What you need to know for the Edmonton Zone hs-TnT Rapid Chest Pain Protocol

Implementation dates:

Site	Go Live Date
University of Alberta Hospital	June 21st, 2022
Sturgeon Hospital	June 23rd, 2022
Misericordia Hospital	July 19th, 2022
Grey Nuns Hospital	July 21st, 2022
*Royal Alexandra Hospital	September 27th, 2022

* Northeast Health Centre will remain with the Beckman hs-TnI assay and the 3 hr chest pain protocol. Roche hs-TnT and Beckman hs-TnI are not interchangeable and should not be used for trending.

Working Group Members:

Department of Emergency Medicine, University of Alberta Hospital, Alberta Health Services
(Drs. Shandra Doran, Brian Rowe)

Department of Emergency Medicine, Royal Alexandra Hospital, Alberta Health Services
(Drs. Dennis Lefebvre)

Division of Cardiology, Mazankowski Heart Institute, University of Alberta Hospital, Alberta Health Services
(Drs. Michelle Graham, Sean van Diepen, Robert Welsh)

Department of Laboratory Medicine and Pathology, University of Alberta Hospital, Alberta Precision Laboratories
(Drs. Albert Tsui, Josh Raizman, Miranda Brun, Kareena Schnabl)

Table of Contents

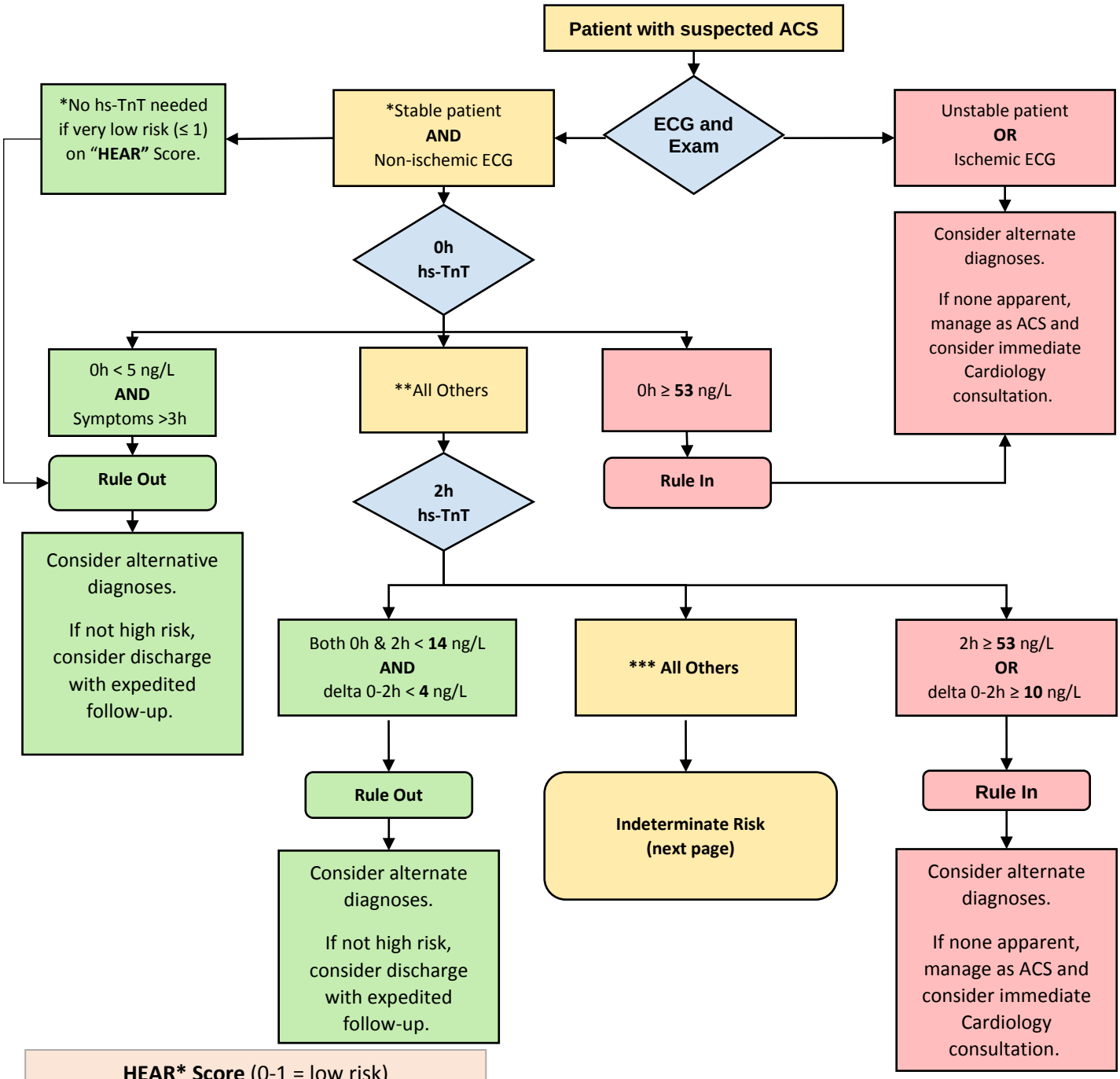
1. Background on High Sensitivity Troponin Assay and Diagnosis of AMI

- The Beckman Coulter high sensitivity troponin I (hs-TnI) assay has been in use with the 3-hour rapid chest pain pathway at the following sites since November 9, 2020: UAH, RAH, GNH, MCH, SGH, SPK, LEH, STO, and NEC. See the APL Laboratory Bulletin distributed on November 3, 2020.
- Although the evaluation of the 3-hour rapid chest pain pathway demonstrated many improvements in care, there remained a number assays in use in Alberta. A province-wide chemistry instrument request for proposal (RFP was initiated to align laboratory practices across the province.
- The successful RFP applicant was Roche Cobas chemistry instruments which supports a high sensitivity troponin T (hs-TnT) assay (the assay in use in southern Alberta for ~10 years).
- Consequently, the Roche hs-TnT assay is being implemented at all large-volume urban and regional hospitals in the province.
- This change will be implemented in the Edmonton Zone at the UAH, RAH, GNH, MCH, and SGH as part of a provincial laboratory standardization initiative (Starting June 21st, 2022).
- **Please note:** many smaller Edmonton Zone EDs and Urgent Care Centers (UCC) will not have the physical capacity to house this instrument, so will remain on hs-TnI and conventional TnI testing (for now) (Refer to Appendix and November 3, 2022 hs-TnI Survival Guide).
- While conversion to Roche instruments will change the way troponin is tested and reported, the units remain the same (ng/L)
- Numerical values, reference interval (i.e. upper 99th percentile reference limit), rule-in/out cut-points, and chest pain algorithm for hs-TnT will change as well from the currently reported values used in hs-TnI.
- The use of a hs-TnT assay in conjunction with a 2-hour rapid protocol has been successfully used other hospitals across Canada (including Calgary), and a decision to adopt this pathway has been made.
- Based on clinical trials in the literature, the Roche hs-TnT assay has a clinical sensitivity and negative predictive value for rule out AMI of 98.7 – 99.9%, and 99.8%, respectively [1-4]. The clinical specificity and positive predictive value for rule-in AMI is 92.3%% and 58.8%, respectively [1-4].
- Values obtained from Roche hs-TnT can only compare with results from the same method (i.e., hs-TnT), and cannot compare/trend with Beckman hs-TnI results.
- The new hs-TnT 2-hour protocol recommended for use in the Edmonton zone will utilize troponin testing at time point zero, two, and four hours. This is expected to allow rapid decision making, reduce length of stay in the ED, expedite serial testing, and align chest pain protocols at major hospital settings across the province.

2. Edmonton Rapid Chest Pain Protocols (2-hour Roche hs-TnT)

(*For sites using Beckman hs-TnI and 3-hour protocol, refer to previous hs-TnI survival guide)
The below schematic outlines the Edmonton rapid chest pain protocol using the Roche hs-TnT assay.

Part I:



HEAR* Score (0-1 = low risk)

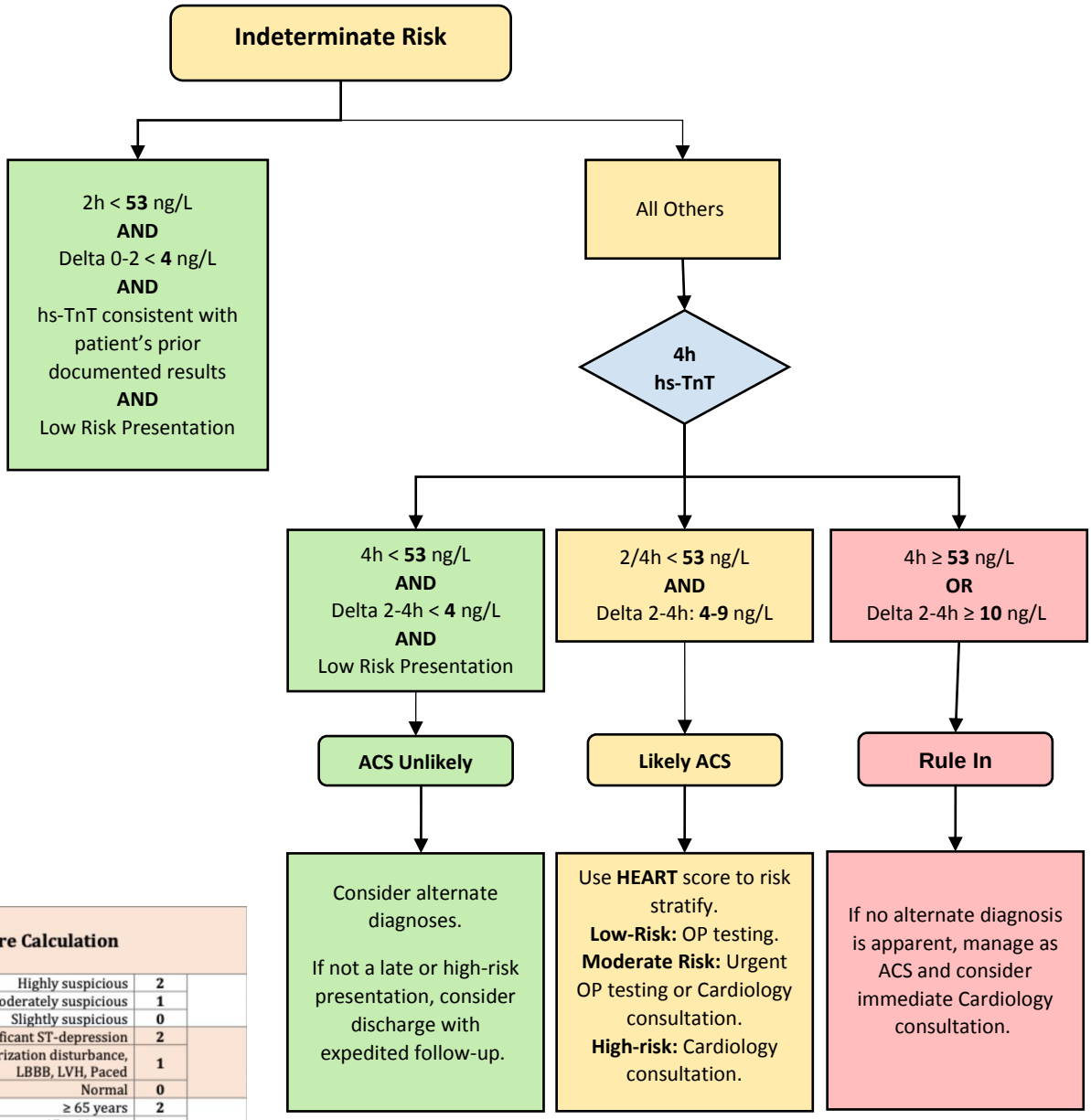
History	Highly suspicious		2
	Moderately suspicious		1
	Slightly suspicious		0
ECG	Significant ST-depression		2
	Non-specific repolarization disturbance, LBBB, LVH, Paced		1
	Normal		0
Age	≥ 65 years		2
	45 – 64 years		1
	≤ 44 years		0
Risk Factors	☐ Diabetes ☐ Current smoker ☐ HTN (diagnosed) ☐ HL (diagnosed) ☐ Family hx CAD ☐ Obesity	≥ 3 risk factors or history of atherosclerotic disease	2
		1 or 2 risk factors	1
		No risk factors known	0

Note:
* Consider using a structured risk assessment tool such as the HEAR (HEART without the TnT testing) to aid decision making for **very low** risk patients.

** For all patients with abnormal hs-TnT results, check the medical record for prior results. Many patients have stable abnormalities in hs-TnT and measured concentrations similar to the patient's baseline are reassuring.

*** The **indeterminate risk pathway** arm relies on expert opinion, the experience in Calgary, and our Edmonton Zone hs-TnI chest pain pathway (initiated 2019). It aligns with current guideline recommendations.

Part II:



HEART Score Calculation			
History	Highly suspicious		2
	Moderately suspicious		1
	Slightly suspicious		0
ECG	Significant ST-depression		2
	Non-specific repolarization disturbance, LBBB, LVH, Paced		1
	Normal		0
Age	≥ 65 years		2
	45 – 64 years		1
	≤ 44 years		0
Risk Factors	☐ Diabetes ☐ Current smoker ☐ HTN (diagnosed) ☐ HL (diagnosed) ☐ Family hx CAD ☐ Obesity	≥ 3 risk factors or history of atherosclerotic disease	2
		1 or 2 risk factors	1
		No risk factors known	0
hs-cTnT (Peak)	> 3x normal limit (43ng/L or greater)		2
	1-3x normal limit (14-42ng/L)		1
	< normal limit (<14ng/L)		0
		Total (10 maximum)	

HEART Score Interpretation	
Low Risk	0-3
Moderate Risk	4-6
High Risk	7-10

Note:
* Consider using a structured risk assessment tool such as the HEART score to aid decision making for all patients without indications for Cardiology consultation.

** For all patients with abnormal hs-TnT results, check the medical record for prior results. Many patients have stable abnormalities in hs-TnT and measured concentrations similar to the patient's baseline are reassuring.

***The **indeterminate risk pathway** arm relies on expert opinion, the experience in Calgary, and our Edmonton Zone hs-TnI chest pain pathway (started 2019). It aligns with current guideline recommendations.

Part I: No hs-TnT Testing:

- Approximately 10% of patients presenting with chest pain don't receive hs-TnI testing in the current Edmonton Zone 3-hour chest pain protocol.
- Presumably this decision-making is based on low-risk assessment; however, we propose using the HEAR score (HEART score without the hs-TnT results).
- Patients with HEAR scores of 0 or 1 have ***very low risk*** of MACE at 30 days (< 1%).

- **Please note:** patients using cocaine or other stimulant medications should have troponin testing, as they are higher risk than very low-risk patients with more frequent increases in troponin values

Modified HEART Score → HEAR

- A study published this year in the *Emerg Med Journal* by Smith, LM *et al.* looked to streamline assessment of low risk chest pain patients[9]. This study examined assessing patients without incorporating troponin results (HEAR).
- In order to assist in risk stratifying the patients with a normal ECG who may fall into the low-risk category with respect chest pain we propose utilizing the **HEAR** aspects of the HEART score: History, ECG, Age, cardiac risk factors.

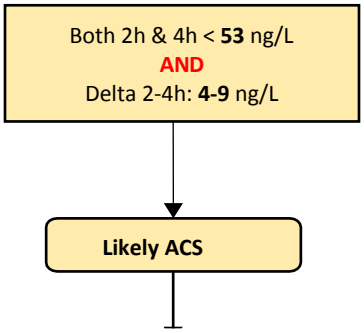
History	**Slightly suspicious** 0		
	Moderately suspicious +1		
	Highly suspicious +2		
EKG 1 point: No ST deviation but LBBB, LVH, repolarization changes (e.g. digoxin); 2 points: ST deviation not due to LBBB, LVH, or digoxin	**Normal** 0		
	Non-specific repolarization disturbance +1		
	Significant ST deviation +2		
Age	**<45** 0	45-64 +1	≥65 +2
Risk factors Risk factors: HTN, hypercholesterolemia, DM, obesity (BMI >30 kg/m^2), smoking (current, or smoking cessation ≤3 mo), positive family history (parent or sibling with CVD before age 65); atherosclerotic disease: prior MI, PCI/CABG, CVA/TIA, or peripheral arterial disease	**No known risk factors** 0		
	1-2 risk factors +1		
	≥3 risk factors or history of atherosclerotic disease +2		

Part I: with hs-TnT Testing:

- All other patients should receive hs-TnT testing.
- If ACS is a strong possibility, consider ordering both a 0h and 2h level on initial submission of lab investigations. This may expedite the pathway as ordering the 2h level can be missed/delayed during a busy period.
- Assuming biomarkers are collected at least **3 hours** following the start of chest pain/symptoms suggestive of ACS:
    - Levels of **< 5 ng/**L are considered safe for rule-out with a single test.
    - Levels of **≥ 53 ng/L** are considered safe for rule-in with a single test;
    - Levels of **5**-**52 ng/L** are indeterminate and need additional hs-TnI testing in **2** hours to determine the delta (or change) in hs-TnT:
        - Delta **< 4 ng/L** are safe to rule-out AMI;
        - Delta **4 – 9 ng/L** require risk stratification using the **HEART** score;
        - Delta **≥ 10 ng/L** are considered rule-in AMI.
- **Rule-out AMI** patients (**~**75% of cases in recent hs-TnI 3-hour rule) – follow-up with their regular primary care provider.
- **Likely AMI** patients (**~**7% of cases in recent hs-TnI 3-hour rule) – consult Cardiology.
- **Indeterminate AMI** category (expected ~10% of cases in recent hs-TnI 3-hour rule) – repeat a 4hour hs-TnT level Delta **4 – 9 ng/L** and then risk stratify:
    - Low**-**risk **HEART** Score – outpatient referral for EST/maximize medical management;
    - Moderate**-**risk **HEART** Score – suggested outpatient referral for ***urgent*** *provocative testing*. If unavailable, consultation with Cardiologist;
    - High-risk **HEART** Score – consultation with Cardiologist.
- HEART SCORE[7]
    - Clinical decision rule allowing rapid risk stratification of undifferentiated chest pain patients, according to their short-term risk for a Major Adverse Cardiac Event (MACE).
    - Cumulative score 0 – 10 of increasing risk for MACE.
    - MACE defined as all-cause mortality, myocardial infarction, or coronary revascularization within 30 days.
    - HEART categories (MACE Risk):
        - 0-3 = low risk (1-2%);
        - 4-6 = moderate risk (12-17%);
        - 7-10 = high risk (50-65%).

Note: HEART score has been validated with hs-TnT assay [5-8].

- In order to assist in risk stratifying the patients that fall into the **Indeterminate Risk** category with respect to the hs-TnT values we propose utilizing the HEART Score: History, ECG, Age, cardiac risk factors, and hs-TnT values.
- Patients in Indeterminate category for rapid chest pain protocol:



  - Low Risk HEART Score (0-3 points) – outpatient referral for EST/maximize medical management;
  - Moderate Risk HEART Score (4-6 points) – if dynamic ST and T-wave changes identified in the ED, cardiology consultation is recommended. If not, outpatient referral for ***urgent (< 48 hour)*** cardiac testing/maximize medical management, or consultation with Cardiology Staff if testing cannot be reliably obtained;
  - High-Risk HEART Score (7-10 points) – consultation with Cardiologist.

3. Clinical Vignettes

Case #1:
A 32-year-old male presents to the ED with right-sided chest pain worse with movement over the past day. He has occasionally had pain like this before and wonders if he is having a heart attack after his co-worker had one at work. He denies diaphoresis, nausea/vomiting, pre-syncope, or shortness of breath. He is pain free in the ED when assessed after taking two Ibuprofen tablets. He states that he is otherwise healthy, denies smoking and/or illicit drug use. You do not identify any concerning features on his ECG. The HEAR Score = 0 (low-risk) and you elect ***not*** to send off lab work, including hs-TnT. He has no family doctor and you suggest he get one/return to the ED if symptoms worsen. **Note:** if the CP were < 3 hours duration, then hs-TnT measurement might be considered.

Case #2:
A 49-year -old female presents to the ED with stuttering epigastric/retrosternal chest pain over the past day. She denies having had pain like this before. She identifies nausea and mild shortness of breath with the pain. She is pain free in the ED when assessed. She states that she is otherwise healthy and is a non-smoker. You identify her to be PERC negative for PE and you do not identify any concerning features on her ECG. The 0-hour hs-TnT measurement is **< 5 ng/L** (**Rule-out AMI**); a second biomarker test is not required. She has a family doctor and you discharge her back into his/her care.

Case #3:
A 64-year-old male presents via EMS with left sided chest pain that began last night and the patient tried to "sleep it off". The patient has had chest pain NYD in the past, often with exertion, and states that this pain feels very similar to those episodes. The ECG indicates non-specific ST segment changes. The hs-TnT is reported as **137 ng/L (Rule-in AMI)**. You initiate NSTEMI treatment and consult Cardiology.

Case #4:
A 61-year-old female presents to the ED with chest pain that began four hours ago while the patient was at work. She has T2DM, hypertension and is still smoking cigarettes but she informs you she is trying to quit. You do not note any specific changes on the ECG, although there is a question of hyper-acute T waves. You send off a cardiac workup, place the patient on cardiac monitoring, ask for a repeat ECG and order

ASA. Initial hs-TnT measurement is reported as **32 ng/L (Indeterminate AMI)**. You are managing this patient's discomfort and order a 2-hour troponin. Your repeat ECG does not show any ST segment elevation; however, you wonder about possibly some subtle depression evolving. Repeat hs-TnT is 34 ng/L. This result still remains below the **53 ng/**L cutoff, and the delta is 2 ng/L **(< 4 ng/L),** which suggests low-risk and keeps her within the indeterminate range of the chest pain protocol. Using the HEART assessment, the patient is scored as 1+1+1+2 = 5, which puts her in the moderate risk category. You attempt to arrange for an urgent out-patient EST or MIBI and if that is not available you could consult Cardiology.

Case #5:
A 68-year-old male presents to the ED with chest pain that began two hours ago while the patient was working in the garden. He has hypertension and is a 30 park year cigarette smoker. You do not note any specific ischemic changes on the ECG. You send off a cardiac workup, place the patient on cardiac monitoring, ask for a repeat ECG and order ASA. The initial hs-TnT measurement is reported as **25 ng/L (Indeterminate AMI)**. You are managing this patient's discomfort and order a repeat 2- hour hs-TnT (both because of the initial hs-TnT value and because the chest pain was < 3 hours in duration). Your repeat ECG does not demonstrate any ST segment elevation. Repeat hs-TnT is **32 ng/L**. This result still remains below the **53 ng/**L cutoff, and the delta is **7 ng/L (5-10 ng/L),** which keeps him within the indeterminate range of the chest pain protocol.

A 4-hour hs-TnT is ordered, and the results return as follows:
Scenario A: 4 hour hs-TnT is **58 ng/L; Delta 2-4 hour is 26 ng/L** (Rule-in ACS) – You would consult Cardiology.
Scenario B: 4 hour hs-TnT is **33 ng/L; Delta 2-4 hour is 1 ng/L** (4 hr hs-TnT < 53 ng/L and delta = 4-9 ng/L). Using the HEART score the patient is scored as 1+0+2+1+1= **5** (MACE 12-63%), which puts him in the moderate-risk category. You could arrange for urgent provocative testing or consult Cardiology if that is not available.

4. Laboratory Changes to Troponin Testing

4.1. Sites Using the Roche hs-TnT Method in Conjunction with 2-hour Rapid Chest Pain Protocol

- University of Alberta Hospital
- Misericordia Hospital
- Grey Nuns Hospital
- Sturgeon Hospital
- Royal Alexandra Hospital (Northeast Health Centre will remain with Beckman hs-TnI and the 3hr chest pain pathway)

4.2. Summary of Roche hs-TnT Reporting:

	Reporting details	Notes
Units	ng/L (whole numbers)	N/A
Reference interval	< 14 ng/L	Values above this limit will be flagged as high.
Critical Value	≥ 53	Only outpatient / community troponin critical value will be phoned out to ordering provider
Reporting limits	3 to 100,000 ng/L	N/A
Delta value	Reported for 0-2 hour delta and 2-4 hour delta	Reported if a previous hs-TnT value on the same patient and method is within 4 hours
Comments	Pathway interpretive comments & Method identification comments	N/A

4.3. Interpretive Comments Reported with hsTnT

A) In-Hospital Patients:

hs-TnT Result (ng/L)	Comment	Flagging
< 5	For patients with a non-ischemic ECG, a Troponin T, High Sensitivity of 4 ng/L or less on presentation is highly sensitive for excluding acute myocardial infarction, provided the specimen was collected more than 3-hours from symptom onset. However, for patients with symptoms less than **3 hours** duration or concerning clinical presentations, repeat troponin testing at 2-hours after the initial sample is recommended. Please note that patients with ischemic ECG changes and/or high-risk clinical presentations should be considered for further evaluation irrespective of troponin results.	Normal
5-13	Troponin T, High Sensitivity is below the upper reference limit (14 ng/L) and results are not consistent with myocardial infarction or injury. However, patients with acute symptoms (less than **3 hours**) or concerning clinical presentations should undergo repeat troponin testing at 2-hours after the initial sample. • A 2-hour change of 3ng/L or less is highly sensitive for excluding acute myocardial infarction. • A 2-hour change of 4-9 ng/L may indicate acute myocardial injury. Repeat clinical evaluation, ECG and troponin at 4-hours after the initial sample is recommended. • A 2-hour change of 10ng/L suggests an acute myocardial injury and may represent acute myocardial infarction in the appropriate clinical scenario. Please note that patients with ischemic ECG changes and/or high-risk clinical presentations should be considered for further evaluation irrespective of troponin results.	Normal
14-52	Troponin T, High Sensitivity has a non-specific/non-diagnostic elevation. Interpretation is highly dependent on clinical presentation and patient history. New elevations are concerning; however, many patients have chronic elevations in troponin and measured concentrations near the patient's baseline are reassuring. Patients with acute symptoms (less than **3 hours**) or concerning clinical presentations should undergo repeat troponin testing at 2-hours after the initial sample. • A 2-hour change of 3 ng/L or less suggests acute myocardial infarction is unlikely. • A 2-hour change of 4-9 ng/L may indicate acute myocardial injury. Repeat clinical evaluation, ECG and troponin at 4-hours after the initial sample is recommended. • A 2-hour change of 10 ng/L suggests an acute myocardial injury and may represent acute myocardial infarction in the appropriate clinical scenario. Please note that patients with ischemic ECG changes and/or high-risk clinical presentations should be considered for further evaluation irrespective of troponin results.	High
≥ 53	Clear elevation of Troponin T, High Sensitivity consistent with acute myocardial injury or infarction in the appropriate clinical context. Repeat troponin testing at 2-hours after the initial sample may be helpful to assess for ongoing myocardial injury.	Critical

B) Community Patients

hs-TnT result (ng/L)	Comment	Flagging
< 14	Troponin T, High Sensitivity is below the upper reference limit (14 ng/L) and results are not consistent with myocardial infarction or injury, provided the specimen was collected more than **3 hours** from the onset of symptoms. Patients with active symptoms, ischemic ECG changes and/or concerning clinical presentations should be considered for urgent evaluation irrespective of troponin results.	Normal
14-52	Troponin T, High Sensitivity has a non-specific/non-diagnostic elevation. Interpretation is highly dependent on clinical presentation and patient history. New elevations are concerning; however, many patients have chronic elevations in troponin and measured concentrations near the patient's baseline are reassuring. Patients with active symptoms. Ischemic ECG changes and/or concerning clinical presentations should be considered for urgent evaluation irrespective of troponin results.	High
≥ 53	Clear elevation of Troponin T, High Sensitivity consistent with myocardial injury or infarction. Interpretation is highly dependent on clinical presentation and patient history. Many patients have chronic elevations in troponin and measured concentrations near the patient's baseline are reassuring. New troponin elevations are concerning and urgent assessment in an emergency department may be indicated in the appropriate clinical context.	Critical

5. Specific Caveats for Roche hs-TnT Assay

Bias Compared to Beckman hs-TnI

- Troponin values from different methods should not be compared and used for trending.
- There is a big difference in troponin values between Roche hs-TnT and Beckman hs-TnI (approximate average range from -100% to + 800%).
- In patients with renal disease, hs-TnT can be higher than expected due to reduced clearance function.[10]
- In patients with skeletal myopathies, hs-TnT can be higher than expected which might be due to the release of skeletal troponin isoform detected by the hs-TnT assays.[11,12]

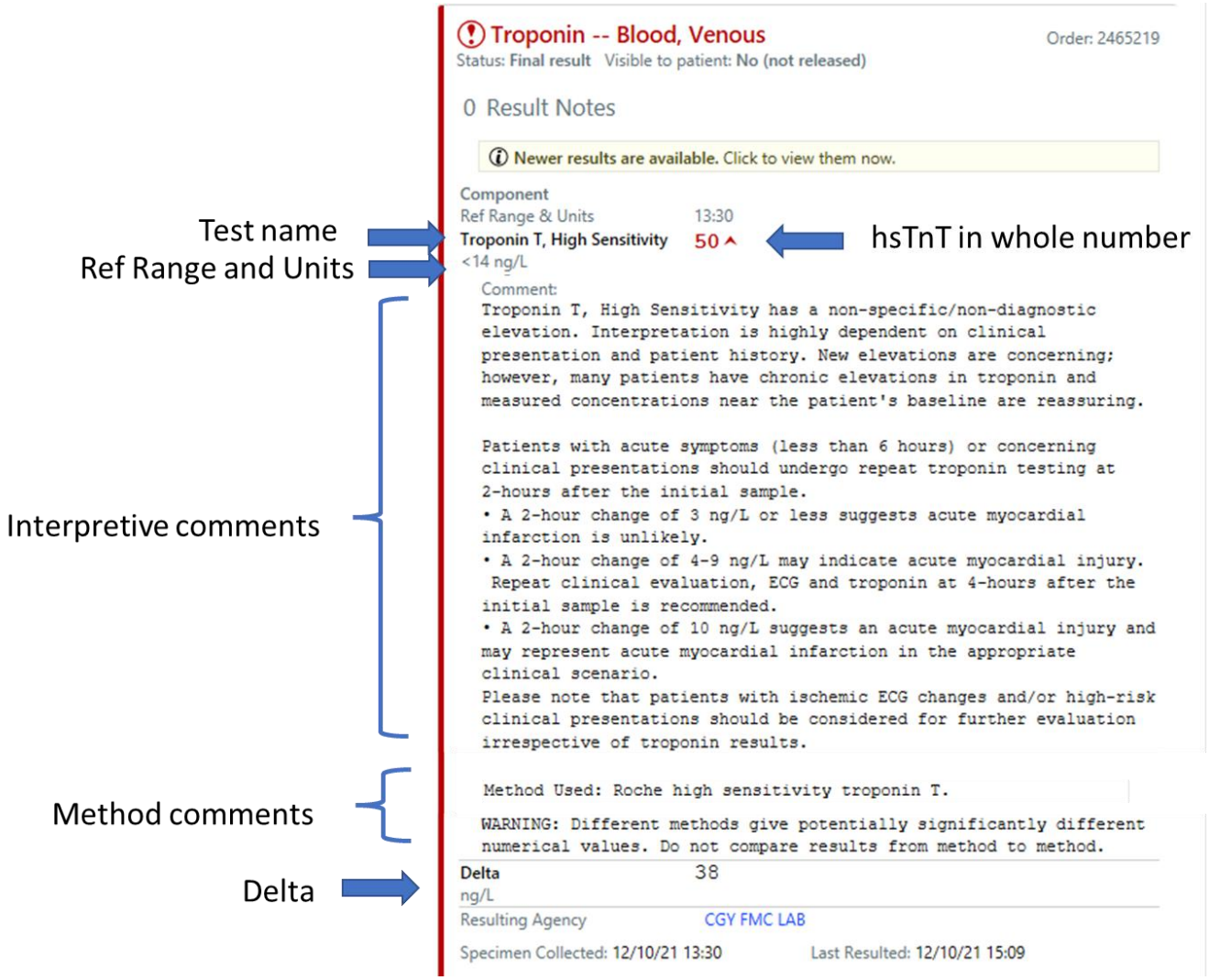
Hemolysis

- Studies from the manufacturer, in-house, and the literature suggested that hemolyzed sample can falsely decrease hs-TnT results.
- Hemolyzed specimens may require re-collection, thus delaying turnaround time.
- Hemolyzed specimens can be due to traumatic blood collection, prolonged use of tourniquet, use of butterfly needles, and vigorous mixing of blood tubes. These can be avoided by following AHS best practice for blood collection or request the lab for collection.
- In certain situations with persistent hemolyzed samples in subsequent collections (e.g., suspected in vivo hemolysis), the laboratory will report hs-TnT results with comments.

6. Screen Shot Examples of hs-TnT Reports

Epic Chart Review Screenshot

Note: a similar reporting format will be seen for Netcare



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8. Appendix

Summary of different troponin assays in Edmonton zone after September 2022:

Site	Troponin assay	Chest Pain protocol
University of Alberta Hospital	Roche hs-TnT	2-hour
Royal Alexandra Hospital		
Grey Nuns Hospital		
Misericordia Hospital		
Sturgeon Hospital		
Strathcona Community Hospital	Beckman hs-TnI	3-hour
Leduc Community Hospital		
Westview Health Center		
Northeast Health Centre		
Fort Saskatchewan Community Hospital	Siemens Stratus conventional TnI	6-hour
East Edmonton Urgent Care Centre		
Devon General Hospital		
Redwater Health Center		
DynaLIFE Medical Labs (community)	Siemens Atellica hs-TnI	Not Applicable