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Current Approach and Treatment of Myocardial Infarction Associated with Cocaine Use

Paula Miranda, MD [1], **Nicolas Veas, MD** [2]

[1] (Pontificia Universidad Católica de Chile), Internal Medicine Residency (Complejo Asistencial Hospital Dr. Sótero del Río)
[2] Interventional Cardiology, complejo asistencial Dr Sotero del Río.

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ABSTRACT

Introduction: The global crisis of illicit substance consumption, particularly cocaine, extends beyond individual users, impacting social, cultural, and institutional levels. Cocaine use is associated with a myriad of illicit activities and significantly affects public health, especially in underdeveloped countries. This study examines the cardiovascular risks linked to cocaine use, focusing on conditions such as chest pain and acute myocardial infarction.

Methodology: A comprehensive review of the literature was conducted to explore the epidemiology, pathophysiology, and treatment strategies for cocaine-associated cardiovascular events. Data on cocaine use prevalence and related cardiovascular incidents were analyzed, alongside mechanisms of cocaine-induced myocardial damage and treatment protocols.

Results: Cocaine use has increased, particularly among young adults, leading to higher prevalence rates of cardiovascular events, including acute myocardial infarction. Cocaine induces vasoconstriction, arrhythmias, and oxidative stress, contributing to myocardial ischemia and infarction. The literature reveals a significant incidence of severe coronary atherosclerosis and multivessel disease among young cocaine users experiencing acute myocardial infarction. Immediate intervention strategies, including dual antiplatelet therapy and percutaneous coronary intervention, are essential but must be tailored to the unique challenges posed by cocaine's effects.

Conclusions: Cocaine elevates the risk of severe cardiovascular events, necessitating targeted prevention and treatment strategies. The management of acute myocardial infarction in cocaine users requires a personalized approach, considering the drug's complex impact on cardiovascular health. Preventive measures and early intervention are crucial to mitigating the heightened risk of myocardial infarction and other cardiac events in this population.

Introduction:

The phenomenon of illicit substance consumption and the disorders arising from its use represent a crisis of global proportions, with ramifications extending beyond the individual boundaries of drug users and deeply impacting various domains. This issue not only directly affects consumers but also leaves a detrimental mark on those with personal and professional ties to them, generating significant repercussions across multiple social, cultural, and institutional levels. Furthermore, it is linked to numerous illicit and dangerous activities, including minor offenses, weapon trafficking, money laundering, labor exploitation, human trafficking, and violent crimes such as homicide and kidnapping. Its effects are even more harmful in underdeveloped countries, impacting public health due to its associated comorbidities, and affecting and promoting the development of various pathologies in young patients even from school age.

One of the most used banned substances is cocaine, being extensively manufactured, distributed, marketed, and consumed globally. The history of cocaine alongside humans, and its use as a substance capable of invigorating the spirit and body, in addition to revitalizing the soul and bringing it closer to the gods, dates to pre-Columbian cultures[1,2] throughout the Andean region[3,4]. Its use in humans was first recorded and described by Amerigo Vespucci, and its isolation from coca leaves was documented in 1860 by Albert Niemann, with its chemical formula elucidated in 1865 by Wilhelm Lossen[5]. Its usage became popular during the 1970s and 1980s, subsequently slightly declining, though experiencing a resurgence in consumption during recent decades.

Cocaine exerts various cardiovascular effects, primarily through its potent sympathomimetic properties. It induces intense vasoconstriction by increasing the levels of catecholamines, leading to elevated blood pressure and heart rate. These effects result in a significant increase in myocardial oxygen demand while simultaneously reducing oxygen supply due to the constriction of coronary arteries. Cocaine also promotes thrombogenesis and endothelial dysfunction, contributing to the development of atherosclerosis and increasing the risk of acute myocardial infarction. The combination of these mechanisms makes cocaine a powerful trigger for various cardiovascular events, including arrhythmias, myocardial ischemia, and sudden cardiac death, even in young, otherwise healthy individuals. In this paper, we explore those risks, specifically focusing on conditions such as chest pain and acute myocardial infarction. We will review and discuss various aspects of acute myocardial infarction in the context of cocaine consumption, emphasizing treatment strategies and exploring revascularization alternatives.

Epidemiology:

Technological advancements and the modernization of cocaine production, together with more sophisticated operations and organization across the production and distribution chain, have led to its increased prevalence, particularly among younger populations[6]. As a result, cocaine has become more common even in primary and secondary schools in countries at various levels of development[7].

Variations in the reported prevalence of cocaine use and related disorders are evident across different studies and populations. According to 2022 North American statistics, the estimated prevalence of past-year use of cocaine is approximately 2% for adults aged 18 and older, and 1.9% for individuals aged 12 and older. Notably, the highest prevalence (3.7%) occurs among young adults aged 18 to 25 years[8]. In Canada (2022), the same age group shows a concerning prevalence of past-year use of 7.4%[9]. In European countries (2023), the Netherlands reports the highest prevalence of use in the last 12 months among adults aged 15 to 64 years (2.5%) and Spain has the highest lifetime prevalence of use (12%). Among young adults (15 to 34 years), Ireland and the Netherlands report a past-year use prevalence of 4.8% and 4.7% respectively, and a lifetime use prevalence of 10.6% and 11% respectively[10]. This is particularly relevant to the topic addressed in this paper, given the early onset of acute myocardial infarction and acute toxicity associated with cocaine.

In the case of South America, the prevalence of past-year drug use among adults aged 15 to 64 is approximately 1.6% (4.7 million users)[11]. In Chile, the figures reported are lower, positioning it as a country with a moderate prevalence of consumption compared to the rest of the region, although there is likely an underdiagnosis of the actual problem. According to data from the Chilean National Service for the Prevention and Rehabilitation of Drug and Alcohol Use (2023), the prevalence of cocaine use has increased in recent years; it is estimated that around 0.9% of Chileans aged 12 to 65 have used cocaine during the last year[12].

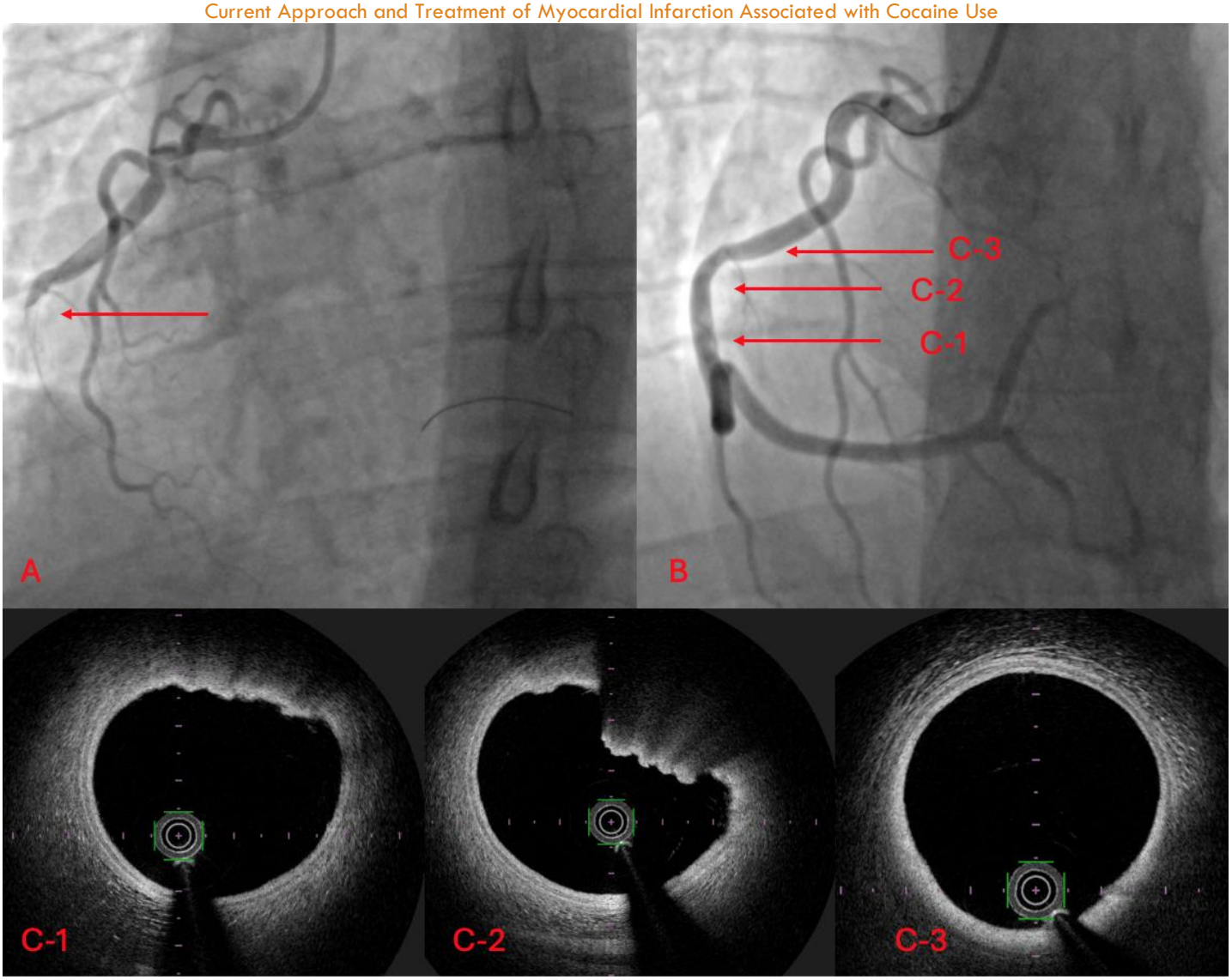

Figure 1: A.- RCA basal angiogram. Shows mid RCA occlusion associated with high thrombus burden. Treated with intracoronary thrombolytic therapy and thrombus aspiration. B.- Second look after 1 week shows RCA recanalization, TIMI 3 flow, and correlation with OCT. C-1-2-3: Shows, from distal to proximal, red thrombus without plaque rupture or dissection, compatible with plaque erosion.

Pathophysiology:

Cocaine consumption can cause a diverse set of disorders, especially vascular and endothelial damage, which can occur in any part of the body and affect all systems. Numerous mechanisms contribute to its pathophysiology, notably impacting the nervous and cardiovascular systems; it inhibits the reuptake of key neurotransmitters such as norepinephrine, dopamine, and serotonin at neuronal synapses[13]. This action increases the availability of catecholamines and dopamine at postsynaptic receptors[14], acting as a potent sympathomimetic agent. This induces the classic effects associated with its use, such as euphoria and mood elevation[15], which are the main reasons users seek it.

Through adrenergic stimulation, calcium imbalance, release of endothelin 1, and reduction in nitric oxide availability[16], cocaine produces vasoconstriction. This can affect the entire vascular tree of the body, even at low doses of the drug. This constrictive action on blood vessels can increase blood pressure and decrease blood flow to various organs, placing individuals at risk of severe cardiovascular events, such as heart attacks and strokes. The vasoconstriction caused by cocaine can be particularly hazardous in individuals with pre-existing cardiovascular conditions.

At the cellular level, cocaine has profound effects by blocking potassium channels and altering calcium dynamics, specifically by enhancing the current in L-type calcium channels. Additionally, it inhibits the entry of sodium, disrupting essential ionic balances crucial for normal cell function[17]. This interference with ion channels can lead to arrhythmias and other cardiac abnormalities. The disruption of calcium flow is particularly significant because it can trigger cellular hyperactivity, severe dysfunction in cardiac muscle fibers or even apoptosis. Beyond these immediate impacts, cocaine induces oxidative stress by promoting the production of reactive oxygen species (ROS). This increase in ROS levels can cause oxidative damage to cell membranes, proteins, and DNA, contributing significantly to the deterioration of cellular health[18]. The oxidative stress response can further exacerbate inflammation and cell death.

The increased availability of catecholamines, along with both direct and indirect endothelial damage, coagulation disorders, and changes in calcium metabolism that lead to vasoconstriction of the coronary tree, contribute to several significant cardiovascular effects. These include myocardial ischemia, coronary atherogenesis, hypertension, arrhythmias, aortic dissection or aneurysms, pulmonary hypertension, and various cardiomyopathies[19].

Several mechanisms underlie 'toxic' or drug-associated cardiomyopathy and the acute onset of left myocardial dysfunction. These mechanisms involve excessive sympathetic stimulation, which is both toxic and detrimental, as well as increased oxygen consumption by the myocardium, contributing to ventricular dysfunction[20]. Notably, even asymptomatic cocaine users have shown ventricular alterations in the left ventricle[21]. A study conducted on long-term cocaine users (average of 14 years), who were asymptomatic, showed that 71% of the sample had cardiovascular abnormalities, as assessed by magnetic resonance imaging[22]. Furthermore, the literature cites cases of reversible Takotsubo-type cardiomyopathy, attributed to elevated catecholamine levels that induce toxicity and vasospasm[23]. Additionally, evidence suggests cardiovascular benefits following the cessation of cocaine use in various clinical contexts[24].

Cocaine-associated acute myocardial infarction:

Among the most significant cardiovascular effects of cocaine are angina and myocardial ischemia, with chest pain being the most common cardiovascular symptom and the most frequent reason for emergency department visits among cocaine users; among individuals presenting at emergency services with chest pain, the overall prevalence of acute myocardial infarction is relatively low (5-6%), but it increases among those with comorbidities that confer a higher cardiovascular risk[25,26]. As presented in the previous section, various mechanisms are involved in its pathophysiology that cause ischemia and myocardial infarction. These mechanisms may be compounded by user risk factors such as a history of atheromatosis or other cardiovascular diseases, tobacco use, and comorbidities like diabetes mellitus.

Vasoconstriction, mediated by alpha-adrenergic stimulation and alterations in ionic and vasoactive molecules flows, as well as increased myocardial oxygen demand due to beta-adrenergic stimulation, are among the phenomena that explain alterations in the oxygen supply-demand relationship to the muscle. This can result in ischemia and, ultimately, myocardial infarction, particularly in cases with underlying atherosclerotic disease—whether or not related to cocaine use. This condition may be premature and often is triggered by vascular and endothelial injury, along with increased thrombogenesis due to associated coagulation disorders.

Cocaine users have a higher risk than the general population of experiencing acute myocardial infarctions[27]; significant and severe coronary atherosclerosis, including multivessel disease, frequently occurs in young, regular cocaine users experiencing acute myocardial infarction[28]. In adult men under 50 years old who experience an acute myocardial infarction with ST segment elevation, and have a history of cocaine use, there is evidence of at least one critical coronary atherosclerotic lesion in 76% of patients and multivessel disease in 65%[29]. Prognosis for acute myocardial infarction is similar between illicit drug users and those without such a history[30]. A retrospective analysis in Mexico among patients under 46 years old presenting early myocardial infarction with ST-segment elevation revealed that 22.3% had a history of illicit drug use or alcohol abuse or dependence, with marijuana and cocaine being the most used substances[31]. Similarly, a retrospective analysis at the Amsterdam Hospital showed that among adults under 50 years old hospitalized for acute myocardial infarction, a quarter had a history of recreational substance use, with a cocaine usage prevalence of 4.8%[32]. Table 1 summarizes the differences and characteristics of myocardial infarction in patients with and without a history of cocaine use.

	STEMI-CR	STEMI
Age (average years)	40	65
Hypertension	+	+++
Diabetes		
Smoker	+++	
Female sex		+++
Thrombus aspiration	+++	
PCI without stent	+++	
One-vesel desease	+++	
Mortality		**+++**

Table 1: Differences and characteristics of myocardial infarction in patients with (CR= cocaine-related) and without a history of cocaine use.

In terms of timing, most patients with acute myocardial infarction experience it within 3 hours of cocaine consumption[33]. In patients with "normal" coronary arteries (without atherosclerotic disease), myocardial infarction is likely attributed to increased myocardial oxygen consumption, vasoconstriction of large epicardial arteries or small coronary resistance vessels, and coronary thrombosis[34].

Treatment:

RESUSCITATION AND INITIAL MEDICAL THERAPY:

Patients presenting with signs and symptoms suggestive of acute coronary syndrome should initially be approached and managed in the same manner as those without a history of cocaine use, with certain considerations. They should receive dual antiplatelet therapy, especially in the case of ST-segment elevation, and when there is no suspicion of acute aortic syndrome. For the management of angina, nitroglycerin is a safe drug, which can be administered sublingually or intravenously, depending on the symptoms, the evolution, and the hemodynamics of the patient.

About calcium channel blockers, although they have been shown to prevent and reverse coronary vasoconstriction in various models[35,36], primary studies are scarce and their role in chest pain and acute coronary syndrome in this context has not been well established. They optimize coronary flow and myocardial oxygen demand/consumption, although they have not been shown to improve significant outcomes or decrease MACE. Their use should be cautious and in the absence of signs suggestive of hypotension, left ventricular dysfunction, and/or heart failure, ideally in young patients without cardiovascular history for the management of angina that persists after resuscitation, in

the initial confrontation and nitroglycerin therapy in a stage prior to myocardial revascularization. Its role as an antianginal can be maintained in conjunction with nitroglycerin if the latter alone does not stop the symptoms when myocardial injury is ruled out.

The use of beta-blockers in the context of acute coronary syndrome associated with cocaine has been empirically discouraged and contraindicated. This caution arises due to the risk of exacerbating vasoconstriction or reinfarction, triggered by predominantly alpha-adrenergic stimulation effects when using either selective or non-selective beta-blockers, such as labetalol, which predominantly act on beta-adrenergic receptors. However, studies and articles have appeared in the literature concluding that they have not shown an increase in in-hospital mortality from any cause or an increase in cases of acute myocardial infarction when used in the context of chest pain[37] in patients with a history of use or in hospitalizations after cocaine use. In any case, as with those without a history of use, immediate use or in the first phase of confrontation of these patients is not suggested, until ensuring the absence of signs suggestive of hypotension and/or imminent heart failure. They may be considered in cases where they are indicated for secondary prevention or in cases of heart failure with reduced ejection fraction, when consumption has ceased and the risk of use remains low, but there is a lack of higher quality evidence to draw conclusions in this context.

Managing type 2 myocardial infarction associated with cocaine use involves addressing the unique pathophysiological mechanisms of this condition. It is caused by an imbalance between myocardial oxygen supply and demand, which can be exacerbated by cocaine-induced vasoconstriction, increased heart rate, and elevated blood pressure. Initial management focuses on stabilizing the patient with supportive care, including oxygen therapy, nitrates, and benzodiazepines to alleviate anxiety and reduce sympathetic stimulation. Continuous monitoring and the use of antiplatelet therapy are essential to manage thrombotic complications. In cases where significant coronary artery disease is present, revascularization procedures such as percutaneous coronary intervention may be indicated. Comprehensive care also involves addressing the underlying substance use disorder with appropriate counseling and interventions to prevent recurrence and reduce long-term cardiovascular risk.

REPERFUSION:
Based on the characteristics of the patient and the entity and subtype of acute coronary syndrome or acute myocardial infarction to be treated, management and reperfusion present different considerations that must be considered by the treating team. In the subgroup of patients with acute myocardial infarction with persistent ST-segment elevation on the electrocardiogram, the initial diagnostic and therapeutic approach is similar to those without a history of cocaine use with slight differences. If the electrocardiographic study meets the established criteria for non-transitory ST-segment elevation and/or equivalent changes or usual criteria established in clinical guidelines, immediate coronary angiography should be performed and eventually percutaneous angioplasty with revascularization when feasible.

ST-segment elevation has lower specificity in adolescents and young adults for myocardial infarction[38] compared to older age groups, so in case of availability of immediate or early coronary angiography according to established protocols, the administration of systemic fibrinolytic therapy as initial treatment is not recommended due to its associated complications that increase when there is a history of use[39] (among other phenomena, probably explained by a generalized vascular, endothelial, and blood disease, not only present in the coronary tree). Considering the above, this therapy should only be considered when percutaneous interventional management is not feasible (due to distance and/or transfer time or other factors) after having insisted on the transfer to a high-complexity center, or if there is no availability of intervention by a trained hemodynamic team.

Regarding percutaneous angioplasty, the pathophysiology and effects that cocaine produces at metabolic, endothelial, blood and vascular levels, added to the uncertainty that exists for the practitioner regarding the patient's adherence to dual antiplatelet therapy, installation of stents or endoprosthesis is not recommended in the absence of a significant and/or critical atherosclerotic lesion or plaque after a successful aspiration of thrombotic material and intracoronary fibrinolysis when appropriate with successful reperfusion of the threatened myocardial territory. Without reliable data, we recommend the performance of intracoronary imaging, especially Optical Coherence Tomography (OCT), to confirm or rule out alterations such as rupture and/or erosion of the plaque or coronary dissection, to treat according to protocols and clinical guidelines according to the result and evaluation of the interventional team (Figure 1).

In the case of severe lesions or plaques or other alterations that require intervention with endoprostheses, the installation of the latest generation devices with evidence supporting their safety even with limited use of dual antiplatelet therapy for at least 30 days (for example, Onyx 1) should be considered[40]; in cases of extreme or total uncertainty regarding the use of treatment for at least 1 month, the use of polymer-free stents over bare-metal stents[41] is recommended.

In acute coronary syndromes without ST-segment elevation, the invasive approach in those who present an indication (which is extrapolated from the current management of acute coronary syndrome in general) seems to be associated with a decrease in morbidity[42]; the invasive method (whether PCI or CABG) should be selected based on various variables, highlighting among them the feasibility of adherence to therapy by the patient, their support network or instances of governmental or institutional social support, and the possibility of care requiring such interventions upon discharge.

Conclusion:

Cocaine use is directly linked to a significant increase in the risk of severe cardiovascular events, such as acute myocardial infarction, particularly among young, habitual users. The vasoconstrictive properties of cocaine, along with disruptions in the flow of ions and vasoactive molecules and an increased demand for myocardial

oxygen, contribute to ischemia and potentially, infarction, especially in the presence of underlying atherosclerotic disease. Moreover, cocaine consumption can exacerbate or precipitate pre-existing cardiac conditions and significantly increase the likelihood of cardiac events, even in asymptomatic users, underscoring the need for preventive strategies and awareness of the specific dangers associated with this drug.

The treatment of acute myocardial infarction in cocaine users involves unique challenges and requires a personalized approach. Initially, these patients should receive standard therapy, like non-users, but with specific considerations, such as avoiding selective beta-blockers in the early stages. Early diagnosis and timely reperfusion therapy are critical to improving outcomes.

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