Management of Cocaine-Associated Chest Pain and Myocardial Infarction: A Scientific Statement From the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology

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AHA Scientific Statement

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The goals of the present article are to provide a critical review of the literature on cocaine-associated chest pain and myocardial infarction (MI) and to give guidance for diagnostic and therapeutic interventions. Classification of recommendations and levels of evidence are expressed in the American College of Cardiology/American Heart Association (ACC/AHA) format as follows:

- **Class I**: Conditions for which there is evidence for and/or general agreement that the procedure or treatment is beneficial, useful, and effective.
- **Class II**: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
  - **Class IIa**: Weight of evidence/opinion is in favor of usefulness/efficacy.
  - **Class IIb**: Usefulness/efficacy is less well established by evidence/opinion.
- **Class III**: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.

- **Level of Evidence A**: Data derived from multiple randomized clinical trials.
- **Level of Evidence B**: Data derived from a single randomized trial or nonrandomized studies.
- **Level of Evidence C**: Only consensus opinion of experts, case studies, or standard of care.

Methods

The Writing Committee conducted a comprehensive search of the medical literature concerning cocaine-associated chest pain and MI. The literature search included English-language publications on humans and animals from 1960 to 2007. In addition to broad-based searching concerning cocaine, specific targeted searches were performed on cocaine and the following topics: MI, chest pain, emergency department (ED), aspirin, nitroglycerin, calcium channel blocker, benzodiazepine, thrombolytics, phentolamine, heparin, primary angioplasty, ECG, and stress testing. Literature citations were generally limited to published articles listed in Index Medicus. The article was reviewed by 4 outside reviewers nominated by the AHA.

Epidemiology

Cocaine is the second most commonly used illicit drug in the United States, with only marijuana being abused more frequently.[1] Cocaine is also the illicit drug that leads to the most ED visits.[2] The 2004 National Survey on Drug Use and Health estimated that 14% of people 12 years of age or older (34 million individuals) in the United States have tried cocaine at least once,[3] and over 2000 individuals per day use cocaine for the first time.[4] In the 2002 to 2003 calendar year, more than 1.5 million (0.6%) Americans ≥12 years of age had abused cocaine in the past year. Cocaine use is concentrated among select demographics: individuals 18 to 25 years of age (1.2%) have the highest rate of cocaine use; males (0.9%) had more than twice the use rate of females (0.4%); and rates according to race are 1.1% for blacks, 0.9% for Hispanics, 0.5% for whites, and 0.1% for Asians.[6]

In 2005, there were 448 481 cocaine-related visits to EDs in the United States.[7] Chest discomfort has been reported in 40% of patients who present to the ED after cocaine use.[8] The

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Drug Abuse Warning Network (DAWN) reported that in the last 6 months of 2004, there were ≈126 000 cocaine-related ED visits in the United States, or ≈40% of all ED visits related to substance abuse (illicit or otherwise).[9] The most frequent age group for these visits was 35 to 44 years of age; this group accounted for 37% of all cocaine-related ED encounters. Cocaine-related ED visits increased by 47% from 1999 to 2002.[2] Thus, the number of ED encounters with patients with cocaine-associated chest pain will likely be increasing.

Pathophysiology

Cocaine has multiple cardiovascular and hematologic effects that likely contribute to the development of myocardial ischemia and/or MI. Cocaine blocks the reuptake of norepinephrine and dopamine at the presynaptic adrenergic terminals, causing an accumulation of catecholamines at the postsynaptic receptor and thus acting as a powerful sympathomimetic agent.[10,11] Cocaine causes increased heart rate and blood pressure in a dose-dependent fashion.[12] In humans, intranasal cocaine use resulted in an increase in heart rate (17±16% beats/min), mean systemic arterial pressure (8±7% mm Hg), cardiac index (18±18% liters/min per m^2), and dP/dt (18±20% mm Hg/s).[13] The chronotropic effects of cocaine use are intensified in the setting of alcohol use.[14] In addition, cocaine administration can reduce left ventricular function and increase end-systolic wall stress.[15] By increasing heart rate, blood pressure, and contractility, cocaine leads to increased myocardial demand.

Even small doses of cocaine taken intranasally have been associated with vasoconstriction of coronary arteries.[16] Coronary vasoconstriction may be more accentuated in patients with preexisting coronary artery disease.[17] Many cocaine users tend to be young men who also smoke cigarettes.[18,19] The combination of cocaine and cigarette use results in greater increases in heart rate and vasoconstriction than either cocaine use or cigarette smoking alone.[20] Vasoconstriction in the setting of cocaine use is most likely secondary to stimulation of the α-adrenergic receptors in smooth muscle cells in the coronary arteries, as pure α-adrenergic antagonists reduce coronary vasoconstriction in cocaine users.[20] In addition to α-adrenergic stimulation, cocaine has been shown to increase levels of endothelin-1, which is a powerful vasoconstrictor,[21] and to decrease production of nitric oxide, which is a vasodilator.[22] Thus, cocaine decreases oxygen supply and induces myocardial ischemia through a variety of mechanisms.

Acute thrombosis of coronary arteries shortly after cocaine use has been described.[23] The propensity for thrombus formation in the setting of cocaine intake may be mediated by an increase in plasminogen-activator inhibitor.[24] Cocaine use has also been associated with an increase in platelet count,[25] increased platelet activation,[26] and platelet hyperaggregability.[27] Autopsy studies demonstrated the presence of coronary atherosclerosis in young cocaine users along with associated thrombus formation; thus, cocaine use is associated with premature coronary atherosclerosis and thrombosis.[28] Cocaine users have elevated levels of C-reactive protein, von Willebrand factor, and fibrinogen that may also contribute to thrombosis.[29] Cocaine, therefore, causes myocardial ischemia or MI in a multifactorial fashion that includes: (1) increasing myocardial oxygen demand by increasing heart rate, blood pressure, and contractility; (2) decreasing oxygen supply via vasoconstriction; (3) inducing a prothrombotic state by stimulating platelet activation and altering the balance between procoagulant and anticoagulant factors; and (4) accelerating atherosclerosis.

Incidence of Myocardial Infarction

Since an early description by Coleman and colleagues,[30] many reports have emerged that link cocaine use to myocardial ischemia and MI. Many of the initial studies reported a temporal association between cocaine use and MI,[19,31,32] whereas multiple experimental and observational studies subsequently elucidated the mechanisms for cocaine-associated MI.[13,16,23,25–27,33–35]

In the COCaine Associated CHest PAin (COCHPA) study, cocaine-associated MI occurred in 6% of patients who presented to the ED with chest pain after cocaine use.[19] In that prospective multicenter study, the diagnosis of MI was made by creatine kinase-MB isoenzyme measurements among 246 patients presenting to the ED with chest pain after cocaine ingestion.[19] Weber and colleagues[36] found a similar 6% rate of MI in patients with cocaine-associated chest pain in a retrospective analysis in an urban university–affiliated hospital.

Other studies of cocaine-associated chest pain have reported lower incidences of MI. The prospective Acute Cardiac Ischemia-Time Insensitive Predictive Instrument (ACI-TIPI) study reported a 0.7% rate of MI among 293 patients with preceding cocaine ingestion who presented to the ED with chest pain or other ischemic symptoms[37]; another study documented a 2.8% rate of MI in a series of 218 patients with similar presentation.[38] The ACI-TIPI study involved urban, suburban, and semirural hospitals and enrolled patients with chest pain, left arm pain, jaw pain, epigastric pain, dyspnea, dizziness, and palpitations. In contrast, the COCHPA trial involved a solely urban population that presented only with chest pain. These differences may explain the different rates of MI. Although the overall incidence of cocaine-associated MI varies between studies from 0.7% to 6% of those presenting with chest pain after cocaine ingestion (some of the variance may relate to differences in MI diagnostic criteria), cocaine appears to be an important contributor to MI among the young. In a study of 130 patients with cocaine-associated MI, the average age was only 38 years.[39]

Clinical Presentation

Cardiopulmonary complaints are the most frequently reported symptoms among cocaine users (occurring in up to 56%), with chest pain being the single most frequent symptom.[8] Cocaine-associated chest pain is usually perceived as pressure-like in quality.[19] Other frequent symptoms include dyspnea, anxiety, palpitations, dizziness, and nausea.[8] Dyspnea and diaphoresis are particularly common, occurring in 60% and 40% of patients, respectively.[19] In one study, only 44% of 91 patients with cocaine-associated MI reported antecedent chest pain.[32] Thus, the presence of chest pain

appears to have little value for discriminating an ischemic from nonischemic cause in these patients. In another study of 130 patients with cocaine-associated MI, there was equal distribution between anterior (45%) and inferior (44%) MI, and most were non-Q wave (61%).[40]

Cocaine-associated chest pain may be caused by not only MI but also by aortic dissection, and this must be considered in the differential diagnosis. Information concerning cocaine-induced aortic dissection is limited, but one study of 38 consecutive patients with aortic dissection in a US urban center demonstrated a surprisingly high number (14, 37%) that were associated with cocaine use.[41] Among 921 cases in the International Registry of Aortic Dissection (IRAD) in which a history of cocaine use was known, however, only 0.5% of aortic dissection cases were associated with cocaine use.[42] In addition to MI and aortic dissection, cocaine use may lead to pulmonary hypertension and associated chest pain and dyspnea.[43] Finally, an acute pulmonary syndrome called "crack lung," which involves hypoxemia, hemoptysis, respiratory failure, and diffuse pulmonary infiltrates and occurs after inhalation of freebase cocaine, has been described.[44]

Timing Between Cocaine Use and Myocardial Infarction

Cocaine-associated MI appears to occur most often soon after cocaine ingestion. In one study, two thirds of MI events occurred within 3 hours of cocaine ingestion.[32] In a survey of 3946 patients with recent MI, 38 patients admitted to cocaine use in the preceding year, and 9 patients reported ingestion in the 60 minutes preceding the onset of MI symptoms.[18] This survey reported a striking 24-fold higher risk of MI in the first hour after cocaine use, with a rapid decrease in risk after this time.[18]

Investigators have noted, however, that the onset of ischemic symptoms could still occur several hours after cocaine ingestion, at a time when the blood concentration is low or undetectable. Amin et al[45] reported an 18-hour median length of time between cocaine use and MI onset among 22 patients presenting with chest pain after cocaine ingestion. This accounted for an unusually high rate of MI of 31% in this retrospective analysis, whereas other studies reported a range extending from 1 minute to up to 4 days.[32] These findings are attributed to cocaine metabolites, which rise in concentrations several hours after cocaine ingestion, persist in the circulation for up to 24 hours, and may cause delayed or recurrent coronary vasoconstriction.[46]

Patient Characteristics

The Cocaine-Associated Myocardial Infarction study retrospectively identified 130 patients who sustained a total of 136 cocaine-associated MI events. In this cohort, the majority of patients were young (mean age 38 years), nonwhite (72%), and smokers (91%) and had a history of cocaine use in the preceding 24 hours (88%).[47] Mittleman et al[18] also demonstrated that cocaine users with recent MI were more likely to be male (87%), current cigarette smokers (84%), young (44 years of age), and nonwhite (63%) than a comparable group with MI and no recent cocaine use. These characteristics appear to be similar in most patients presenting with cocaine-associated chest pain,[19] making it exceedingly difficult to predict those at risk for MI, given the low incidence of cocaine-associated MI.[19,36–38]

Complications and Prognosis

In the 130 patients in the Cocaine-Associated Myocardial Infarction study, 38% had cardiac complications.[47] Heart failure occurred in 7% and arrhythmias in up to 43%, which accounted for the majority of these complications. The arrhythmias included ventricular tachycardia (18%), supraventricular tachycardia (5%), and bradyarrhythmia (20%). Notably, 90% of these complications occurred within the first 12 hours after presentation to the hospital and did not lead to significant adverse events, with an in-hospital mortality rate of 0%. In addition, in a study of 22 patients who suffered cardiac arrest in the setting of cocaine use, only 10 (46%) died compared with 32 of 41 (78%) aged-matched controls ($P<0.01$).[48]

Many patients continue cocaine use after their initial hospitalization and have a higher cumulative risk for MI and associated complications. Hollander and Hoffman[32] reported a 58% incidence of recurrent ischemic events after discharge among a group of 24 patients presenting with cocaine-associated MI. In another cohort of 203 patients with cocaine-associated chest pain followed up for 1 year, 60% reported continued cocaine use.[39] Although no MI or death occurred among those claiming abstinence, 2 nonfatal MIs and 6 deaths occurred in patients with persistent cocaine use (although none were attributed to MI). Weber et al[49] reported a 1.6% rate of nonfatal MI during a 30-day follow-up of patients who presented with cocaine-associated chest pain and in whom MI was excluded. All 4 events occurred in patients who continued cocaine use.

Diagnostic Strategies

The use of cocaine can be ascertained by self-reports or by urine analysis.[50] Self-reported use of cocaine can be obtained easily and nonintrusively; however, a potential significant drawback is underreporting by patients. Qualitative immunoassay detection of the cocaine metabolite benzoylecgonine in the urine is the most commonly used laboratory method, but cocaine can also be detected in blood and hair. Cocaine use is reported as positive when the level of benzoylecgonine is above a standard cut-off value (usually 300 ng/mL). As benzoylecgonine has a urinary half-life of 6 to 8 hours, it can be detected in the urine for about 24 to 48 hours after cocaine use. In a study of 18 patients who had ingested cocaine intranasally, the mean time to the first negative specimen was 43.6 ± 17.1 (range 16 to 66) hours.[51] Among individuals with long-term cocaine use (who may ingest up to 10 g/d), benzoylecgonine has been detected 22 days after last ingestion.[52] Quantitative methods are also available, but they are more expensive and potentially misleading because of individual variability in cocaine metabolism and excretion.[53]

Establishing cocaine use in a patient presenting with chest pain should depend primarily on self-reporting. As the use of cocaine may influence treatment strategies, patients being evaluated for possible acute coronary syndrome (ACS)

should be queried about the use of cocaine; this especially applies to younger patients. Not enough information exists to definitely recommend the routine screening of particular subgroups of patients. The qualitative determination of cocaine metabolites in the urine should be done only in specific cases, including when the patient is unable to communicate and no other reliable source of the history is available. When confronted with patients with no or few risk factors for coronary artery disease presenting with MI, especially those who are young or have a history of illicit drug use, however, measuring cocaine urine metabolites may be prudent. The evaluation of cocaine-associated chest pain in the ED is in general the same as evaluation of patients for possible ACS without cocaine use: ECG, serial cardiac markers, and some form of stress testing.

Electrocardiogram

An abnormal ECG has been reported in 56% to 84% of patients with cocaine-associated chest pain; however, many of these patients are young and commonly have the normal variant of early repolarization, which may be interpreted by physicians as an abnormal ECG finding.[44] Gitter and colleagues[54] reported an early repolarization pattern in 32% of patients with cocaine-associated chest pain, a left ventricular hypertrophy pattern in 16%, and a normal ECG in only 32% of patients. Overall, 42% of patients in their cohort of 101 patients manifested electrocardiographic ST-segment elevation, although all of them eventually had MI excluded by cardiac marker testing.[54] In the COCHPA study, the sensitivity of an ECG revealing ischemia or MI to predict a true MI was only 36%.[19] The specificity, positive predictive value, and negative predictive value of the ECG were 89.9%, 17.9%, and 95.8%, respectively.[19] In a series of 238 patients with chest pain after cocaine use, 33% had normal ECGs, 23% had nonspecific changes, 13% had a left ventricular hypertrophy pattern, 6% had left ventricular hypertrophy and early repolarization patterns, and 13% had early repolarization pattern only. ECG findings specific for ischemia or infarction were present in only a minority of patients; 2% had changes typical for ST-segment–elevation MI and 6% had changes specific for acute ischemia.[7,38]

Cardiac Biomarkers

Cocaine ingestion may cause rhabdomyolysis with consequent elevation in myoglobin and total creatine kinase levels, which may confound the diagnosis of cocaine-associated MI.[54,55] In one study, total creatine kinase elevation occurred in 75% of patients, including 65% without MI.[45] Cardiac troponins are the most sensitive and specific markers for the diagnosis of cocaine-associated MI[55]; therefore, their use is preferred in patients with possible ACS in the setting of cocaine use.

Myocardial Perfusion Imaging

Rest myocardial perfusion imaging has been evaluated in the ED in low- to moderate-risk patients after cocaine use. Of 216 patients, only 5 had positive results; 2 of the 5 patients with an abnormal scan had an MI documented by cardiac marker criteria. Of those with negative results seen with imaging studies, only 2 were found to have significant coronary artery disease. The high rate of negative studies might also have been due to the fact that only half of the patients were injected during an episode of chest pain. The sensitivity for MI was therefore 100% (95% confidence interval, 50% to 100%), with a specificity of 99% (95% confidence interval, 96% to 100%). Of 67 patients that had follow-up stress perfusion studies, 4 (6%) had a reversible defect during stress. Three of the 4 underwent angiography, with significant coronary artery disease found in 2.[38]

Echocardiography

Compared with nonusers, long-term cocaine users have a higher left ventricular mass index (mean 103 ± 24 g/m^2 among users compared with 77 ± 14 g/m^2 in nonusers) and thickness of the posterior wall (>1.2 cm in 44% of users compared with 11% in nonusers).[56] As the cavity size was normal in all patients, it was postulated that long-term cocaine use appears to be associated with concentric left ventricular hypertrophy.[56] These findings potentially explain the baseline ECG changes associated with cocaine use. This may also decrease the utility of echocardiography to look for ischemia in the evaluation of chest pain, as left ventricular hypertrophy often masks regional wall motion abnormalities.[57] Echocardiography also yields information concerning systolic and diastolic function and valvular structure that may affect treatment strategies.

Dobutamine stress echocardiography has been safely performed in subjects admitted with chest pain after cocaine use, provided they exhibited no signs of ongoing cocaine toxicity.[58] Among 24 patients with chest pain but no specific ECG changes or positive cardiac markers, dobutamine stress echocardiography was successfully completed in 19 patients who achieved their target heart rates. Two patients did not have adequate resting images, 1 test was terminated because of atrial conduction abnormalities, 1 test was cancelled because of baseline wall motion abnormalities, and 1 patient failed to achieve the target heart rate. None of the patients had an exaggerated adrenergic response (defined as development of systolic blood pressure >200 mm Hg or a tachyarrhythmia), and only 1 patient had new wall motion abnormalities with dobutamine infusion.

The appropriate diagnostic evaluation for these patients remains unclear. Practitioners should follow general principles for risk stratification of patients with possible ACS. In light of the underlying electrocardiographic abnormalities, if a stress test is ordered, most patients would benefit from stress testing with imaging, either echocardiography or nuclear.[38,58]

Coronary Angiography

In a study of 734 patients (mean age 43 ± 7 years) evaluated for symptoms compatible with ischemia after cocaine use, 90 underwent coronary angiography.[59] In this selected, higher-risk group, 50% had no significant stenosis, 32% had single-vessel disease, 10% had 2-vessel disease, and 5.6% had 3-vessel disease. Of patients with proven MI, 77% had significant coronary artery disease. Of patients without MI, only 35% had significant coronary artery disease.[59] In a

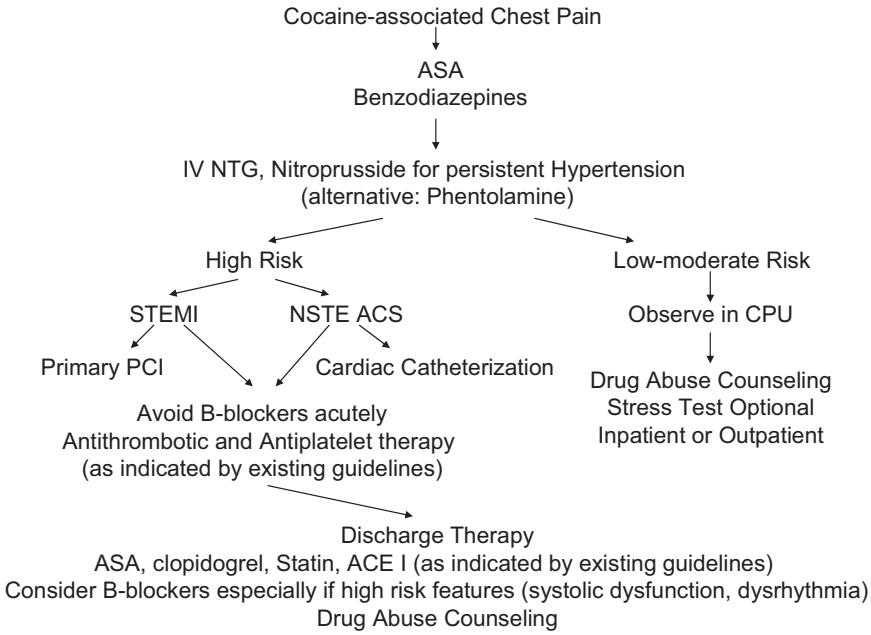

Figure. Therapeutic and diagnostic recommendations in cocaine-associated chest pain. ASA indicates aspirin; NTG, nitroglycerin; STEMI, ST-segment–elevation MI; NSTE ACS, non–ST-segment–elevation ACS; CPU, chest pain unit; PCI, percutaneous coronary intervention; B-blockers, β-blockers; and ACE, angiotensin-converting enzyme inhibitor.

smaller report of 91 cases of cocaine-associated MI, 54 patients underwent coronary angiography,[32] and 34 (55%) of those patients were found to have significant coronary artery disease or thrombotic occlusion. In another study of patients with proven MI after cocaine use, 80% of patients had significant coronary artery disease.[13]

Evaluation in a Chest Pain Unit

As only 0.7% to 6% of patients with cocaine-associated chest pain have an MI,[36,37] risk stratification of these patients in an observation unit may significantly reduce unnecessary admissions and improve resource utilization. In a prospective randomized study,[49] 344 patients were evaluated for cocaine-associated chest pain. Forty-two (12%) high-risk patients with ST-segment elevation or depression >1 mm, elevated serum cardiac markers, recurrent chest pain, or hemodynamic instability were directly admitted. Of the 42 patients admitted, 10 (24%) had an MI and another 10 (24%) were diagnosed with unstable angina. The other 302 intermediate- to low-risk patients were successfully evaluated in an observation unit for 6 to 12 hours with clinical and ECG monitoring and repeat cardiac troponin I determination. The observation period was followed by nonmandatory stress testing before discharge. Patients were treated with aspirin and nitrates, and 30% received benzodiazepines as well.

Among the patients evaluated in the observation unit, there were no cardiovascular deaths; however, 4 of 256 (2%) patients sustained a nonfatal MI. Before discharge, 158 (52%) patients underwent a stress test. Only 4 (3%) had positive results and underwent angiography. Two patients had multivessel disease, 1 had nonocclusive disease, and 1 had no evidence of coronary artery disease. In a retrospective review of 197 patients with cocaine-associated chest pain evaluated in a chest pain unit, 171 (87%) were discharged and 12% required hospital admission. Only 1 patient (4.5%) developed an MI. Of the patients sent home, only 1 (1%) had a cardiac complication.[60]

These studies suggest that risk stratification on the basis of well-established criteria, including ECG changes and positive cardiac troponin,[61] is feasible and safe in patients with chest pain associated with cocaine use. Patients at high risk should be admitted to monitored beds. High-risk patients have a 23% incidence of MI, and another 23% will ultimately be diagnosed with unstable angina.[49] Among patients in whom coronary angiography was performed, over 75% had significant coronary artery stenoses. The in-hospital course will likely be uneventful with over 90% of patients categorized as uncomplicated, Killip class I.[49] In the absence of ischemic electrocardiographic changes or positive cardiac markers, intermediate- and low-risk patients can be safely managed in a chest pain observation unit for 9 to 12 hours, which can obviate the need for hospital admission in the majority of these patients. The likelihood of underlying coronary artery disease or adverse cardiac events in patients in which MI is ruled out is low. In the study by Weber et al,[49] no differences in 30-day outcomes among patients managed with or without stress testing before discharge were seen. We recommend that stress testing be optional for patients with cocaine-associated chest pain who have had an uneventful 9 to 12 hours of observation. Stress testing can be performed at the time of observation or on an outpatient basis and should be considered depending on cardiac risk factors and ongoing symptoms.

Therapeutic Strategies

General Considerations

Patients with cocaine-associated chest pain, unstable angina, or MI should be treated similarly to those with traditional ACS or possible ACS,[62,63] with some notable exceptions (Figure). No randomized, placebo-controlled trials regarding therapies to improve outcomes of patients sustaining a cocaine-associated MI have been reported. Therapeutic recommendations are based on animal studies, cardiac catheterization studies, observational studies, case series, and case

Table. Scientific Strength for Treatment Recommendations for Initial Management of Cocaine-Associated Myocardial Ischemia or Infarction

Therapy	Classification of Recommendation/Level of Evidence	Controlled Clinical Trials	Cardiac Catheterization Laboratory Studies	Case Series or Observational Studies	Case Reports	Controlled In Vivo Animal Experiments
Benzodiazepines	I/B	X			X	X
Aspirin	I/C			X		
Nitroglycerin	I/B	X	X	X		
Calcium channel blocker	IIb/C		X			X
Phentolamine	IIb/C		X		X	X
β-Blockers	III/C		X		X	X
Labetalol	III/C		X		X	X

No. of patients in studies/reports: benzodiazepines, 67; nitroglycerin, 67; phentolamine, 45; calcium channel blocker, 15; β-blockers without α-blocking properties, 30; labetalol, 15; and fibrinolytics, 66.

reports (Table). Unlike patients with ACS unrelated to cocaine use, cocaine users should be provided with intravenous benzodiazepines as early management.[32,64–66] In the setting of cocaine use, benzodiazepines relieve chest pain and have beneficial cardiac hemodynamic effects.[67,68] The neuropsychiatric symptoms and cardiovascular complications of cocaine use are interrelated; therefore, management of neuropsychiatric manifestations favorably impacts the systemic manifestations of cocaine toxicity. In animal models, benzodiazepines decrease the central stimulatory effects of cocaine, thereby indirectly reducing cardiovascular toxicity.

Hypertension and tachycardia may not require direct treatment. In a patient with definite ACS, these signs need to be addressed. In a patient with chest pain of unclear origin, hypertension and tachycardia should be treated conservatively. Resolution of anxiety with a benzodiazepine will often lead to resolution of the hypertension and tachycardia. When sedation is not successful, hypertension can be managed with sodium nitroprusside, nitroglycerin, or intravenous phentolamine.[16,46]

ST-Segment–Elevation Myocardial Infarction

Timely percutaneous coronary intervention by experienced operators in high-volume centers is preferred over fibrinolytics in ST-segment–elevation MI and is even more desirable in the setting of cocaine use.[64–66,68–70] Many young patients have benign early repolarization, and only a small percentage of patients with cocaine-associated chest pain syndromes and J-point elevation are actually having an MI.[44,54] Case reports document adverse outcomes, such as a higher rate of intracranial hemorrhage, after fibrinolytic administration in patients who use cocaine.[71–73] Fibrinolytic therapy should be reserved for patients who are clearly having an ST-segment–elevation MI who cannot receive direct percutaneous coronary intervention.[63,64,66,68,70]

No data are available regarding the use of drug-eluting stents in patients who abuse cocaine, but they would be expected to decrease in-stent restenosis as compared with bare metal stents as in patients who do not use cocaine. Moreover, few data are available regarding drug-eluting stent use in ST-elevation MI patients who have not ingested cocaine. Patients with ongoing cocaine abuse may have poor compliance with the long-term antiplatelet regimen of aspirin and clopidogrel, potentially increasing their risk for subacute and late thrombosis. Therefore, we recommend very careful consideration of the probability of long-term compliance before a drug-eluting stent is used in a patient with cocaine-associated MI. In most cases, a bare metal stent would be preferable. Patients with non–ST-elevation MI or unstable angina are at higher risk for subsequent events and may benefit from an early invasive approach with cardiac catheterization and revascularization, just as patients with ACS unrelated to cocaine do.[74]

β-Blockers

Coronary artery vasoconstriction is exacerbated by the administration of propranolol.[75] The unopposed α-adrenergic effect leads to worsening coronary vasoconstriction and increased blood pressure.[76–78] Multiple experimental models have shown that β-adrenergic antagonists lead to decreased coronary blood flow, increased seizure frequency, and increased mortality.[79–82] The use of the selective β_1 antagonist metoprolol has not been studied in cocaine-associated chest pain, but the short-acting selective β_1 antagonist esmolol resulted in significant increases in blood pressure in up to 25% of patients.[83,84] Although β-blocker administration is recommended for patients with MI unrelated to cocaine because it can lead to lower mortality rates, deaths from cocaine-associated MI are exceedingly low, altering the risk–benefit ratio.[47] The ACC/AHA ST-segment–elevation MI guidelines state, "Beta-blockers should not be administered to patients with STEMI precipitated by cocaine use because of the risk of exacerbating coronary spasm" (p E38).[63] The 2005 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care state "propranolol is contraindicated in cocaine overdose" (p 130) and "propranolol is contraindicated for cocaine induced ACS" (p 129).[85] The use of β-adrenergic antagonists for the treatment of cocaine toxicity should be avoided in the acute setting.[64–66,68] The use of carvedilol has not been studied in the setting of cocaine-associated chest pain. At discharge, β-blockers should be considered for patients with coronary artery disease or left ventricular dysfunction in certain situations (see the section on Discharge Management and Secondary Prevention).

Although theoretically more attractive than propranolol, labetalol does not appear to offer any advantages.[86] Labetalol is both an α- and β-blocker but has substantially more β- than α-adrenergic antagonist effects.[87] Labetalol increases the risk of

seizure and death in animal models of cocaine toxicity[79] and does not reverse coronary artery vasoconstriction in humans.[86]

Nitroglycerin

One case series and 2 randomized controlled trials have shown that nitroglycerin relieves cocaine-associated chest pain.[67,88,89] Nitroglycerin is similar to benzodiazepines with respect to the relief of cocaine-associated chest pain.[67] Cardiac catheterization studies demonstrate that nitroglycerin reverses cocaine-associated vasoconstriction.[46] Nitroglycerin can also be used to control hypertension when a patient does not respond to benzodiazepines.

Calcium Channel Blockers

The role of calcium channel blockers for the treatment of cocaine-associated chest pain has not been well defined. Pretreatment of cocaine-intoxicated animals with calcium channel blockers has had variable results with respect to survival, seizures, and cardiac dysrhythmias.[79,90–94] In cardiac catheterization studies, verapamil reverses cocaine-associated coronary artery vasoconstriction.[95] Large-scale multicenter clinical trials in patients with ACS unrelated to cocaine use have not demonstrated any beneficial effects of calcium channel blockers on important outcomes such as survival, however, and in certain subgroups, calcium channel blockers may worsen mortality rates. Short-acting nifedipine should never be used, and verapamil or diltiazem should be avoided in patients with evidence of heart failure or left ventricular dysfunction.[96,97] Thus, the role of calcium channel blockers in the treatment of patients with cocaine-associated ACS remains uncertain. Calcium channel blockers should not be used as a first-line treatment but may be considered for patients who do not respond to benzodiazepines and nitroglycerin.

Phentolamine

There are anecdotal reports about the safety and efficacy of phentolamine, an α-antagonist, for the treatment of cocaine-associated ACS.[64–66,68,98] Randomized controlled trials in the cardiac catheterization laboratory have provided much of the evidence for the treatment of patients with cocaine-associated coronary vasoconstriction. In these studies, adult patients were given a low dose of cocaine intranasally (2 mg/kg). After cocaine use, patients developed an increased heart rate, blood pressure, and coronary vascular resistance, as well as narrowing of the coronary arterial diameter by 13%.[16] The administration of phentolamine returned coronary arterial diameter to baseline, suggesting that phentolamine may be useful for the treatment of cocaine-associated ischemia.

Other Therapeutic Agents

Cocaine injures the vascular endothelium, increases platelet aggregation, and impairs normal fibrinolytic pathways.[24,25,27,99] As a result, the potential benefit of antiplatelet and antithrombin agents is biologically plausible.[64–66,68,100] Treatment with aspirin, glycoprotein IIb/IIIa antagonists, clopidogrel, unfractionated heparin, low-molecular-weight heparin, or direct thrombin inhibitors has not been well studied in this patient population, although these treatments have been used in some cases and are theoretically useful.[101,102] We recommend aspirin be routinely administered and unfractionated heparin or low-molecular-weight heparin be given to patients with cocaine-associated MI unless there is a contraindication. Aspirin has been shown to be safe when used in an observation unit in patients with cocaine-associated chest pain.[49]

Ventricular Tachyarrhythmias

The treatment of ventricular arrhythmias depends on the time interval between cocaine use, arrhythmia onset, and treatment. Ventricular arrhythmias occurring immediately after cocaine use result from the local anesthetic (sodium channel) effects on the myocardium. These arrhythmias may respond to the administration of sodium bicarbonate, similar to arrhythmias associated with other type IA and type IC agents.[103,104] In addition, one animal model suggested that lidocaine exacerbated cocaine-associated seizures and arrhythmias as a result of similar effects on sodium channels[105]; however, this finding has not been confirmed in other animal models.[103,106,107] Bicarbonate therapy may be preferable and has been used effectively.[108] Ventricular arrhythmias that occur several hours after the last use of cocaine are usually secondary to ischemia, the management of which should be the first goal for treatment. Standard management for ventricular arrhythmias, including lidocaine, is reasonable for persistent or recurrent ventricular arrhythmias.[109] No data exist concerning the efficacy of amiodarone in clinical cocaine intoxication.

Discharge Management and Secondary Prevention

Cessation of cocaine use should be the primary goal of secondary prevention. Recurrent chest pain is less common and MI and death are rare among patients who discontinue cocaine.[39,49] No established drug treatments exist for cocaine dependency, however, and recidivism is high among patients with cocaine-associated chest pain (60% admit to cocaine use in the next year).[39] Several options for psychosocial intervention exist, including individual and group counseling, psychotherapy, and cognitive therapy. Preliminary data suggest that a combination of intensive group and individual drug counseling has the greatest impact on recurrent cocaine use.[110]

Aggressive modification of traditional risk factors is indicated for patients with MI or with evidence of atherosclerosis. This includes smoking cessation, hypertension control, diabetes control, and aggressive lipid-lowering therapy with a target low-density lipoprotein level $<$70 mg/dL. Although these strategies have not been tested specifically for patients who use cocaine, they are standard for patients with underlying coronary artery disease.

Patients with 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 to patients who undergo percutaneous coronary intervention with bare metal stents and for at least 1 year for those treated with drug-eluting stents.[111] Among patients treated medically (ie, without percutaneous coronary intervention), the combination of antiplatelet therapy with aspirin and clopidogrel is clearly of benefit among

patients with unstable angina and non–ST-segment–elevation MI not precipitated by cocaine use,[112] but this regimen has not been studied in patients with cocaine-associated chest pain and MI. Selective use of the combination of aspirin and clopidogrel may be considered for those patients with cocaine-associated MI who have evidence of underlying coronary artery disease. Nitrates and calcium channel blockers may be administered to treat anginal symptoms but are not indicated for routine use. Angiotensin-converting enzyme inhibitors should be used in patients with left ventricular systolic dysfunction.[113]

As noted above, β-adrenergic antagonists should not be administered acutely in patients with cocaine-associated chest pain and/or MI because of concerns about provoking or exacerbating coronary spasm. Postdischarge use of β-blockers, although clearly beneficial among patients with previous MI and cardiomyopathy who do not abuse cocaine, merits special consideration in the setting of cocaine abuse. Because recidivism is high among patients with cocaine-associated chest pain,[39] chronic β-blocker use should be reserved for those with the strongest indications, including those with documented MI, left ventricular systolic dysfunction, or ventricular arrhythmias, in whom the benefits may outweigh the risks even among patients at risk for recurrent use of cocaine. This decision should be individualized on the basis of careful risk–benefit assessment and after counseling the patient about the potential negative interactions between recurrent cocaine use and β-blockade.

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*Modest.

†Significant.

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KEY WORDS: AHA Scientific Statement ■ cocaine ■ substance-related disorders ■ myocardial infarction