

**Nova Scotia Guidelines For
Non-ST Elevation Acute Coronary Syndrome (NSTEMACS)**

SYNOPSIS

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Diagnosis of NSTEMACS

Clinical history

- Obtain a clinical history and perform a physical examination immediately.

ECG monitoring

- Establish continuous electrocardiogram (ECG) monitoring and secure venous access during initial assessment, to facilitate rapid detection and treatment of arrhythmias.
- Obtain a standard 12-lead ECG within 10 minutes of first medical contact.

Troponin measurement

- Obtain blood for troponin measurement on presentation, and other key blood work (e.g. blood glucose [BG], creatinine, complete blood count) as soon as possible after ECG is obtained. If initial troponin is not elevated then measurement should be repeated 6–12 hours later, as levels may not rise for several hours after onset of symptoms.

Imaging investigations

- A chest x-ray should be performed in the majority of patients, and other investigations considered as appropriate to the clinical circumstances (e.g. computed tomography [CT] imaging, echocardiography). **Additional imaging investigations should not unnecessarily delay treatment for definite Acute Coronary Syndrome (ACS).**

Definitions

- If non-ST elevation acute coronary syndrome (NSTEMACS) is suspected, once troponin result is available, determine whether appropriate diagnostic label is unstable angina (normal troponin) or non-ST elevation myocardial infarction (non-STEMI; elevated troponin).
- The definition of MI should be according to the diagnostic criteria proposed by the American College of Cardiology and the European Society of Cardiology.

Risk stratification

- Perform risk stratification early based upon history, physical findings and investigation results and repeat as clinical situation evolves.

Immediate Treatment of Suspected NSTEMI/ACS

Oxygen

- Oxygen (O₂) should be administered immediately (2–6 L/min) to patients with suspected ACS who have evidence of respiratory distress or hypoxemia (O₂ saturation <90%).

Antiplatelet therapy

- Acetylsalicylic acid (ASA) (160–325 mg non-enteric coated oral loading dose) should be administered immediately and continued throughout the hospital stay (81–325 mg once daily) in all patients with suspected ACS who do not have contraindications and who have not been taking ASA previously. The dose should be minimized (81 mg once daily) in patients also taking clopidogrel or warfarin, to help reduce the risk of bleeding complications.
- Patients with contraindications to ASA, regardless of age, should be treated immediately with clopidogrel (300-mg oral loading dose).
- Clopidogrel (300-mg oral loading dose) should be administered in addition to ASA as soon as possible to patients with definite NSTEMI/ACS who do not have bleeding or other contraindications.
- Clopidogrel (75 mg once daily) should be continued throughout the hospital stay in patients with definite NSTEMI/ACS who do not have bleeding or other contraindications, and who are not scheduled to undergo early (within 5 days) coronary artery bypass surgery.

Nitroglycerin

- Nitroglycerin (0.3–0.6 mg every 5 minutes; total of 3 doses) should be administered sublingually (spray or tablet) to hemodynamically stable patients with suspected ACS and continuing symptoms.
- Intravenous (IV) nitroglycerin (10–200 µg/min infusion) can be considered in patients with continuing symptoms, despite administration of O₂, sublingual nitroglycerin and a beta blocker.

Beta blocker therapy

- Immediate administration of a beta blocker should be considered in hemodynamically stable patients with suspected ACS, particularly if they have continuing symptoms. Oral treatment is recommended in most cases, but IV therapy (e.g. IV metoprolol 5 mg every 5 minutes, up to 3 times) can be

considered in hemodynamically stable patients with continuing symptoms despite administration of O₂ and nitroglycerin.

Morphine

- Morphine (2–4 mg IV or subcutaneously [SC]) or other opiate analgesics can be considered in hemodynamically stable patients with suspected ACS and continuing severe symptoms despite administration of O₂, nitroglycerin and a beta blocker.

Additional Immediate Treatment

Glycoprotein IIb/IIIa receptor inhibitor therapy

- For patients with definite NSTEMACS and refractory ischemia or other high-risk features, IV infusion of a small molecule platelet glycoprotein IIb/IIIa receptor inhibitor (eptifibatide or tirofiban) should be considered in patients without bleeding or other contraindications. Early triage to the cardiac catheterization laboratory should be discussed with the on-call interventional cardiologist.

Fondaparinux

- The factor Xa inhibitor fondaparinux is the **preferred** antithrombin drug for definite NSTEMACS in Nova Scotia.
- Fondaparinux (2.5 mg SC on the day of admission, followed by 2.5 mg once daily thereafter) should be administered immediately to the majority of patients with definite NSTEMACS who do not have bleeding or other contraindications.
- In fondaparinux-treated patients who go on to percutaneous coronary intervention (PCI), fondaparinux can be discontinued after the procedure in the majority of patients. In patients managed with a conservative strategy, fondaparinux can be continued until hospital discharge if necessary, to a maximum of 8 days.

Unfractionated heparin

- Unfractionated heparin (UFH) should be used instead of fondaparinux in patients with definite NSTEMACS under the following circumstances:
 - severe renal impairment (creatinine clearance <30 mL/minute)
 - patients with mechanical heart valves
 - patients with very high-risk features mandating urgent (within 12 hours) cardiac catheterization, PCI or coronary artery bypass surgery

Cardiac Catheterization and Revascularization

Triage for cardiac catheterization and revascularization

- Access to cardiac catheterization and revascularization should be prioritized according to risk.
- NSTEMI patients are typically at significantly higher risk of death and recurrent MI than patients with unstable angina. The majority of NSTEMI patients should therefore be considered for early cardiac catheterization provided the benefits of invasive assessment and revascularization are felt to outweigh the risks. Conversely, lower-risk unstable angina patients need not necessarily undergo early cardiac catheterization, provided that non-invasive testing rules out easily inducible or widespread myocardial ischemia.
- Important considerations when weighing the benefits and risks of cardiac catheterization and revascularization include:
 - presence of peripheral arterial disease that might affect arterial access
 - renal function and anticipated risk of contrast nephropathy/renal failure
 - bleeding risk
 - ability to tolerate and comply with prolonged dual antiplatelet therapy in the event of drug-eluting stent insertion
 - patient frailty and fitness/willingness to undergo an invasive procedure
 - cognitive issues that might affect ability to provide procedure consent
 - other major life-threatening illness
- The following features should be considered in determining the need for and timing of cardiac catheterization:
 - High-risk features** (catheterization \pm PCI within 24–48 hours; Coronary Artery Bypass Grafting (CABG) within 3–5 days)
 - hypotension^a or definite evidence of heart failure
 - recurrent ventricular arrhythmias
 - transient ST elevation
 - new ST depression ≥ 2 mm in ≥ 3 leads
 - recurrent or refractory ischemia despite initial therapy^b
 - TIMI risk score 5–7
 - ^a with other supportive evidence of ischemia
 - ^b definite new or dynamic ST segment changes required to justify urgent status in patients with unstable angina (normal troponin level)
 - Intermediate-risk features** (catheterization \pm PCI within 3–5 days; CABG within 2–3 weeks)
 - NSTEMI with no high-risk features, but known left ventricular ejection fraction (LVEF) $< 40\%$
 - TIMI risk score 3–4

Low-risk features (catheterization \pm PCI within 5–7 days; CABG within 5–7 weeks)

- NSTEMI with no high- or intermediate-risk features^c
- suspected unstable angina with recurrent symptoms but no ECG changes
- unstable angina with easily inducible (<3 METs) or widespread ischemia on non-invasive testing, or some other marker of increased risk^d
- TIMI risk score 1–2^e

^c low-risk NSTEMI patients can have invasive assessment deferred to an early outpatient setting (<2 weeks) provided that non-invasive testing does not indicate easily inducible (<3 METs) or widespread ischemia or some other marker of increased risk^d

^d e.g. hypotensive response, sustained ST depression, exercise-induced ventricular tachycardia, large territory of reversible ischemia, multiple perfusion defects, low LVEF <40%

^e low-risk unstable angina patients with a TIMI risk score of 1–2 need not necessarily undergo early invasive assessment if non-invasive testing rules out easily inducible or widespread ischemia

Mode of revascularization

- In general, the factors influencing the most appropriate mode of revascularization (PCI or CABG) in patients with NSTEMACS should be the same as for patients with stable coronary artery disease (CAD). PCI is usually preferred in patients with single and double-vessel CAD not involving the left main stem. CABG is strongly preferred in patients with left main stem disease and usually preferable in patients with multi-vessel disease, especially when associated with poor left ventricular systolic function and/or diabetes.

Treatment of hyperglycemia/diabetes

- Tight glycaemic control is advised for all NSTEMACS patients who present with hyperglycemia (random blood glucose [BG] >11.0, or fasting BG >7.0 mmol/L).
- During the first 48 hours there should be a low threshold for use of insulin to maintain a BG of 7.0–10.0 mmol/L. After 48 hours, standard diabetes management is recommended including oral antihyperglycemic agents and/or insulin as appropriate.
- Caution is recommended in considering the use of thiazolidinediones in patients with cardiovascular disease.
- The long-term therapy goals should conform to the current Canadian Diabetes Association guidelines: fasting BG 4.0–7.0 mmol/L and A1C \leq 7.0%, if achievable safely.

Pharmacologic Secondary Preventive Therapy

Antiplatelet therapy

- ASA (81–325 mg once daily) should be continued indefinitely in all NSTEMI/ACS patients without contraindications. The dose of ASA should be minimized (81 mg once daily) in patients also taking clopidogrel or warfarin to help reduce the risk of bleeding complications.
- Clopidogrel (75 mg once daily), in addition to ASA, is recommended on discharge for all definite NSTEMI/ACS patients in the absence of contraindications. The duration of clopidogrel therapy should be tailored according to patient risk and the type of stent inserted in those who undergo PCI. (See Table 1, below.)

Table 1. Recommended duration of clopidogrel therapy

Recommended clopidogrel duration	Patients not undergoing PCI	Patients undergoing PCI
3 months	Patients at low risk of recurrent events	Patients at low risk of recurrent events treated only with bare metal stent
12 months	Patients at increased risk of recurrent events ^a	Patients receiving ≥1 drug-eluting stent (DES) or who are at increased risk of recurrent events ^a regardless of stent type
>12 months	Patients at very high risk of recurrent events ^b	Some patients receiving multiple (≥3) DES or undergoing complex PCI ^c or patients at very high risk of recurrent events ^b regardless of stent type

^a e.g. second ACS within 12 months, complex or extensive CAD (especially if not amenable to revascularization), associated peripheral arterial or cerebrovascular disease

^b e.g. patients with degenerate saphenous vein bypass grafts or who also have peripheral vascular **and** cerebrovascular disease

^c DES implanted in left main stem or bifurcation configuration

Beta blocker therapy

- Beta blocker therapy should be initiated early and continued throughout hospitalization in all patients with definite NSTEMI/ACS and no contraindications.
- The majority of patients with definite NSTEMI/ACS should be considered for long-term beta blocker therapy in the absence of contraindications or side effects. Long-term therapy may not be necessary or appropriate in low-risk patients (e.g. normotensive patients with preserved left ventricular systolic function who have been completely revascularized).

- Use of cardioselective beta blockers is generally recommended in NSTEMI patients with preserved left ventricular function. Preferred agents in patients with left ventricular systolic dysfunction are bisoprolol and carvedilol.
- In patients with ongoing symptoms, with contraindications to beta blockade, treatment with a calcium channel blocker can be considered. Short-acting dihydropyridines should be avoided. Non-dihydropyridines (verapamil and diltiazem) should be avoided in patients with a LVEF <40%.

Lipid-lowering therapy

- HMG CoA reductase inhibitors (statins) are recommended for the majority of patients with definite NSTEMI in the absence of contraindications, irrespective of baseline lipid values.
- The choice of statin and the dose initiated should take into consideration the long-term lipid targets for patients with established CAD recommended by the Canadian Cardiovascular Society.
 - *Primary target:* LDL-C <2.0 mmol/L
 - *Secondary targets:* TC to HDL-C ratio <4; in patients with established atherosclerosis, treatment to lower LDL-C by at least 50% is generally appropriate
- Some patients may require combination therapy with other agents, such as ezetimibe, niacin or fibrates to achieve their target lipid values.

Angiotensin-converting enzyme inhibitor therapy

- No randomized clinical trials have specifically tested the safety and efficacy of angiotensin-converting enzyme (ACE) inhibitors in patients with NSTEMI. These agents should be used selectively in patients with definite NSTEMI who are felt to be at specifically increased risk of adverse cardiac events.
- In the absence of contraindications, long-term treatment with an ACE inhibitor is recommended in NSTEMI patients with:
 - Congestive heart failure (CHF) during hospitalization or LVEF <40%
 - diabetes mellitus
 - hypertension
 - extensive CAD
 - definite peripheral arterial or cerebrovascular disease
- Long-term ACE inhibitor therapy may not be appropriate or necessary in low-risk patients, e.g. normotensive, non-diabetic patients with preserved left ventricular systolic function and minor CAD.
- NSTEMI patients with contraindications to, or who are intolerant of, ACE inhibitors and who are felt to be at increased risk of adverse events can be considered for treatment with an angiotensin receptor blocker.

Table 2. Glycemic, BP and lipid targets

Parameter	Target
A1C	≤7.0%
BP Patients without diabetes Patients with diabetes or chronic kidney disease	<140/90 mm Hg <130/80 mm Hg
LDL-C*	<2.0 mmol/L
TC to HDL-C ratio**	<4.0
LDL-C lowering**	≥50%

* Primary target; ** Secondary targets,
A1C = glycated hemoglobin, BP = blood pressure, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol

Non-pharmacologic Secondary Preventive Therapy

Smoking cessation

- Cigarette smokers should be urged to quit in order to reduce their risk of recurrent cardiac events and death. Exposure to second-hand smoke should also be avoided.
- Referral to a local smoking cessation program should be arranged.

Diabetes education

- NSTEMI patients with diabetes should be offered initial and ongoing needs-based diabetes education in a timely manner to enhance self-care practices and behaviours.
- Referral to a Diabetes Education Centre for ongoing education and management of diabetes and cardiac risk factors is recommended.

Nutrition intervention

- A heart-healthy diet is recommended. Such a diet is limited in sodium (<2.4 g/day), cholesterol (<200 mg/day), total fat (<25-35% of total energy intake), saturated (<7%) and trans fats, and carbohydrates, and increased in monounsaturated (up to 20%) and polyunsaturated fats (up to 10%), and fruits and vegetables. Other therapeutic diet modifications may be needed according to co-morbidities; written nutrition information to this effect should be provided.
- Patients should be encouraged to achieve and maintain a healthy weight (body mass index [BMI] 18.5–24.9 kg/m²) and waist circumference (<102 cm men; <88 cm women). Overweight and obese patients should be offered support and advice. Dietary energy content should be aimed at reducing body weight by ~10% from baseline. With success, further weight loss can be attempted to achieve a BMI of <27 kg/m² and ideally <25 kg/m².

- A clinical dietitian should be consulted for a comprehensive nutrition assessment in nutritionally compromised patients.

Exercise

- Regular, moderate-intensity aerobic exercise for 30–60 minutes most days of the week is recommended. Exercise training in a medically supervised environment should be considered for moderate- and high-risk patients.

Secondary prevention programs for cardiovascular disease

- Secondary prevention programs are recommended, particularly for patients with multiple modifiable risk factors and for moderate- to high-risk patients in whom supervised exercise training is warranted.
- Referral to secondary prevention programs should be arranged prior to hospital discharge. Program entry should be within the recommended time frame of 30 days.

Other Aspects of Management and Follow-up

Analgesic therapy

- In patients with chronic musculoskeletal or other pain, the requirement for analgesic therapy should be assessed prior to discharge. ASA and small doses of narcotics are the preferred analgesic options. Nonsteroidal anti-inflammatory drugs (NSAIDs) with increasing degrees of COX-2 selectivity should be avoided.

Patient education about activities of daily living

- Patients should be given specific instructions about physical and sexual activity, driving and return to work before discharge.

Role of the family physician

- It is anticipated that family physicians will play a central role in long-term risk factor modification by ensuring that ACS patients receive appropriate lifestyle counselling and evidence-based secondary preventive drug therapy. Family physicians should ensure that drug doses are evidence-based and titrated when appropriate, in pursuit of recommended glycemic, BP and lipid targets. (See Table 2.)

Screening for depression

- Depression is common, frequently under-recognized and correlates with a poorer prognosis in ACS patients. Specialists and family physicians should screen for depression and refer/treat accordingly.

Influenza vaccination

- As recommended by Health Canada, the majority of patients with CAD should receive annual influenza vaccination.