



Diagnosis and management of acute coronary syndrome

Diagnostic et prise en charge du syndrome coronarien aigu

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Abstract The prevalence of cardiovascular disease is growing rapidly in developing countries, leading to an increasing incidence of acute coronary syndrome (ACS). The modalities available for diagnosing and treating this disease continue to evolve, and considerations must be made of local resources when making diagnostic and therapeutic choices. This article provides an evidence-based guide to the management of ACS, with specific recommendations for clinicians working in low and middle-income countries (LAMICs). Diagnosis of ACS, including both non ST-elevation (NSTEMI) and ST elevation (STEMI) ACS, focuses on risk stratification, vigilance for subtle or atypical presentations, and consideration of alternative causes of chest pain. The diagnostic process involves assessment of risk factors, knowledge of high yield history and physical exam findings (including variations that may exist in various populations), and utilization of appropriate diagnostic tests. Aspirin should be used as initial treatment in conjunction with an additional anti-platelet drug. Prasugrel is preferred over clopidogrel if the patient is having STE-ACS and planned for percutaneous coronary intervention (PCI). Bivalirudin should be the first choice for anti-coagulation in STE-ACS, followed by enoxaparin (which does not require a drip), and then unfractionated heparin. For the patient with NSTEMI-ACS and an increased bleeding risk, fondaparinux should be considered in place of enoxaparin. Oxygen should be administered to patients with breathlessness, signs of heart failure, shock, or arterial oxymoglobin saturation less than 94%. Beta blockade should be given if there are no signs of instability such as heart rate greater than 100 beats per minute or hypotension. Nitrates or morphine may be given to control symptoms, but do not confer morbidity or mortality advantages

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and are therefore not critical if a patient is comfortable. PCI should be performed if indicated and available. Fibrinolysis should be administered instead if delay to PCI would be greater than 90 min.

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Abstract La prévalence des maladies cardiovasculaires connaît une croissance rapide dans les pays en développement, entraînant une incidence croissante du syndrome coronarien aigu (SCA). Les modalités de diagnostic et de traitement de cette maladie continuent d'évoluer, et il convient de tenir compte des ressources locales lors de la réalisation d'un diagnostic et la détermination des options thérapeutiques. Cet article constitue un guide à la prise en charge du SCA fondé sur l'expérience, et fournit des recommandations spécifiques destinées aux médecins hospitaliers travaillant dans les pays à bas et moyen revenu. Le diagnostic du SCA, y compris les SCA sans élévation du ST et avec élévation du ST, se concentre sur la stratification du risque, la vigilance relative aux manifestations subtiles ou atypiques, et la prise en considération d'autres causes des douleurs poitrinaires. Le processus de diagnostic implique l'évaluation des facteurs de risque, la connaissance des antécédents médicaux défavorables et les conclusions de l'examen physique (des variantes étant susceptibles d'exister dans les différentes populations), ainsi que l'utilisation de tests de diagnostic appropriés. Il est recommandé d'utiliser de l'aspirine à titre de traitement initial, parallèlement à un antiagrégant plaquettaire supplémentaire. Le prasugrel est préféré au clopidogrel si le patient présente un SCA avec élévation du ST et qu'une intervention coronaire percutanée (ICP) est prévue. La bivaldurine devrait être le premier choix pour éviter la coagulation dans les SCA avec élévation du ST, suivie de l'énoxaparine (qui ne nécessite pas de perfusion), puis d'héparine non fractionnée. Pour les patients présentant un SCA sans élévation du ST et en cas de risque de saignement accru, le fondaparinux devrait être envisagé à la place de l'énoxaparine. Les patients souffrant de dyspnée, présentant des signes d'insuffisance cardiaque, de choc ou de saturation oxyhémoglobinée artérielle inférieure à 94% doivent se voir administrer de l'oxygène. Des bêtabloquants ne devraient être administrés que dans le cas où aucun signe d'instabilité n'est observé, comme un rythme cardiaque supérieur à 100 pulsations par minute ou de l'hypotension. Des nitrates ou de la morphine peuvent être administrés afin de contrôler les symptômes mais n'apportent aucun bénéfice en termes de morbidité ou de mortalité, et ne sont donc pas essentiels si le patient n'est pas mal à l'aise. Une ICP ne devrait être réalisée que si cela est indiqué et qu'une telle intervention est disponible. Une fibrinolyse devrait être réalisée à la place si le délai pour réaliser une ICP est supérieur à 90 min.

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Introduction

Cardiovascular disease (CVD) is the most common cause of mortality in the world, resulting in over 17 million deaths annually.¹ This disease state can take on many different manifestations, such as rheumatic heart disease, heart failure, hypertension, stroke, and coronary artery disease (CAD). Coronary artery disease, which can cause acute coronary syndrome (ACS), is responsible for nearly half of the total worldwide deaths attributable to CVD.² In Africa, CVD is second only to infectious diseases as the most frequent etiology of death, and is the source of a substantial degree of chronic illness and disability.³

In spite of being largely preventable with modification of risk factors and appropriate medical therapy, the overall global prevalence of CVD and CAD is anticipated to rise in the coming years. These trends will disproportionately affect developing countries, and it is projected that the burden of these diseases in Africa will double.³ State of the art treatment is costly – the United States spends approximately \$300 billion annually on CVD, a cost that is expected to triple by 2030.⁴ Even when faced with limited resources, however, many effective interventions remain available to emergency physicians and other acute care providers for the management of ACS.

Pathophysiology

Acute coronary syndrome is broken down based on the presence or absence of ST elevations on the patient's electrocardiogram (ECG). Atherosclerotic plaques accumulate within the coronary arteries over time, with stenotic lesions of at least 60% resulting in ischemia to the myocardium with exertion. These unstable lipid-rich plaques may acutely rupture, leading to platelet activation and formation of a thrombus. This process may cause a sudden stenosis or frank occlusion, which in turn restricts blood flow to the myocardium and, coupled with vasospasm and reperfusion injury, leading to myocyte death.⁵

Definition

As set forth by the Global Myocardial Infarction (MI) Task Force, the definition of MI has been refined multiple times to account for the increasing sensitivity of biomarker assays (i.e., cardiac troponin) and the variety of conditions in which these biomarkers may be present. Fundamentally, the diagnosis requires evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia. The most recent revision of these guidelines include separate thresholds for cardiac tro-

ponin in peri-procedural patients, specifically in the context of recent percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).⁶

The clinical and epidemiological need for a definition of MI that does not require cardiac biomarker testing for use in resource-constrained settings has been acknowledged, and additional criteria have been developed by the WHO (Table 1). Fulfilling the diagnosis of a “probable MI” outlined in Category C of Table 1 involves ruling out alternative explanations for the patient’s symptoms, strategies for which are discussed below.

Diagnosis

The diagnosis of ACS can pose a difficult clinical challenge. The presenting complaints can be myriad and atypical, and even a classic description of ischemic chest pain may in fact represent a pulmonary embolus, an aortic dissection, or another life-threatening process (Tables 2 and 3). Vital signs and addressing the ABC’s are the first step in the approach to these patients. Obtaining a rapid history and physical exam with particular attention paid to breath sounds, heart sounds, the presence of jugular venous distension, and peripheral circulation can help rule in or rule out time-sensitive diagnoses like tension pneumothorax and pericardial tamponade (Table 2).

An important early objective in working up patients presenting with potential ACS is risk stratification. Although no decision rule exists that allows one to definitively exclude the diagnosis of ACS based solely on history, ECG, and a single measurement of biomarkers, having knowledge of risk factors (Tables 3 and 4) and being able to appropriately stratify a patient will aid the physician in the interpretation of subsequent test results as well as in determining the disposition.⁸

Risk stratification should begin by screening for diagnoses that require emergent intervention, and an ECG should be the initial screening tool to look for evidence of ischemic heart disease. The management algorithm will be determined by the presence or absence of ST elevations (STE-ACS, also known as STEMI) (Table 5), although in the patient with persisting chest pain and a negative initial ECG, serial studies may reveal an early and evolving AMI. Prolonged “door-to-ECG” times greater than 10 min have been linked with adverse clinical outcomes in patients presenting with STE-ACS.¹²

Additional ECG features, such as left bundle-branch blocks (LBBB), may make a clear-cut diagnosis of STE-ACS difficult. Some ST-segment patterns are suggestive of an MI in this setting: 1. ST-segment pattern 1 mm or greater and concordant (in the same direction as the main deflection) with the QRS complex, 2. ST-segment depression 1 mm or more in leads V1, V2, or V3, or 3. ST-segment elevation 5 mm or greater and discordant with the QRS complex.¹³ If suspicion for an MI is high in a patient with an LBBB that is presumed to be new (or similarly, if ventricular pacing is present), the patient should be considered for immediate angiography and reperfusion.¹⁴

Serum cardiac biomarkers should be obtained if available, although therapy should not wait for these results in the presence of STE-ACS. The recent development of highly sensitive troponin assays will enable the physician to detect the presence (or absence) of an acute myocardial infarction within 3 h of

onset, rather than the 6–8 h required with traditional troponin-I assays.¹⁵

Ancillary imaging studies such as chest X-ray and cardiac ultrasound can aid in further refining of the differential diagnosis. More sophisticated imaging tests, such as CT coronary angiography, have been demonstrated to provide a reliable anatomical basis for excluding ACS and to allow safe, expedited discharge from the ED.¹⁸

If the ECG is not diagnostic of STE-ACS and cardiac biomarkers are positive, the patient can be diagnosed as having non-ST-elevated ACS (NSTEMI-ACS, also known as NSTEMI). If both ECG and serial biomarkers are negative, definitive ruling in or out of ACS may require a stress test.¹⁹ Alternatively, in a patient who is at medium or high risk, coronary angiography can define the extent of the coronary lesions as well as provide a means of re-establishing patency.

Management – pharmacology

The management of all forms of ACS is directed toward reversing the pathogenic platelet activation, thrombus formation, and vasospasm, with the goal of restoring perfusion to the distal myocardium. The primary intervention in a case of suspected or confirmed ACS is aspirin therapy, which targets platelet activation by irreversibly inhibiting cyclooxygenase 1-mediated thromboxane A2 synthesis.²⁰ This treatment alone can provide a reduction in mortality of approximately 25%.^{16,21}

In addition to aspirin administration as early out-of-hospital or emergency department management, laboratory studies have suggested that augmenting the metabolic substrate for ischemic myocardium could mitigate the extent of an eventual infarction. The IMMEDIATE trial studied the effect of giving glucose-insulin-potassium in the pre-hospital setting for suspected ACS, but did not find a difference in progression to MI or 30-day mortality when compared with glucose placebo.²² Routine oxygen therapy, even in the absence of hypoxia, would seem to be an intuitively beneficial intervention for similar reasons, although the limited trials to date have not supported this practice and have even suggested the possibility of harm.^{23,24}

Pain control should be addressed early through relief of myocardial stress and promotion of enhanced oxygen delivery. Nitroglycerin facilitates both of these goals through coronary artery dilation and redistribution of blood to ischemic regions, and is the first line therapy in the absence of hypotension or right ventricular infarction.²⁵ Morphine is considered second-line treatment, although it has not been shown to improve outcomes and in one observational study was associated with a higher adjusted risk of mortality.²⁶ Beta blockers are not recommended early in the course of an acute MI if risk factors are present for the development of cardiogenic shock, such as heart rate greater than 100 beats per minute or any episodes of hypotension.²⁷

Antagonists to the platelet P2Y12 ADP receptor, such as clopidogrel and prasugrel, have also been shown to have benefit, both as monotherapy and when used in combination with aspirin. This dual antiplatelet approach is one of the cornerstones of current therapy, although the commensurate risk of

Table 1 Criteria for acute myocardial infarction by setting (reproduced).^{6,7}

Category A: Settings without resource constraints

- Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:
 - Symptoms of ischemia.
 - New or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBBB).
 - Development of pathological Q waves in the ECG.
 - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
 - Identification of an intracoronary thrombus by angiography or autopsy.
- Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.
- Percutaneous coronary intervention (PCI) related MI is arbitrarily defined by elevation of cTn values ($> 5 \times 99$ th percentile URL) in patients with normal baseline values (≤ 99 th percentile URL) or a rise of cTn values $> 20\%$ if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischemia or (ii) new ischemic ECG changes or (iii) angiographic findings consistent with a procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.
- Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL.
- Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker values ($> 10 \times 99$ th percentile URL) in patients with normal baseline cTn values (≤ 99 th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Category B: Settings without cardiac biomarkers

- Both of the following criteria are present:
 - Symptoms of ischemia (ischemic symptoms include various combinations of chest, upper extremity, jaw or epigastric discomfort with exertion or at rest; the discomfort usually lasts ≤ 20 min, often is diffuse, not localized, not positional, not affected by movement of the region, and it may be accompanied by dyspnea, diaphoresis, nausea or syncope).
 - Development of unequivocal pathological Q waves (no pathological Q wave in the first ECG or in the event set of ECG/s followed by a record with a pathological Q wave—any Q wave in leads V2–V3 ≥ 0.02 s or QS complex in leads V2 and V3. Q-wave ≥ 0.03 s and ≥ 0.1 mV deep or QS complex in leads I, II, aVL, aVF or V4–V6 in any two leads of a contiguous lead grouping I, aVL, V6: V4–V6: II, III, aVF).
- Or, death with a history of coronary heart disease and/or documented cardiac pain within 72 h before death and no evidence of non-coronary cause of death, or autopsy evidence of chronic coronary heart disease, including coronary atherosclerosis and myocardial scarring.

Category C: Settings without means of utilizing categories A or B (probable MI)

- Either one of the following is present in a person with symptoms of ischemia (described above), without evidence of a non-coronary reason:
 - Development of unequivocal pathological Q waves.
 - Incomplete information on cardiac biomarkers (preferably troponin) provided that myocardial damage of other reasons and other clinical considerations that can cause a rise in cardiac biomarkers are excluded.
- Or, autopsy findings suggestive of MI but not conclusive.

bleeding can be substantial.²⁰ Currently, clopidogrel is commonly used in the setting of NSTEMI-ACS, while prasugrel has demonstrated marginal superiority in STE-ACS patients undergoing PCI.²⁸ The on-going Trilogy ACS study is comparing both agents in the setting of NSTEMI-ACS and findings are anticipated in the second half of 2012.²⁹

Recent trials looking at more efficacious 2nd generation P2Y₁₂ antagonists, such as ticagrelor, and PAR-1 thrombin antagonists (so-called “triple therapy”) have found success in outcomes from ischemic heart disease, but have also noted serious complications from heightened bleeding risk, particularly in patients with prior stroke.³⁰

GPIIb/IIIa inhibitors prevent platelet aggregation via the fibrinogen receptor. These agents are helpful at the time of PCI but not when given up-front in the emergency department or if fibrinolysis is pursued.¹⁶ Anticoagulation therapy such as unfractionated heparin, enoxaparin, or fondaparinux is useful prior to PCI or fibrinolysis. Bivalirudin is an anticoagulant that eliminates the need for simultaneous administration of a GPIIb/IIIa inhibitor, and as part of pre-hospital treatment of STE-ACS was found to significantly reduce the rate of CV events when compared with abciximab and heparin.³¹

Table 2 Immediate and life-threatening causes of chest pain.⁸

Acute coronary syndrome	Pericarditis with tamponade
Pulmonary embolism	Tension pneumothorax
Esophageal rupture	Aortic dissection

Lipid-lowering therapy (HMG-CoA reductase inhibition) has been demonstrated to be a powerful adjunct in secondary prevention of cardiovascular events.³² Statins should be started on all patients who suffer from an acute MI early in their hospital admission, irrespective of cholesterol concentration. Best available evidence suggests high-dose treatment with atorvastatin if tolerated by the patient.¹⁴

Management – PCI/fibrinolysis

The rationale for the difference in approach to STE-ACS versus NSTEMI-ACS is the rapidity with which blood flow must be re-established in the former to avoid irreversible transmural damage. Mortality outcomes in the event of STE-ACS worsen significantly with delay to time of definitive treatment, prompting the American College of Cardiology/American Heart Association recommendations that door-to-balloon time (from ED arrival to the catheterization lab) and door-to-needle time (ED arrival to fibrinolysis) optimally occur within 90 min and 30 min, respectively.^{33–35}

The challenge posed by meeting the 30 min target for fibrinolysis was analyzed in a study by Maharaj et al. of 3 hospitals in Cape Town, which found a median door-to-needle time of 54 min. The timing was comparable to that reported by medical centers in the Middle East, Pakistan, India, and Vancouver, and identified atypical presentations, system delays, and lack of appropriately trained clinicians as barriers.³⁵

Many fibrinolytic agents exist, although the choice of drug is less important than the rapidity with which it is administered.³⁴ First generation medications such as streptokinase are antigenic, resulting in allergic reactions in approximately 6% of patients treated. Alteplase, also known as tissue plasminogen activator (tPA), is second generation and has a shorter half-life (< 5 min), requiring IV infusion over 60–90 min.

Table 4 Risk factors for CAD chiefly derived from an international population.^{10,11}

Diabetes	Hypertension	Age and sex
Hypercholesterolemia		Obesity
Family history of CAD		Smoking history

Table 5 STE-ACS (STEMI) diagnostic criteria (reproduced).^{16,17}

American College of Cardiology/American Heart Association ST-Segment Elevation Myocardial Infarction (STEMI) Diagnosis Guidelines
In a patient presenting with active chest pain, a 12-lead electrocardiogram showing:
1. ST-segment elevation ≥ 1 mm (0.1 mV) in 2 or more adjacent limb leads
2. ST-segment elevation ≥ 1 mm (0.1 mV) in precordial leads V4 through V6
3. ST-segment elevation ≥ 2 mm (0.2 mV) in precordial leads V1 through V3, or
4. New left bundle-branch block
Therapy should not be delayed while awaiting results of cardiac biomarkers. Reciprocal depressions (ST depressions in the leads corresponding to the opposite side of the heart) make the diagnosis of STEMI more specific.

The third generation fibrinolytics such as reteplase and tenecteplase have the advantage of allowing for weight-based bolus administration³⁶, of the two, tenecteplase is often preferred, as it requires only a single dose.

Percutaneous coronary intervention (PCI) has been shown to be superior to fibrinolytic drug therapy both in reduction of mortality from re-infarction and need for eventual coronary artery bypass grafting.³⁵ Availability of PCI has historically been based at hospitals with on-site capability to perform cardiac surgery, making fibrinolysis the default option for definitive therapy at many institutions worldwide. This paradigm may currently be changing with the impressive safety profile of international centers performing primary PCI without surgical backup.³⁷

Table 3 Value of chest pain symptoms toward likelihood of acute myocardial infarction (AMI).⁹

Pain descriptor	Positive likelihood Ratio (95% CI)
Increased likelihood of AMI	• 4.7 (1.9–12)
• Radiation to right arm or shoulder	• 4.1 (2.5–6.5)
• Radiation to both arms or shoulders	• 2.4 (1.5–3.8)
• Associated with exertion	• 2.3 (1.7–3.1)
• Radiation to left arm	• 2.0 (1.9–2.2)
• Associated with diaphoresis	• 1.9 (1.7–2.3)
• Associated with nausea or vomiting	• 1.8 (1.6–2.0)
• Worse than previous angina or similar to previous MI	• 1.3 (1.2–1.5)
• Described as pressure	
Decreased likelihood of AMI	• 0.2 (0.1–0.3)
• Described as pleuritic	• 0.3 (0.2–0.5)
• Described as positional	• 0.3 (0.2–0.5)
• Described as sharp	• 0.3 (0.2–0.4)
• Reproducible with palpation	• 0.8 (0.7–0.9)
• Inframammary location	• 0.8 (0.6–0.9)
• Not associated with exertion	

In South Africa as a whole, the ACCESS study found that fibrinolysis was performed in the minority of patients, even in the absence of contraindications (Table 6). This choice of therapeutic strategy was speculated to be due to the accessibility of urgent angiography in the 29 participating sites. Overall, these hospitals were aggressive in pursuing invasive treatment relative to other countries included in the larger ACCESS registry, but also had favorable 1-year mortality outcomes and lower rates of re-admission for bleeding and recurrent ischemic events.³⁸

Special considerations

Therapeutic hypothermia

Therapeutic hypothermia (TH) can preserve neurologic function in a comatose patient following cardiac arrest, as well as provide cardiac protection by limiting infarct size in the event of STE-ACS. One of the main obstacles to more widespread use of TH in this context is the potential for delay to PCI, due to difficulties in rapid cooling to the goal temperature of 32–36 degrees centigrade. Intravenous infusion of refrigerated fluids is the quickest way to achieve this temperature, although newer surface, intranasal, and peritoneal cooling devices are currently being investigated.³⁹

Renal Dysfunction

The presence of renal dysfunction may serve as an independent risk factor for CVD. In a study by Chang et al., patients presenting to the ED with undifferentiated chest pain and comorbid renal insufficiency were at an increased 30-day risk of all cause CV events, including death, nonfatal AMI, and revascularization. Patients with an established diagnosis of ACS and renal insufficiency have been shown to have worse in-hospital mortality, even when adjusted for other factors.⁴⁰

Human immune deficiency virus (HIV)

HIV has been documented to confer risk of premature CAD and ACS. The virus itself can promote atherosclerosis through dyslipidaemia, endothelial dysfunction, and inflammation, as well as derangement of the coagulation profile leading to a pro-thrombotic state. Protease inhibitors, as a component of highly active antiretroviral therapy, are known to have similar effects. Consequently, patients with HIV, regardless of treatment status, may present with ACS at a younger age and with fewer traditional risk factors.^{41,42}

Substance abuse

Cocaine use is a common precipitant of chest pain and ACS, particularly in younger patients presenting to the ED. The pathophysiology of ACS development in this population depends on the same processes as in non-cocaine associated ACS, although the causal relationship between cocaine use and development of CAD has been debated in the literature. The largest study to date has concluded that cocaine use has not been shown to be independently associated with clinically significant CAD.⁴³

Table 6 Absolute contraindications for fibrinolysis use in ST-elevation myocardial infarction.^{14,34}

Any prior intracranial hemorrhage
Known structural cerebral vascular lesion (e.g. AVM)
Known malignant intracranial neoplasm (primary or metastatic)
Ischemic stroke within 6 months
EXCEPT acute ischemic stroke within 3 h
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses)
Significant trauma/surgery/head injury (within preceding 3 weeks)
Gastrointestinal bleeding within the past month
Non-compressible punctures in the past 24 h (e.g. liver biopsy, lumbar puncture)
ICH, intracranial hemorrhage; AVM, arteriovenous malformation

Similarly, a study by Ali et al. looked at the characteristics and outcomes of patients with ACS who also chewed khat, a plant with stimulant properties that is thought to induce coronary artery spasm. These patients were noted to have fewer CV risk factors and were less likely to have a history of CAD, but were more likely to present with STE-ACS and had worse overall outcomes over the course of 1 year.⁴⁴

Treatment summary, by therapeutic category

See Table 7 for recommended drug doses.

Antiplatelet therapy

Aspirin therapy should be given to all patients with suspected ACS (unless allergic or active gastrointestinal hemorrhage present)

- NSTE-ACS: Additionally, administer clopidogrel.
 - STE-ACS: If patient going for primary PCI, use prasugrel.
 - If prasugrel unavailable or patient is not going for PCI, use clopidogrel.

Anticoagulation

- NSTE-ACS: Enoxaparin has the best level of evidence and safety profile for initial anticoagulation.
 - If patient at increased bleeding risk, consider fondaparinux in place of enoxaparin.
 - If enoxaparin and fondaparinux unavailable, use unfractionated heparin, titrating to aPTT between 50 and 70.
- STE-ACS: If PCI planned, use bivalirudin.
 - If bivalirudin unavailable, or if there is no plan for PCI, use enoxaparin.
 - If enoxaparin unavailable, use unfractionated heparin.

Supportive care

STE-ACS or NSTE-ACS

- Provide supplemental oxygen to patients with breathlessness, signs of heart failure, shock, or an arterial oxygen saturation < 94%.

Table 7 Drug dosages in treatment of ACS.^{14,45,46}

<i>Antiplatelet therapy</i>	
Aspirin	160–325 mg (non-enteric coated)
Clopidogrel	300–600 mg PO
Prasugrel	60 mg PO
<i>Anticoagulation therapy</i>	
	Unfractionated heparin
Loading dose	
60 units/kg	
IV, followed	
by 12 units/	
kg/h IV	
Enoxaparin	NSTE-ACS: 1 mg/kg SC STE-ACS: 1 mg/kg SC + 30 mg IV
Fondaparinux	2.5 mg SC
Bivalirudin	0.75 mg/kg IV + 1.75 mg/kg/hour
<i>Anti-ischemic/supportive therapy</i>	
Nitroglycerin	0.4 mg SL q5 min – up to 3 doses
Morphine	3 – 5 mg IV, repeat every few minutes PRN
Metoprolol	25 mg PO or 5 mg IV
<i>Fibrinolytics</i>	
Tenecteplase	Single weight-based bolus: 30–50 mg IV
Retepase	10 units IV bolus, followed by another 10 units IV bolus 30 min later
Alteplase	15 mg IV bolus, followed by 0.75 mg/kg (not to exceed 50 mg) infused × 30 min, then 0.50 mg/kg (not to exceed 35 mg) infused over 1 h
Streptokinase	1.5 million units infused over 1 h
<i>Lipid-lowering therapy</i>	
Atorvastatin	80 mg daily

- Administer sublingual nitroglycerin (NTG) if patient is normotensive, does not have evidence of right ventricular ischemia, and has on-going pain. Nitrates should not be administered to patients with bradycardia (< 50/min) or tachycardia in the absence of heart failure (> 100/min), or to patients who have taken a phosphodiesterase inhibitor for erectile dysfunction within 24 h (or 48 h if tadalafil has been used). If refractory, initiate IV NTG, titrating to 10% reduction in MAP (or 30% reduction if hypertensive).
- Intravenous morphine is reasonable to use if pain is not relieved with NTG and the patient is not hypotensive or hypovolemic.
- Beta blockers (for example, metoprolol) may be considered if heart rate is 60–100 beats per minute, blood pressure is normal or elevated, and there is no concern for current or impending instability.

Revascularization

- STE-ACS: PCI is the optimal treatment modality if available within 90 min of presentation.
- If unable to perform within 90 min, or if unavailable, fibrinolytics should otherwise be administered within 30 min of presentation.
- Tenecteplase is a good first choice, as it is dosed as a single weight-based bolus.
- If tenecteplase is unavailable, alternatives include reteplase, alteplase, or streptokinase, in order of decreasing preference.
- NSTE-ACS: PCI is recommended for high-risk patients if it can be performed within 48 h.

Treatment summary, by diagnosis

See Table 7 for recommended drug doses.

NSTE-ACS or STE-ACS

- Aspirin therapy should be given to all patients with suspected ACS (unless allergic or active gastrointestinal hemorrhage present).
- Provide supplemental oxygen to patients with breathlessness, signs of heart failure, shock, or an arterial oxygen saturation < 94%.
- Administer sublingual nitroglycerin (NTG) if patient is normotensive, does not have evidence of right ventricular ischemia, and has on-going pain. Nitrates should not be administered to patients with bradycardia (< 50/min) or tachycardia in the absence of heart failure (> 100/min), or to patients who have taken a phosphodiesterase inhibitor for erectile dysfunction within 24 h (or 48 h if tadalafil has been used). If refractory, initiate IV NTG, titrating to 10% reduction in MAP (or 30% reduction if hypertensive).
- Intravenous morphine is reasonable to use if pain is not relieved with NTG and the patient is not hypotensive or hypovolemic.
- Beta blockers (for example, metoprolol) may be considered if heart rate is 60–100 beats per minute, blood pressure is normal or elevated, and there is no concern for current or impending instability.

NSTE-ACS

- Administer clopidogrel for additional anti-platelet therapy.
- Enoxaparin has the best level of evidence and safety profile for initial anticoagulation.

- o If patient at increased bleeding risk, consider fondaparinux in place of enoxaparin.
- o If enoxaparin and fondaparinux unavailable, use unfractionated heparin, titrating to aPTT between 50 and 70.
- PCI is recommended for high-risk patients if it can be performed within 48 h.

STE-ACS

- PCI is the optimal treatment modality if available within 90 min of presentation. If patient going for primary PCI:
 - o Administer prasugrel for additional anti-platelet therapy.
 - If prasugrel unavailable, use clopidogrel.
 - o Use bivalirudin for anticoagulation.
 - If unavailable, use enoxaparin. If enoxaparin unavailable, use unfractionated heparin.
- If unable to perform PCI within 90 min, or if unavailable, fibrinolytics should otherwise be administered within 30 min of presentation.
 - o Administer clopidogrel for additional anti-platelet therapy.
 - o Use enoxaparin for anticoagulation. If unavailable, use unfractionated heparin.
 - o Tenecteplase is a good first choice for fibrinolysis, as it is dosed as a single weight-based bolus. If tenecteplase is unavailable, alternatives include reteplase, alteplase, or streptokinase, in order of decreasing preference.

Conclusion

Extensive evidence has emerged from numerous clinical trials on ACS. The studies described in this paper indicate that a combination of careful history, ECG interpretation, and cardiac enzymes can allow for the reliable diagnosis of ACS. Once diagnosed, a concise set of treatments can significantly improve patient outcomes. The exact set of treatments underutilized can be adjusted to local resource availability. There is currently a global expansion of centers offering primary PCI for patients suffering STE-ACS, as well as the work toward broadening the accessibility of essential pharmacotherapy, such as the efforts toward the polypill.⁴⁷ Though the burden of cardiovascular disease and incidence of ACS are expected to increase in coming years, emergency physicians and other acute care providers in any practice setting should feel well equipped to face them.

African relevance

- In Africa, cardiovascular disease is second only to infectious diseases as the most frequent etiology of death; this paper describes current and projected acute coronary syndrome (ACS) epidemiology in Africa.
- Includes diagnostic and treatment algorithms based on most current published data, with provision of alternative strategies for clinicians in resource-limited settings.
- Offers insights into management of patients with comorbidities frequently seen in Africa, such as HIV.

What's new?

- In Africa, coronary vascular disease is second only to infectious disease as the most frequent etiology of death and its prevalence is expected to double in coming years.
- Patients with HIV, regardless of treatment status, may present with ACS at a younger age and with fewer traditional risk factors.
- Fibrinolysis has traditionally been the default option for definitive ACS therapy worldwide, although this paradigm may be changing.

Appendix A. Short answer questions

Test your understanding of the contents of this original paper (answers can be found at the end of the regular features section).

1. Which historical finding most increases the likelihood of an acute myocardial infarction?
 - a. Described as pressure
 - b. Radiation to left arm
 - c. Associated with exertion
 - d. Radiation to right arm or shoulder
 - e. Similar to previous myocardial infarction
2. Which of the following is an absolute contraindication to using fibrinolysis in ST-elevation ACS?
 - a. Suspected aortic dissection
 - b. Significant closed head trauma within 3 months
 - c. Known malignant intracranial neoplasm
 - d. Any prior ICH
 - e. All of the above
3. Which fibrinolytic agent used for acute myocardial infarction can be administered as a single weight-based bolus?
 - a. Reteplase
 - b. Tenecteplase
 - c. sAlteplase
 - d. Streptokinase
 - e. Urokinase

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