Immediate Effects of Intravenous Cocaine on the Thoracic Aorta and Coronary Arteries*

A Transesophageal Echocardiographic Study

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Study objectives and design: Arterial vasoconstriction is thought to play a role in the etiology of cocaine-induced cardiovascular complications, but little is known about the immediate effects of cocaine on the thoracic aorta and coronary arteries. To examine these effects, we used transesophageal echocardiography to examine the thoracic aorta and coronary arteries before and immediately after intravenous (IV) cocaine (1.2 mg/kg) in 15 subjects.

Measurements and results: Immediately after cocaine infusion, average heart rate, systolic BP, and double product were increased compared with baseline (22%, 15%, 35%, respectively). There was no significant change in the diameters of the ascending aorta (27.5 vs 27.1 mm; p=0.85), the descending aorta (19.8 vs 20.4 mm; p=0.62), or the left main coronary artery (4.3 vs 4.7 mm; p=0.15). However, there was a trend for an increase in coronary blood flow immediately after cocaine (226 vs 309 mL/min; p=0.10).

Conclusions: We conclude that in the 15 subjects studied, there was no evidence of thoracic aorta or coronary artery vasoconstriction immediately after IV cocaine. Instead, we found that the diameters of the thoracic aorta and the left main coronary artery were unchanged, and that there was a trend for augmentation of coronary artery blood flow. (CHEST 1996; 110:147-54)

Key words: aorta; cocaine; coronary arteries; heart; transesophageal echocardiography; vasoconstriction

Abbreviations: LAD=left anterior descending coronary artery; TEE=transesophageal echocardiography; VTI=velocity-time integral

Cocaine use has been associated with a number of life-threatening cardiovascular complications, including dissection and rupture of the thoracic aorta and myocardial ischemia and infarction.1,5 Arterial vasoconstriction is thought to play a role in the etiology of these life-threatening cardiovascular complications, and this theory is supported by a number of studies documenting cocaine-induced vasoconstriction of the thoracic aorta 6 and coronary arteries.7-10

Cocaine has been shown to cause vasoconstriction of the thoracic aorta in in vitro preparations.6 When segments of rabbit aorta were placed in baths with increasing concentrations of cocaine, the segments demonstrated increasing levels of vasoconstriction. In clinical studies, cocaine has been shown to cause peripheral vasoconstriction leading to increases in systemic BP.1 Thus, vasoconstriction of the thoracic aorta in the setting of increased systemic BP has been suggested as the mechanism by which cocaine causes dissection and rupture of the thoracic aorta.11

Besides its effects on the thoracic aorta, cocaine has also been shown to cause vasoconstriction of the coronary arteries.7-10 Clinical studies suggest that in the subacute period (15 to 60 min after administration), cocaine causes a reduction in coronary artery diameter.7,8 During this time, cocaine increases myocardial oxygen demand via an increase in heart rate and BP.1 Thus, vasoconstriction of the coronary arteries in the setting of increased myocardial oxygen demand has been suggested as the mechanism by which cocaine causes myocardial ischemia and infarction.1,4

Although a number of studies have documented
Table 1—Clinical Characteristics of 15 Subjects Who Received IV Cocaine During TEE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year, mean ± SD</td>
<td>34±6</td>
</tr>
<tr>
<td>Systolic BP, mm Hg, mean ± SD</td>
<td>115±10</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg, mean ± SD</td>
<td>74±8</td>
</tr>
<tr>
<td>Duration of cocaine use, yr, mean ± SD</td>
<td>14±5</td>
</tr>
<tr>
<td>Cocaine use (last 12 mo)</td>
<td></td>
</tr>
<tr>
<td>Average, times/mo</td>
<td>7±6</td>
</tr>
<tr>
<td>Range, times/mo</td>
<td>1-20</td>
</tr>
<tr>
<td>Alcohol use (last 12 mo)</td>
<td></td>
</tr>
<tr>
<td>Percent who used over last 12 mo</td>
<td>93</td>
</tr>
<tr>
<td>Average, times/mo</td>
<td>14±13</td>
</tr>
<tr>
<td>Range, times/mo</td>
<td>1.5-30</td>
</tr>
<tr>
<td>Range, No. of drinks per episode</td>
<td>4±3</td>
</tr>
<tr>
<td>Duration of alcohol use, yr, mean ± SD</td>
<td>17±8</td>
</tr>
<tr>
<td>Tobacco use</td>
<td></td>
</tr>
<tr>
<td>Percent who used over last 12 mo</td>
<td>80</td>
</tr>
<tr>
<td>No. of cigarettes/day, mean ± SD</td>
<td>13±10</td>
</tr>
<tr>
<td>Duration of tobacco use, yr, mean ± SD</td>
<td>14±9</td>
</tr>
<tr>
<td>Other drug use (% who used over last 12 mo)</td>
<td></td>
</tr>
<tr>
<td>Marijuana*</td>
<td>83</td>
</tr>
<tr>
<td>Opiates</td>
<td>90</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>60</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>40</td>
</tr>
<tr>
<td>LSD*†</td>
<td>25</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>20</td>
</tr>
</tbody>
</table>

*n=11
†LSD=lysergic acid diethylamide.

Cocaine-induced arterial vasoconstriction in the subacute period, relatively little is known about the immediate effects of cocaine (0 to 15 min after administration) on the thoracic aorta and coronary arteries. In contrast with most studies examining the subacute effects of cocaine, Friedrichs et al.12 found that IV cocaine caused an immediate dilatation of the coronary arteries and an increase in coronary blood flow in anesthetized beagles. Similarly, Zimring et al.13 described coronary artery vasodilation immediately after IV cocaine administration in an open chest pig model. To our knowledge, these results have not been reported in humans. Thus, in order to examine the immediate effects of cocaine on the thoracic aorta and coronary arteries in humans, we administered IV cocaine to 15 subjects during transesophageal echocardiography (TEE). Our purpose was to examine whether IV cocaine causes (1) an immediate vasoconstriction of the thoracic aorta and coronary arteries, and (2) an immediate decrease in coronary blood flow.

MATERIALS AND METHODS

Subjects

Fifteen paid volunteers were recruited for the study. Inclusion criteria included (1) age 20 to 45 years, (2) current IV cocaine use, and (3) no evidence of cardiac, neurologic, or systemic illness. Subjects were screened with comprehensive history, physical, and laboratory examinations (including ECGs) (Table 1). HIV-positive subjects and pregnant women were excluded from the study. All subjects gave written informed consent for both IV cocaine administration and TEE, and the research protocol was approved by the Committee on Human Research at the University of California, San Francisco.

Cocaine Administration

Subjects were asked not to use cocaine for 24 h prior to the echocardiographic study, not to eat or drink for 8 h prior, and not to use tobacco on the day of the study. After a baseline TEE study was performed, the subjects received 1.2 mg/kg of cocaine hydrochloride (10 mg/mL diluted in normal saline solution) injected IV over 2 min. Infusions were given by an indwelling venous catheter in the left forearm via an infusion pump.

Monitoring

Subjects were monitored for a minimum of 30 min before the insertion of the transesophageal probe and for at least 3 h after the probe was removed. The following physiologic variables were recorded: heart rate, BP, skin temperature, core temperature, oxygen saturation, and intoxication ratings. Heart rate and BP were recorded with a patient monitor (Physio-Control VSM-2; Physio-Control Corp; Redmond, Wash); skin temperature with a thermometer taped to the left index finger; core temperature with a thermometer inserted in the subject’s right ear; and oxygen saturation with a continuous pulse oximeter. Intoxication ratings were obtained by subjects pointing to a visual analog scale ranging from 0 to 100. A value of 0 was equivalent to not feeling intoxicated at all, and a value of 100 was equivalent to feeling the most intoxicated the subject had ever been after an IV dose of cocaine. Except for intoxication ratings, all variables were recorded prior to probe insertion (3 measurements over ≥0.5 h), every minute during the TEE study, and then every 0.5 h for 3 h. Intoxication ratings were obtained at baseline and at 1, 2, 5, 7, 10, and 15 min after cocaine administration.

Blood Samples

To measure cocaine levels, blood samples were obtained from an indwelling catheter in the right arm. Samples were obtained prior to probe insertion and at 2 and 180 min after cocaine administration. Blood samples were frozen and were later analyzed by gas chromatography.14

Transesophageal Echocardiography

Procedure: All TEE studies were performed by the same sonographer using a machine (Hewlett Packard Sonos 1500 series) and a bipline probe. Studies were recorded on 0.5-inch videotape (SVHS). Random numbers and multiple video cassettes were employed so that echocardiographic studies could later be analyzed in a blinded manner.

TEE studies were performed following the standard procedure in our laboratory. Following sedation with IV midazolam (1 to 8 mg) and topical pharyngeal anesthesia (Cetacaine) (3 to 7 sprays), a baseline TEE study was performed as follows. A videotape cassette was placed in the machine, and random numbers were entered for subject identification and precocaine status. Using the transverse plane, the descending thoracic aorta was visualized at 2 levels: (1) the level of the left atrial appendage, and (2) 30 to 40 cm from the subject’s incisors. The coronary arteries were then visualized in the transverse plane beginning at their origins just above the aortic valve. Pulse-wave Doppler was used to measure blood flow velocity in the left anterior descending coronary artery (LAD). Color-flow Doppler was used to guide placement of the sample volume at the point of greatest color intensity. The imaging plane was then adjusted by transducer rotation or flexion/extension to visualize the circumflex and right coronary arteries. Finally, the ascending aorta was visualized in the longitudinal plane.
Following the baseline study, the videocassette was replaced and a new random number was entered indicating postcocaine status (multiple cassettes were used to ensure reviewer blinding). Beginning 2 min after the initiation of the cocaine infusion, a repeated TEE study was performed following the same format as the baseline study. Both baseline and postcocaine studies required about 15 min, and the TEE probe was never in place longer than 45 min.

**Analysis:** Paired TEE studies were presented to a blinded reviewer for off-line analysis with a dedicated computerized analysis system (Cineview Plus; Freeland GTI; Louisville, Colo). Because the studies were identified only by random numbers, the reviewer was unaware of which study was baseline and which was postcocaine. All measurements made by the reviewer were made during three cardiac cycles and averaged.

Using electronic calipers, the reviewer measured the aortic diameter at 3 points: (1) the ascending aorta—1 cm above the aortic valve; (2) the descending aorta—at the level of the left atrial appendage; and (3) the descending aorta—30 to 40 cm from the subject’s incisors.

Similarly, coronary artery diameters were measured at 4 points: (1) 0.3 cm from the origin of the left main coronary artery; (2) the proximal LAD; (3) the proximal circumflex coronary artery; and (4) the proximal right coronary artery. Blood flow in the mid-LAD was assessed quantitatively by pulse-wave Doppler. Using the computerized analysis system, measurements were made of peak and mean blood flow velocities in systole and diastole. The systolic/diastolic ratio of peak velocities was calculated and the velocity-time integral (VTI) was measured. Finally, coronary blood flow for each subject was calculated by multiplying the cross-sectional area of the left main coronary artery by the average heart rate and the VTI before and immediately after cocaine. Similar to measurements of thoracic aorta and coronary artery diameters, all Doppler measurements were repeated three times and averaged.

**Statistical Analysis**

Continuous variables are presented as the mean±SD. Preco- cocaine and postcocaine measurements of thoracic aorta diameter, coronary artery diameter, and coronary blood flow were compared using paired Student’s *t* tests. All hypothesis testing was two tailed, and a *p* value<0.05 was considered to be statistically significant.

**RESULTS**

**Subjects**

We studied 15 long-term IV cocaine users (12 men and 3 women) with an average age of 34 years (Table 1). Subjects used cocaine approximately two times per week in the year before the study. Most subjects also used alcohol and tobacco, as well as a number of other illicit substances in addition to cocaine.

**Dosages**

Peak plasma levels of cocaine and peak intoxication ratings suggest that the dosages used in this study were comparable to dosages commonly self-administered in nonmedical settings.15-18 The mean plasma cocaine concentration measured 2 min after cocaine administration was 496 ng/mL. This concentration is greater than that seen in some postmortem studies of patients who died of cocaine-induced cardiac complications. These studies found blood concentrations of cocaine as low as 100 ng/mL in some IV users.16 Although previous studies in animals documented arterial vasoconstriction in association with higher cocaine concentrations, the dosages used in these studies were many times greater than the dosages commonly employed by cocaine users.

In contrast with the plasma cocaine concentrations, intoxication ratings revealed that only 1 of 15 subjects...
we conducted using a TEE probe insertion, immediately after IV cocaine, heart rate increased by 22% (from a mean ± SD of 79±19 to 96±22 beats/min; p<0.01), systolic BP by 15% (from 108±13 to 124±13 mm Hg; p<0.01), and double product by 35% (from 8,788±2,716 to 11,905±3,332 mm Hg×beats/min; p<0.01). Skin temperature and core temperature were not significantly different from baseline values. Importantly, no subject reported chest pain or dyspnea during the study.

**Thoracic Aorta Response to Cocaine**

Optimal visualization of the ascending thoracic aorta before and immediately after cocaine was present in 8 subjects and of the descending thoracic aorta in 11 subjects. Baseline TEE studies showed that none of the subjects had atherosclerotic disease involving the ascending or descending thoracic aorta. Precocaine and postcocaine measurements showed no significant change in thoracic aorta diameter (Table 2). The mean diameter of the ascending aorta was 27.5 mm at baseline and 27.1 mm after cocaine. The mean diameter of the descending aorta was 19.8 mm at baseline and 20.4 mm after cocaine.

**Coronary Artery Response to Cocaine**

Optimal visualization of the left main coronary artery before and immediately after cocaine was present for ten subjects (Fig 2), for the LAD in three subjects, for the circumflex coronary artery in two subjects, and for the right coronary artery in one subject. Baseline TEE studies showed no evidence of proximal coronary artery calcification or stenosis in any of the subjects studied. Similar to the measurements of the thoracic aorta, there were no significant changes in

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**Table 2—Diameters of the Thoracic Aorta and Left Main Coronary Artery Before and Immediately After IV Cocaine**

<table>
<thead>
<tr>
<th>Diameter, mm</th>
<th>Pre cocaine</th>
<th>Post cocaine</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aorta (n=8)1</td>
<td>27.5±0.4</td>
<td>27.1±0.6</td>
<td>0.85</td>
</tr>
<tr>
<td>Descending aorta</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of left atrial appendage (n=11)</td>
<td>20.1±1.8</td>
<td>20.6±3.7</td>
<td>0.62</td>
</tr>
<tr>
<td>30-40 cm from incisors1 (n=9)</td>
<td>19.5±1.9</td>
<td>20.2±2.6</td>
<td>0.15</td>
</tr>
<tr>
<td>Left main coronary artery (n=10)</td>
<td>4.3±0.9</td>
<td>4.7±0.6</td>
<td>0.15</td>
</tr>
</tbody>
</table>

*Data are presented only for subjects who had measurable diameters before and after cocaine.

1 Measured 1 cm above the aortic valve.

2 Distance measured from scale located on surface of TEE probe.

reported a high rating of 50 or more while 8 subjects reported high ratings of 50 or less. In a previous study we conducted using the same dose of IV cocaine,19 10 of the 20 subjects reported intoxication ratings of 90 or greater. Thus, although cocaine dosages were the same in both studies (1.2 mg/kg), premedication with midazolam in the present study appeared to blunt the perception of intoxication.

**Physiologic Effects**

Cocaine administration caused acute elevations in heart rate, systolic BP, and double product (Fig 1). Compared with baseline measurements after TEE probe insertion, immediately after IV cocaine, heart rate increased by 22% (from a mean ± SD of 79±19 to 96±22 beats/min; p<0.01), systolic BP by 15% (from 108±13 to 124±13 mm Hg; p<0.01), and double product by 35% (from 8,788±2,716 to 11,905±3,332 mm Hg×beats/min; p<0.01). Skin temperature and core temperature were not significantly different from baseline values. Importantly, no subject reported chest pain or dyspnea during the study.

**Thoracic Aorta Response to Cocaine**

Optimal visualization of the ascending thoracic aorta before and immediately after cocaine was present in 8 subjects and of the descending thoracic aorta in 11 subjects. Baseline TEE studies showed that none of the subjects had atherosclerotic disease involving the ascending or descending thoracic aorta. Precocaine and postcocaine measurements showed no significant change in thoracic aorta diameter (Table 2). The mean diameter of the ascending aorta was 27.5 mm at baseline and 27.1 mm after cocaine. The mean diameter of the descending aorta was 19.8 mm at baseline and 20.4 mm after cocaine.

**Coronary Artery Response to Cocaine**

Optimal visualization of the left main coronary artery before and immediately after cocaine was present for ten subjects (Fig 2), for the LAD in three subjects, for the circumflex coronary artery in two subjects, and for the right coronary artery in one subject. Baseline TEE studies showed no evidence of proximal coronary artery calcification or stenosis in any of the subjects studied. Similar to the measurements of the thoracic aorta, there were no significant changes in

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**Figure 2.** Left main coronary artery arising from the left coronary cusp of the ascending aorta. View obtained by TEE in the transverse plane. The pulse wave Doppler sampling frame is in the proximal LAD.
coronary artery diameters after cocaine (Table 2), and the measurements obtained suggested little likelihood of coronary vasoconstriction (LAD: 2.6±0.8 to 3.4±0.4 mm; circumflex: 2.8±0.8 to 3.4±0.7 mm; right coronary artery: 3.2 to 3.7 mm).

Doppler measurements of blood flow in the LAD were obtainable for 13 subjects before and after cocaine (Fig 3 and Table 3). These data demonstrate that there was no significant change in the VTI immediately after cocaine. Because cocaine increased heart rate, however, there was an increase in mean diastolic velocity, but no change in mean systolic blood flow velocity. Based on coronary artery diameter and Doppler measurements, there appeared to be a trend for increased coronary blood flow in the left main coronary artery after cocaine (226 vs 309 mL/min; p=0.10). Approximately one half of this increase in blood flow was due to an increase in coronary artery diameter and approximately one half was due to the cocaine-induced increase in heart rate.

**DISCUSSION**

Our study was designed to examine whether IV cocaine causes (1) an immediate vasoconstriction of the thoracic aorta and coronary arteries, and (2) an immediate decrease in coronary blood flow. In contrast with previous studies, we found little evidence of cocaine-induced vasoconstriction of the thoracic aorta or coronary arteries immediately after IV cocaine, and we observed a trend for an increase in blood flow in the left main coronary artery.

**Thoracic Aorta**

Experimental and clinical reports suggest that vasoconstriction of the thoracic aorta in the setting of increased systemic BP may be the mechanism by which cocaine causes dissection and rupture of the thoracic aorta. Several *in vitro* studies have demonstrated cocaine-induced vasoconstriction of the thoracic aorta, and several clinical case reports have documented co-

<table>
<thead>
<tr>
<th></th>
<th>Precocaine</th>
<th>Postcocaine</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main coronary artery</td>
<td>226±129</td>
<td>309±100</td>
<td>0.10</td>
</tr>
<tr>
<td>LAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VTI (n=13)</td>
<td>1.9±0.5</td>
<td>2.0±0.6</td>
<td>0.43</td>
</tr>
<tr>
<td>Diastolic velocity, m/s (n=13)</td>
<td>0.45±0.10</td>
<td>0.55±0.19</td>
<td>0.01</td>
</tr>
<tr>
<td>Peak</td>
<td>0.32±0.08</td>
<td>0.41±0.14</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean</td>
<td>0.37±0.10</td>
<td>0.37±0.11</td>
<td>0.95</td>
</tr>
<tr>
<td>Systolic velocity, m/s (n=12)</td>
<td>0.30±0.07</td>
<td>0.29±0.10</td>
<td>0.80</td>
</tr>
<tr>
<td>Peak</td>
<td>0.30±0.07</td>
<td>0.29±0.10</td>
<td>0.80</td>
</tr>
<tr>
<td>Mean</td>
<td>0.69±0.08</td>
<td>0.69±0.08</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*Blood flow velocities were determined by pulse-wave Doppler assessment in the mid-LAD.*
caine-induced dissection and rupture of the thoracic aorta.

Shibata et al. examined *in vitro* preparations of rabbit aorta. These investigators found increasing levels of vasoconstriction when segments of rabbit aorta were placed in baths with increasing concentrations of cocaine. Similarly, Egashira et al. found a dose-dependent relationship between cocaine concentration and aortic vasoconstriction in an *in vitro* ferret model. These results suggest that vasoconstriction of the thoracic aorta in the setting of increased systemic BP may cause increased aortic shear forces and be responsible for cases of cocaine-induced dissection and rupture of the thoracic aorta.

This hypothesis is supported by clinical case reports linking cocaine use and aortic dissection and rupture. These reports document ten cases of aortic dissection and rupture that occurred shortly after cocaine use. Patients ranged in age from 26 to 58 years, and 8 of the 10 were men. Type A and type B dissections were noted, and four of the patients died. Thus, both experimental studies and clinical case reports support the idea that cocaine use may cause dissection and rupture of the thoracic aorta, and that these cardiovascular complications may be due to vasoconstriction of the thoracic aorta in the setting of elevated systemic BP.

In contrast with these previous studies, we found little evidence that IV cocaine causes vasoconstriction of the thoracic aorta. Furthermore, we found that typical doses of cocaine cause only modest increases in heart rate and BP. On average, 1.2 mg/kg of cocaine increased heart rate by 22%, systolic BP by 15%, and double product by 35%. In a previous study we conducted using the same dose of cocaine but without premedication with midazolam,19 heart rate increased from 69 to 99 beats/min, systolic BP from 106 to 128 mm Hg, and rate pressure product from 7,400 to 12,600 mm Hg·beats/min. Thus, our results indicate that IV cocaine does not cause acute vasoconstriction of the thoracic aorta and that the increases in systemic BP caused by cocaine are only modest. These results suggest that cocaine-induced vasoconstriction of the thoracic aorta in the setting of increased systemic BP is an unlikely explanation for cases of cocaine-induced aortic dissection and rupture. Alternative explanations may include increased aortic shear forces due to cocaine-induced increases in cardiac output, severe BP elevations due to large overdoses of cocaine, cocaine-induced aortic vasculitis, and chronic ischemia of the aortic media due to cocaine-induced vasoconstriction of the vaso vasorum.

**Coronary Arteries**

Similar to the previous studies examining cocaine and the aorta, a number of experimental and clinical reports have also documented cocaine-induced vasoconstriction of the coronary arteries. Animal studies that used unusually high doses of IV cocaine documented significant vasoconstriction of the coronary arteries. Hale et al. found a 15% reduction (range, 2 to 29%) of the circumflex coronary artery diameter in anesthetized dogs 3 to 5 min after receiving 10 mg/kg of IV cocaine. Hayes et al. found a 46% reduction in coronary artery cross-sectional area at 60 min after administering 9 mg/kg IV cocaine to dogs. Similar findings have been reported by Kuhn et al. and by Egashira et al.

Human studies, using more typical doses, also suggest that cocaine causes coronary artery vasoconstriction. Lange et al. performed coronary arteriography in 45 subjects before and after intranasal cocaine (2 mg/kg) and found that cocaine induced an 8 to 12% reduction in coronary artery diameter. These investigators also found that vasoconstriction was even more prominent at sites of coronary atherosclerosis and that this effect was exacerbated by exposure to tobacco smoke. Thus, both experimental and clinical studies suggest that cocaine induces coronary artery vasoconstriction, and a number of investigators have suggested that this may be the mechanism by which cocaine induces myocardial ischemia and infarction.

In contrast with the results of previous investigators who examined the subacute effects of cocaine, we found little evidence for coronary artery vasoconstriction immediately after cocaine. We found a trend for an increase in coronary artery blood flow after cocaine, approximately one half of which was due to an increase in coronary artery diameter and one half of which was due to the cocaine-induced increase in heart rate. Our results are similar to those of Friedrichs et al. and Zimring et al. These investigators examined coronary blood flow in animal models and found that cocaine caused a transient increase in both coronary artery diameter and blood flow.

A possible explanation of our findings is that the hyperdynamic state induced by cocaine leads to increased systemic BP, increased coronary artery perfusion pressure, and subsequent coronary artery distention. It may be that only after cocaine-induced heart rate and BP elevations subside do the vasoconstrictive effects of cocaine become apparent. These results may help explain why most cocaine-induced cardiovascular complications occur hours to days after cocaine administration.

**Limitations**

Several possible limitations of our study should be mentioned. First, we examined a relatively small number of patients and we were unable to obtain optimal precocaine and postcocaine images for all patients. Nevertheless, the large size of the thoracic aorta
relative to TEE’s resolution of approximately 1 mm suggests that our observations regarding aortic diameter are credible. In addition, there was an almost uniform trend for an increase in coronary artery diameter after cocaine, so we are confident that we did not miss significant coronary vasoconstriction.

Second, because pulse-wave Doppler assessment of blood flow in the left main coronary artery is not possible during TEE, we substituted the VTIs obtained in the proximal LAD. Because the VT is greater in the left main coronary artery than in the LAD, we may have underestimated the coronary blood flow in the left main coronary artery. Nevertheless, there was no significant change in the VTIs obtained in the proximal LAD before and after cocaine. Thus, it seems reasonable to assume that there was little, if any, change in the VTIs of the left main coronary artery.

Third, cocaine-induced cardiovascular complications may occur only when extremely high doses of cocaine are used. Although the dose of cocaine we used was similar to dosages used in nonmedical settings, many cocaine users administer cocaine multiple times over the course of several hours. Thus, cumulative cocaine levels may be much higher in patients with cardiovascular complications compared with the subjects we studied and, consequently, cocaine-induced vasoconstriction of large arteries may be seen only in these settings.

Fourth, other effects of cocaine have been implicated in the etiology of cocaine-induced cardiovascular complications. For example, cocaine-induced vasculitis and coronary thrombosis may be at least partially responsible for cocaine-induced cardiovascular complications, and our study was unable to examine these effects.

Finally, the responses of the thoracic aorta and coronary arteries to cocaine may have been blunted by the midazolam that was used to sedate the subjects prior to TEE. The subjects we studied had a high tolerance to midazolam and consequently required high dosages (up to 8 mg). When we compared the central and the systemic responses of these subjects with those of subjects in a previous study who did not receive midazolam, we found that intoxication ratings, heart rate, and BP responses were blunted. Thus, it is possible that the midazolam we used for premedication may have attenuated the effects of cocaine on coronary vascular tone. This possibility is intriguing and should be investigated in future studies.

CONCLUSION

In summary, we used TEE to investigate the immediate response of the thoracic aorta and coronary arteries to IV cocaine. We found that immediately after IV cocaine administration, there was little evidence of aortic or coronary artery vasoconstriction. In fact, because of a cocaine-induced increase in heart rate and a nonsignificant increase in coronary artery diameter, we observed a modest increase in coronary blood flow after cocaine. From these results, we conclude that vasoconstriction of the thoracic aorta and coronary arteries does not occur immediately after IV cocaine.

Readers should not be falsely reassured by our findings. Many cocaine-induced cardiovascular complications occur hours to days after cocaine use. Although our results suggest that arterial vasoconstriction does not occur immediately after cocaine, we cannot exclude the possibility that aortic or coronary vasoconstriction in the subacute period is the mechanism by which cocaine induces late cardiovascular complications.

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