

ORIGINAL ARTICLE

Validation of a Brief Observation Period for Patients with Cocaine-Associated Chest Pain

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ABSTRACT

BACKGROUND

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Retrospective studies of patients with cocaine-associated chest pain suggest that a strategy of discharging patients from the emergency department after a 12-hour observation period if they do not have evidence of ischemia should be associated with a very low rate of complications.

METHODS

We prospectively evaluated the safety of a 9-to-12-hour observation period in patients with cocaine-associated chest pain who were at low-to-intermediate risk of cardiovascular events. Consecutive patients who reported or tested positive for cocaine use and who received protocol-driven care in a chest-pain observation unit were included. Patients who had normal levels of troponin I, without new ischemic changes on electrocardiography, and who had no cardiovascular complications (dysrhythmias, acute myocardial infarction, or recurrent symptoms) during the 9-to-12-hour observation period were discharged from the unit. The main outcome was death from cardiovascular causes at 30 days.

RESULTS

Three hundred forty-four patients with cocaine-associated chest pain were evaluated. Forty-two of these patients (12 percent) were directly admitted to the hospital. The study cohort comprised the remaining 302 patients. During the 30-day follow-up period, none of the patients died of a cardiovascular event (0 percent; 95 percent confidence interval, 0 to 0.99), and only 4 of the 256 patients for whom detailed follow-up data were available had a nonfatal myocardial infarction (1.6 percent; 95 percent confidence interval, 0.1 to 3.1). All four nonfatal myocardial infarctions occurred in patients who continued to use cocaine.

CONCLUSIONS

Patients with cocaine-associated chest pain who do not have evidence of ischemia or cardiovascular complications over a 9-to-12-hour period in a chest-pain observation unit have a very low risk of death or myocardial infarction during the 30 days after discharge.

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ACCORDING TO 1999 DATA, AN ESTIMATED 25 million U.S. citizens have used cocaine at least once, 3.7 million have used cocaine in the past year, and 1.5 million have used cocaine in the past month.¹ As cocaine use has become more widespread, the number of cocaine-related cardiovascular events has increased.² During the hour after cocaine is used, the risk of myocardial infarction is 24 times the base-line risk.³ Cocaine users have a lifetime risk of nonfatal myocardial infarction that is seven times the risk of non-users. Cocaine accounts for up to 25 percent of acute myocardial infarctions in patients 18 to 45 years of age.⁴

In 2000, there were 175,000 cocaine-related visits to an emergency department in the United States.⁵ In such visits, chest discomfort occurs in 40 percent of the patients,⁶ 57 percent of whom are admitted to the hospital; their admission lasts an average of three days.⁷ The cost of caring for these patients exceeds \$83 million annually in hospitalization expenses alone.⁷

Currently, no criteria have been identified that allow the safe and rapid discharge of patients who present to the emergency department with cocaine-associated chest pain. In one series, 15 percent of patients with cocaine-associated myocardial infarction were inadvertently released before the discovery of myocardial infarction.⁸ For patients with chest pain who are at low risk for cardiovascular events and who have not recently used cocaine, 12-hour observation periods are safe and cost effective.⁹⁻¹¹ Although a similar observation period may be appropriate for patients with cocaine-associated chest discomfort, prospective evaluation is needed.

Most patients with cocaine-associated chest pain continue to use cocaine, even after hospitalization to rule out acute coronary syndromes.¹² Therefore, it is possible that the low complication rate observed among these patients in an inpatient setting may not apply to patients after release from a chest-pain evaluation unit,^{8,13} when some patients may rapidly resume cocaine use. For that reason, we believed it imperative to document the safety of early release in a prospective, "real-world" setting. The purpose of the current study was to validate prospectively the use of a 9-to-12-hour observation period in patients with cocaine-associated chest pain.

METHODS

STUDY DESIGN

From January 1, 1998, to January 1, 2000, consecutive patients with cocaine-associated chest pain who were evaluated in a chest-pain observation unit were enrolled in a longitudinal cohort study to assess morbidity and mortality from cardiovascular causes at 30 days. The institutional review board of Hurley Medical Center in Flint, Michigan, approved the study.

PATIENTS AND SETTING

Patients 18 years of age or older were included in the study if, when they presented to the emergency department, they reported that they had used cocaine during the week before presentation^{8,12,13} or if the results of toxicologic urine screening revealed cocaine metabolites; if chest discomfort was their chief symptom; and if their symptoms were consistent with a low-to-intermediate likelihood of unstable angina.¹⁴ All the patients who met the inclusion criteria were evaluated in the emergency department chest-pain observation unit.

Patients were excluded if they had chest pain that could be explained by local trauma, radiographic abnormalities, or other clearly noncardiac causes. In addition, high-risk patients were directly admitted to the hospital and were excluded from the analysis; high-risk patients were defined as those whose initial electrocardiogram suggested the presence of ischemia or acute myocardial infarction, ST-segment elevation or depression of 1 mm or more that persisted for at least one minute; elevated serum levels of cardiac markers; recurrent ischemic chest pain; or hemodynamic instability. A daily log of data from all the patients evaluated was maintained and compared against study-enrollment data to ensure that all eligible patients were enrolled.

INITIAL EVALUATION

Structured collection of data was performed with the use of a closed-question instrument that has been assessed in this patient population and has been found to have excellent interrater reliability. The demographic characteristics of the patients, their medical history, the time of their most recent cocaine use, their route of cocaine administration, and their presenting symptoms were recorded.

The investigative team classified each electrocardiogram into one of six categories with the use of a closed-question instrument designed specifically

for this patient population. The possible classifications were as follows: normal, nonspecific ST-T changes, abnormal but not diagnostic of ischemia, diagnostic of ischemia or previous infarction not known to be old, diagnostic of ischemia or previous infarction known to be old, or suggestive of acute myocardial infarction.¹⁵ Interrater reliability, assessed for data from 321 patients, was excellent (Cohen's kappa, 0.69; weighted kappa, 0.95).

OBSERVATION-UNIT PROTOCOL

A detailed discussion of the observation-unit protocol has previously been published.¹¹ Cardiac markers were measured at the time of presentation in the emergency department and three, six, and nine hours after presentation. Continuous 12-lead ST-segment monitoring (Vectra XA, Hewlett-Packard Diagnostics) was performed by physician assistants. Measurement of cardiac troponin I (Access Accu TnI, Beckman Coulter) was selected instead of measurement of the MB fraction of creatine kinase because previously published data suggest that troponin I is the marker protein most specific for myocardial injury in patients who have recently used cocaine.¹⁶ The levels of this marker were considered to be elevated if any measurement exceeded the institutional threshold for normal. The presence or absence (and, if present, the time of occurrence) of congestive heart failure, ventricular tachycardia, supraventricular tachyarrhythmia, and bradyarrhythmia was noted. Finally, in accordance with the institutional standard of care, toxicologic urine screening (Synchron LX Systems) was performed in patients 50 years of age or younger whose chief symptom was chest pain presumed to be of ischemic origin and in all the patients evaluated in the observation unit.

After completion of the first nine hours of the observation protocol, a cardiology consultation was obtained. Initially, all the patients without evidence of myocardial necrosis or ischemia at rest underwent graded exercise testing according to the modified Bruce protocol. Patients with positive stress tests were admitted to the hospital for further evaluation. A positive stress test was defined as one in which there was ST-segment elevation or depression greater than 1 mm, with or without chest discomfort. If the stress test was negative, patients were discharged and referred to an internist or cardiologist within 48 hours. An indeterminate stress test was defined as one in which the patient was unable to complete the protocol or unable to obtain 85 percent of the maximal predicted heart rate. Pa-

tients with indeterminate results on exercise stress testing underwent pharmacologic stress testing with the use of dipyridamole. The study design initially included provocative testing in all the patients. Because of the very low rate of positive stress tests, the observation-unit protocol was changed; stress testing before discharge ceased to be mandatory, and patients were referred to their physicians for outpatient stress testing.

At the time of discharge, all the patients received written instructions regarding the risks of cocaine use.

FOLLOW-UP

At the time of presentation, each patient was asked to provide the addresses and telephone numbers of his or her home, business, and a relative. Alternative contact information, such as pager numbers and telephone numbers for drug rehabilitation centers and homeless shelters, when applicable, were also obtained. Patients were contacted at least 30 days after discharge and asked about recurrent chest pain, the occurrence of the previously defined complications, and myocardial infarction. If both a patient and his or her contact person were unavailable, telegrams were sent to all known addresses requesting that the patient contact us. If we were able to contact the patient directly, we also asked him or her about continued cocaine use, but if a relative or colleague was contacted, we did not inquire about substance abuse. If these methods failed to provide survival information, a review of the medical records with respect to repeated visits and a search of the National Death Index were performed. Written informed consent for follow-up was obtained from the patients. Because other data were collected as part of routine care, the institutional review board did not require informed consent for their use in this study.

All follow-up data were confirmed with a hospital-based search of the medical records one year after the initial visit. All reported adverse events (including myocardial infarction or death) were also confirmed by a review of the records. No deaths or cardiovascular complications that had not already been reported by patients or their proxies were detected by record review.

STATISTICAL ANALYSIS

Data were analyzed on an intention-to-treat basis. Calculations of sample size were based on the expectation that there would be no fatal cardiovascular events. Therefore, we required a sample of 300

patients to reduce the upper limit of the confidence interval for the likelihood of a fatal cardiovascular event to less than 1 percent. All the data were analyzed with the use of SAS statistical software.

RESULTS

PATIENTS

During the study period, 344 patients with chest pain reported cocaine use or tested positive for cocaine. Of these patients, 42 were admitted to the hospital for further evaluation (Table 1). The remaining 302 patients who entered the observation unit constituted the study cohort. Their characteristics at presentation are shown in Table 2. The patients in this study were similar to previous cohorts of patients with cocaine-associated chest pain.

Only two patients (1 percent) required a search of the National Death Index to ascertain survival data. The majority of patients were directly contacted (249 [82 percent]); in other cases information was obtained from a household relative (22 patients [7 percent]), a relative or friend not residing with the patient (24 patients [8 percent]), or a primary care provider (5 patients [2 percent]). All these proxy respondents were in contact with the patient at the time the information was obtained.

Toxicologic urine screening was positive in 282 of the 301 patients tested (94 percent). Cocaine use was self-reported by 247 of the 302 patients in the cohort (82 percent). Of these, 237 reported that they had used cocaine within the preceding week (96 percent), and 169 (68 percent) reported that they had used it within 24 hours before presentation. All the patients who did not report their own cocaine use tested positive for cocaine metabolites in the urine. The most common route was inhalation of "crack" cocaine (by 203 patients); other routes were nasal insufflation (by 51 patients) and intravenous injection (by 10 patients). Some patients administered cocaine by more than one route.

The duration of chest pain was known in 290 of the 302 patients (96 percent). In 171 of these 290 patients (59 percent), the duration was less than six hours; in 118 (41 percent), it was less than three hours; and in 45 (16 percent), it was less than one hour.

COURSE IN THE CHEST-PAIN OBSERVATION UNIT

Interventions in the chest-pain observation unit most commonly included aspirin (given to 93 percent of the patients), nitrates (given to 90 percent), and benzodiazepines (given to 30 percent). None

of the patients received fibrinolytic agents, and only four received beta antagonists (1 percent). In none of the patients did congestive heart failure or dysrhythmias develop in the observation unit.

One hundred fifty-eight of the 302 patients underwent stress testing before discharge from the hospital. Four of these patients had positive results on stress testing (3 percent); all four underwent cardiac catheterization. Two had multivessel coronary artery disease, one had nonocclusive coronary disease, and one had normal coronary arteries.

Table 1. Clinical Course of the 42 Patients Admitted Directly to the Hospital.

Event	No. of Patients
Cardiovascular complications	
Myocardial infarction	10
Unstable angina	10
Congestive heart failure	3*†
Sustained ventricular dysrhythmias	2*‡
Diagnostic testing	
Cardiac catheterization	
Test performed	21
Coronary artery disease (>70% stenosis)	16
Stress testing§	
Test performed	7
Positive results	1
Echocardiography	
Test performed	13
Abnormal findings¶	10
Cardiovascular interventions	
Percutaneous intervention	12*
Coronary-artery bypass surgery	1*

* These patients had a final diagnosis of either acute myocardial infarction or unstable angina.

† Congestive heart failure was present on arrival in all three patients.

‡ Ventricular dysrhythmias occurred within nine hours after arrival in both patients.

§ None of the patients who had a negative stress test underwent cardiac catheterization.

¶ Regional wall-motion abnormalities were present in four patients; global hypokinesis without a regional wall-motion abnormality was present in five patients; an ejection fraction of 45 percent or less was present in eight patients; and severe valvular disease was present in one patient. (Some of the patients had more than one finding.)

Table 2. Demographic, Historical, and Presenting Characteristics of the 302 Study Patients.

Characteristic	Value	Characteristic	Value
Mean (\pmSD) age — yr	37.6 \pm 9.3	Characteristics of chest pain (cont.)	
Male sex — no. (%)	198 (66)	Associated symptoms \ddagger	
Race or ethnic group — no. (%)		Shortness of breath	190 (63)
Black	211 (70)	Diaphoresis	104 (34)
Hispanic	7 (2)	Palpitations	41 (14)
White	75 (25)	Nausea	90 (30)
Other or unknown	9 (3)	Vomiting	24 (8)
Cardiac risk factors — no. (%)$\ast\ddagger$		Syncope	8 (3)
Hypertension	51 (17)	Vital signs at presentation — no. (%)	
Hypercholesterolemia	12 (4)	Systolic blood pressure	
Family history of coronary artery disease	93 (31)	\geq 140 mm Hg	109 (36)
Diabetes mellitus	10 (3)	>90–139 mm Hg	187 (62)
Current tobacco use	255 (84)	\leq 90 mm Hg	6 (2)
Medical history — no. (%)\ast		Diastolic blood pressure	
Self-reported chest pain	137 (45)	>90 mm Hg	55 (18)
Myocardial infarction	6 (2)	\leq 90 mm Hg	247 (82)
Congestive heart failure	3 (1)	Heart rate	
Arrhythmias	4 (1)	>100 beats/min	67 (22)
Characteristics of chest pain — no. (%)		60–100 beats/min	218 (72)
Location		<60 beats/min	17 (6)
Substernal	226 (75)	Respiratory rate	
Left side only	55 (18)	>25 breaths/min	13 (4)
Right side only	10 (3)	10–25 breaths/min	289 (96)
Other or unknown	11 (4)	Electrocardiogram	
Quality		Normal	122 (40)
Pressure, tightness, or squeezing	174 (58)	Nonspecific ST-T changes	121 (40)
Sharp or stabbing	80 (26)	Abnormal but not diagnostic of ischemia	42 (14)
Aching or dull	18 (6)	Diagnostic of ischemia known to be old	11 (4)
Burning or sensation of indigestion	10 (3)	Diagnostic of ischemia not known to be old	6 (2)
Other or unknown	20 (7)		
Pleuritic component	70 (23)		

* Cardiac risk factors and previous medical problems were reported by the patients.

\ddagger Several patients had more than one cardiac risk factor. Twenty-five patients had no cardiac risk factors (8 percent), 165 had one risk factor (55 percent), 85 had two risk factors (28 percent), 23 had three risk factors (8 percent), and 4 had four or more risk factors (1 percent).

\ddagger Some of the patients had more than one symptom.

MAIN OUTCOMES

Thirty-day survival data were available for 300 patients (99 percent of the study cohort). The remaining two patients did not appear in the National Death Index. There were no deaths from cardiovascular causes (0 percent; 95 percent confidence interval, 0 to 0.99). There were, however, two deaths (one due to a gunshot wound and the other due to a heroin overdose). Detailed follow-up information was available for 256 patients (Table 3). Twenty-

five percent of the patients reported recurrent cocaine use. None of the patients had sustained ventricular dysrhythmias (0 percent; 95 percent confidence interval, 0 to 1.2). Four patients had a nonfatal myocardial infarction during the 30-day follow-up period (1.6 percent; 95 percent confidence interval, 0.1 to 3.1). All four had continued to use cocaine (Table 4). In addition, all four had at least two cardiac risk factors (which was the case for only 37 percent of the overall cohort).

DISCUSSION

Our data prospectively validate previous work suggesting that patients with cocaine-associated chest pain are at low risk for death and cardiovascular complications after presentation to the emergency department. In the Cocaine Associated Chest Pain (COCHPA) study,⁸ none of 246 patients had a sustained ventricular dysrhythmia after arrival, and congestive heart failure developed in only 2 percent. Tokarski et al.¹⁷ observed an uncomplicated hospital course in 42 patients with cocaine-associated chest pain and normal or nondiagnostic initial electrocardiograms. Amin et al.¹⁸ reported one case of congestive heart failure and one case of nonsustained ventricular tachycardia among 22 patients with acute myocardial infarction due to cocaine use.

Table 3. Outcomes at 30 Days in the Study Patients.

Outcome	No. of Patients	Percent (95% CI)*
Death from cardiovascular causes	0/302	0 (0–0.99)
Ventricular dysrhythmias	0/256	0 (0–1.2)
Nonfatal myocardial infarction	4/256	1.6 (0.1–3.1)
Recurrent chest pain	63/255	24.7 (19.4–30.0)
Recurrent cocaine use	64/254	25.2 (19.9–30.5)
Cocaine counseling after discharge	21/251	8.4 (4.9–11.8)

* CI denotes confidence interval.

Table 4. Characteristics of the Four Patients with Nonfatal Myocardial Infarction during the 30-Day Follow-up Period.

Characteristics at Presentation	Findings on Initial Evaluation	Diagnoses at Discharge	Cardiac Medications at Discharge	Course after Discharge
42-year-old male smoker; taking no medications	Acute myocardial infarction ruled out; abnormal result on dipyridamole stress testing; after admission, nonocclusive disease found on catheterization	Noncardiac chest pain, alcoholic cardiomyopathy, diabetes mellitus	Aspirin, insulin	Continued to use cocaine after initial evaluation; had a myocardial infarction despite nonocclusive coronary artery disease
39-year-old female smoker with hypertension and congestive heart failure; taking digoxin, furosemide, spironolactone, and captopril	Acute myocardial infarction ruled out	Noncardiac chest pain, hypertension, alcoholic cardiomyopathy	Aspirin, digoxin, furosemide, spironolactone, captopril	Continued to use cocaine after initial evaluation; had a myocardial infarction; was found to have nonocclusive coronary artery disease
58-year-old male smoker with diabetes mellitus; taking metoprolol and glyburide	Acute myocardial infarction ruled out; indeterminate result on exercise stress test and then a normal result on dipyridamole sestamibi scanning	Noncardiac chest pain, diabetes mellitus	Aspirin, glyburide	Continued to use cocaine after initial evaluation; was referred for outpatient cardiac catheterization; 3 days after discharge and before catheterization, he presented with a myocardial infarction; was found to have two-vessel coronary disease on catheterization; underwent coronary-artery bypass grafting
41-year-old male smoker with hypertension; taking aspirin and atenolol	Acute myocardial infarction ruled out	Noncardiac chest pain, hypertension	Aspirin	Continued to use cocaine after initial evaluation; had a myocardial infarction; was found to have severe two-vessel disease on catheterization; underwent angioplasty of both vessels

Serious cardiovascular complications were infrequent in low-risk patients with cocaine-associated chest pain.^{8,17-20}

A retrospective study of 136 patients with cocaine-associated myocardial infarction at 29 institutions found that most of the serious complications occurred before or soon after hospital presentation.¹³ All the patients with cardiovascular complications were identified by observation over a 12-hour period, by the finding of ischemia or infarction on an initial electrocardiogram, or by the finding of an elevated level of the MB fraction of creatine kinase within 12 hours after presentation. The authors concluded that fewer than 1.6 of every 1000 patients with cocaine-associated chest pain would be expected to have short-term cardiovascular complications that were not identified during a 12-hour observation period.¹³

Several retrospective studies also support these conclusions. In a study by Kushman et al.,²¹ there was only 1 death within 30 days among 179 patients with cocaine-associated chest pain who were admitted to a chest-pain unit. Kontos et al.,²² who obtained 30-day follow-up information on 115 of 133 patients with cocaine-associated chest pain who were released from the emergency department, did not identify any cardiovascular complications. The one-year actuarial survival was 98 percent in a subgroup of 203 patients from the COCHPA study¹²; most of the deaths were related to preexisting conditions (for example, complications of infection with the human immunodeficiency virus), and death or nonfatal myocardial infarction occurred only in the patients who continued to use cocaine.

The recognition that patients with cocaine-associated chest pain continue to use cocaine, even after hospitalization, has previously prevented widespread adoption of short-term, "rule-out" protocols in this population of patients. It may not be possible to extend the safety profiles documented during inpatient evaluations to the outpatient setting, where an increased likelihood of recurrent cocaine use might lead to an increased risk of cardiovascular complications.^{8,13} Most of the serious complications are associated with continued drug use.¹² Hospitalization may facilitate access to social-work services and drug-use counseling.

Of the 344 patients in the current study who presented to the emergency department with cocaine-associated chest pain, 42 (12 percent) were considered to be at high risk for cardiovascular complications and were directly admitted to the hospi-

tal. Of these 42 patients, 20 received a diagnosis of an acute coronary syndrome, a finding that confirms the high-risk nature of the cohort. These numbers are similar to the results of previous studies that found a 6 percent rate of myocardial infarction in patients with cocaine-associated chest pain,^{8,23} a rate that is higher than that in young patients who do not use cocaine.²⁴

On the other hand, our results support the safety of short-term, "rule-out" protocols for patients with cocaine-associated chest pain who are at low to intermediate risk for cardiovascular events. The outcomes are similar to those reported for 9-to-12-hour protocols in patients who do not use cocaine.^{11,25} In our study, there were no deaths from cardiovascular causes. Only four of the patients had a nonfatal myocardial infarction during the follow-up period, and all four had at least two cardiac risk factors. Two of these patients did not undergo stress testing; the other two had abnormal results on stress testing. Two of the four patients were ultimately found to have clinically significant coronary disease. Although not all patients with cocaine-associated chest pain require urgent evaluation of potential coronary disease, we advocate expedited evaluation of potential coronary disease (within one to two weeks after presentation) for patients with traditional cardiac risk factors, since the vasoconstrictive effects of cocaine are enhanced in the presence of underlying atherosclerosis.²⁶ All four of the patients with subsequent myocardial infarction continued to use cocaine. Therefore, cocaine counseling and drug-treatment strategies should also be emphasized.¹²

Several potential limitations of our study design merit discussion. We did not perform urine testing in all the patients. However, to reduce the selection and ascertainment bias present in previous studies of patients with cocaine-associated chest pain, analysis of the urine for cocaine metabolites was performed in all the patients 50 years of age or younger who presented to the emergency department with potentially ischemic chest pain and in all the patients who were admitted to the chest-pain observation unit, regardless of age. In an effort to be consistent with prior studies,^{8,12,13} we included all patients who had used cocaine during the previous week, although the period during which cocaine can result in myocardial ischemia remains unknown. Although we did not contact all the patients directly, we obtained 30-day follow-up data for a very high proportion of the patients by using multiple

sources to locate the patients. We did not collect data on exercise testing or the use of cardiac medications after discharge.

Our results demonstrate the safety of a 9-to-12-hour observation period for patients who present with cocaine-associated chest pain. Patients with cocaine-associated chest pain should still be evaluated for potential acute coronary syndromes, but those who do not have recurrent symptoms, in-

creased levels of markers of myocardial necrosis, or dysrhythmias can be safely released after a 9-to-12-hour observation period. We recommend that institutions implementing such protocols incorporate strategies for substance-abuse treatment, since there is an increased likelihood of nonfatal myocardial infarction in patients who continue to use cocaine.

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