

## **ND Cardiac System STEMI, NSTEMI, & Acute Coronary Syndrome Guide**

### **Tertiary Hospital One Call:**

#### **Altru Health System – Grand Forks**

Phone: 701-780-5206 or 1-855-425-8781

Fax: 701-780-1097

#### **CHI St. Alexius Health - Bismarck**

Phone: 701-530-7699 or 1-877-735-7699

Fax: 701-530-7005

#### **Essentia Health System - Fargo**

Phone: 701-364-CALL (2255) or

844-865-CALL (2255)

Fax: 701-364-8405

#### **Sanford Health System- Bismarck**

Phone: 1-855-550-1225

Fax: 701-323-5751

#### **Sanford Health System- Fargo**

Phone: 701-234-6304 or 1-877-647-1225

Fax: 701-234-7203

#### **Trinity Health System - Minot**

Phone: 701-857-3000 or 1-800-223-1596

Fax: 701-857-3260

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# ACS Risk Stratification Guide

Revised 5/2022

Patient presenting with chest pain or anginal equivalent.

YES ↓

12 Lead ECG obtained and interpreted ≤10 minute

YES ↓

ST elevation at the J point in at least 2 contiguous leads of ≥2 mm (0.2 mV) in men or ≥1.5 mm (0.15 mV) in women in leads V2-V3 and/or of ≥ 1 mm (0.1mV) in other contiguous chest leads or the limb leads  
 OR New or presumed new LBBB (discuss with cardiologist)  
 OR isolated ST depression >2 mm in V1-V3  
 OR Cardiogenic Shock –  
 OR Sustained Ventricular Tachycardia

YES →

**Emergent**  
 Contact tertiary center to arrange for immediate transfer  
 -Dispatch EMS  
 -If patient is a STEMI, follow statewide STEMI Guideline

**Obtain serial ECG at 5–10-minute intervals if symptoms persist or change** NO ↓

Hemodynamic instability  
 OR other evidence of life-threatening differential chest pain diagnosis\*: pulmonary embolism, aortic aneurysm, aortic dissection, pericardial tamponade, tension pneumothorax (\*Life threatening Differential Chest Pain Diagnoses supplemental guide)

YES →

NO ↓

Troponin\*, CBC, BMP, Portable Chest X-ray  
 ASA 324 mg chewable PO or 300 mg PR  
 Nitroglycerine prn - Hold for inferior MI -Hold 24 hrs. for Sildenafil or Vardenafil, or within 48 hrs. of Tadalafil  
 Oxygen at 2 LPM if SpO2 <90%, titrate to maintain SpO2 90-94%  
 Morphine for analgesia prn

↓

ST depression >0.5 mm in ≥2 leads  
 OR Dynamic T Wave Inversion  
 OR Positive Biomarkers  
 OR HEART Score 7-10

YES →

**High Risk**  
 Follow Non-ST-Elevation ACS Guideline

NO ↓

Persistent chest pain  
 OR Classic angina increased with exertion, decreased with rest/NTG  
 OR Known CAD or PVD  
 OR HEART Score 4-6

YES →

**Intermediate Risk**  
 Follow Intermediate Risk Guideline

NO ↓

No ECG Changes  
 AND Negative Biomarkers  
 AND Heart Score 0-3

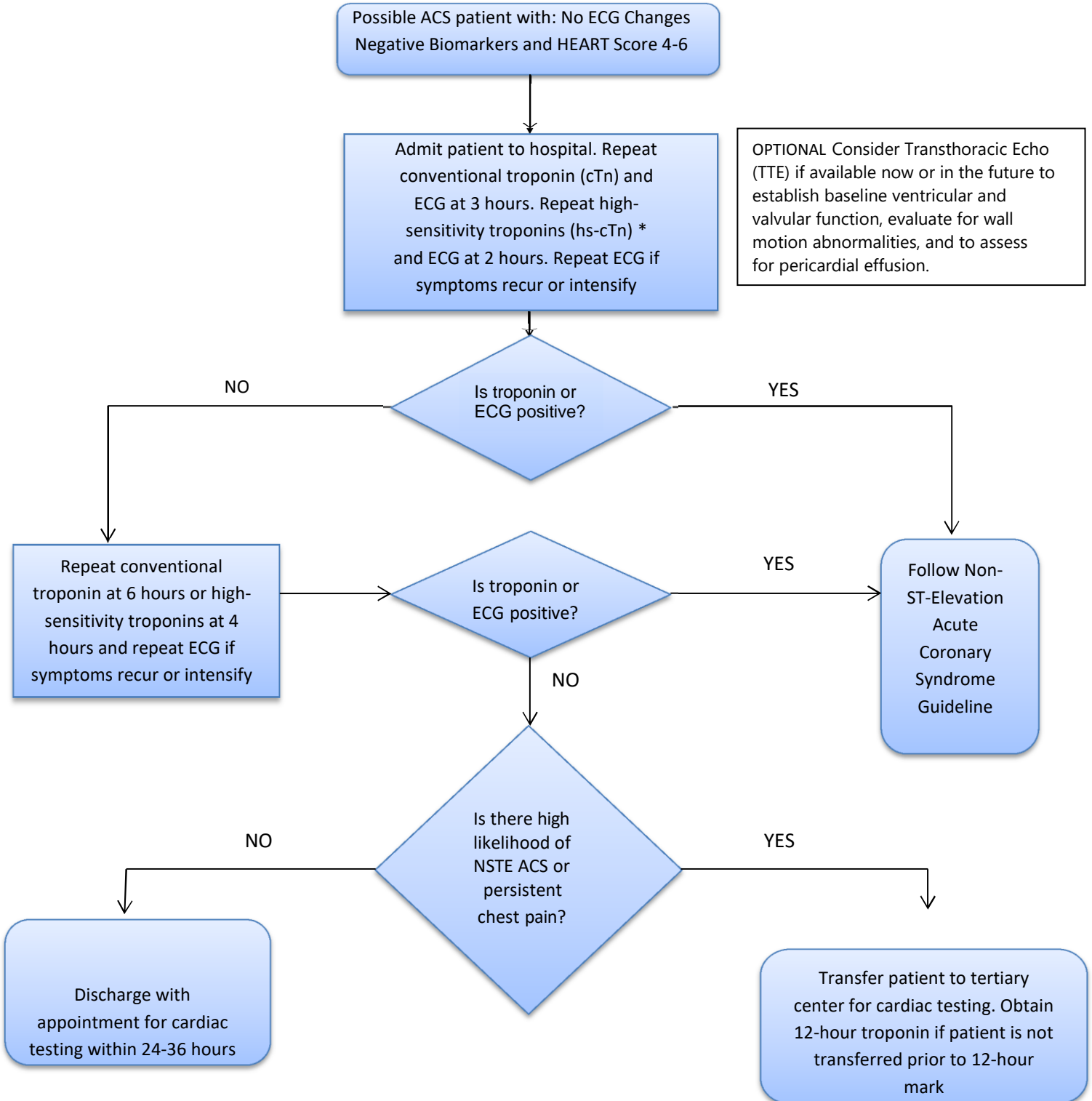
YES →

**Low Risk**  
 Follow Low Risk Guideline

The HEART Score for Chest Pain Patients in the ED		
History	<ul style="list-style-type: none"> <li>Highly Suspicious</li> <li>Moderately Suspicious</li> <li>Slightly or Non-Suspicious</li> </ul>	<ul style="list-style-type: none"> <li>2 points</li> <li>1 point</li> <li>0 points</li> </ul>
ECG	<ul style="list-style-type: none"> <li>Significant ST-Depression</li> <li>Nonspecific Repolarization</li> <li>Normal</li> </ul>	<ul style="list-style-type: none"> <li>2 points</li> <li>1 point</li> <li>0 points</li> </ul>
Age	<ul style="list-style-type: none"> <li>≥65 years</li> <li>≥45-&lt;65 years</li> <li>&lt;45 years</li> </ul>	<ul style="list-style-type: none"> <li>2 points</li> <li>1 point</li> <li>0 points</li> </ul>
Risk Factors (DM, current or recent smoker, HTN, HLP, family history of CAD, obesity)	<ul style="list-style-type: none"> <li>&gt;3 Risk Factors or History of CAD</li> <li>1-2 Risk Factors</li> <li>No Risk Factors</li> </ul>	<ul style="list-style-type: none"> <li>2 points</li> <li>1 point</li> <li>0 points</li> </ul>
Conventional Troponin	<ul style="list-style-type: none"> <li>≥3 x normal limit</li> <li>&gt;1-&lt;3 x normal limit</li> <li>≤ normal limit</li> </ul>	<ul style="list-style-type: none"> <li>2 points</li> <li>1 point</li> <li>0 points</li> </ul>
High-Sensitivity Troponins	<ul style="list-style-type: none"> <li>&gt;3x normal limit: Females &lt;48ng/L, Males &lt;102ng/L</li> <li>1-3x normal limit: Females 16-48ng/L, Males 34-102ng/L</li> <li>&lt;normal limit: Females &lt;16ng/L, Males &lt;34ng/L</li> </ul>	<ul style="list-style-type: none"> <li>2 points</li> <li>1 point</li> <li>0 points</li> </ul>
Score 0-3: 2.5% MACE over next 6 weeks (Discharge Home) Score 4-6: 20.3% MACE over next 6 weeks (Admit for Observation) Score 7-10: 72.7% MACE over next 6 weeks (Early Invasive Strategies)		

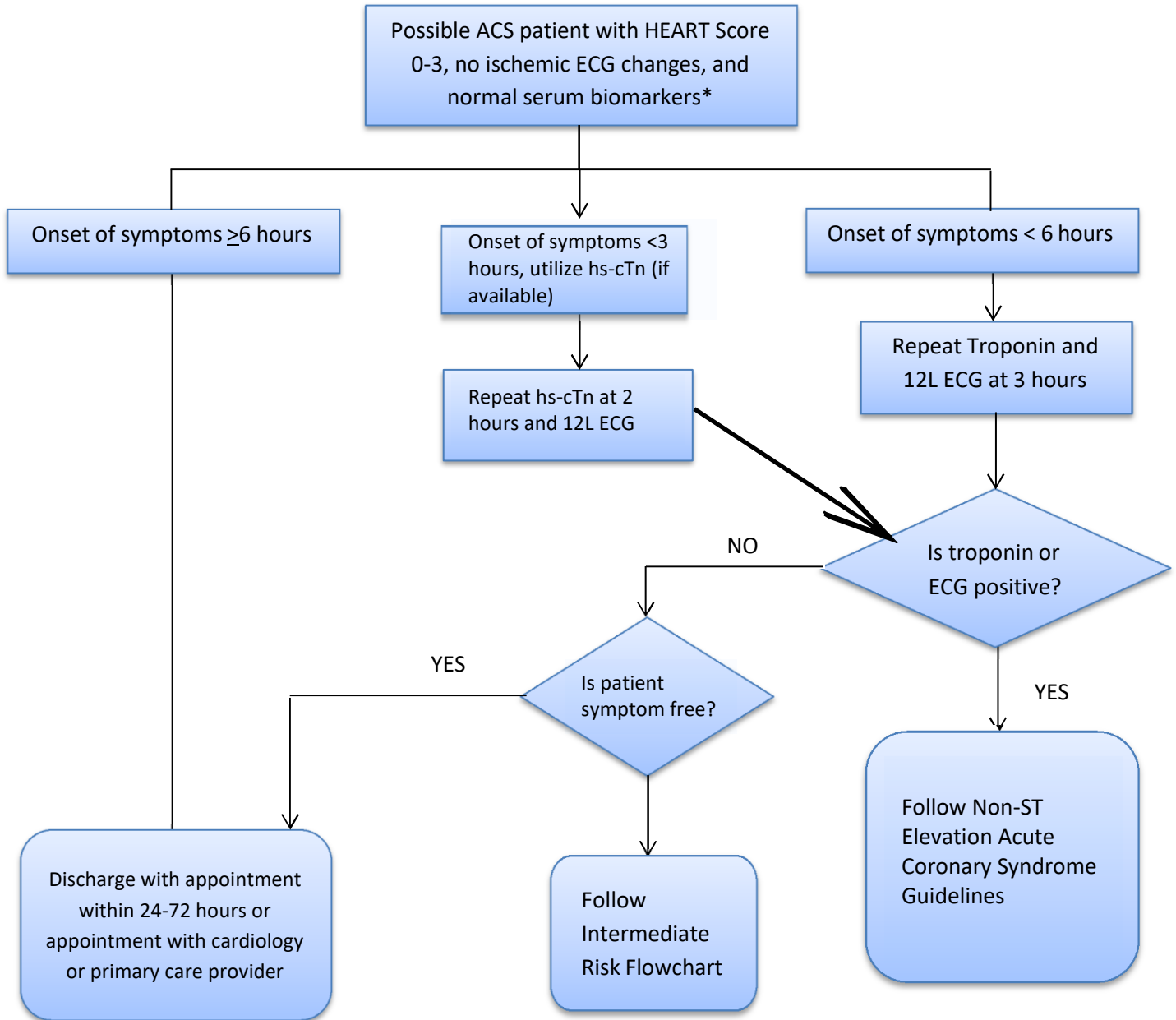
\*High-Sensitivity Troponins (hs-cTn) Preferred

## Intermediate Risk ACS Flowchart



\*High-Sensitivity Troponins (hs-cTn) Preferred  
See reference for Cardiac Testing pg. 9-10

## Low Risk ACS Flowchart



\*High-Sensitivity Troponins (hs-cTn) Preferred

# ND STEMI

## Inter-Hospital Transfer Guideline

(ST-Segment Elevation Myocardial Infarction)

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#### ***Ideal STEMI Treatment Goals:***

- **First Medical Contact-to-First ECG** time  $\leq$  10 minutes unless pre-hospital ECG obtained
- All eligible patients receive **Reperfusion** (PCI or fibrinolysis) therapy
- Fibrinolytic–eligible patients with **Door-to-Needle** time  $\leq$  30 minutes
- Reperfusion – eligible patients transferred to a PCI receiving center with referring center **Door in- Door out** time (*Length of Stay*)  $\leq$  45 minutes
- Referring Center ED **Door-to-PCI device time**  $\leq$  100 minutes (*includes transport time*)
- All STEMI patients without a contraindication receiving **aspirin** before ED discharge
- **Upon Transfer Fax the following documents to the accepting facility:** 12 L ECG, ED Record, Lab Results, Current Medication Record, ND STEMI documentation

#### ***Patients with a contraindication to transfer or PCI/Medical Therapy Option:***

- Documentation of contraindication or Patient refusal to transfer for PCI or medical treatment
- Aspirin within 24 hours of hospital arrival, and aspirin at discharge
- Beta blocker at discharge
- High intensity statin at discharge
- P2Y12 (Plavix or Brilinta) at discharge
- STEMI patients who smoke receive smoking cessation counseling at discharge
- Scheduled Cardiology Consultation within 1-2 weeks at discharge
- Cardiac Rehabilitation referral at discharge

Revised 5/2022

# ND STEMI Guideline (ST-Segment Elevation Myocardial Infarction)

Revised 5/2022



MISSION:  
LIFELINE

## Diagnostic Criteria for STEMI

- ST elevation at the J point in at least 2 contiguous leads of  $\geq 2$  mm (0.2 mV) in men or  $\geq 1.5$  mm (0.15 mV) in women in leads V2–V3 and/or of  $\geq 1$  mm (0.1 mV) in other contiguous chest leads or the limb leads.
- New or presumably new LBBB at presentation occurs infrequently, may interfere with ST-elevation analysis, and should not be considered diagnostic of acute myocardial infarction (MI) in isolation. If doubt persists, immediate referral for invasive angiography may be necessary. Consult with Cardiology.
- ECG demonstrates evidence of ST depression suspect of a Posterior MI consult with PCI receiving center
- If initial ECG is not diagnostic but suspicion is high for STEMI obtain serial ECG at 5–10-minute intervals

**ACTIVATE EMS TRANSFER TEAM**

**ACTIVATE STEMI ALERT at Receiving PCI Hospital**

### STANDARD ORDERS & LABS

- Apply Continuous Cardiac Monitor
  - Insert (2) peripheral IV large bore Saline lock
  - Troponin (hs-cTn preferred)
  - BMP  Magnesium
  - CBC  Glucose
  - INR  aPTT
- Do not delay transfer awaiting results

### CONSIDER:

Estimated transfer time in minutes to PCI facility take into account first medical contact time:

Air: \_\_\_\_\_ and/or Ground: \_\_\_\_\_

**ASSESS:** Symptom Onset Date: \_\_\_\_\_ Time: \_\_\_\_\_

**Code Status**  Full Code  DNR

*-If patient wishes to remain DNR Status, consult receiving facility MD prior to initiation of transfer*

**REVIEW:** Thrombolytic Contraindications Page 7

### OPTIONAL MEDICATION

- Nitroglycerin IV** or 0.4 mg SL  
-Hold for inferior MI  
-Evaluate if erectile dysfunction or pulmonary hypertension medications taken in the past 24 hours including: Sildenafil (Viagra, Revatio), Vardenafil (Levitra, Staxyn), or Avanafil (Stendra), Tadalafil (Cialis, Adcirca). -Hold nitrates for 48 hours following the last dose.
- Analgesia as needed**
- Ondansetron** (Zofran) 4 mg PO or IV
- Metoprolol Tartrate**  25 mg PO  
**CONTRAINDICATION FOR METOPROLOL TARTRATE:** *Do not give if any of the following: signs of heart failure or shock, heart rate less than 60 or more than 110, systolic blood pressure less than 100-, second- or third-degree heart block, severe asthma, or reactive airway disease*

**Choose One Reperfusion Pathway**

Time of First Medical Contact to PCI arrival Expected to be **LESS THAN  $\leq$  100 minutes**

**PRIMARY PCI**  
**Direct to CATH LAB for Emergent PCI**

- Aspirin** 324 mg chewed or 300mg rectally
  - Ticagrelor (Brilinta) 180 mg PO preferred OR**
    - Clopidogrel (Plavix) 600 mg PO**  
-DO NOT give both Plavix & Brilinta
  - Heparin IV Bolus** (60 Units/kg, max 4,000 Units)
  - Transport patient directly** to Cath Lab for PCI (Percutaneous Coronary Intervention)
    - Goal Arrival to Departure < 30 minutes unless awaiting air transport
  - Oxygen as needed** to keep SpO2 90-94%
- DO NOT give Thrombolytics **TNKase, rPA, or TPA**

Time of First Medical Contact to PCI arrival anticipated to be **GREATER THAN  $\geq$  100 minutes**

**THROMBOLYTIC Therapy**

- Aspirin** 324 mg chewed or 300mg rectally
- Tenecteplase IV (TNKase)** per attached protocol
  - Facility Arrival to lytic administration goal **LESS THAN  $\leq$  30 minutes**
- Plavix 300 mg PO**  
-If patient > 75 yrs. consult with cardiologist and reduce dosage to 75 mg PO
- Heparin IV Bolus** (60 Units/kg, max 4,000 Units)
- Heparin IV Drip** (12 Units/kg/hr., max 1,000 Units/hr.)
- Transport patient urgently directly** to PCI capable hospital
  - Goal Arrival to Departure < 45 minutes unless awaiting air transport

## ND STEMI (ST-Segment Elevation Myocardial Infarction) Guideline

Tenecteplase (TNKase) Dosing			Weight:	lb.	kg	Height:	in.	Age:	yrs.																																																																											
Patient weight (kg)	TNK (mg)	TNK (mL)																																																																																		
Less than 60 kg	30 mg	6 mL	<b>Allergies:</b> _____ <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 60%;">Medication</th> <th style="width: 10%;">Dose</th> <th style="width: 10%;">Time Start</th> <th style="width: 10%;">Time Stop</th> <th style="width: 10%;">RN (Initials)</th> </tr> </thead> <tbody> <tr> <td>Aspirin (81 mg chew x 4)</td> <td>324 mg</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Ticagrelor (Brilinta) PO (PPCI therapy arm only) -Do not give ticagrelor (Brilinta) and Plavix together</td> <td>180 mg</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Clopidogrel (Plavix) PO PPCI therapy dose</td> <td>600 mg</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Clopidogrel (Plavix) PO Lytic therapy dose If &gt;75 y/o, give 75mg</td> <td>300 mg 75mg</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Heparin IV Bolus PCI Dose 60 U/kg, max 4000 Units Lytic Dose 60 U/kg, max 4000 Units</td> <td>Units</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Heparin IV Infusion Lytic Dose 12 U/kg/hr. max 1000 U/hr.</td> <td>Units/hr.</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Tenecteplase (TNKase) IV -Do not give ticagrelor (Brilinta) with Lytic (TNK)</td> <td>mg (= mL)</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Nitroglycerin Sublingual -Erectile Dysfunction Medication within past 24 hrs. <input type="checkbox"/> Yes <input type="checkbox"/> No</td> <td>0.4 mg 0.4 mg 0.4 mg</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Nitroglycerin IV Infusion</td> <td>mcg/min</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Morphine Sulfate IV</td> <td>mg</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Fentanyl IV</td> <td>mcg</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Ondansetron (Zofran) PO</td> <td>4 mg</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Ondansetron (Zofran) IV</td> <td>4 mg</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Metoprolol Tartrate 25 mg or 50 mg PO</td> <td>mg</td> <td></td> <td></td> <td></td> </tr> </tbody> </table>							Medication	Dose	Time Start	Time Stop	RN (Initials)	Aspirin (81 mg chew x 4)	324 mg				Ticagrelor (Brilinta) PO (PPCI therapy arm only) -Do not give ticagrelor (Brilinta) and Plavix together	180 mg				Clopidogrel (Plavix) PO PPCI therapy dose	600 mg				Clopidogrel (Plavix) PO Lytic therapy dose If >75 y/o, give 75mg	300 mg 75mg				Heparin IV Bolus PCI Dose 60 U/kg, max 4000 Units Lytic Dose 60 U/kg, max 4000 Units	Units				Heparin IV Infusion Lytic Dose 12 U/kg/hr. max 1000 U/hr.	Units/hr.				Tenecteplase (TNKase) IV -Do not give ticagrelor (Brilinta) with Lytic (TNK)	mg (= mL)				Nitroglycerin Sublingual -Erectile Dysfunction Medication within past 24 hrs. <input type="checkbox"/> Yes <input type="checkbox"/> No	0.4 mg 0.4 mg 0.4 mg				Nitroglycerin IV Infusion	mcg/min				Morphine Sulfate IV	mg				Fentanyl IV	mcg				Ondansetron (Zofran) PO	4 mg				Ondansetron (Zofran) IV	4 mg				Metoprolol Tartrate 25 mg or 50 mg PO	mg			
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<b>ABSOLUTE CONTRAINDICATIONS FOR FIBRINOLYSIS (TNK) IN STEMI</b> 1. Any prior intracranial hemorrhage 2. Known structural cerebral vascular lesion (e.g., arteriovenous malformation) 3. Known malignant intracranial neoplasm (primary or metastatic) 4. Ischemic stroke within 3 months except acute ischemic stroke within 4.5 hours 5. Suspected aortic dissection 6. Active bleeding or bleeding diathesis (excluding menses) 7. Significant closed-head or facial trauma within 3 months 8. Chest Pain/Symptom Onset > 12 hours																																																																																				
<b>RELATIVE CONTRAINDICATIONS FOR FIBRINOLYSIS: (TNK) IN STEMI</b> 1. History of chronic, severe, poorly controlled hypertension 2. Severe uncontrolled hypertension on presentation (SBP more than 180 or DBP more than 110 mmHg) 3. History of prior ischemic stroke more than 3 months, dementia, or known intracranial pathology not covered in contraindications 4. Traumatic or prolonged CPR (over 10 minutes) 5. Major surgery (within last 3 weeks) 6. Recent internal bleeding (within last 2-4 weeks) 7. Noncompressible vascular punctures 8. Streptokinase/anistreplase: prior exposure (more than 5 days ago) or prior allergic reaction to these agents 9. Pregnancy 10. Active peptic ulcer 11. Current use of anticoagulants: the higher the INR _____ 12. Symptom Onset > 6 hrs. prior to presentation consult Cardiology																																																																																				

Notes: \_\_\_\_\_

RN Name (Print): \_\_\_\_\_ RN Signature: \_\_\_\_\_ RN Initials: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_

**Data Elements in the ND State STEMI Registry**

1. **Initial Symptom Onset Time** \_\_\_\_\_  
Date: \_\_\_\_\_ Time: \_\_\_\_\_
2. **FMC EMS Agency:** \_\_\_\_\_
3. **Referring Hospital Arrival (Door-in)**  
Date: \_\_\_\_\_ Time: \_\_\_\_\_
4. **Referring Hospital 1<sup>st</sup> ECG Time:** \_\_\_\_\_
5. **STEMI ECG Time:** \_\_\_\_\_
6. **STEMI Activation (STEMI Receiving contacted)**  
Date: \_\_\_\_\_ Time: \_\_\_\_\_
7. **Referring Hospital Departure (Door-out)**  
Date: \_\_\_\_\_ Time: \_\_\_\_\_
8. **Transfer EMS Agency Name:** \_\_\_\_\_

- Call Report when patient leaves your hospital and confirm update departure time and ETA
- Copy ECG, ED physician and Nurses documentation and send with patient – DO NOT delay transport**
- Fax** All paperwork to referring Hospital (ECG, Vital Signs, Labs, Orders, Physician Order, Notes, Medication administration record)

Patient Name: \_\_\_\_\_





## Non-ST-Elevation Acute Coronary Syndrome Guideline

### Diagnostic Criteria

- New >0.5 mm ST segment depression or new >2 mm anterior T-wave inversion and/or positive biomarkers
- If patient experiences persistent or worsening symptoms obtain serial ECGs at 15–30-minute intervals to monitor for new onset ST elevation

- Contact PCI Center to arrange for transfer of patient
- Dispatch EMS service once transfer is confirmed

### ACC/AHA Guideline Based Treatment

#### **Standard orders and labs**

- Assess vital signs stat, repeat per unit routine
- Continuous cardiac monitoring (telemetry)
- Insert 1-2 large bore peripheral saline lock IV(s)
- Obtain following labs: CBC, BMP, PT/INR, PTT, Troponin I at 3 and 6 hours or hs-cTn at 2 and 4 hours (if stay is extended)
- Oxygen at 2 LPM if SpO<sub>2</sub><90%, titrate to maintain SpO<sub>2</sub> 90-94%

#### **Standard Medications**-*Discuss with accepting provider prior to administration*

- **Aspirin 324 mg** (chewable non-enteric coated 81 mg x 4) orally stat x 1 or if patient is unable to swallow give: **Aspirin 300 mg** rectally
- **Ticagrelor** (Brilinta) 180 mg orally stat x 1 **OR**  
**Clopidogrel** (Plavix) 300 mg orally stat x 1 (do not give both Ticagrelor and Clopidogrel)

#### **Heparin**-*Adjust dose according to weight-based protocol if patient stay is extended*

- **Heparin 60 units/kg IV bolus** (max bolus 4000 units)
- **Heparin IV drip 15 units/kg/hr.** (max 1000 units/hr.)

#### **Optional Labs**

- BNP, HCG

#### **Optional Medications**

- **Nitroglycerine** 0.4 mg SL every 5 minutes x 3 as needed for chest discomfort
- **Nitroglycerine** IV continuous infusion as needed for chest pain  
*-Hold Nitro if recent phosphodiesterase inhibitor, 24 h of sildenafil or vardenafil, or within 48 h of tadalafil.*
- For severe uncontrolled pain, consider use of **Morphine** or other narcotic analgesic of choice IV as needed.
- **Ondansetron** (Zofran) 4 mg IV as needed for nausea/vomiting x 1
- **Metoprolol Tartrate** (Lopressor) 25 mg orally x 1  
*-Hold Beta Blocker if Signs of heart failure or shock, SBP less than 110, Heart rate less than 60 bpm or heart block, severe asthma, or reactive airway disease*

- Transfer patient to PCI center for possible early invasive strategy
- Send with or fax the following documents to accepting facility: 12L ECG, ED record, lab results, current medication record, EMS record

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# Cardiac Testing

Revised 5/2022

## Diagnostic Testing may include:

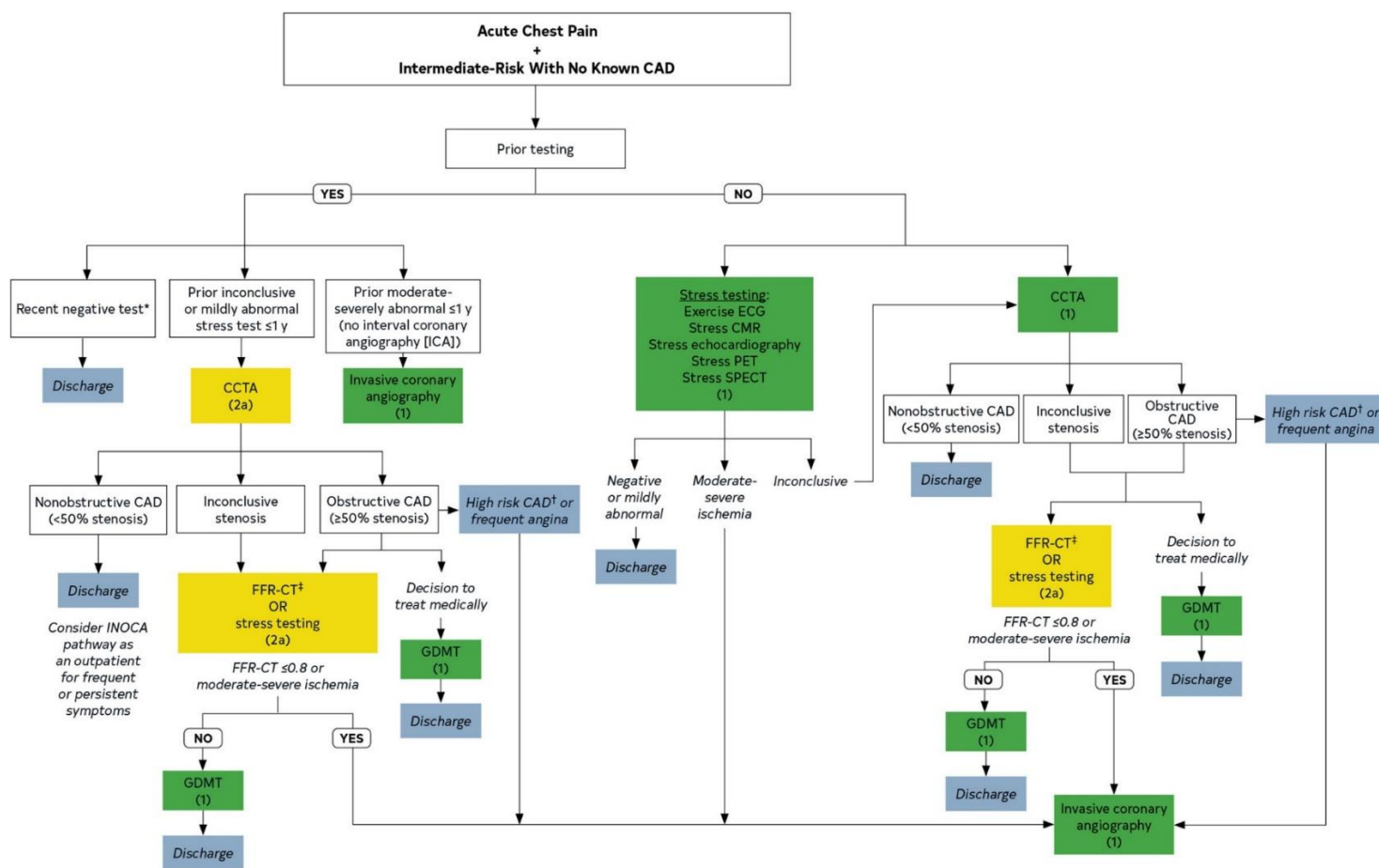
- Exercise ECG Coronary Computed Tomography Angiography
- Echocardiography/Stress Echocardiography Invasive Coronary Angiography
- Stress Nuclear (PET or SPECT) Myocardial Perfusion Imaging
- Cardiovascular Magnetic Resonance Imaging

## Anatomic Testing may include:

- Coronary Computed Tomography Angiography
- Invasive Coronary Angiography

For further direction on choosing proper provocative testing, see attached algorithms from the 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Chest Pain Guideline and cardiac testing algorithms:

- Patients With Suspected ACS at Intermediate Risk With No Known CAD
- Patients With Suspected ACS at Intermediate Risk With Known CAD

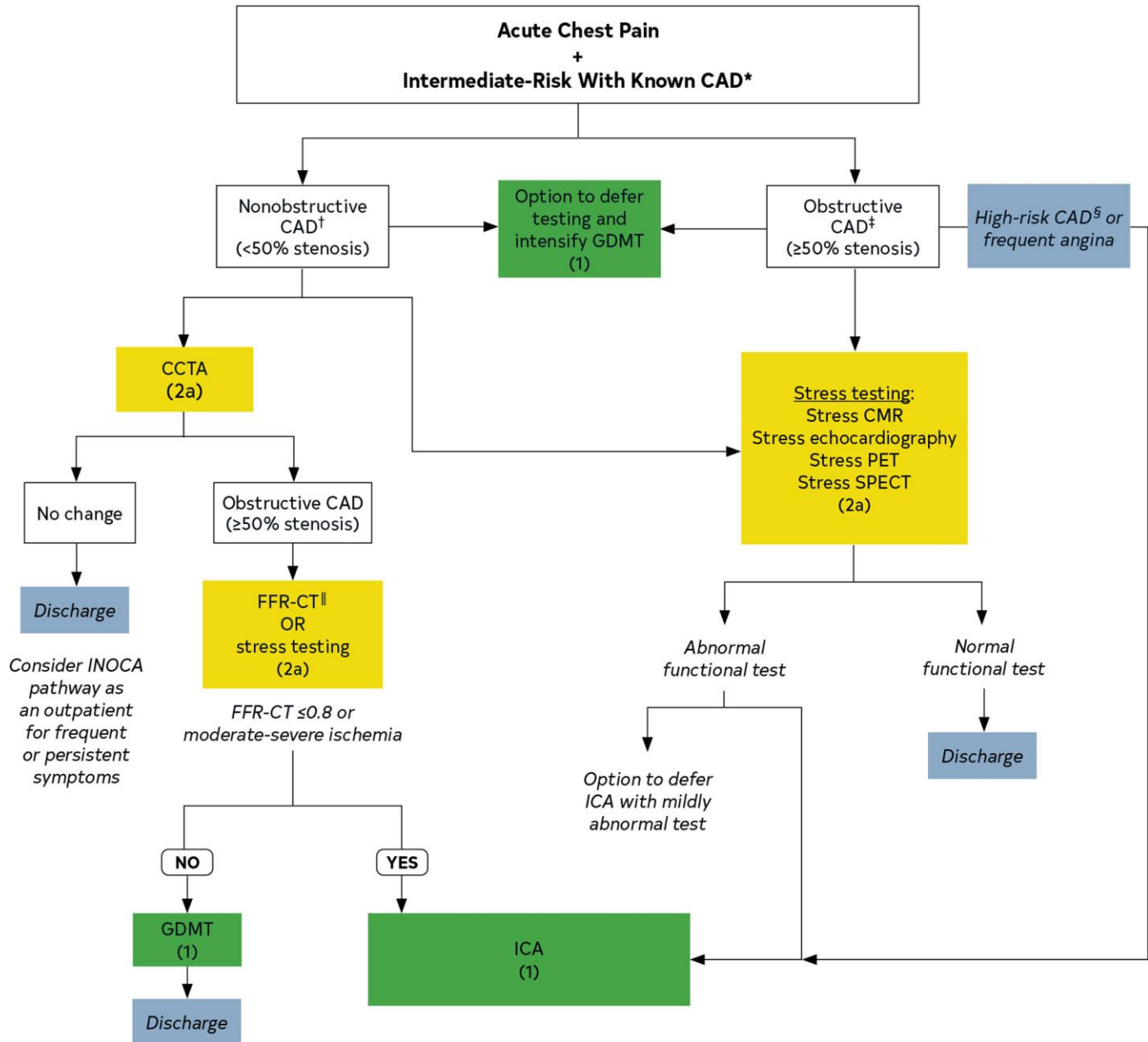


**Figure 9. Evaluation Algorithm for Patients With Suspected ACS at Intermediate Risk With No Known CAD**

Test choice should be guided by local availability and expertise. \*Recent negative test: normal CCTA  $\leq 2$  years (no plaque/no stenosis) OR negative stress test  $\leq 1$  year, given adequate stress. †High-risk CAD means left main stenosis  $\geq 50\%$ ; anatomically significant 3-vessel disease ( $\geq 70\%$  stenosis). ‡For FFR-CT, turnaround times may impact prompt clinical care decisions. However, the use of FFR-CT does not require additional testing, as would be the case when adding stress testing. CAD indicates coronary artery disease; CCTA, coronary CT angiography; CMR, cardiovascular magnetic resonance imaging; CT, computed tomography; FFR-CT, fractional flow reserve with CT; GDMT, guideline-directed medical therapy; ICA, invasive coronary angiography; INOCA, ischemia and non obstructive coronary artery disease; PET, positron emission tomography; and SPECT, single-photon emission CT.

## Cardiac Testing

Revised 5/2022



**Figure 10. Evaluation Algorithm for Patients With Suspected ACS at Intermediate Risk With Known CAD**

Test choice should be guided by local availability and expertise. \*Known CAD is prior MI, revascularization, known obstructive or nonobstructive CAD on invasive or CCTA. †If extensive plaque is present a high-quality CCTA is unlikely to be achieved, and stress testing is preferred ‡Obstructive CAD includes prior coronary artery bypass graft/percutaneous coronary intervention. §High-risk CAD means left main stenosis  $\geq 50\%$ ; anatomically significant 3-vessel disease ( $\geq 70\%$  stenosis). ¶FFR-CT turnaround times may impact prompt clinical care decisions. ACS indicates acute coronary syndrome; CAD, coronary artery disease; CCTA, coronary CT angiography; CMR, cardiovascular magnetic resonance; CT, computed tomography; FFR-CT, fractional flow reserve with CT; GDMT, guideline-directed medical therapy; ICA, invasive coronary angiography; INOCA, ischemia and no obstructive coronary artery disease; PET, positron emission tomography; and SPECT, single-photon emission CT.

**Reference:** 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines J Am Coll Cardiol. Oct 28, 2021. Published DOI: 10.1016/j.jacc.2021.07.053