
    - **9.8% in pts without troponin elevation**
  - **Mild troponin elevation more predictive of critical CAD than "suspected angina"**

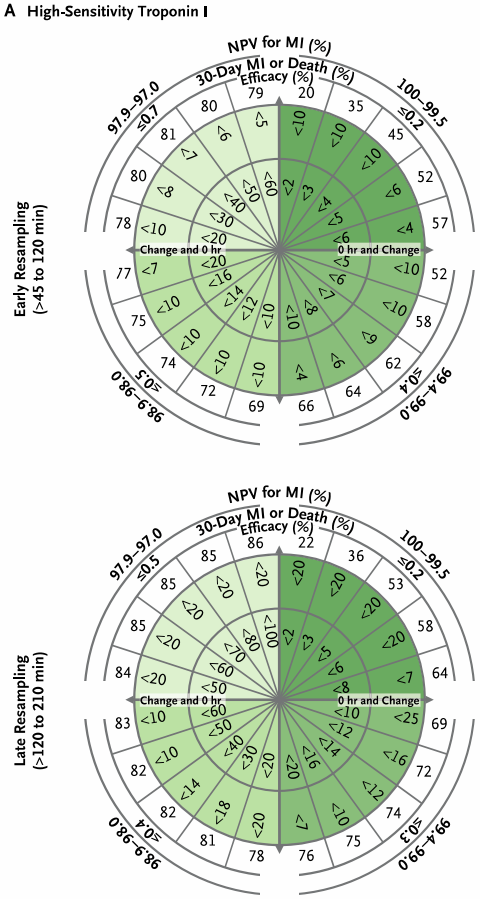
High Sensitivity Troponin Pathway

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Application of High-Sensitivity Troponin in Suspected Myocardial Infarction

J.T. Neumann, R. Twerenbold, F. Ojeda, N.A. Sörensen, A.R. Chapman, A.S.V. Shah, A. Anand, J. Boeddinghaus, T. Nestelberger, P. Badertscher, A. Mokhtari, J.W. Pickering, R.W. Troughton, J. Greenslade, W. Parsonage, M. Mueller-Hennessen, T. Gori, T. Jernberg, N. Morris, C. Liebetrau, C. Hamm, H.A. Katus, T. Münzel, U. Landmesser, V. Salomaa, L. Iacoviello, M.M. Ferrario, S. Giampaoli, F. Kee, B. Thorand, A. Peters, R. Borchini, T. Jørgensen, S. Söderberg, S. Sans, H. Tunstall-Pedoe, K. Kuulasmaa, T. Renné, K.J. Lackner, A. Worster, R. Body, U. Ekelund, P.A. Kavsak, T. Keller, B. Lindahl, P. Wild, E. Giannitsis, M. Than, L.A. Cullen, N.L. Mills, C. Mueller, T. Zeller, D. Westermann, and S. Blankenberg, for the COMPASS-MI Study Group*



Negative Troponins

- **Appropriately timed, serial, negative hsTNs exclude AMI and predict extremely low 30 day death/AMI**

Negative Troponins

Bjurman et al. Biomarkers. 2021

- **Swedish pts w CP/SOB evaluated in ED and discharged home.**
  - **99^{th} percentile for hsTnT <14ng/L**
- **<u>90 day mortality</u> (6426 pts)**
  - **hsTn < 7 = 0.2%**
  - **hsTn 7-14 = 0.6%**

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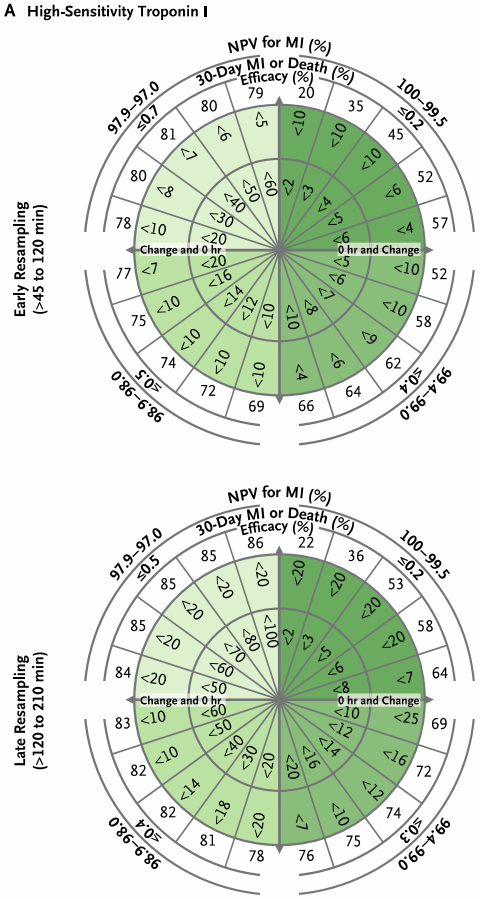
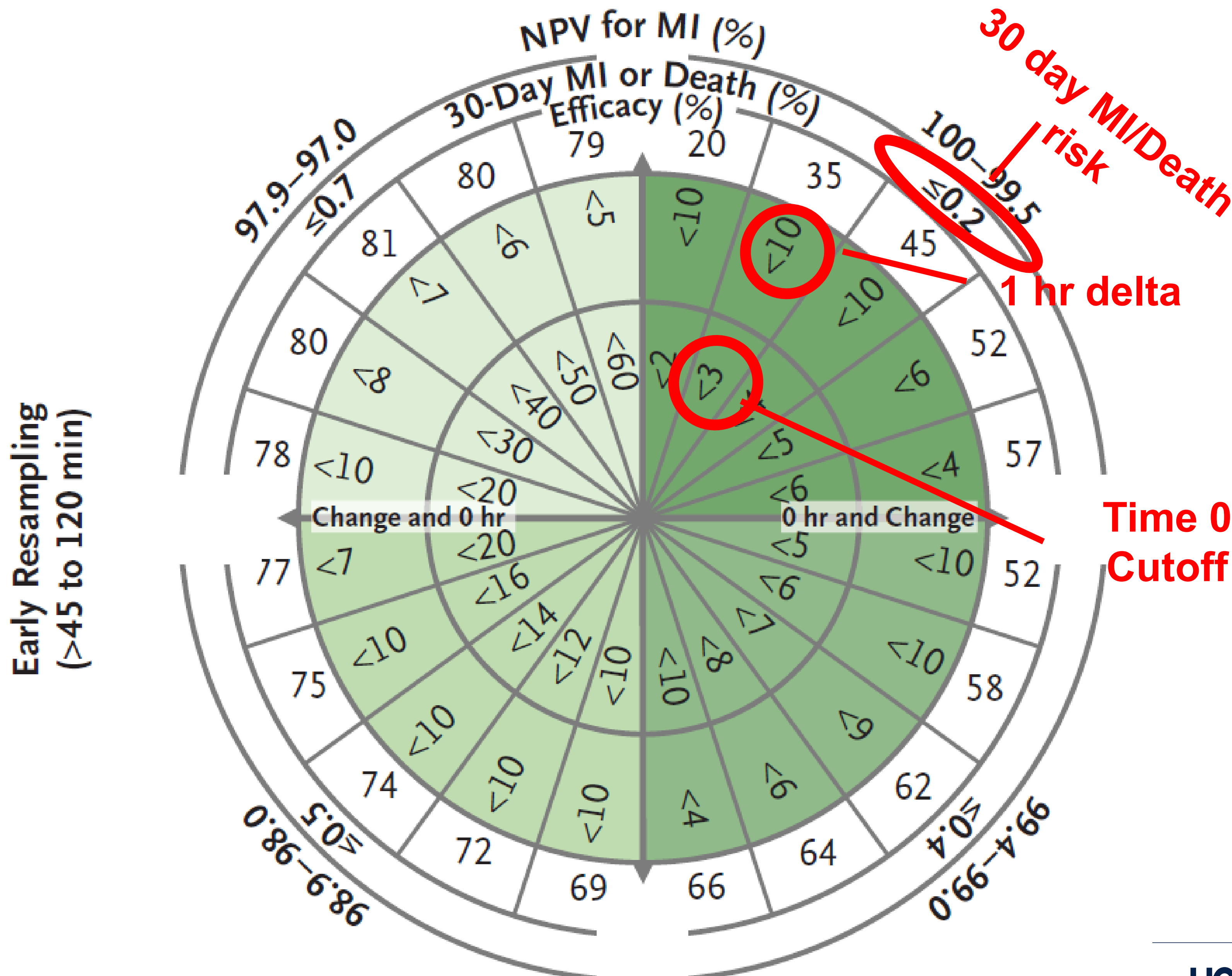


A High-Sensitivity Troponin I



UCSF

ZSFG hsTrop Path Outcomes

Usage: >20,000 (100% uptake)

Usage per Day: 26 +/- 5

Results

- **79% Rule Out**
- **Avoided 10 chest pain admits / week**
- **Mean time to discharge reduced from 7.5 hrs => 3 hrs**

ZSFG hsTrop Path Safety

Sensitivity, % (95% CI)	100%, (71-100%)
Specificity	85%, (81-89%)
Positive Predictive Value	14%, (6-21%)
Negative Predictive Value	99.8%
30 Day Risk of Death or MI	0.025%

vs HEART Score MACE Rate: 2% (CI 1.2%-3.3%)

What Should We Do With Mildly Elevated, Non-Rising Troponins?

Differential Diagnosis

- Unstable Angina
- Myocardial Injury/ Troponin Leak
  - Tachyarrhythmia, severe hypertension, marathon running, stimulant use, CHF exacerbation, hypotension, lack of clearance from renal failure, other

What Should We Do With Mildly Elevated, Non-Rising Troponins?

- Most of these will NOT be due to an acute coronary event!
- However, they are at increased risk of 30 day AMI/death
  - 1 in 20-50 pts w mild, non-rising elevations

  Vs
  - 1 in 500 pts with negative troponins

Sending home a patient w low, non-rising hsTrops

- Always repeat an abnormal level to make sure it is not rising
  - Ex. renal failure pt with chronic elevation
- Their risk is lower risk if:
  - at least several episodes with similar levels in the past
  - their coronary anatomy is known and there are no critical lesions
  - with a longer observation period with repeat troponin and EKG

Sending home a patient w low, non-rising hsTrops

- **Use shared decision making - patients may be comfortable with a risk of AMI/death at 30 days that you are not.**
-

Case Study: Severe Hypertension with Chest Pain and Headache

- Dx – Severe hypertension due to non-compliance with consequent mild, non-rising troponin elevation
- Hypertension is treated. Pt feels better and really wants to go home. After With Shared Decision Making, pt is discharged home with recommended f/u
- Pt misses their followup and you do not hear from them again

Take Home Points

1. Should I rule out AMI liberally?

YES

- **AMI frequently has atypical presentations.**
- **Knowledge of previous anatomy should not significantly impact decision to rule out AMI in ED**
- **Do not fear getting a mildly positive elevation**

Take Home Points

2. Should AMI type affect ED management?

NO.

- **Rising troponins may be from Type 2 AMI (i.e. not from coronary thrombus), but you can't tell in the ED and mortality is still significant**

Take Home Points

3. Should I perform further evaluation for ACS in patients with negative, appropriately timed hsTNs?

- **Almost never with negative hsTNs**
  - **the Major Adverse Cardiac Event risk is extremely low**
- **Rarely with negative csTNs**
  - **Very low MACE rate**

Take Home Points

4. Should I further evaluate all patients with slightly elevated, non-rising troponins?

Probably but…

- **Reasonable to discharge without further eval if repeat the level doesn't rise AND**
  - **Known absence of significant CAD**
  - **Or multiple episodes with similar levels and they have survived this far**
  - **Or pt is willing to accept some risk of MACE at 30 days (1 in 20 is a rough starting point)**

Take Home Points

5. Should I check troponins in patients with tachyarrhythmias who have dyspnea or chest discomfort?

Probably!

- **Do so if they have symptoms and are at risk for CAD (middle aged / older)**
- **Elevated levels in these patients predict significant CAD and MACE – think of it as a poor man's cardiac stress test!**

Questions?

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Bibliography

- Bjurman C et al. Patients discharged with elevated baseline high-sensitive cardiac troponin T from the emergency department, Biomarkers 2021:26:5, 410-416
- Lawton JS et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: a report of the ACC/AHA Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2022;79:e21-e129.
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