Consensus statement on the use of high sensitivity cardiac toponins

SA Heart 2012

- Since the introduction of Troponin I and T (Tn), their levels have assumed a pivotal role in the diagnosis, prognosis and strategy selection for ACS other than STEMI
- Early Tn assays had only moderate sensitivity for cardiomyocyte injury. Successive generations of assays have increased sensitivity progressively.
- High sensitivity troponin (HsTn) assays is defined as:
  - The coefficient of variation (CV) (imprecision) should be <10% at or below the upper limit of normal, which is the 99th percentile of the reference range

- Former Tn assays were either “positive” or “negative” for cardiomyocyte injury
- However, it is now clear almost everyone has detectable levels of Tn in their circulation, and in particularly so in the presence of cardiovascular disease such as heart failure, HT, LV hypertrophy, stable coronary artery disease, DM or renal dysfunction.
- This increased sensitivity with a concomitant loss of specificity has resulted in significant numbers of “false positive” tests for ACS, resulting in unnecessary hospitalization, angiography, etc; thus culminating in unwarranted inconvenience and risk to patients as well as misuse of resources

Pre-analytical and analytical issues

- There is one hsTnT assay and several hsTnI assays on the market (be familiar with the assay that your laboratory uses)
- Serum or plasma (preferably heparinised) are appropriate samples, but serial measurements in a given patient must be done from the same sample type to minimize variation
- It was agreed that, **whole numbers** and specifically **ng/L** will be used as the unit of measurement by all laboratories
- The upper limit of normal for hsTn is the 99th percentile of the normal population. For hs assays the CV should be < 10%, although a CV 10-20% is clinically useful
- Falsely high or low results are rare but possible due to heterophile antibodies and human auto-antibodies interfering with the assay

HsTn in ACS

- Advantages:
  - Earlier identification of MI, making former former Tn assays, myoglobin and CK-MB redundant.
  - Speed up chest pain triage to 4 hours (vs 7 hours)
  - Better ‘rule-out’ test than the former (↑ NPV)
  - Able to predict the risk for subsequent MI and/or death in some patients
- Improved sensitivity comes at a cost of decreased specificity
  - Thus hsTn levels may be mildly raised in a number of settings e.g stable coronary artery disease, heart failure, LV hypertrophy, cor pulmonale, renal failure and even the normal population

The consensus of the meeting was:

- The diagnosis of STEMI is made by typical ECG findings in patients with a suggestive clinical presentation, and not by elevation of troponins (or any other cardiac biomarker). Treatment must be initiated immediately and not delayed until assays are completed
- Although in unstable angina hsTn remains normal, admission for further management may be warranted
- The use of hsTn abolishes the need for other biomarkers, specifically myoglobin and CK-MB
- An initial normal hsTn level in a patient with a reliable history of chest pain onset > 6 hours prior to sampling, **rules out MI**

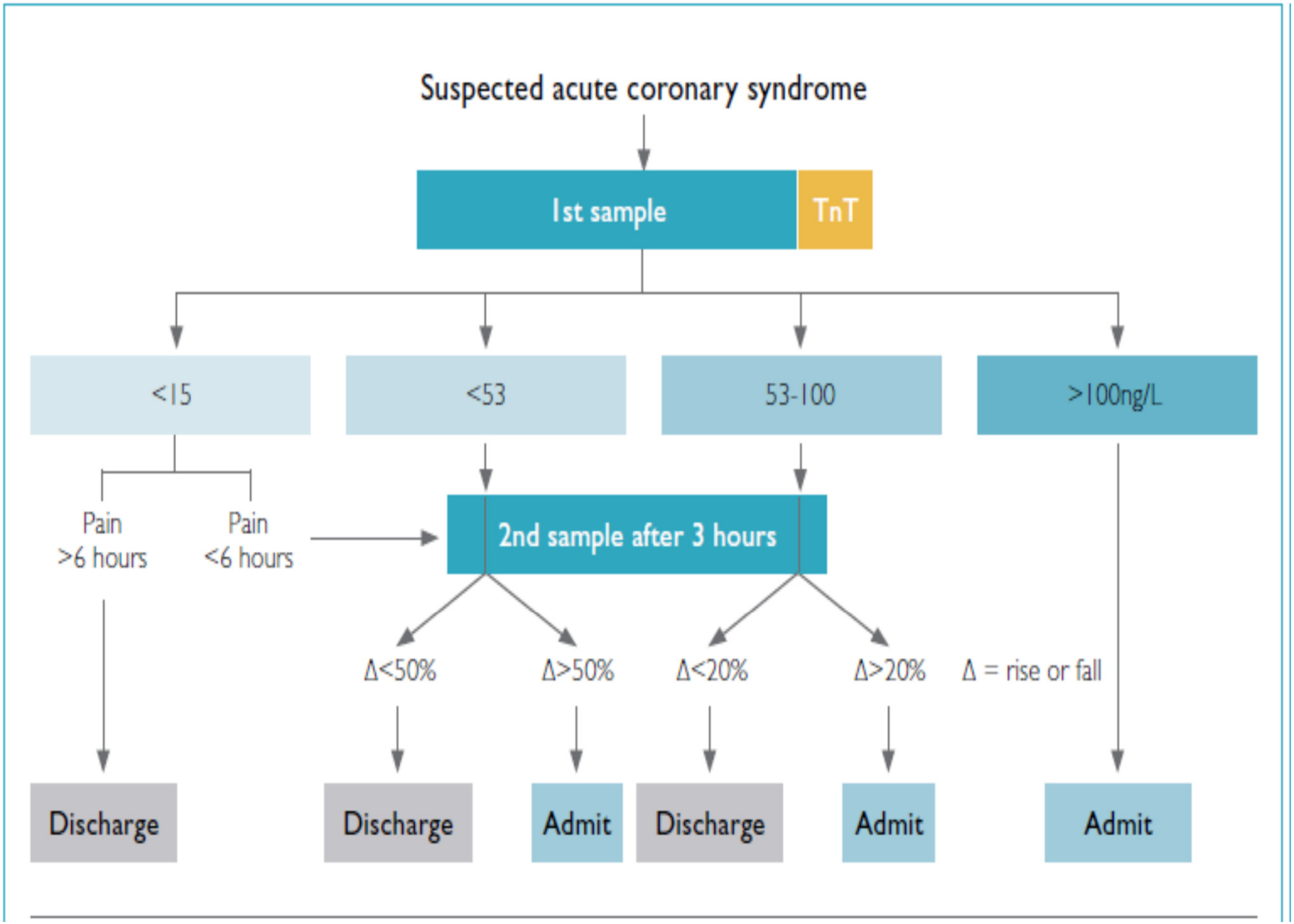
- A hsTn value above the WHO cut-off value rules in MI

TABLE 1: List of contemporary sensitive troponin assays available in South Africa, with the values relevant to the algorithm in Figure 1 (ng/L).

Assay		99th percentile (upper limit of normal)	WHO MI rule-in*
Roche hsTnT	TnT	14	100
Abbott ARCHITECT	TnI	28	300
Beckman AccuTnI	TnI	40	500
Siemens Centaur Ultra	TnI	40	600
Siemens Dimension RxL	TnI	70	600
Siemens Stratus CS	TnI	70	600

*Information from manufacturers

- Serial samples demonstrating rising or falling levels of hsTn differentiate acute for chronic cardiomyocyte necrosis
- The timing of the 2nd of serial samples should be no sooner than 3 hours after the first
- The percentage change (rise or fall) in hsTn levels in 2 samples 3 hours apart is used to establish the diagnosis of MI when the Tn level is below the WHO cut-off.
  - TnI a 50 % in initial value is diagnostic of MI
  - TnT if initial value < 53ng/L a 50% change is diagnostic
  - TnT if initial value 53-100 ng/L a 20% change is diagnostic
- The biomeker of choice for the diagnosis of MI associated with percutaneous coronary interventions remains controversial
- The use of hsTn for risk stratification is not recommended in the general population


Suspected acute coronary syndrome
1st sample
TnT
<15
<53
53-100
>100ng/L
Pain >6 hours
Pain <6 hours
2nd sample after 3 hours
Δ<50%
Δ>50%
Δ<20%
Δ>20%
Δ = rise or fall
Discharge
Discharge
Admit
Discharge
Admit
Admit

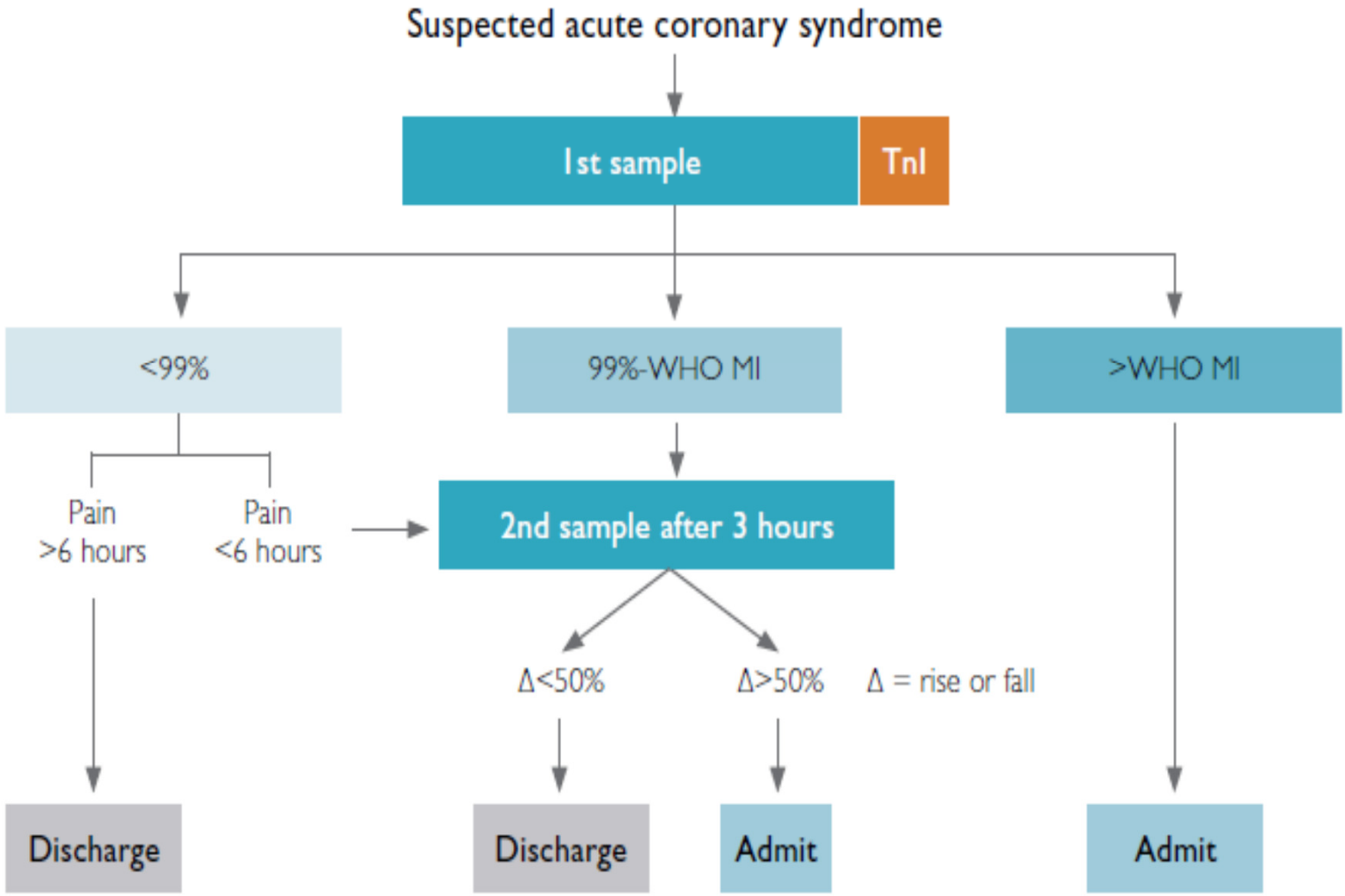


FIGURE 1: Algorithms for interpretation of high-sensitivity cardiac troponin levels in suspected acute coronary syndrome. Note that there are different algorithms for TnT and TnI. For TnI, the numerical values indicated in Table I must be inserted.