

Evaluation and Management of the Patient Who Has Cocaine-associated Chest Pain

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Erythroxylon coca, the shrub from which cocaine is naturally derived, grows indigenously in South America. Cocaine was first identified as the active alkaloid in the coca leaf in 1857. As far back as the twelfth century, Incas used cocaine-filled saliva as local anesthesia for ritual trephinations [1]. In 1884, it was recognized medically as a local anesthetic [2]. In the early twentieth century, cocaine was used briefly as an ingredient in Coca-Cola. In 1906, the United States began to control cocaine use, and in 1914 the Harrison Narcotic Act labeled cocaine as a narcotic. It became a schedule II drug in the 1970s. During the last several decades, recreational cocaine use has increased, and reports of side effects have grown exponentially. As of 2003, 34.9 million citizens of the United States (14.7%) have used cocaine at least once, with 2.3 million citizens using cocaine within the past month [3].

Pharmacology

Cocaine is absorbed through application to the mucosa, ingestion, inhalation, and direct intravenous injection. Effects from nasal insufflation begin rapidly with peak concentrations typically reached within 30 to 60 minutes. Intravenous and inhalational routes of cocaine use produce near-immediate distribution throughout the circulation. “Crack” is the direct precipitate of

free-base cocaine that results from alkalization of aqueous cocaine hydrochloride.

The relative contributions of cocaine and its metabolites to the clinical effects remain somewhat unclear. Cocaine is hydrolyzed rapidly by liver and plasma esterases to ecgonine methylester (EME), which accounts for 30% to 50% of the parent product. Nonenzymatic hydrolysis results in the formation of the other major metabolite, benzoylecgonine (approximately 40% of the parent product). The biologic half-life of cocaine is 0.5 to 1.5 hours; Benzoylecgonine and EME, the major metabolites of cocaine, have half-lives of 5 to 8 hours and 3.5 to 6 hours, respectively [4].

Minor metabolites, norcocaine and ecgonine, account for the majority of the other degradation products. Early studies suggested that cocaine and norcocaine accounted for majority of the vascular effects of cocaine [5]. Recent studies, however, demonstrate an active role for many of the metabolites. Most studies suggest that cocaine and norcocaine are the most potent vasoconstrictors; benzoylecgonine and ecgonine have less of an effect. Some studies suggest that EME may result in mild cerebral vasodilation [6,7]. Sodium-channel antagonist effects occur with cocaine and norcocaine [8]. Sodium-channel antagonist effects do not occur with benzoylecgonine or EME [8].

Cocaethylene is a unique metabolite that results from the combined use of alcohol and cocaine [9]. In clinical studies, cocaethylene produces hemodynamic effects comparable to those of cocaine. Cocaethylene has a direct myocardial depressant effect [10] that is independent of any coronary artery vasoconstriction [11]. The permeability of

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human endothelial cells to low-density lipoproteins is increased by both cocaine and cocaethylene, potentially suggesting a mechanism for the accelerated atherosclerosis seen with cocaine [12].

Pathophysiology

Cocaine has diverse actions in humans. It directly blocks fast sodium channels, stabilizing the axonal membrane, with a resultant local anesthetic effect. Blockade of myocardial fast sodium channels causes cocaine to have type I antidysrhythmic properties [13,14]. Cocaine interferes with the uptake of neurotransmitters at the nerve terminal. Cocaine functions as a vasoconstrictive agent. These three properties account for most of the toxicity seen in the clinical setting.

The initial effect on the cardiovascular system is a transient bradycardia, secondary to stimulation of the vagal nuclei. Tachycardia typically ensues, predominantly from increased central sympathetic stimulation. Cocaine has a cardiostimulatory effect through sensitization to epinephrine and norepinephrine. It prevents neuronal reuptake of these catecholamines and increases the release of norepinephrine from adrenergic nerve terminals, leading to enhanced sympathetic effects. The vasopressor effects of cocaine are mostly mediated by norepinephrine of sympathetic neural origin, and the tachycardiac effects of cocaine are mostly mediated by epinephrine of adrenal medullary origin [15].

The pathophysiology of cocaine-associated myocardial ischemia is multifactorial. Chronic cocaine users develop left ventricular hypertrophy, premature atherosclerosis, and coronary aneurysms and ectasia [16]. Acutely, cocaine causes coronary arterial vasoconstriction, in situ thrombus formation, platelet aggregation, and increased myocardial oxygen demand. The combination of increased myocardial oxygen demand (from hypertension, tachycardia, and left ventricular hypertrophy) in the setting of decreased blood flow (from atherosclerosis, platelet aggregation, and thrombus formation) and coronary vasoconstriction results in myocardial ischemia.

Cocaine produces coronary vasoconstriction of the epicardial coronaries that can be reversed by phentolamine, an alpha-adrenergic antagonist [17] and exacerbated by propranolol, a beta-adrenergic antagonist [18]. Cocaine-induced vasoconstriction occurs in both diseased and nondiseased coronary artery segments; however, the magnitude of the

effect is more pronounced in the diseased segments [19]. Tobacco smoking induces coronary artery vasoconstriction through an alpha-adrenergic mechanism similar to that of cocaine [20]. Most cocaine-using patients are also cigarette smokers, and the combination of near-simultaneous tobacco and cocaine use has a synergistic effect on epicardial coronary artery vasoconstriction [21]. Cocaine also impedes microvascular blood flow in the heart [22].

Platelet activation and thrombus formation also occur secondary to cocaine. Cocaine activates platelets directly [23] and indirectly through an alpha-adrenergic-mediated increase in platelet aggregability [24]. Adenosine diphosphate-induced platelet aggregation is enhanced [25], and tissue plasminogen activator inhibitor is increased [26] in the presence of cocaine. Thrombus formation can occur in patients who have cocaine-associated myocardial infarction (MI) whether or not underlying coronary artery disease is present [2,22].

Chronic users of cocaine may be prone to early atherosclerosis, as demonstrated by autopsy studies of young cocaine users [27–29]. Although initial reports of cocaine-associated MI emphasized a lower-than-expected prevalence of coronary artery disease, many, if not most, patients who have cocaine-associated MI have underlying coronary artery disease. Large clinical series have found that 31% to 67% of patients who have cocaine-associated MI have atherosclerotic coronary artery disease [2,16,22,27]. Coronary artery disease is less common in patients who have MI associated with cocaine than in cocaine-free patients; however, it is still more common than in controls [22]. Chronic cocaine use has also recently been associated with coronary artery ectasia and aneurysms [16]. In a consecutive series of 112 cocaine users who underwent angiography, 30% had coronary ectasia and aneurysms. MI had occurred in 65% of the patients who had coronary ectasia and aneurysms, including patients who did not have significant coronary artery stenosis [16]. Epicardial [30] and intramyocardial coronary artery disease [31] is also present in patients who have chest pain in the absence of MI.

Cocaine use has also been identified as a possible cause of aortic dissection. One study in an inner-city setting reported 38 cases of acute aortic dissection over a 20-year period, 14 of which (37%) were associated with cocaine use [32]. Although the International Registry for Aortic Dissection suggests that cocaine use is involved in less than 1% of aortic dissections, this diagnosis may

be underappreciated and must be considered in patients presenting with cocaine-associated chest pain [33,34].

Initial approach to the patient in the emergency department

Patients who have potential cocaine toxicity should receive a complete evaluation including a history of cocaine use, recognition of signs and symptoms consistent with sympathetic nervous system excess, and evaluation of organ-specific complaints. It is imperative to determine whether signs and symptoms are caused by cocaine itself, underlying unrelated structural abnormalities, or cocaine-induced structural abnormalities.

The differential diagnosis of cocaine-associated chest pain is similar to the differential diagnosis of chest pain unrelated to cocaine except that the likelihood of a patient having a serious event in the absence of traditional risk factors for that particular disease is increased. Potentially serious causes of chest pain are cardiovascular, pulmonary, and vascular in origin and include myocardial ischemia and infarction, aortic dissection, pulmonary embolism, pneumothorax, pneumomediastinum, and noncardiogenic pulmonary edema [35]. Less serious causes of chest pain following cocaine use include traumatic injury and rhabdomyolysis.

The risk of MI is increased 24-fold in the hour following cocaine use [36]. Approximately 6% of patients who have cocaine-associated chest pain are actually having an acute MI [37,38], and another 15% have an acute coronary syndrome [37]. The classic patient who has cocaine-associated MI is a young, male tobacco smoker with a history of repetitive cocaine use and few other cardiac risk factors [2,37–50]; however, cocaine-associated MI has been reported in patients over 60 years old [2,37,39]. Demographic or historical factors do not reliably predict or exclude acute MI [37]. Likewise, location of chest pain, duration of chest pain, quality of chest pain, and symptoms associated with chest pain are not predictive of MI [37].

The duration of time for which a patient is at risk for MI or ischemia following cocaine use is unknown, because it has been postulated that cocaine-associated acute coronary syndromes (myocardial ischemia and infarction) can also occur secondary to cocaine withdrawal [2,37,45,47]. Spontaneous episodes of ST-elevation myocardial infarction

(STEMI) have been documented for up to 6 weeks after withdrawal of cocaine [47]. These patients often do not have classic chest pain syndromes. The chest pain can be delayed for hours to days after their most recent use of cocaine, although most cocaine-related MIs occur within 24 hours of last use [36,37,39,43,50]. Both STEMI and non-STEMI can occur [2,40,51]. Chronic cocaine use is also associated with premature atherosclerosis and coronary ectasia; these patients can present with MI that is not temporally related to cocaine use.

Electrocardiography

Interpretation of the EKG in patients who have cocaine-associated chest pain can be difficult, because patients can have nondiagnostic EKGs in the setting of ischemia as well as abnormal EKGs in the absence of ischemia. MI occurs in patients who have normal or nonspecific EKGs [37,48]. In one series, patients who had MI were as likely to present with normal or nonspecific EKGs as with ischemic EKGs, thereby, resulting in the emergency department release of 15% of patients who have MI [37]. The sensitivity of the EKG for MI is less than in other patients who have acute MI (approximately 36%) [37].

Conversely, EKGs are abnormal in 56% to 84% of patients who have cocaine-associated chest pain [37,40,50,52], and up to 43% of patients who do not have MI may meet standard EKG criteria for use of reperfusion therapy [50]. J-point and ST-segment elevation secondary to early repolarization or left ventricular hypertrophy makes the identification of ischemia more difficult in these patients [50,53].

Cardiac markers

Cardiac markers are elevated in MI, but false elevations of creatine kinase-MB fraction are common [48,54,55]. Elevations in creatine kinase and creatine kinase-MB occur in the absence of MI [54,55] because of cocaine-induced skeletal muscle injury and rhabdomyolysis. Following the use of cocaine, approximately 50% of patients have elevations in serum creatine kinase with or without myocardial injury [37]. Rising enzyme patterns are more likely to occur in patients who have MI [37,48], whereas initial elevations that rapidly decline less commonly indicate infarction [37,48]. Additionally, in the setting of an elevated absolute creatine kinase-MB, reliance should not be placed entirely on the creatine kinase-MB

relative index, because the creatine kinase-MB relative index may be falsely low when concurrent MI and skeletal muscle rhabdomyolysis occur. Cardiac troponin I and T are more specific than creatine kinase-MB for myocardial injury when concomitant skeletal muscle injury exists. Use of cardiac troponin I or T may enhance the diagnostic accuracy of MI in patients who have cocaine-associated ischemia and therefore is preferred [54,55].

Urine drug testing

Patients may initially deny cocaine use. As a result, urine drug testing can be helpful. Relatively little cocaine is excreted unchanged in the urine [56]. Because of a long elimination half-life, assays for cocaine and cocaine metabolites generally will detect benzoylecgonine for up to 48 to 72 hours after use.

Other diagnostic tests

Laboratory evaluation may include a complete blood cell count, electrolytes, glucose, blood urea nitrogen, creatinine, arterial blood gas analysis, urinalysis, creatine kinase, and cardiac marker determinations. Excess sympathetic stimulation may result in hyperglycemia and hypokalemia. Patients who have acute cocaine toxicity can have severe acid-based disturbances as well as rhabdomyolysis [57]. A chest radiograph should be obtained in patients who have cardiopulmonary complaints. It may help demonstrate noncardiac causes for the chest pain.

Initial disposition decision

Patients who have acute STEMI should receive immediate reperfusion therapy. Direct percutaneous coronary intervention (PCI) is preferred in light of the frequently complex clinical presentation and risk of thrombolytics. Patients who have cocaine-associated MI who are likely to develop complications can be identified with a high degree of accuracy during the initial 12 hours of hospitalization [58]. Patients who have cocaine-associated chest pain and do not have infarction have an extremely low frequency of delayed complications [37,39,50]. Cost-effective evaluation strategies, such as 9- to 12-hour observation periods, are appropriate for many patients who have cocaine-associated chest pain, because these patients seem to have a low incidence of cardiovascular complications. Weber and colleagues [59]

demonstrated the safety of a 12-hour observation protocol in 302 patients who had cocaine-associated chest pain.

EKG evidence of ischemia, elevated cardiac markers, and cardiovascular complications occurring before or within 12 hours of arrival predict late complications [58]. These patients should be admitted to monitored beds. Other patients who have cocaine-associated chest pain can be evaluated safely in a 12-hour observation unit [59].

Initial treatment considerations

The initial treatment should focus on airway, breathing, and circulation. Specific treatments are based on the specific sign, symptom, or organ system affected. Because of the direct relationship between the neuropsychiatric and other systemic complications, management of neuropsychiatric manifestations affects the systemic manifestations of cocaine toxicity.

Patients who have suspected cocaine-induced ischemia or MI should be treated similarly to those with traditional acute coronary syndromes, with some notable exceptions. Aspirin, nitroglycerin, and heparin remain important initial therapies. Intravenous benzodiazepines should be provided as early management [2,39,44,60–62]. They will decrease the central stimulatory effects of cocaine, thereby indirectly reducing the cardiovascular toxicity of cocaine. Beta antagonists are contraindicated, because they may exacerbate cocaine-induced coronary artery vasoconstriction [39,44,61,62]. Another management difference between the management of cocaine-using patients and those who have STEMI is a preference for PCI over fibrinolysis [39,44,51,61,62]. Finally, there are anecdotal reports of the safety and efficacy of phentolamine, an alpha antagonist, for treatment of cocaine-associated acute coronary syndromes [39,44,61–62].

Studies in the cardiac catheterization laboratory have largely provided the evidence-based approach to patients who have cocaine-associated coronary vasoconstriction. In these studies, adult patients who had not previously used cocaine were given a low dose of intranasal cocaine (2 mg/kg). Patients developed an increase in heart rate, blood pressure, and coronary vascular resistance with the coronary arterial diameter narrowed by 13% [17]. With administration of phentolamine, the coronary arterial diameter returned to baseline [17]. This finding suggests that phentolamine

may be useful for treatment of cocaine-induced ischemia. Based on these data, case reports, and anecdotal experience, the International Guidelines for Emergency Cardiovascular Care recommend alpha-adrenergic antagonists (phentolamine) for the treatment of cocaine-associated acute coronary syndrome [61,62].

Case series and one randomized, controlled trial show that nitroglycerin relieves cocaine-associated chest pain [60,63]. Cardiac catheterization studies demonstrate that nitroglycerin reverses cocaine-induced vasoconstriction [64]. Benzodiazepines have a salutary effect on the hyperdynamic effects of cocaine and relieve chest pain [60]. Benzodiazepines are similar to nitroglycerin with respect to effects on pain relief, cardiac dynamics, and left ventricular function in patients who have cocaine-associated chest pain [60].

The role of calcium-channel blockers for the treatment of cocaine-associated chest pain remains ill defined. Pretreatment of cocaine-intoxicated animals with calcium-channel blockers has had variable results with respect to survival, seizures, and cardiac dysrhythmias [65–71]. In cardiac catheterization studies, verapamil reverses cocaine-induced coronary artery vasoconstriction [72]. Large-scale multicenter clinical trials in patients who have acute coronary syndromes unrelated to cocaine have not demonstrated any beneficial effects of calcium-channel blockers on important outcomes such as survival. Thus, the role of calcium-channel blockers in patients who have cocaine-induced acute coronary syndrome has not yet been defined.

Cocaine induced coronary artery vasoconstriction is clearly exacerbated by the administration of propranolol [18]. An unopposed alpha-adrenergic effect may occur, which leads to vasoconstriction and an increased blood pressure [73–75]. Multiple experimental models have shown that beta-adrenergic antagonists lead to decreased coronary blood flow, increased seizure frequency, and high fatality rates [71,76–79]. The use of short-acting beta-adrenergic antagonists such as esmolol has resulted in significant increases in blood pressure in up to 25% of patients [80,81]. Therefore, the use of beta-adrenergic antagonists for the treatment of cocaine toxicity is contraindicated [39,44,61,62].

Labetalol does not seem to offer any advantages over propranolol. It has substantially more beta-adrenergic antagonism than alpha-adrenergic antagonist effects [82]. Labetalol increases the risk of seizure and death in animal models of

cocaine toxicity [71] and does not reverse coronary artery vasoconstriction in humans [83]. Nitroglycerin or phentolamine is considered a better option to achieve vasodilation [39,44,61,62].

Cocaine injures the vascular endothelium, increases platelet aggregation, and impairs normal fibrinolytic pathways [84]. As a result, the use of antiplatelet and antithrombin agents makes theoretical sense [39,44,61,62,85]. Fibrinolytic administration poses problems, however. Many young patients have benign early repolarization, and only a small percentage of patients who have cocaine-associated chest pain syndromes and J-point elevation are actually in the midst of an acute MI [50,53]. Patients are frequently hypertensive, and aortic dissection must be considered. Several case reports document adverse outcomes following fibrinolytic administration in cocaine-using patients [86–88]. Patients who have cocaine-associated STEMI have a low mortality; therefore, the benefit of early fibrinolytic administration is less than in patients who have STEMI unrelated to cocaine, and the risk is higher. Therefore, fibrinolytic therapy should be reserved for patients who are definitely having STEMI and cannot receive primary PCI [36,60,61,85]. With the increasing availability of primary PCI including transfer, this situation should rarely occur. More aggressive antiplatelet therapy with glycoprotein IIb/IIIa antagonists and clopidogrel may be useful in patients who have cocaine-associated acute coronary syndromes, but they have not been well studied in this patient population [89].

Hypertension and tachycardia alone rarely require specific treatment but may need to be addressed in a patient who has definite acute coronary syndromes. In a patient with chest pain of unclear cause, hypertension and tachycardia alone should be treated conservatively. Resolution of anxiety, agitation, and ischemia often lead to resolution of the hypertension and tachycardia. When necessary, treatment directed toward the central effects of cocaine, such as the benzodiazepines, usually reduces blood pressure and heart rate. When sedation is unsuccessful, hypertension can be managed with sodium nitroprusside, nitroglycerin, or intravenous phentolamine [17,64].

Most atrial arrhythmias respond to sedative hypnotics. When they do not, verapamil or diltiazem may be indicated. The treatment of ventricular arrhythmias depends upon the time between cocaine use, arrhythmia onset, and treatment. Ventricular arrhythmias occurring immediately after cocaine use should be presumed to occur from the

local anesthetic (sodium-channel) effects on the myocardium. They may respond to the administration of sodium bicarbonate, similar to arrhythmias associated with other type IA and type IC agents [14,90]. In addition, one animal model suggested that lidocaine exacerbates cocaine-induced seizures and arrhythmias as a result of similar effects on sodium channels [91]; however, this finding has not been confirmed in other animal models [14,92,93]. Bicarbonate therapy may be preferable and has been used effectively [94].

Ventricular arrhythmias that develop several hours after the last use of cocaine often occur as a result of ischemia. Standard management for ventricular arrhythmias, including lidocaine, is indicated and seems to be safe [95]. There are no data concerning the efficacy of amiodarone in clinical cocaine intoxication. Torsades de pointes is a rare complication of cocaine use [96] and should be managed with intravenous magnesium sulfate and overdrive pacing.

Other cardiovascular effects of cocaine

Cocaine also causes significant cardiovascular conditions besides those that result in chest pain. Cocaine has a direct myocardial-depressant effect [13,97]. Chronic cocaine use leads to a dilated cardiomyopathy, possibly from recurrent or diffuse ischemia with subsequent “stunned” myocardium [98]. Alternatively, it may have a direct effect on myocardial contractility. Direct infusion of cocaine into human coronary arteries increases left ventricular end-diastolic pressures and end-systolic volume and decreases left ventricular ejection fraction [99]. Left ventricular function may improve when cocaine use is halted [100].

Intravenous cocaine use increases the risk of bacterial endocarditis, even more than intravenous heroin use, presumably because of the increased frequency of injection to sustain effects [101,102]. Direct effects of cocaine on endovascular tissues and the immune system may also play a role [102].

Aortic dissection is a rare but life-threatening complication of cocaine abuse and must be considered in the differential diagnosis. In a consecutive series, 37% of acute aortic dissections in an inner-city hospital were associated with cocaine use. This patient cohort was younger than expected with a high percentage of African American males with untreated hypertension [32].

Higher doses of cocaine are associated with virtually all types of tachyarrhythmias. Atrial

fibrillation, atrial flutter, supraventricular tachycardias, ventricular premature contractions, accelerated idioventricular rhythms, ventricular tachycardia, torsades de pointes, and ventricular fibrillation may occur as a result of cocaine. High doses of cocaine lead to infranodal and intraventricular conduction delays and lethal ventricular arrhythmias secondary to prolonged QRS and QT intervals [103,104]. Prolonged QT intervals have been noted in patients who have recently used cocaine and who have not had arrhythmias [53]. These effects are probably mediated by the local anesthetic sodium-channel blockade. In addition to the local anesthetic effects, arrhythmias may also occur as a result of cocaine-induced acute coronary syndrome [13,95]. Low doses of cocaine can result in a transient bradycardia.

In-hospital management

There is limited specific information available regarding the in-hospital management of patients who have cocaine-related cardiovascular disease. Therefore, as a general rule, treatment guidelines follow those recommended for patients who have acute coronary syndromes not associated with cocaine Table 1 [105,106].

ST-elevation myocardial infarction

The diagnosis of STEMI can be more challenging in patients who have acute cocaine toxicity because of the atypical presentation and challenges with interpretation of the EKG, including left ventricular hypertrophy and early repolarization. Patients who have acute cocaine toxicity frequently are younger than expected and are hypertensive, and aortic dissection must be considered in the differential diagnosis. Therefore cardiac catheterization with direct PCI is the preferred method of reperfusion, and fibrinolytic therapy should be reserved for patients when cardiac catheterization is not available. With the development of transfer systems for STEMI, fibrinolytic therapy should rarely be required. The method of revascularization and subsequent management should follow guidelines for treatment of patients who do not have a history of cocaine abuse, with a few exceptions. There are no data available regarding the use of drug-eluting stents in patients who abuse cocaine, but they would be expected to decrease target lesion revascularization compared with bare metal stents.

Patients with ongoing cocaine abuse may have poor compliance with the required chronic antiplatelet regimen of aspirin and clopidogrel, which could potentially increase the risk of subacute thrombosis. Therefore each patient's potential for drug rehabilitation and compliance history needs to be considered in the stent choice. Patients who have accelerated atherosclerosis, coronary aneurysms, and ectasia require aggressive risk factor modification and antiplatelet therapy. Long-term clopidogrel should be considered in addition to aspirin. Patients who have left ventricular dysfunction should receive angiotensin-converting enzyme inhibitor therapy. Although patients who have STEMI would be expected to benefit from long-term beta blockade, caution should be

used in patients expected to have continued exposure to cocaine.

High-risk unstable angina/non-ST-segment elevation myocardial infarction

Patients who have elevated cardiac enzymes or abnormal EKGs are at higher risk for subsequent events and benefit from an early invasive approach with cardiac catheterization and revascularization [107]. Although no specific data exist for cocaine-related unstable angina/non-STEMI, it is reasonable to believe these patients would benefit from a similar approach. It is important to use drug rehabilitation as well as aggressive risk factor modification in these patients, because

Table 1
Treatment summary for specific cocaine-related medical conditions

Medical Condition	Treatments
Cardiovascular complications	
Dysrhythmias	
Sinus tachycardia	observation oxygen diazepam 5 mg IV or lorazepam 2–4 mg IV titrated to effect
Supraventricular tachycardia	oxygen diazepam 5 mg IV or lorazepam 2–4 mg IV consider diltiazem 20 mg IV or verapamil 5 mg IV adenosine 6 mg or 12 mg IV cardioversion if hemodynamically unstable
Ventricular dysrhythmias	oxygen sodium bicarbonate 1–2 meq/kg lidocaine 1.5 mg/kg IV bolus followed by 2 mg/min infusion defibrillation if hemodynamically unstable diazepam 5 mg IV or lorazepam 2–4 mg IV
Acute coronary syndrome	oxygen diazepam 5–10 mg IV or lorazepam 2–4 mg IV soluble aspirin 325 mg nitroglycerin 1/150 sublingual × three every 5 minutes followed by an infusion titrated to a mean arterial pressure reduction of 10% or relief of chest pain. morphine sulfate 2 mg IV every 5 minutes titrated to pain relief phentolamine 1 mg IV; repeat in 5 minutes verapamil 5–10 mg IV heparin or enoxaparin percutaneous intervention (angioplasty and stent placement) glycoprotein IIb/IIIa inhibitors
Hypertension	observation diazepam 5–10 mg IV or lorazepam 2–4 mg IV titrated to effect phentolamine 1 mg IV; repeat in 5 minutes nitroglycerin or nitroprusside continuous infusion titrated to effect
Pulmonary edema	lasix 20–40 mg IV morphine sulfate 2 mg IV every 5 minutes titrated to pain relief or respiratory status nitroglycerin infusion titrated to blood pressure consider phentolamine or nitroprusside

Adapted from Hollander JE and Hoffman RS. Cocaine. In Godlfrank LR, Flomenbaum NE, Lewin NA, et al, editors. Goldfrank's toxicologic emergency. 6th edition. Stamford (CT): Appleton and Lange.; 1998. p. 1071–89.

there is a high likelihood of recurrence. In one review of patients who had cocaine-associated MI followed for median of 4.5 months, 12 of 24 patients had recurrent ischemic pain; 8 of whom sustained a second MI, suggesting that these patients are at high risk for subsequent events [2].

Low-risk unstable angina

Most patients who have cocaine-related chest pain have low-risk unstable angina and can be treated satisfactorily with a 12-hour observation protocol [59].

Patients who have cocaine-associated chest pain have a 1-year survival rate of 98% and an incidence of late MI of only 1% [49]. Most deaths occur because of concurrent medical problems (such as HIV disease). Because patients who have cocaine-associated chest pain are not at high risk for MI or death during the ensuing year, urgent cardiac evaluation is probably not necessary for patients in whom MI is ruled out. Evaluation for possible underlying coronary artery disease may be accomplished on a more elective basis. Continued cocaine usage, however, is associated with an increased likelihood of recurrent chest pain, and therefore aggressive drug rehabilitation may be useful [49].

The appropriate diagnostic evaluation for these patients remains unclear and therefore should follow general principles for risk stratification in patients who have coronary artery disease. In light of the underlying EKG abnormalities, most patients would benefit from imaging with stress testing, either echocardiography or nuclear. Many patients who have cocaine-related chest pain have pain related to coronary vasoconstriction or increased myocardial demand and therefore have negative stress evaluations. There have been remarkable advances in cardiac imaging in the last few years. Both cardiac MRI and CT angiography have theoretical advantages over conventional stress imaging for detection of premature atherosclerosis and coronary artery aneurysms, but there are currently no data available specific to cocaine-related chest pain.

Secondary prevention

Cessation of cocaine use is the hallmark of secondary prevention. Recurrent chest pain is less common and MI and death are rare in patients who discontinue cocaine use [49]. Aggressive risk

factor modification is indicated in patients who have MI or evidence of premature atherosclerosis, coronary artery aneurysm, or ectasia. This risk factor modification includes smoking cessation, hypertension control, diabetes control, and aggressive lipid-lowering therapy with a target low-density lipoprotein level below 70. Although these strategies have not been tested specifically for patients who have cocaine-associated chest pain, they are standard of care for patients who have underlying coronary artery disease.

Patients who have evidence of MI or atherosclerosis should receive long-term antiplatelet therapy with aspirin. In addition to aspirin, clopidogrel should be given for at least 1 month with bare metal stents or for 3 to 6 months with currently available drug-eluting stents. Long-term combination antiplatelet therapy with aspirin and clopidogrel may be beneficial in patients who have extensive atherosclerosis, coronary ectasia, or aneurysm, but this possibility has not been studied. The role of nitrates and calcium-channel blockers remains speculative and should be used for symptomatic relief. The use of beta-adrenergic antagonists, although useful in patients who have had a previous MI and cardiomyopathy, needs special consideration in the setting of cocaine abuse. Because recidivism is high in patients who have cocaine-associated chest pain (60% admit to cocaine use within the next year [49]), beta-blocker therapy probably should be avoided in certain patients.

Summary

Patients who have chest pain following the use of cocaine have become more common in emergency departments throughout the United States, with approximately 6% of these patients sustaining an acute MI. The authors have described the rationale for recommending aspirin, benzodiazepines, and nitroglycerin as first-line treatments and calcium-channel blockade or phentolamine as possible second-line therapies and have summarized the controversies surrounding the use of fibrinolytic agents. Admission for observation is one reasonable approach to the management of the low-risk cohort. Evaluation for underlying coronary artery disease is reasonable, particularly in patients who have acute MI. Patients who do not have infarction can undergo evaluation for possible coronary artery disease on an outpatient basis. Routine interventions for secondary prophylaxis as well as cocaine rehabilitation should

be used in this patient population, because the long-term prognosis seems somewhat dependent upon the ability of the patient to discontinue cocaine use.

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