Acute Coronary Syndromes

Unstable Angina and Non–ST Elevation Myocardial Infarction

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KEYWORDS

• Unstable angina • Non–ST elevation MI • Acute coronary syndromes • Management • Revascularization • Antiplatelet • Antithrombotic

KEY POINTS

- Improvements in primary prevention and acute management strategies have led to a reduction in in-hospital mortality associated with non–ST elevation acute coronary syndromes (NSTE-ACS); however, the incidence of NSTE-ACS continues to be stable, largely because of an aging population and use of highly sensitive biomarkers for diagnosis of myocardial injury.
- Newer antiplatelet agents, including prasugrel and ticagrelor, have been shown to have superior efficacy compared with clopidogrel and have been approved for the treatment of patients with NSTE-ACS as an alternative to clopidogrel and as part of oral dual antiplatelet therapy.
- Early invasive strategy with diagnostic angiography and intervention within 12 to 24 hours is a reasonable treatment strategy in all NSTE-ACS, especially in the highest-risk patients.
- Early revascularization after NSTE-ACS is beneficial in patients with mild to moderate chronic kidney disease.
- A statin of high to moderate intensity should be administered to all patients with NSTE-ACS by hospital discharge without using the low-density lipoprotein–cholesterol as a target goal.

Unstable angina (UA) and non–ST elevation myocardial infarction (NSTEMI) are collectively known as non–ST elevation acute coronary syndromes (NSTE-ACSs). Improvements in prevention strategies and acute treatments for NSTE-ACSs led to marked improvement in their outcomes. According to data from the National Registry of Myocardial Infarction (1990–2006), in-hospital NSTEMI mortality declined significantly from 7.1% to 5.2%, which was partially attributable to improvements in acute treatments.[1] In the Worcester registry, the 1-year postdischarge case fatality rates for NSTEMI declined from 23.1% in 1997 to 18.7% in 2005.[2] In contrast, the increased sensitivity of new biomarkers for the diagnosis of myocardial infarction (MI) and the increasing prevalence of cardiovascular (CV) risk factors (such as diabetes and obesity) resulted in their increased incidence and prevalence (**Fig. 1**). Data from Kaiser Permanente Northern California showed that the adjusted mortality decreased significantly for NSTEMI between 1999 and 2008, but the age-adjusted and sex-adjusted incidence rate of hospitalizations did not change significantly over time.[3] Therefore, NSTE-ACSs remain common causes of morbidity and mortality in the United States.

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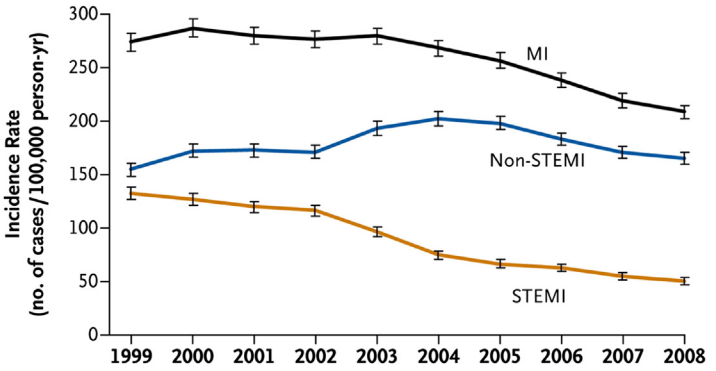

Fig. 1. Age-adjusted and sex-adjusted incidence rates of acute MI, 1999 to 2008. STEMI, ST elevation MI. (*From* Yeh RW, Sidney S, Chandra M, et al. Population trends in the incidence and outcomes of acute myocardial infarction. N Engl J Med 2010;362(23): 2155–65; with permission.)

PATHOPHYSIOLOGY

UA and NSTEMI are characterized by an acute imbalance between myocardial oxygen supply and demand. The most common cause is coronary artery narrowing from a disrupted atherosclerotic plaque with superimposed acute thrombosis that suddenly and significantly compromises coronary blood flow but is usually not 100% occlusive (as in ST elevation MI [STEMI]).[4] Additional causes include coronary artery spasm, severe luminal narrowing from atherosclerosis or restenosis after percutaneous coronary intervention (PCI), and coronary dissection as well as extrinsic factors (such as severe hypotension, tachycardia, anemia, and thyrotoxicosis) in the setting of underlying luminal narrowing of the coronary arteries by atherosclerosis.

DIAGNOSIS AND RISK STRATIFICATION

Medical history, physical examination, electrocardiograms (ECGs), and an initial measurement of cardiac biomarkers should be done rapidly to develop a working diagnosis, establish the acuity of the event and the hazards of death and adverse events, and promptly triage patients to the appropriate treatment strategy. Serial ECGs and measurements of cardiac biomarkers of necrosis are critical to the accurate diagnosis of NSTE-ACS and are complemented by echocardiography, coronary angiography, and other imaging modalities. NSTE-ACS usually presents with ischemic symptoms (angina pectoris or its equivalent) along with new ST segment depression or prominent T-wave inversion on the ECG. The presence of increased biomarkers, usually an increase and/or decrease in cardiac troponin (cTn) value exceeding the 99th percentile upper limits of normal, confirms myonecrosis and differentiates NSTEMI from UA (**Box 1**).[5]

Risk stratification using various scoring systems such as the TIMI (Thrombolysis in Myocardial Infarction),[6] GRACE (Global Registry of Acute Coronary Events),[7] and the PURSUIT (Platelet glycoprotein IIb/IIIa in Unstable agina: Receptor Suppression Using Integrilin)[8] risk scores have been developed to assess patients' prognosis and help guide clinical decision making. All patients with NSTE-ACSs should undergo initial medical stabilization; early administration of antiplatelet, antithrombotic, and anti-ischemic drugs; and should be treated appropriately with either an early invasive or initial conservative strategy depending on their initial risk assessment (**Fig. 2**).

ANTIPLATELET THERAPY

Aspirin

Multiple trials have shown the benefits of aspirin, including improved survival, in patients with ACS.[9–12] Aspirin inhibits cyclooxygenase-1 within the platelet preventing the formation of thromboxane A2 and thus inhibiting platelet aggregation.[13] Aspirin should be administered to all patients with NSTE-ACS as soon as possible after hospital presentation and continued indefinitely thereafter.[14] Doses of aspirin between 75 mg and 1500 mg showed similar reduction in vascular effects but are associated with a dose-dependent increase in bleeding hazards. Thus, following the acute hospitalization period, it is reasonable to use a maintenance dose of 81 mg of aspirin per day in preference to higher maintenance doses in patients with NSTE-ACS. Patients allergic to aspirin should be placed on clopidogrel indefinitely or should undergo aspirin desensitization.

Clopidogrel

Clopidogrel, the most widely used thienopyridine, causes irreversible inhibition of the $P2Y_{12}$ receptor and inhibits platelet aggregation by a different