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Cocaine consumption and acute coronary syndromes: a cross sectional study from the Swiss registry AMIS Plus

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Summary

INTRODUCTION: Cocaine abuse is a relevant public health issue which causes medical, psychological and social drawbacks. Only limited data are currently available on outcomes of acute coronary syndromes (ACS) in cocaine-addicted patients. The aim of this study was to evaluate the cardiovascular impact of cocaine in a population of patients enrolled in the Swiss nationwide AMIS Plus registry, with a focus on in-hospital outcomes.

METHODS: We retrospectively analysed data of patients enrolled in the Swiss AMIS Plus registry from 1 January 2007 to 31 December 2018. Baseline and in-hospital data of ACS patients with self-reported regular cocaine abuse were compared with the remaining AMIS Plus population and a sex and age-matched group of non-cocaine user ACS patients (ratio 1:5, 540 patients). Primary endpoints were in-hospital death and major adverse cardiac and cardiovascular events (MACCEs).

RESULTS: A total of 20,036 patients were included in the AMIS Plus registry for ACS in the study period, of whom 110 (0.5%) reported regular cocaine abuse. As compared with the remaining AMIS population, cocaine users were significantly younger (46.4 ± 10.8 vs 66.4 ± 13.2 years, p <0.001), presented more frequently with out-of-hospital cardiac arrest (11.8% vs 4.7%, p <0.001) and ST-elevation myocardial infarction (68.2% vs 54.7%, p = 0.007). Of the traditional cardiovascular risk factors, there was a higher incidence of positive family history and active smoking, but a lower incidence of arterial hypertension, diabetes and obesity. In-hospital mortality (3.6% vs 4.4%, p = 1) and MACCEs (5.4% vs 5.5%, p = 0.83) were comparable. When compared with an age-matched non-cocaine user ACS population, cocaine users were more frequently smokers (87.6% vs 63.6%, p <0.001) but less frequently obese (10.4% vs 25.6%, p = 0.001). Clinical presentation was comparable between the two groups. However, cocaine abuse was associated with a higher incidence of in-hospital death (3.7% vs 0.7%, p <0.05) and MACCEs (5.6% vs 1.3%, p <0.05).

CONCLUSION: Cocaine abuse increases the risk of mortality by a factor of 5 and the risk of major adverse cardiac and cardiovascular events by a factor of 4 as compared with a sex and age-matched population hospitalised after an acute coronary syndrome.

Keywords: *acute coronary syndrome*, *cocaine*, *Swiss AMIS Plus registry*

Introduction

Cocaine is a plant-based illicit drug that is produced from the extract of the South American *Erythroxylon coca* plant's leaves. Generally taken by nasal insufflation, cocaine can also be injected or smoked in the crystal form of crack. Examples of frequently seen effects are a sense of wellbeing, euphoria and a self-perceived sensation of improved physical and mental performance. From a European perspective, cocaine consumption has a lifetime prevalence of 5.1%, so one can assume that 17 million European citizens will consume cocaine at least once during their lifetime [1].

Recent data from the European Monitoring Centre for drugs and drug addiction showed that four Swiss cities are among the top ten cities in Europe for cocaine use [1], indicating a worrying epidemic spread of this illicit drug throughout Switzerland. Easy access and relatively low cost have contributed towards making cocaine the most widespread stimulant illicit drug in Switzerland, with an

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Author contributions
All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

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estimated consumption of about 14 kilograms every day within its borders [2].

The cardiovascular effects of cocaine have been thoroughly evaluated and its association with acute myocardial infarction was documented more than 30 years ago by Coleman [3]. Several different mechanisms explain its detrimental effects on the cardiovascular system. Cocaine can induce coronary vasospasm and premature atherosclerosis, promote intracoronary thrombosis and increase sympathomimetic activity [4–11]. Despite the well-known association and the burden of available evidence, obtaining reliable data on this subset of patients, as well as guiding therapeutic choices, is challenging given the difficulties in identifying abusers and the lack of evidence regarding tailored therapies because of the systematic exclusion of this population from randomised trials. From a prognostic perspective, difficulties in obtaining data on illicit drug abuse means that it is hard to reach any conclusions concerning its deleterious effect or to derive risk stratification tools capable of predicting clinical outcomes.

Thus, the aim of this analysis was to evaluate the prevalence of self-reported cocaine abuse in the setting of acute coronary syndromes (ACS) and the cardiovascular impact of cocaine consumption in a population of patients enrolled in the nationwide AMIS Plus Registry, with a particular focus on in-hospital outcomes.

Methods

AMIS (Acute Myocardial Infarction in Switzerland) Plus is a nationwide prospective registry established in 1997, which collects data of patients admitted in more than 80 Swiss hospitals with the final diagnosis of ST-segment elevation myocardial infarction (STEMI), non-STEMI and (since 2000) unstable angina pectoris. Data is collected through a standardised questionnaire containing more than 280 variables and completed by treating doctors or trained nurses. Data collection is centralised at the Epidemiology, Biostatistic and Prevention Institute of the University of Zurich. All data are checked for completeness, plausibility and consistency by the AMIS Plus Data Centre and treating physicians are consulted in the event of incomplete data. Since 2010, external monitoring is regularly performed at randomly selected hospitals. The registry was approved (NCT01305785) by the Swiss Federal Ethics Committee for Clinical Studies the Swiss Board for Data Security and the appropriate Cantonal Ethic Commissions (Nr - KEK-ZH-Nr.20140210/StV-Nr.05/05). The study protocol conforms to the ethical guidelines of the Declaration of Helsinki. Details on the AMIS Plus registry have been described previously [12, 13].

Data on self-reported cocaine consumption have been collected since 2007. Patients were routinely questioned about any substance abuse and classified by disclosure of cocaine consumption. In suspect cases (e.g. out-of-hospital cardiac arrest in young patients with a suggestive environment) toxicological screening was performed when deemed necessary by treating physicians, but this was not undertaken routinely. For the present analysis we considered patients enrolled in the registry between 1 January 2007 and 31 December 2018.

Baseline and in-hospital data of patients with ACS and cocaine use were compared with the remaining AMIS Plus population as well as a sex and age-matched ACS population (ratio 1:5) without any history of cocaine consumption.

Cardiovascular risk factors were defined as follows: smoker, if the patient was smoking at the time of the cardiovascular event; alcohol consumption, if the patient was consuming more than one drink a day at least 4 days per week; diabetes, hypertension and dyslipidaemia, if the patient was under treatment or had been previously diagnosed by a physician; positive family history, if a patient's first-degree relative had a ischaemic heart disease when younger than 60 years; obesity, if the patient had a body mass index $\geq$30 kg/m^2.

In-hospital outcomes were evaluated and defined as follows: cardiogenic shock as persistent hypotension (systolic blood pressure <90 mm Hg) with clinical signs of severe reduction in cardiac index; stroke or transient ischaemic attack as any event due to ischaemic, thrombotic or haemorrhagic disturbance confirmed by a neurologist or imaging; re-infarction: clinical signs or symptoms of ischaemia with ECG changes indicative of new ischemia (new ST-changes or new left bundle branch block and a new rise of biomarkers following the initial infarction; bleeding was recorded if deemed clinically relevant by the individual physician caring for the patient. Primary endpoints were in-hospital death and major adverse cardiac and cardiovascular events (MACCEs), the latter defined as the combined endpoint of re-infarction, stroke and/or death, which means that if a patient presented after the ACS an in-hospital re-infarction or stroke and then died, those were considered per definition as a single MACCE.

Statistics

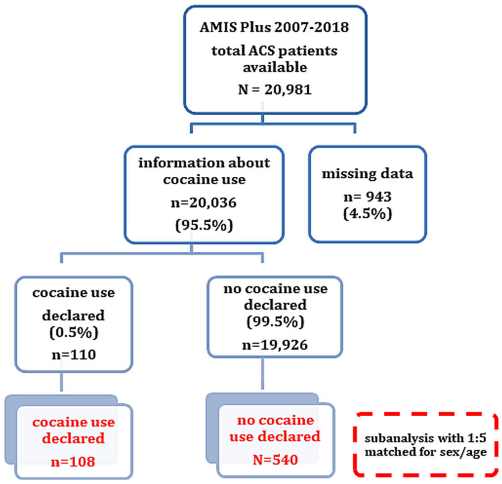
For the description of baseline patient characteristics and in-hospital data according to cocaine consumption, continuous normally distributed variables are expressed as mean and standard deviation (SD) and compared using the Student's two-tailed unpaired t-test. For categorical variables, results are presented as percentages and analysed using the Pearson chi-square test or Fisher's exact test as appropriate. Continuous nonnormally distributed variables are expressed as medians and interquartile ranges (IQRs) and analysed using the Mann– Whitney U test. In the event of missing data, we fused n/N (number of patients with a characteristic/number of patients with available data) instead of an imputation procedure. A two-sided p-value less than 0.05 was considered statistically significant.

To correct for baseline imbalances, we analysed a propensity matched sample from the crude population. For the computation of the propensity score, age and sex were included in a nonparsimonious logistic regression with cocaine consumption as the dependent variable. Matching was performed in proportions of 1:5. The validity of logistic regression was assessed using the Hosmer-Lemeshow test. Propensity matching was performed using the package Matching in R.12 The IBM SPSS Statistics Version 25 (IBM Corp; Armonk, New York, USA) was used for other statistical analyses.

Results

A total of 20,981 patients with acute coronary syndromes were included in the AMIS Plus registry from 1 January 2007 to 31 December 2018. Information on cocaine consumption was available for 95.5% (n = 20,036) of patients. One hundred and ten (0.5%) self-declared regular cocaine consumption during hospitalisation. Figure 1 shows patient flow in the registry including both the non-matched and the matched population.

Figure 1: Flow-chart. ACS = acute coronary syndrome.



Patient characteristics

ACS patients reporting cocaine abuse (COC+) were significantly younger (46.4 ± 10.8 vs 66.4 ± 13.2 years, p <0.001) and almost exclusively males (94.6% vs 76.8%, p < 0.001) as compared with the AMIS Plus non-cocaine user population. In addition, self-reported alcohol consumption, smoking habits and family history for cardiovascular events were more frequent in cocaine-using patients. On the other hand, cocaine-using patients showed a lower incidence of traditional cardiovascular risk factors such as arterial hypertension, diabetes and obesity (table 1). They also had lower rates of a previous history of heart failure, peripheral vascular disease, cerebrovascular disease and cancer. Out-of-hospital cardiac arrest (11.8% vs 4.7%, p = 0.002) and STEMI (68.2% vs 54.7%, p = 0.007) were significantly more frequent in cocaine users compared with the remaining AMIS population. Acquired immunodeficiency syndrome was significantly more frequent in the cocaine group as compared with the remaining AMIS population (8.3% vs 0.1%, p <0.001).

Acute treatment

As shown on table 2, acute medical treatment with antiplatelet therapy, vasodilators and statins was similar for both groups. Diuretics and beta-blockers were less frequently prescribed for cocaine users, whereas vasopressors (13% vs 6.7%, p = 0.019) were more frequently adopted. Coronary angiography was performed in 88.2% of cocaine users and in 82.1% of the remaining AMIS population, with a numerical, borderline non-significant, difference between groups (p = 0.059); the extent of coronary artery dis-

Table 1: Baseline characteristics.

	AMIS plus population	Cocaine abusers	p-value	Propensity matched population	Cocaine abusers	p-value
n/N (%)	19,926 (99.5)	110 (0.5)		540	108	
Female sex, (%)	5413/19,926 (27.2)	7/110 (6.4)	**<0.001**	34/540 (6.3)	7/108 (6.5)	1
Age in years, mean (SD)	66.4 (13.2)	46.4 (10.8)	**<0.001**	46.8 (10.3)	46.8 (10.4)	0.98
Resuscitation prior to admission n, (%)	939/19,926 (4.7)	13/110 (11.8)	**0.002**	39/540 (7.2)	13/108 (12.0)	0.12
STEMI, n (%)	10891/19,926 (54.7)	75/110 (68.2)	**0.007**	341/540 (63.1)	73/108 (67.6)	0.44
BMI (kg/m^2)	27.1 (4.8)	25.8 (3.8)	**0.002**	27.7 (4.5)	25.8 (3.8)	**<0.001**
Risk factors						
– Family history, n (%)	5288/16,329 (32.4)	40/76 (52.6)	**<0.001**	195/487 (40.0)	40/76 (52.6)	**0.045**
– Smoking, n (%)	6776/18,141 (37.4)	93/106 (87.7)	**<0.001**	327/514 (63.6)	92/105 (87.6)	**<0.001**
– Dyslipidaemia, n (%)	10906/17,950 (60.8)	49/95 (51.6)	0.07	273/497 (54.9)	49/94 (52.1)	0.65
– Hypertension (%)	12183/19,127 (63.7)	30/100 (30.0)	**<0.001**	210/514 (40.9)	30/98 (30.6)	0.07
– Diabetes n,(%)	3910/19,347 (20.2)	6/106 (5.7)	**<0.001**	60/525 (11.4)	6/104 (5.8)	0.11
– Obesity (BMI >30 kg/m^2), n (%)	3873/17,741 (21.8)	10/97 (10.3)	**0.006**	124/485 (25.6)	10/96 (10.4)	**0.001**
– Regular alcohol intake, n (%)	3107/18,004 (17.3)	53/81 (65.4)	**<0.001**	91/494 (18.4)	52/80 (65.0)	**<0.001**
Previous stable angina pectoris, n (%)	3085/19,618 (15.7)	10/108 (9.3)	0.089	65/537 (12.1)	10/106 (9.4)	0.51
Previous AMI, n (%)	3376/19,621 (17.2)	13/108 (12.0)	0.2	53/537 (9.9)	12/106 (11.3)	0.6
Previous PCI, n (%)	3252/19,618 (16.6)	12/108 (11.1)	0.16	54/537 (10.1)	11/106 (10.4)	0.86
Previous CABG, n (%)	1005/19,618 (5.1)	0/108 (0)	**0.007**	3/537 (0.6)	0/106	1
Comorbidities						
– Heart failure, n (%)	652/19,620 (3.3)	1/109 (0.9)	0.27	6/532 (1.1)	1/107 (0.9)	1
– Peripheral vascular disease, n (%)	973/19,620 (5.0)	3/109 (2.8)	0.38	9/532 (1.7)	3/107 (2.8)	0.43
Cerebrovascular disease n,(%)	1059/19,620 (5.4)	2/109 (1.8)	0.13	10/532 (1.9)	2/107 (1.9)	1
– Cancer diseases, n (%)	1084/19,620 (5.5)	1/109 (0.9)	**0.032**	9/532 (1.7)	1/107 (0.9)	1
– AIDS (stage C), n (%)	17/19,620 (0.1)	9/109 (8.3)	**<0.001**	2/532 (0.4)	9/107 (8.4)	**<0.001**
Ischaemic region anterior, n (%)	6910/19,924 (34.7)	53/110 (48.2)	**0.004**	226/540 (41.9)	51/108 (47.2)	0.34

AIDS = acquired immunodeficiency syndrome; AMI = acute myocardial infarction; BMI = body mass index; CABG = previous coronary artery bypass graft; PCI = percutaneous coronary intervention; SD = standard deviation; STEMI = ST-elevation myocardial infarction

ease was different with a prevalent single vessel disease (p = 0.002) treated by percutaneous coronary intervention during the index procedure in 96.9% of the cocaine users as compared to 86.8% of the remaining AMIS population.

In-hospital outcomes

Cocaine addicted patients had a shorter hospital stay than non-cocaine users (median 4 days, IQR 2–7 vs 5 days, IQR 2–8 days; p= 0.049). There was no difference between cocaine users and the AMIS Plus population in terms of in-hospital events rates, such as recurrent ischaemic episodes, cardiogenic shock, re-infarction, bleeding or cerebrovascular events (table 3). In-hospital mortality (3.6% vs 4.4%, p = 1) and MACCEs (5.5% vs 5.4%, p = 0.83) rates were comparable between cocaine users and the entire cohort of AMIS patients (fig. 2).

Propensity score matched population

After propensity score matching, 540 non-cocaine users were selected from the AMIS Plus population. In line with the general AMIS population, positive family history and smoking were confirmed to be significantly more strongly represented in the cocaine-using group. In addition, the cocaine group showed a lower incidence of obesity and a greater rate of reported alcohol consumption than the age/sex-matched population. Details of other cardiovascular risks factors are listed in table 1. Apart from a higher incidence of acquired immunodeficiency syndrome in cocaine users (8.4% vs 0.4%, p <0.001), no differences were observed among other significant comorbidities.

With regard to clinical presentation, incidence of out-of-hospital cardiac arrest and STEMI were comparable between the cocaine users and the matched group, with ob-

Table 2: Therapies at admission and angiographic findings.

	AMIS Plus population	Cocaine abusers	p-value	Propensity matched population	Cocaine abusers	p-value
n/N (%)	19,926 (99.5)	110 (0.5)		540	108	
ASA, n (%)	19,056/19,849 (96.0)	106/110 (96.4)	1	527/539 (97.8)	104/108 (96.3)	0.32
P_2Y_{12} inhibitor, n (%)	17,388/19,818 (87.7)	96/110 (87.3)	0.88	508/540 (94.1)	95/108 (88.0)	**0.035**
Beta-blocker, n (%)	11,586/19,694 (58.8)	40/109 (36.7)	**<0.001**	314/536 (58.6)	69/107 (36.4)	**<0.001**
Nitrate, n (%)	876/19,572 (44.8)	53/109 (48.6)	0.44	257/533 (48.2)	53/107 (49.5)	0.83
ACEI/ARB, n (%)	11,604/19,737 (58.8)	60/109 (55.0)	0.44	315/537 (58.7)	59/107 (55.1)	0.52
Diuretic, n (%)	3938/19,582 (20.1)	12/108 (11.1)	**0.025**	50/533 (9.4)	12/106 (11.3)	0.59
Statin, n (%)	15,525/19,740 (78.6)	80/109 (73.4)	0.2	445/538 (82.7)	79/107 (73.8)	**0.041**
Vasopressor, n (%)	1314/19,501 (6.7)	14/108 (13.0)	**0.019**	33/531 (6.2)	14/106 (13.2)	**0.023**
Thrombolysis, n (%)	278/19,912 (1.4)	2/110 (1.8)	0.67	6/540 (1.1)	2/108 (1.9)	0.67
Coronary angiography, n (%)	16,356/19,926 (82.1)	97/110 (88.2)	0.059	489/540 (90.6)	96/108 (88.9)	0.48
Angiographic findings	N = 17,863	N = 106	**<0.001**	N = 523	N = 105	0.49
– One vessel, n (%)	6743 (37.7)	56 (52.8)		276 (52.8)	55 (52.4)	
– Two vessels, n (%)	5155 (28.9)	31 (29.2)		124 (23.7)	31 (29.5)	
– Three vessels, n (%)	5231 (29.3)	14 (13.2)		108 (20.7)	14 (13.3)	
– No abnormality, n (%)	300 (1.7)	3 (2.8)		10 (1.9)	3 (2.9)	
PCI, n (%)	15760/19926 (79.1)	96/110 (87.3)	0.059	480/540 (88.9)	95/108 (88.0)	0.48
PCI with stent, n (%)	14608/15713 (93.0)	83/96 (86.5)	**0.025**	446/480 (92.9)	83/95 (87.4)	0.094
Vessel treated	N = 15,273	N = 96	**0.002**	N = 473	N = 95	**0.009**
– One vessel, n (%)	13,264 (86.8)	93 (96.9)		418 (88.4)	92 (96.8)	
– Multiple vessels, n (%)	2009 (13.2)	3 (3.1)		55 (11.6)	3 (3.2)	
LVEF	N = 12129	N = 80	**0.027**	N = 378	N = 79	**0.018**
– <35%, n (%)	1008 (8.3)	7 (8.8)		22 (5.8)	7 (8.9)	
– 35–50%, n (%)	4210 (34.7)	39 (48.8)		137 (36.2)	38 (48.1)	
– >50%, n (%)	6910 (57.0)	34 (42.5)		219 (57.9)	34 (43.0)	

ACEI = angiotensin-converting enzyme inhibitors; ASA = acetylsalicylic acid; ARB = angiotensin receptor blocker; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention

Table 3: In-hospital outcomes.

	AMIS Plus population	Cocaine abuseres	p-value	Propensity matched population	Cocaine abusers	p-value
n/N (%)	19,926 (99.5)	110 (0.5)		540	108	
Length of stay in days, median (IQR)	5 (2–8)	4 (2–7)	**0.049**	4 (2–7)	4 (2–7)	0.66
Recurrent ischaemic episode, n (%)	289/19,922 (1.5)	0/110	0.41	5/540 (0.9)	0/108 (0.0)	0.6
Cardiogenic shock, n (%)	620/19,920 (3.1)	3/110 (2.7)	1	9/540 (1.7)	3/108 (2.8)	0.43
Reinfarction, n (%)	160/19,922 (0.8)	2/110 (1.8)	0.22	2/540 (0.4	2/108 (1.9)	0.13
Bleeding, any, n (%)	679/19,922 (3.4)	4/110 (3.6)	0.79	15/540 (2.8)	4/108 (3.7)	0.54
Cerebrovascular event, n (%)	141/19,922 (0.7)	2/110 (1.8)	0.19	1/540 (0.2)	2/108 (1.9)	0.074
Mortality, n (%)	867/19,926 (4.4)	4/110 (3.6)	1	4/540 (0.7)	4/108 (3.7)	**0.03**
MACCE, n (%)	1075/19,922 (5.4)	6/110 (5.5)	0.83	7/540 (1.3)	6/108 (5.6)	0.012

IQR = interquartile range; MACCE = major adverse cardiac and cardiovascular event

served rates of 12% and 7.2% (p = 0.12) and 67.6% and 63.1% (p = 0.44), respectively.

Immediate therapies and management

Cocain addicted patients received P2Y12 inhibitors, beta-blockers and statins less frequently, but vasopressors were more frequently used than in the matched population (table 2). Rates of coronary angiography and coronary intervention were comparable between the two groups. The extent of coronary artery disease did not differ significantly between cocaine users and matched controls.

In-hospital outcomes

No difference in the length of hospital stay was observed after matching, with a median length stay of 4 days in both groups. The same applied to rates of in-hospital events. Concerning the primary endpoint, cocaine abusers showed a mortality rate roughly 5 times higher and a MACCE rate roughly 4 times higher than matched, non-cocaine users (fig. 3 and table 3).

Discussion

The present analysis derived from the Swiss national registry on myocardial infarction (AMIS Plus) is, to the best of our knowledge, one of the largest cohorts of cocaine users presenting with acute coronary syndrome.

The main findings of the present analysis are as follows:

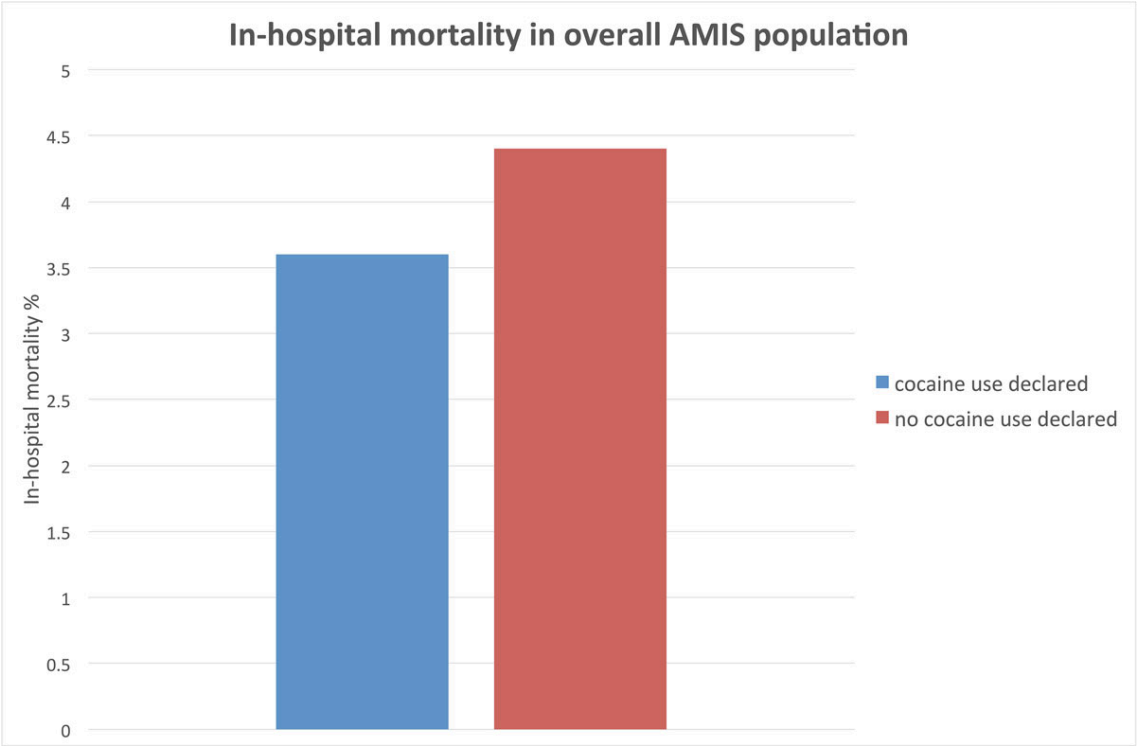
1. As compared with the remaining AMIS population, regular cocaine users were significantly younger, with fewer cardiovascular risk factors and presented more frequently with out-of-hospital-cardiac arrest and STEMI.
2. In-hospital mortality and MACCEs of regular cocaine users were comparable to the general AMIS Plus population. Nonetheless, when compared with an age- and sex-matched population, rates were increased by 5 and 4 times, respectively, highlighting the deleterious prognostic impact of this substance abuse in the ACS setting.

Our study differs from previous reports regarding the association between cocaine and ACS. Firstly, our analysis is based on a European population and secondly, results of a propensity score analysis have been provided in order to balance covariates between cocaine abusers and non-abusers in the ACS setting.

Our analysis shows a prevalence of cocaine consumption of in-hospital ACS patients of 0.5%. It is known that cocaine is the second most widely consumed illicit drug in Switzerland after cannabis, with a lifetime prevalence for consumption of 4.2% and a 12-month prevalence of 0.7% in the general population [14]. Cocaine intoxication is also a major cause for attendance at emergency departments in Switzerland [15, 16]. Our estimate clearly underrates the prevalence of cocaine abusers among ACS patients, but it can be confirmed that at least 1 out of 200 patients admitted with ACS in Switzerland are cocaine users.

When observing the baseline characteristics of cocaine users, the prototypal patient is a male in his fourth decade of life with an otherwise low cardiovascular risk profile when compared with the general AMIS population. Of note, when compared with an age- and sex-matched population, cocaine users showed a lower incidence of obesity, were more frequently smokers and had a family history of cardiovascular diseases. Interestingly, data on the national analysis of drug consumption show that addiction decreases with age, with a prevalence for cocaine consumption of

Figure 2: In-hospital mortality in overall AMIS population.



6.0% for males aged 25–29, 1.6% in subjects aged 30–39 years and only 0.5% in the group aged 40–59 years [17]. This, in association with the evidence that the vast majority of patients showed single vessel disease, emphasises the fact that in the ACS setting, cocaine consumption acts as a trigger against a background of pre-existing coronary artery disease [18]. It is worth pointing out that a greater incidence of alcohol consumption and human immunodeficiency virus disease is observed in this group of patients, highlighting specific aspects of this population with a higher propensity for risky behaviour and polytoxicomania.

Our data, in line with previous analyses [19, 20], show that ACS in cocaine users seems to be associated with a higher rate of STEMI and out-of-hospital cardiac arrest when compared with non-users. Additional variables, such as smoking, which was more frequent in cocaine consumers, might have played an additional role. This worse clinical presentation is linked to a complex imbalance between myocardial oxygen demand/supply and the activation of platelet aggregation mediated by cocaine. Previous work demonstrated how cocaine might deleteriously and simultaneously act as a positive inotropic and chronotropic agent, which increases myocardial oxygen demand [7], a vasoconstrictor, which decreases myocardial oxygen supply [4, 8] including in healthy non-arteriosclerotic vessels [18], and a platelet activator [5, 6].

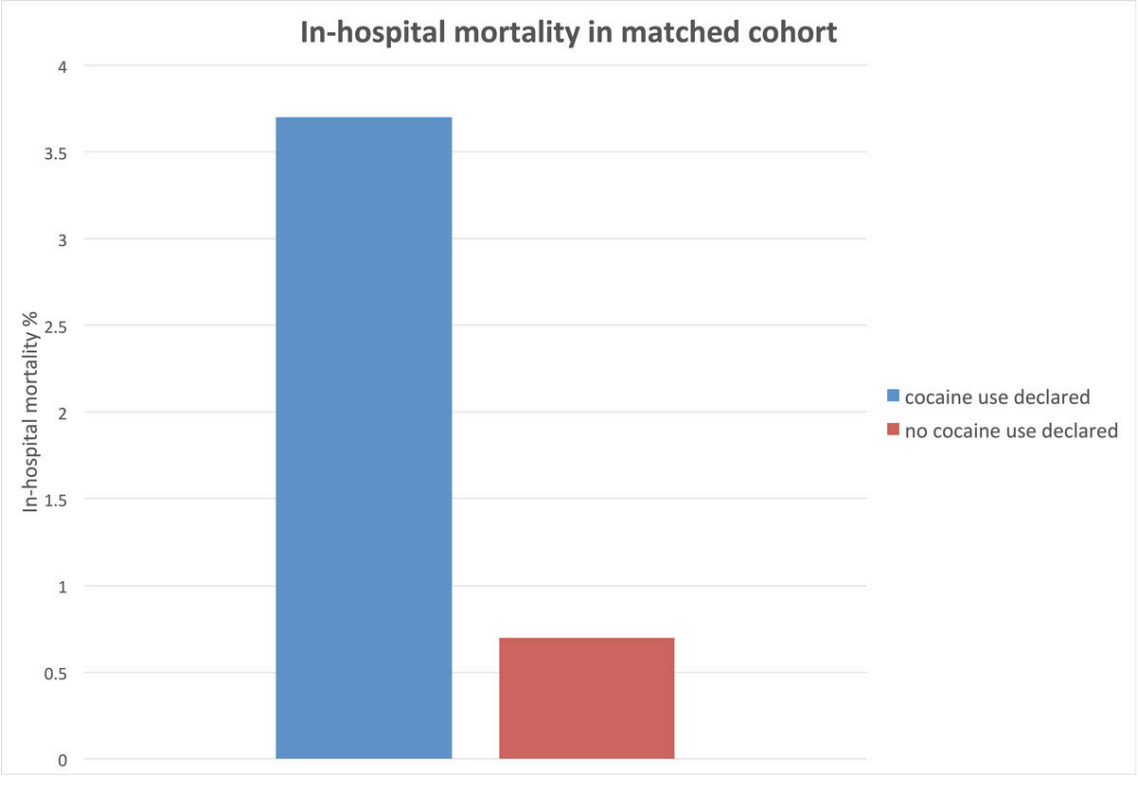
Cocaine users were less likely to be prescribed beta-blockers when compared with the general AMIS population and the matched group because of concerns about a potential alpha-adrenergic-mediated exacerbation of vasospasm [21–24]. No difference in terms of referral for coronary angiography or percutaneous treatment were observed between the groups, while cocaine users acutely showed a moderate impairment of left ventricular function on echocardiography.

In terms of in-hospital outcomes, no differences in mortality or MACCE rates were observed. In other words, outcomes seen in cocaine users are comparable to those of a much older (mean 20 years) ACS population with a significantly greater burden of comorbidities. This deleterious impact is confirmed after propensity score matching. ACS in cocaine users was in fact associated with a 5-fold increase in in-hospital mortality and a 4-fold increase in MACCEs as compared with an age- and sex-matched population. It is worth noting that the difference in the composite endpoint of MACCEs (re-infarction, stroke and/or death) was driven by deaths, with no statistical difference in re-infarction and stroke rates.

This retrospective and registry-based analysis, as per study design, is prone to intrinsic limitations. First of all, data on cocaine consumption were based on voluntary disclosure and toxicological screening was certainly not performed on a routine basis on each patient enrolled in the registry. This clearly underestimates the rate of cocaine users resulting in selection bias, as well as underreporting. Furthermore, we have no information on the timing of cocaine intake in relation to the occurrence of symptoms or the frequency of consumption. These are all factors that could influence the risk of developing an ACS.

Association between cocaine and ACS may be influenced by confounders such as the risk behaviour of cocaine users (more inclined toward smoking, alcohol consumption and HIV infection, which could be associated with the consumption of others intravenous drugs). For the registry, follow-up data are obtained by phone calls only for a limited

Figure 3: In-hospital mortality in matched cohort.



number of patients. This means that reliable long-term follow-up data cannot be provided for cocain-using patients.

In conclusion, data derived from the AMIS plus registry show that cocaine users admitted with ACS are a specific subgroup of patients of a younger age and a lower burden of comorbidities than the general AMIS population. Despite their lower baseline risk, the clinical presentation and in hospital outcomes of cocaine abusers are of concern leading to a 5-fold increase in mortality as compared to an age and sex matched population. This emphasises the clinical importance of cocaine-related ACS and should sensitise clinicians, patients and healthcare providers to this issue and encourage the development of dedicated diagnostic pathways and prognostic scores.

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Potential competing interests

All authors have no conflict of interest to disclose.

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