Provincial Clinical Knowledge Topic

Non-ST-Elevation Acute Coronary Syndromes (NSTE-ACS), Adult – Emergency Department

V 1.0

Revision History

Version	Date of Revision	Description of Revision	Revised By
1.0	June 2018	Version 1 of topic completed	see Acknowledgments

Important Information Before You Begin

The recommendations contained in this knowledge topic have been provincially adjudicated and are based on best practice and available evidence. Clinicians applying these recommendations should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care. This knowledge topic will be reviewed periodically and updated as best practice evidence and practice change.

The information in this topic strives to adhere to Institute for Safe Medication Practices (ISMP) safety standards and align with Quality and Safety initiatives and accreditation requirements such as the Required Organizational Practices. Some examples of these initiatives or groups are: Health Quality Council Alberta (HQCA), Choosing Wisely campaign, Safer Healthcare Now campaign etc.

Guidelines

This topic is based on the following guidelines:

1. 2015 ESC Guidelines for the management of acute coronary syndrome in patients presenting without persistent ST-segment elevation[1]

2. 2014 ACC/AHA guideline for the management of patients with non-ST-elevation acute coronary syndromes[2]

Goals of Management

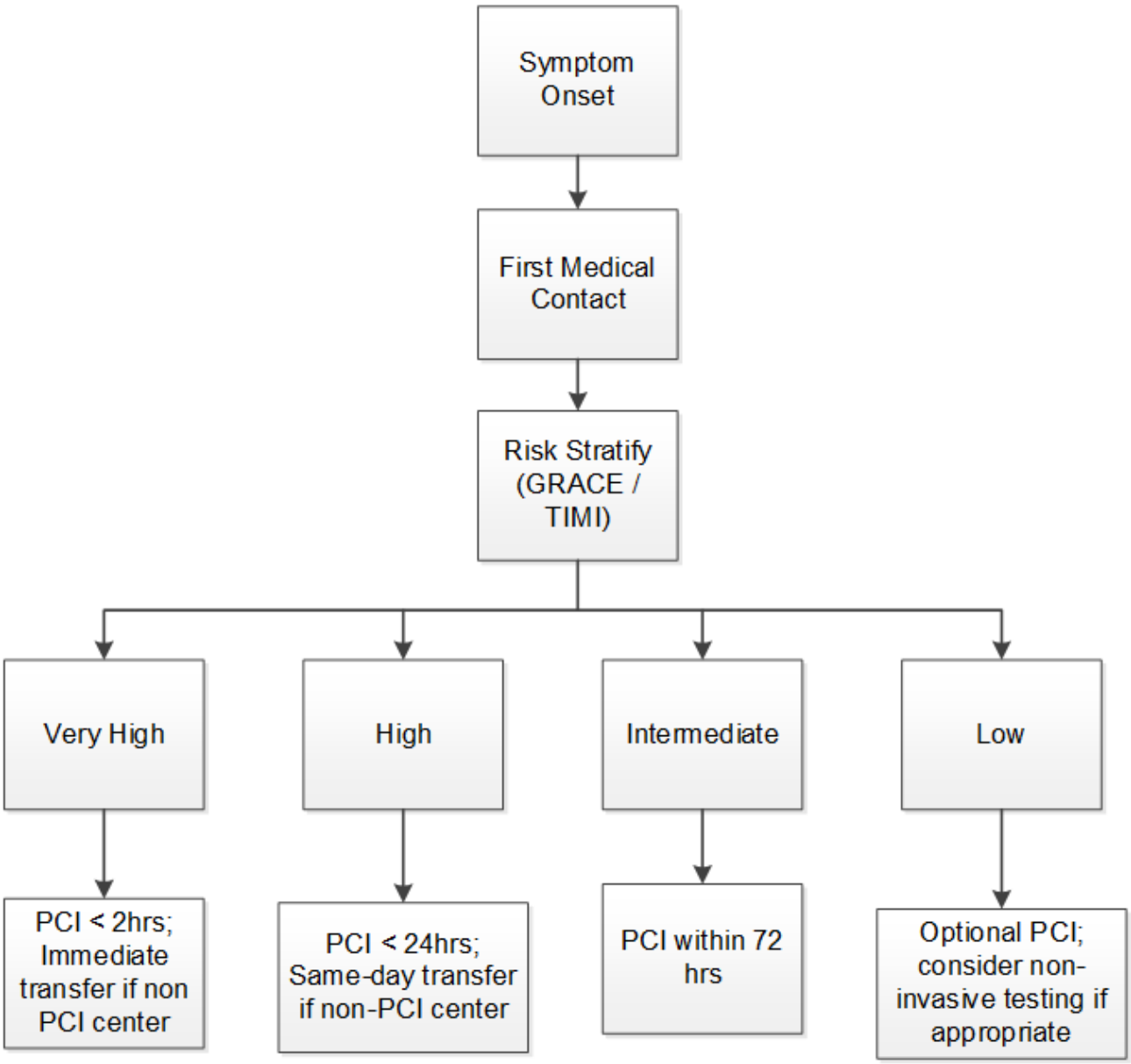
1. Early diagnosis of Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS) via early completion of 12-lead ECG and cardiac biomarkers in patients with symptoms suggestive of acute coronary syndrome (ACS)
2. Initiation of antiplatelet therapy and anti-ischemic / analgesic therapy
3. Initiation of antithrombotic therapy in the appropriate patient
4. Risk-stratify the patient using a validated risk stratification tool (TIMI Risk Score; GRACE Risk Score)
5. Consider disposition to a service / centre capable of percutaneous coronary intervention (PCI), the urgency of which is dictated by risk level (see Clinical Decision Support below)

Clinical Decision Support

Thrombolysis in Myocardial Infarction (TIMI) Risk Score
Online calculator may be found at:
https://www.mdcalc.com/timi-risk-score-ua-nstemi

GRACE Risk Score
Online calculator may be found at:
http://www.gracescore.org/WebSite/default.aspx?ReturnUrl=%2f

Figure 1: Timing of invasive strategy in NSTE-ACS



*Adapted from ESC NSTEMI Guidelines 2015[1]; PCI = percutaneous coronary intervent**ion***

Textual Decision Making Information

1. **Diagnosis:**
   - Identify patients at initial ED presentation who exhibit signs / symptoms suggestive of acute coronary syndrome (ACS) and obtain ECG within 10 minutes of patient arrival to facilitate early diagnosis of NSTE-ACS.
     - Clinicians should retain an index of suspicion for ACS even in the absence of classic ischemic chest pain, especially in patients who are elderly, female, and/or diabetics. Serial ECGs should be performed every 15 to 30 minutes in patients with initially non-diagnostic ECG and ongoing symptoms suggesting cardiac ischemia. Early of detection of STEMI transformation has critical management implications (if a STEMI is diagnosed, please refer to the ***ST-Elevation Myocardial Infarction (STEMI), Adult - Emergency Department Clinical Knowledge Topic***).
     - Presence of high-risk ECG changes, for example De Winter's Peaked T waves in the anterior leads in conjunction with ST depression, should be recognized and prompt an earlier Cardiology Consult regarding the need for urgent reperfusion
     - See ***Chest Pain, Suspected Cardiac, Adult - Emergency Department Clinical Knowledge Topic*** regarding initial workup of suspected cardiac chest pain in the Emergency Department and details of cardiac biomarker testing

2. **Initial Anti-Ischemic and Supportive Care:**
   - Hemodynamic instability is not common in NSTE-ACS, but should be addressed with emergent reperfusion (consultation with the on-call interventional cardiologist will be required)**.**
     - A missed STEMI or transformation to STEMI must be considered if a patient with NSTE-ACS develops hemodynamic instability (if a STEMI is diagnosed, please refer to the ***ST-Elevation Myocardial Infarction (STEMI) – Adult Emergency Department Clinical Knowledge Topic***). Supportive therapies in addition to reperfusion may include intravenous fluids, vasoactive medications, and/or mechanical support, tailored to the individual patient circumstances. Norepinephrine is preferred over doPAMine in patients with cardiogenic shock requiring vasoactive medical therapy due to a lower risk of death and cardiac arrhythmias.
   - Patients with symptoms and/or ECG suggestive of ACS should receive acetylsalicylic acid (ASA) 160 mg chewed in the absence of a history of true ASA allergy (see **Antiplatelet Therapy**, below (See *Chest Pain, Suspected Cardiac, Adult - Emergency Department Clinical Knowledge Topic)*
   - Nitrates may be titrated to relieve symptoms of ischemia and/or pulmonary edema in patients who are not hypotensive and who have not recently taken a phosphodiesterase inhibitor type 5 (e.g. sildenafil within 24 hours, tadalafil within 48 hours)
   - Oxygen should be administered to patients with room air saturations less than 90%
   - Patients who are not hypoxic should not receive supplemental oxygen
   - Beta-blockers should be administered early to patients with NSTE-ACS and ongoing symptoms of ischemia who lack contraindications to their use (hypotension / cardiogenic shock, acute heart failure, bradycardia, 2nd/3rd-degree heart block without a pacemaker, PR greater than 0.24 seconds, active asthma, vasospasm / cocaine-related ischemia, known poor LV function)
     - In patients with NSTE-ACS and ongoing ischemic symptoms and contraindications to the use of beta-blockers, Nitrates should be maximally titrated. If Nitrates have been maximally titrated (e.g. intolerable headaches, hypotension), a non-dihydropyridine calcium channel blocker (CCB; e.g. diltiazem) should be

administered in the absence of contraindications (hypotension, bradycardia, significant LV dysfunction, increased risk for cardiogenic shock, 2nd/3rd-degree AV block without a pacemaker, PR greater than 0.24 seconds)

- Morphine may be considered for additional analgesia in patients unresponsive to nitrates or beta-blockers / calcium channel blockers

3. Antiplatelet Therapy:

- All patients without true ASA allergy should receive chewable acetylsalicylic acid (ASA)
- 160 mg PO once as soon as possible after ED presentation and then enteric coated ASA 81 mg PO daily.
- A $P2Y_{12}$ inhibitor should be administered to patients with confirmed / highly probable NSTE-ACS in the absence of an excessive risk of bleeding:
  - ticagrelor (180 mg PO once and then 90 mg PO BID) should be preferentially administered in the absence of contraindications (history of intracerebral hemorrhage or active bleeding)
    OR
  - clopidogrel (300 mg PO once and then 75 mg PO daily) should be administered when ticagrelor cannot be used or in patients requiring chronic ongoing anticoagulation

*** Note: The timing of ticagrelor or clopidogrel inhibitor administration in patients planned for an invasive strategy is not adequately studied to recommend for or against treatment prior to angiography*

4. Antithrombotic Therapy:

- Anticoagulation should be administered at the time of diagnosis in addition to antiplatelet therapy. The following agents may be considered**:**
  - fondaparinux 2.5 mg subcutaneously every 24 hours
    - If CrCl LESS THAN 30 mL/min, fondaparinux is contraindicated.
  - enoxaparin 1 mg/kg subcutaneously every 12 hours. Always clarify the dose with pharmacy if the patient weighs greater than 100 kg.
    - If eGFR LESS THAN 30 mL/min, consider 1 mg/kg every 24 hours.
    - If eGFR LESS THAN 15 mL/min, enoxaparin is contraindicated; consider UFH.
  - Unfractionated heparin bolus dose followed by infusion. Dosing will depend on whether PCI is imminent and whether GPIIb/IIIa inhibitor use is planned during PCI and thus should be discussed with the interventional cardiologist. Unfractionated heparin bolus dosing and infusion rates should be in compliance with local protocols. Unfractionated heparin is the anticoagulant of choice in the setting of Chronic Kidney disease, especially if CrCl less than 15.

5. Other Therapies:

- Statins should be administered orally within the first 24 hours of presentation within NSTE-ACS if there are no contraindications (true allergy or previous rhabdomyolysis, intractable myalgia, or hepatic toxicity).
- ACE-inhibitors or Angiotensin-Receptor Blockers should be administered orally within the first 24 hours of presentation within NSTE-ACS if there are no contraindications

6. **Disposition:** Figure 1 outlines an approach to the urgency of angiography / revascularization in patients with NSTE-ACS. The timing of invasive treatment is determined by a combination of hemodynamic stability, ongoing symptoms, ECG findings, troponin levels, and standardized risk scoring (e.g. GRACE or TIMI scores)
    - In patients categorized as low risk, an 'ischemia-guided strategy' may be considered wherein the need for invasive investigation (i.e. angiography / PCI) is determined by the results of non-invasive testing (e.g. myocardial perfusion imaging)

Order Set Components

Name of Order Set: Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS) Adult Emergency Order Set

Order Set Keywords: acute coronary syndrome, heart attack, NSTEMI, NSTE-ACS
Order Set Requirements: Grace Scoring tool and TIMI score available as reference

Goals of Care Designation

Conversations leading to the ordering of a Goals of Care Designation (GCD), should take place as early as possible in a patient's course of care. The Goals of Care Designation is created, or the previous GCD is affirmed or changed resulting from this conversation with the patient or, where appropriate, the Alternate Decision-Maker.

Complete the Goals of Care Designation (GCD) Order Set within your electronic system, or if using paper process, complete the Provincial Goals of Care Designation (GCD) paper form (http://www.albertahealthservices.ca/frm-103547.pdf)

Laboratory Investigations - STAT

Hematology

- ☐ Complete Blood Count (CBC)
- ☐ PT (INR)
- ☐ Partial Thromboplastin Time (PTT)

Chemistry

- ☐ Electrolytes (Na, K, Cl, CO2)
- ☐ Glucose random level
- ☐ Creatinine
- ☐ Urea
- ☐ Troponin, STAT
- ☐ Troponin, time-specific _____:_____ *(hh:mm)*

Blood Gases

Consider in patients with Oxygen Saturations of less than 90%, in most patients a VBG (in lieu of ABG is appropriate)

- ☐ Blood Gas Venous *(Caution!! Accuracy of results is affected by tourniquet use. Draw sample without a tourniquet)*
- ☐ Blood Gas Arterial – Current Therapy

In admitted patients, consider:

- ☐ Magnesium
- ☐ ALT

Diagnostic Imaging

General Radiography

Consider to assess for alternative causes of chest pain; be mindful of avoiding delays to reperfusion therapy

- ☐ GR Chest, 2 Projections (Chest X-ray PA and Lateral)
- ☐ GR Chest, 1 Projection portable (Chest X-ray Portable)

Other Investigations

Electrocardiogram (ECG)

- ☐ Electrocardiogram – 12 Lead, STAT
- ☐ Electrocardiogram – 12 Lead, time specific: _____:____ *(hh:mm)*
- ☐ Electrocardiogram – 12 Lead, serial: every _____ min, stop after _____ times
- ☐ Electrocardiogram – 12 Lead, STAT if recurrence of chest pain (conditional order)
- ☐ Electrocardiogram – 15 Lead, STAT *(consider if signs of inferior ischemia or anterior ST depression)*

Intravenous Therapy

- ☐ Intravenous Cannula – Insert: Initiate IV
- ☐ IV Peripheral Saline Flush/Lock: Saline Lock

IV Bolus or Rapid Infusion

- ☐ 0.9% NaCl infusion _____ mL as fast as possible

Maintenance IV Solutions

- ☐ 0.9% NaCl infusion at _____ mL/hour
- ☐ D5W - 0.9% NaCl infusion at _____ mL/hour
- ☐ D5W - 0.45% NaCl infusion at _____ mL/hour
- ☐ Other: _____ *(specify fluid)* at _____ mL/hour

Medications

Administer acetylsalicylic acid (ASA) CHEW tab to ALL patients with suspected NSTE-ACS unless true allergy *(see Clinical Decision Support)*

- ☐ acetylsalicylic acid CHEW tab (ASA) 160 mg PO STAT once UNLESS already administered during current presentation **and then** ASA enteric coated 81 mg PO daily

Anti-ischemic Agents

Consider if systolic BP is greater than 100 mmHg AND patient has chest pain

- ☐ nitroglycerin SL spray or tablets (each dose delivers 0.3 - 0.4 mg nitroglycerin) 1 spray or tablet sublingually every 5 minutes PRN for 3 doses ; Notify authorized prescriber if persistent symptoms after 3 doses; HOLD if SBP less than 100 mmHg

OR

- ☐ nitroglycerin IV continuous – dosing as per local institutional practices until provincial orders available. Titrate to resolution of chest pain AND/OR STOP if SBP < 100mmHg.

OR

- ☐ nitroglycerin **patch;** HOLD if SBP less than 100 mmHg

  Choose ONE:

  - ☐ 0.4 mg/hr topically, apply now, remove after 12 hours
  - ☐ 0.6 mg/hr topically, apply now, remove after 12 hours
  - ☐ 0.8 mg/hr topically, apply now, remove after 12 hours
  - ☐ _____ mg/hr topically, apply now, remove after 12 hours

Consider metoPROLOL if no contraindications and persistent symptoms of myocardial ischemia despite other anti-ischemic therapy, including nitroglycerin.

Suggest 12.5 - 50 mg PO per dose

- ☐ metoPROLOL ____ mg PO once (HOLD if HR LESS than 60 bpm or SBP LESS than 100 mmHg)

Antiplatelet Agents

Administer one of the following IN ADDITION TO acetylsalicylic acid (ASA) to patients with high suspicion of NSTE-ACS

Choose ONE:

- ticagrelor 180 mg PO once **and then** 90 mg PO BID (preferred unless patient has history of intracerebral hemorrhage)

  OR
- clopidogrel 300 mg PO once **and then** clopidogrel 75 mg PO daily (select if ticagrelor cannot be used or if oral anticoagulation is also being used)

Antithrombotic Agents

Administer one of the following to all patients with high suspicion / proven NSTE-ACS

Choose ONE:

- fondaparinux 2.5 mg subcutaneously every 24 hours (contraindicated if CrCl LESS than 30 mL/min)

  OR
- enoxaparin (1 mg/kg)_____ subcutaneously BID (1 mg/kg subcutaneously daily if CrCl less than 30 mL/min; contraindicated if eGFR less than 15 mL/min); review dose after 72 hours

  OR
- unfractionated heparin as per local facility's nomogram

Opiate Analgesia

Consider opiate analgesia if persistent symptoms of ischemic chest pain despite maximal anti-ischemic therapy.

For "susceptible patients" defined as elderly, frail, low body mass, systemically unwell, or on medications known to cause sedation or lower blood pressure we recommend decreasing narcotic dosing by 50%.

- Notify physician or nurse practitioner for reassessment if pain not controlled after administration of maximum dosage.

Recommend avoiding the simultaneous use of more than one opiate analgesic

Suggest 0.5 mg for moderate pain and 1 mg for severe pain

- HYDROmorphone 1 mg IV once
- HYDROmorphone 0.5 to 1 mg IV every 10 minutes PRN for pain (maximum 3 mg total)
- HYDROmorphone _____ mg IV every _____ minutes PRN for pain

Suggest 2.5 mg for moderate pain and 5 mg for severe pain

- morphine 5 mg IV once
- morphine 2.5 to 5 mg IV every 10 minutes PRN for pain (maximum 15 mg total)
- morphine _____ mg IV every _____ minutes PRN for pain

Suggest 25 mcg for moderate pain and 50 mcg for severe pain

- fentaNYL 50 micrograms IV once
- fentaNYL 25 to 50 micrograms IV every 5 minutes PRN for pain (maximum 200 mcg total)
- fentaNYL _____ micrograms IV every _____ minutes PRN for pain

Antiemetics

Avoid dimenhyDRINATE in patients 65 years of age or older due to increased risk of side effects including delirium. Suggest 25 mg for mild/moderate nausea, 50 mg for moderate/severe nausea

- dimenhyDRINATE 50 mg IV/PO once
- dimenhyDRINATE 25 to 50 mg IV/PO every 4 hours PRN for nausea/vomiting

Antiemetics continued…

Oral administration or slow infusion via IVPB are preferred for metoclopramide to reduce the risk of akathisia. Suggest 5 mg for mild/moderate nausea or if CrCl less than 40 mL/min; 10 mg for moderate/severe nausea, and CrCl over 40 mL/min

- metoclopramide 5 mg IV/PO once as well
- metoclopramide 10 mg IV/PO once
- metoclopramide 5 to 10 mg IV/PO every 6 hours PRN for nausea/vomiting

- ondansetron tab 8 mg PO every 8 hours PRN for nausea/vomiting
- ondansetron tab _____ mg PO every _____ hours PRN for nausea/vomiting

4 mg starting dose recommended for IV ondansetron
Avoid ondansetron in patients with prolonged QTc interval

- ondansetron 4 mg IV once
- ondansetron 4 mg IV every 8 hours PRN for nausea/vomiting
- ondansetron _____ mg IV every _____ hours PRN for nausea/vomiting

Due to high cost, should only be used for patients with difficulty swallowing tablets or capsules or for patients actively vomiting without established IV access.

- ondansetron DISINTEGRATING tab 8 mg PO every 8 hours PRN for nausea/vomiting
- ondansetron DISINTEGRATING tab _____ mg PO every _____ hours PRN for nausea/vomiting

Patient Care

Diet / Nutrition

- NPO
- NPO – May Have Sips, May Take Meds

Monitoring

- Vital Signs (perform baseline respiratory rate, pulse, blood pressure, temperature, oxygen saturation and repeat with any chest pain or equivalent symptom)
- Bedside Cardiac Monitoring - Continuous
- Oxygen Saturation Monitoring - Continuous

Respiratory Care

If oxygen saturation is already adequate (GREATER than 90%), no supplemental oxygen is required

- O2 Therapy titrated to maintain oxygen saturation greater than or equal to 90%
- Notify physician if O2 flow required to be increased by greater than 2 L to maintain the same level of oxygenation, if there is a progressive increase in work of breathing, hypotension, or decreased or altered level of consciousness (LOC).

Transitions and Referrals

- Consult interventional cardiology; Reason _____
- Consult cardiology; Reason _____
- Consult internal medicine; Reason _____
- Consult critical care; Reason _____

Admission/Transfer/Discharge Planning

1. Admission to hospital is the general rule for patients diagnosed with NSTE-ACS
2. A significant percentage of patients will require transfer to a centre capable of percutaneous coronary intervention at some point during their admission.
    a. See Figure 1 and Clinical Decision Support section, above, for guidance on the timing of transfer for PCI in NSTE-ACS
    b. Transfer may not be appropriate for patients with extensive comorbidities for whom the risks of revascularization outweigh the potential benefits. Patients whose goals of care are incompatible with an invasive strategy may also be managed at non-PCI-capable centres

Rural Considerations

- Timing / necessity of transfer to a center capable of invasive therapy (PCI)

Analytics

1. Improved selection of anticoagulants for a given patient population in the setting of NSTE-ACS
2. Rates of MACE (Major Adverse Cardiovascular Event) within 30, 60, and 90 days
3. Early recognition of NSTE-ACS transformation to STEMI
4. Early Objective Risk Stratification
5. Time to initial ECG

References

1. Roffi M, et. al. 2015 ESC Guidelines for the management of acute coronary syndrome in patients presenting without persistent ST-segment elevation. Eur Heart J 2016;37:267-315.
2. Amsterdam EA, Wenger NK, Brindis RG, Casey Jr DE, Ganiats TG, Homes Jr DR, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ. 2014 ACC/AHA guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology / American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130:e344-e426.
3. Alnasser SM, Huang W, Gore JM, et al. Late Consequences of Acute Coronary Syndromes: Global Registry of Acute Coronary Events (GRACE) Follow-up. *Am J Med*. 2015;128:766-775.

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