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Traditional Risk Factors and Acute Myocardial Infarction in Patients Hospitalized with Cocaine-associated Chest Pain

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Summary

Background: Cocaine causes coronary artery constriction and may cause acute myocardial infarction (AMI). The role of traditional coronary risk factors in cocaine-associated myocardial infarction is unclear.

Hypothesis: We hypothesized that traditional risk factors play a major role in predicting AMI in patients admitted with cocaine-associated chest pain

Methods: After reviewing 165 admissions for chest pain in patients with a history of recent cocaine use and/or a positive drug screen from January 2001 to December 2004, we identified 151 patients with information available on at least 6 of the following 7 risk factors: gender, hypertension, hyperlipidemia, diabetes, smoking, family history of coronary artery disease (CAD) and known CAD. AMI was diagnosed using WHO criteria. A risk score was calculated on the basis of the number of risk factors, gender and age. Association of AMI was evaluated with the individual risk factors and with the risk score.

Results: AMI was identified in 21 patients (14%). All patients diagnosed with AMI were smokers. Continuous risk score ($p < 0.0001$), highest vs. lowest quartile of risk score ($p = 0.007$), known CAD, age, hyperlipidemia and family history of CAD were individually associated with the diagnosis of AMI ($p \leqslant 0.05$). Each quartile of risk score was associated with increased odds of the diagnosis of AMI and score of 8 or higher was statistically significant.

Conclusion: Several traditional risk factors are associated with the diagnosis of AMI among patients hospitalized with cocaine-associated chest pain and increasing risk factor score was associated with increasing odds of AMI diagnosis.

Key words: cocaine, chest pain, myocardial infarction

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Introduction

The use of the leaves of the Erythroxylon coca to achieve a euphoric effect dates back more than 1,000 years.[1] Cocaine abuse in the United States peaked in 1985 when 5.7 million people (3% of population) used cocaine.[2–4] Among Americans over 12 year of age, 27.7 million, 12% of the population, have used cocaine at some point in their lifetime,[5] and more than 5.9 million, or 2.5% of the entire US population, have used cocaine in the past year.[6]

Cocaine use is associated with both acute and chronic cardiovascular toxicity including myocardial ischemia and infarction, coronary artery vasoconstriction, accelerated coronary atherosclerosis, arrhythmias, cardiomyopathy, myocarditis, malignant hypertension, aortic dissection, *in situ* thrombus formation and sudden cardiac death.[7–9]

Cocaine-associated chest pain accounts for approximately 16% of all cocaine-related admissions[10–12] with 6% of the patients being diagnosed with acute myocardial infarction (AMI).[13–15] The risk of AMI is thought to be 24 times greater in the first hour after cocaine use with a rapid decline thereafter.[16] Currently, no criteria have

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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% of patients with cocaine-associated myocardial infarction were inadvertently released before the discovery of myocardial infarction.[17] This often leads to routine admission of all the patients who present with cocaine-associated chest pain, which creates a significant burden on already limited health resources of the country. For patients with chest pain who are at low risk for cardiovascular events and who have not recently used cocaine, it is known that a brief observation period in the emergency room without an admission to the hospital is safe and cost effective. Whether a similar strategy is appropriate for patients with cocaine-associated chest pain is not known and needs to be evaluated. The objective of this study was to investigate if there is a relationship between the traditional risk factors and the diagnosis of AMI among patients hospitalized with cocaine-associated chest pain and to evaluate the value of traditional risk factors for ischemic heart disease in the prediction of AMI among cocaine users.

Methods

This study was approved by University of Arkansas for Medical Sciences (UAMS) Institutional Review Board. We examined medical records of patients admitted at the UAMS hospital from January 2001 to December 2004 with chest pain in the setting of recent cocaine use. Patients were identified by cross-referencing the ICD codes for chest pain and AMI (including ICD 410 through 410.99, 411 through 411.99, 413 through 413.99, 786.5, 786.50, 786.51, 786.52 and 786.59) with those of cocaine use (including ICD codes 304.20, 304.21, 304.22, 304.23, 305.60, 305.61, 305.62, 305.63) using computer assisted medical records search.

Medical records of all the patients who had ICD codes for chest pain/myocardial infarction and ICD codes for cocaine use, either in the same admission or at any time in their medical records (different admissions) were reviewed to assure capture of patients who may have had both chest pain/myocardial infarction and cocaine use in the same admission. Patients were included in the study if they acknowledged cocaine use within the prior 10 days of presentation to the emergency room or had a positive urine drug screen for cocaine at the admission for a chief complaint of chest pain. The need of screening for cocaine use was determined by the clinicians taking care of the patient, which is a standard practice. Information on risk factors was obtained by reviewing the medical records.

Age, race, gender and other cardiac risk factors (hypertension, smoking status, family history of coronary artery disease [CAD], diabetes, preexisting [known] CAD, and hyperlipidemia) were abstracted from data obtained at admission. For persons with multiple admissions, missing family and smoking history were obtained from any admission where available. Diagnosis of AMI was confirmed on the basis of WHO criteria, which included a combination of symptoms of AMI, EKG changes and abnormal cardiac biomarkers (specifically Troponin I).

Statistical analysis

If 6 of the 7 risk factors (gender, hypertension, smoking, family history of CAD, diabetes, known CAD and hyperlipidemia) were available, a risk score was calculated as the number of risk factors plus an additional point for each 5 years of age over 40 (up to 4 points). The risk score ranged from 0 to 11 with median of five. The scores were divided into approximate quartiles (risk score <3, $n = 39$; score $4–5$, $n = 46$; score $6–7$, $n = 41$; scores >8, $n = 25$). Separate general estimating equations were used to evaluate individual risk factors, continuous risk score, and quartiles of risk score, controlling for repeated admissions. Logistic regression analyses evaluated associations between risk factors and AMI for the first admission ($n = 106$). Mann Whitney U-test was used to compare the Areas Under the receiver operating Characteristic curves (AUC) to evaluate the ability of risk factors or risk score to identify individuals at risk of AMI during individuals' first hospital admissions.

Results

We identified 194 nonduplicate admissions with the ICD codes for chest pain/AMI and cocaine use. We excluded 13 admissions because the medical records were not available for review and 16 others were excluded because recent cocaine use could not be confirmed by either urine drug screen or by chart review, leaving 165 admissions for detailed review. Of the 165 admissions, data for calculating risk scores were available for 151 admissions in 106 patients.

Patient characteristics in all cocaine-associated chest pain admissions (including repeat admissions) are shown in Table 1. Fourteen AMIs were diagnosed at the first admission with 7 additional AMIs diagnosed at repeat admissions. The mean age of patients at first admission was 43 years (range $20–60$ years); and patients were predominantly male (76%), black (83%), smokers (88%), and hypertensive (57%). About half of the patients had a family history of CAD (54%) and hyperlipidemia (49%), while 15% were diabetic and 21% had known CAD. Considering all admissions, age, family history of CAD, hyperlipidemia, known CAD and risk scores were significantly higher for admissions when AMI was diagnosed compared to admission when no AMI was diagnosed. If only first admissions were considered, hyperlipidemia and family history of CAD were no longer statistically significant (Table 1). All patients with the diagnosis of AMI were smokers.

TABLE 1 Characteristics of participants for cocaine-associated chest pain admissions

Characteristic	All admissions				First admission only			
		Acute myocardial infarction				Acute myocardial infarction		
	All (N = 151[a])	Yes (n = 21[a])	No (n = 130[a])	p-value	All (N = 106)	Yes (n = 14)	No (n = 92)	p-value
Age, mean (SD)	43.5 (7.5)	49 (5.7)	42.6 (7.4)	0.0002	43.3 (8.1)	48.4 (5.7)	42.5 (8.1)	0.01
Gender, (% male)	78.8	85.7	77.7	0.4	76.4	78.6	76.1	0.8
Race, (% black)	86.1	81	86.9	0.5	83.0	78.6	83.7	0.6
Smoking, (%)	89.4	100	87.7	0.09	87.7	100	85.9	0.1
Family history CAD, (%)	58.9	81	55.4	0.03	53.8	71.4	51.1	0.2
Hypertension, (%)	66.7	61.9	67.4	0.6	56.6	50	57.6	0.6
Diabetes mellitus, (%)	15.9	23.8	14.6	0.3	15.1	21.4	14.1	0.5
Hyperlipidemia, (%)	46	75	41	0.005	48.9	69.2	45.6	0.1
Known CAD, (%)	23.8	66.7	16.9	<0.0001	20.8	57.1	15.2	0.003
Risk score, mean (SD)	5.2 (2.3)	7.3 (2.2)	4.9 (2.1)	<0.0001	5 (2.2)	6.6 (2.0)	4.7 (2.1)	0.002

[a] Number of admissions, but fewer available for some risk factors due to missing data p-value for chi square and t-test comparisons between groups with and without acute myocardial infarction.
SD, standard deviation.

Logistic regression analyses of individual risk factors' associations with AMI during the first admission, indicated that age was positively and significantly associated with AMI (odds ratio [OR] = 1.12, 95% confidence interval [CI] = 1.03–1.22), and patients with known CAD were about seven times as likely to be diagnosed with AMI as patients without preexisting CAD (OR = 7.4, 95% CI = 2.2–24.7). When repeated admissions were included and analyzed with general estimating equation, the risk of AMI was >3 times as great among persons who were 45 years or older (p = 0.02), who had hyperlipidemia (p = 0.03), or had a family history of CAD (p = 0.06) in comparison to persons without these characteristics. Preexistent CAD resulted in an even greater risk (p<0.0001) (Fig. 1). Each quartile of risk score was associated with increased odds of the diagnosis of AMI whether the first or all admissions were considered and scores of ⩾ 8 were statistically significant (Table 2) (Fig. 2).

With the AUC (sensitivity vs. 1-specificity) as the measure of each statistical model's ability to discriminate risk of AMI among first time admissions, of the seven risk factors studied, only known CAD (AUC = 0.710) produced discrimination that was similar to age (AUC = 0.714). When risk factors were added singly to the logistic model with age, only known CAD (AUC = 0.787) improved the predictability of the model (p = 0.16).

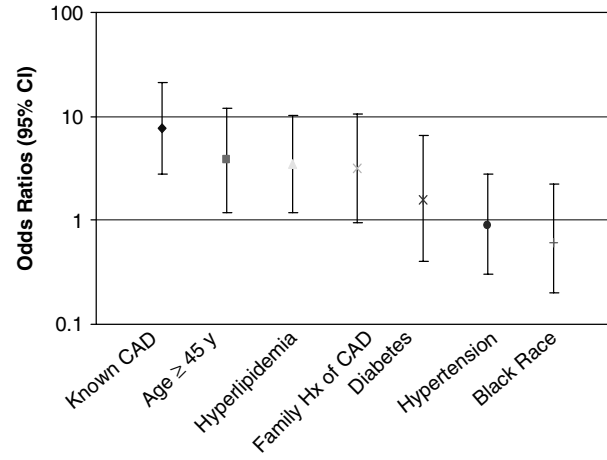

FIG. 1 Odds ratio and 95% confidence intervals (CI) for acute myocardial infarction for individual risk factors from general estimating equations adjusted for repeated admissions. (CAD, coronary artery disease; FHCAD, family history of coronary artery disease).

Discussion

There are a number of mechanisms by which cocaine use might precipitate AMI such as blocking of presynaptic reuptake of epinephrine, norepinephrine, serotonin and dopamine; stimulation of beta adrenergic receptors with subsequent increase in influx of calcium into the cardiac myocytes;[10] stimulation of alpha adrenergic receptors resulting in an increase in inositol triphosphate;[18] and induction of coronary vasoconstriction by inducing release of endothelin-1[19] and inhibiting nitric oxide production.[20] Metabolites such as norcocaine or the enterohepatic circulation may result in delayed or recurrent vasoconstriction several hours after cocaine ingestion.[21] Cocaine also induces structural alterations that enhance permeability of the vascular endothelial cell barrier allowing oxidant species and low density lipoproteins access to the subendothelial layers.[22] This may explain why chronic cocaine use has been associated with accelerated atherosclerosis,[23,24] and why scattered foci of myocyte necrosis have been found after repeated

TABLE 2 Baseline risk factor score quartile[a] associations with acute myocardial infarction in subjects with cocaine-associated chest pain admissions

	First admission only		All admissions	
Risk score[a]	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Quartile 4 (score $\geqslant$ 8)	13.8 (1.4–139)	0.03	21 (2–195)	0.007
Quartile 3 (score 6–7)	6.9 (0.8–60.9)	0.08	7.7 (0.9–65)	0.06
Quartile 2 (score 4–5)	3.7 (0.4–38)	0.3	3.5 (0.3–35)	0.3
Quartile 1 (score $\leqslant$ 3)	1		1	

[a] Calculated based on number on number of risk factors present and age.

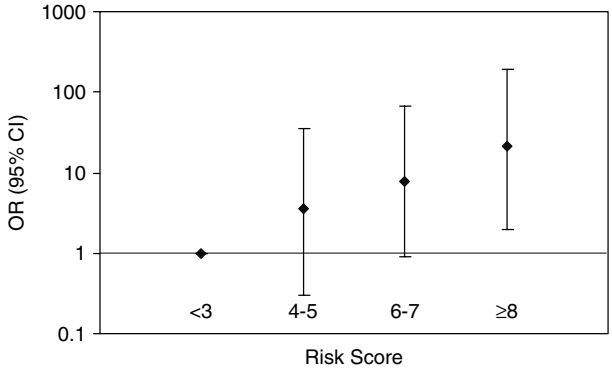

FIG. 2 Magnitude of the association between risk score quartiles and acute myocardial infarction: odds ratios (OR) and 95% confidence intervals (CI) estimated using general estimating equations and controlling for repeated admissions.

use.[18] Thus, our finding of 14% AMIs occurring among cocaine users with chest pain is not surprising.

The 14% incidence of AMI in patients with cocaine-associated chest pain is small, though not insignificant. Previous studies have shown that the incidence of AMI with the use of cocaine may be even lower (6%).[13] The relatively high incidence of AMI in our study may be related to use of troponin rather than creatine kinase as the major diagnostic criterion for identifying AMI and because our study included only patients hospitalized with chest pain. In another study of cocaine-associated AMI, Amin *et al*. determined the characteristics of patients with cocaine-associated AMI, and found no significant difference in the prevalence of traditional CAD risk factors among patients who had AMI vs. those who did not.[25] However, the number of subjects in their study was small which may have limited their ability to identify a role for the traditional risk factors.

It is important to identify individuals abusing cocaine who are at increased risk of developing an AMI to prevent the adverse prognosis that an unmonitored AMI could produce. Algorithms designed for risk stratification may provide a cost-effective emergency room triage of patients with cocaine-associated chest pain. Our study showed that a risk score derived from traditional CAD risk factors was strongly associated with the diagnosis of AMI. This study provides preliminary data that is needed to establish the usefulness of risk stratification among cocaine users with chest pain. If similar associations can be confirmed among all emergency room patients seen for cocaine-associated chest pain, then risk scores should be useful in risk stratification of patients who present with cocaine-associated chest pain. If a suitable level of risk score can be confirmed in other populations, then those with low risk scores may not need to be admitted but can rather be discharged after a brief observation. It is noteworthy that our sample had too few smokers for the association to be statistically significant, but AMI was not diagnosed among nonsmokers.

Most patients with cocaine-associated chest pain continue to use cocaine, even after hospitalization to rule out acute coronary syndromes.[26] Recurrent/continued cocaine use is associated with higher risk of cardiovascular complications.[26] This study can prove useful in counseling hospitalized patients with high risk scores. Their markedly higher risk of having an acute MI in comparison to cocaine users with lower risk score, might serve as an incentive for a generally healthier lifestyle or as a deterrent for future cocaine use.

Overall, many factors, such as population under study, may impact whether a prediction model will be useful in clinical practice. Age, known CAD, hyperlipidemia, family history of CAD, and risk score were associated with AMI when all admissions were considered (all p-values $\leqslant$ 0.06), and several risk factors increased the predictability (AUC) of AMI when added to the models containing age (data not shown). However, only known CAD approached statistical significance.

Limitations of our study are a relatively small sample size, lack of reliable documentation regarding the duration of chest pain, and for frequency, timing and route of cocaine administration. Further, our study was limited to hospitalized patients. Thus, our patients are likely to have been at greater risk of AMI than patients presenting to the emergency room with cocaine-associated chest pain and not deemed eligible for hospitalization. Since, in this study, urine screen for cocaine was at the discretion of the admitting physician, this may have led

to information bias because persons with chest pain and traditional risk factors may have been tested less often for drug use than persons lacking traditional risk factors. Without a history of cocaine use or a urine screen, these patients would not have been included and would underestimate an effect of traditional risk factors. Thus, biases could have resulted in selection of either fewer or more cocaine users with traditional risk factors. Also, some of the significant associations were only found if repeated admissions were considered which suggests some cocaine users are at higher risk than others.

Conclusion

Among patients admitted with cocaine-associated chest pain, a risk score formed from traditional coronary risk factors was strongly associated with the subsequent diagnosis of AMI. Further studies are needed to validate the role of traditional risk factors in patients presenting with cocaine-associated chest pain.

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