Original research

Prevalence and impact of recreational drug use in patients with acute cardiovascular events

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ABSTRACT

Objective While recreational drug use is a risk factor for cardiovascular events, its exact prevalence and prognostic impact in patients admitted for these events are not established. We aimed to assess the prevalence of recreational drug use and its association with in-hospital major adverse events (MAEs) in patients admitted to intensive cardiac care units (ICCU).

Methods In the Addiction in Intensive Cardiac Care Units (ADDICT-ICCU) study, systematic screening for recreational drugs was performed by prospective urinary testing all patients admitted to ICCU in 39 French centres from 7 to 22 April 2021. The primary outcome was prevalence of recreational drug detection. In-hospital MAEs were defined by death, resuscitated cardiac arrest, or haemodynamic shock.

Results Of 1499 consecutive patients (63±15 years, 70% male), 161 (11%) had a positive test for recreational drugs (cannabis 9.1%, opioids 2.1%, cocaine 1.7%, amphetamines 0.7%, 3,4-methylened ioxymethamphetamine (MDMA) 0.6%). Only 57% of these patients declared recreational drug use. Patients who used recreational drugs exhibited a higher MAE rate than others (13% vs 3%, respectively, p<0.001). Recreational drugs were associated with a higher rate of in-hospital MAEs after adjustment for comorbidities (OR 8.84, 95% CI 4.68 to 16.7, p<0.001). After adjustment, cannabis, cocaine, and MDMA, assessed separately, were independently associated with in-hospital MAEs. Multiple drug detection was frequent (28% of positive patients) and associated with an even higher incidence of MAEs (OR 12.7, 95% CI 4.80 to 35.6, p<0.001).

Conclusion The prevalence of recreational drug use in patients hospitalised in ICCU was 11%. Recreational drug detection was independently associated with worse in-hospital outcomes.

Clinical trial registration NCT05063097.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Epidemiological studies have found that recreational drug use can cause several acute cardiovascular events. Prior studies have reported that recent use of cannabis or cocaine in patients with myocardial infarction is associated with worse outcomes during long-term follow-up. However, these studies were often retrospective or post-hoc analyses, usually in young patients, without systematic screening for recreational drugs, and with a risk of recall bias.

WHAT THIS STUDY ADDS

⇒ To our knowledge, this study is the first to measure the prevalence of recreational drugs using a systematic urine drug assay in all consecutive patients admitted to intensive cardiac care units. The use of a systematic urine assay also allows a real quantification of the risk of under-declaration of drug consumption, with almost half of drug-using patients not declaring this consumption. This study is also the first to describe an independent prognostic impact of recreational drugs on the occurrence of intra-hospital outcomes in patients with an acute cardiovascular event.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Recreational drugs are detected in more than one out of 10 consecutive patients admitted to an intensive cardiac care unit, with a risk of underreporting by about one in two patients. The detection of recreational drug use is independently associated with the occurrence of in-hospital outcomes. Public health strategies aimed at offering systematic screening for recreational drugs on admission to intensive care unit could lead to improvement in patient prognosis by allowing optimal management.

INTRODUCTION

Recreational drug use is a common cause of preventable morbidity and mortality worldwide.[1 2] It is estimated that over the past year, around 275

million people used recreational drugs, a 22% increase compared with 2010.[3] In the USA alone, the estimated annual prevalence of recreational drug use is approximately 16% (53.2 million users).[4] Cannabis, cocaine, 3,4-methylenedioxymethamphetamine (MDMA), amphetamines, and heroin or other opioids are the most commonly used recreational substances.[5]

Chronic use of these substances can cause various acute cardiovascular events, including sudden cardiac death, acute coronary syndrome, acute heart failure, aortic dissection, thromboembolic events, myocarditis, and cardiac arrhythmias.[6–8] Prior studies have reported that recent use of cannabis or cocaine in patients with myocardial infarction is associated with worse outcomes during long-term follow-up.[9–11] However, these studies were often retrospective or post-hoc analyses, usually in young patients, without systematic screening for recreational drugs, and with a risk of recall bias.

While the rate of underreporting of recreational substance use among cardiac patients is high, current guidelines recommend only a declarative survey to investigate recreational drug use, but no systematic urine or plasma screening.[12 13] Although many acute cardiovascular events may involve recreational drug use, the prevalence of such drug use in patients hospitalised in intensive cardiac care units (ICCUs), as well as the short-term cardiovascular consequences of it, remains unknown.

For this reason, the Addiction in Intensive Cardiac Care Units (ADDICT-ICCU) study was designed to assess prospectively the prevalence of recreational drug use and its association with the occurrence of in-hospital adverse events in consecutive patients admitted to ICCUs for acute cardiovascular events.

METHODS

Study population

This is a multicentre, prospective, observational study of all consecutive patients aged ≥18 years admitted to ICCUs over 2 weeks in April 2021 at 39 centres across France, which represented all administrative regions in the country (online supplemental eTable 1). The details of the study design have been described and published previously.[14] The main exclusion criterion was hospitalisation for either a planned interventional procedure or more than 24 hours at any hospital facility before admission to the ICCU. This was to prevent the risk of obtaining a negative urine drug assay in patients with recreational drug consumption more than 24 hours before admission. The methodology of the baseline characteristics collection is detailed in online supplemental eMethod 1. The main admission diagnosis was adjudicated by two independent experts at the end of the hospitalisation following the current guidelines of each centre (online supplemental eMethod 2). The treatment of each patient was at the discretion of the treating physicians following the current European Society of Cardiology guidelines. The study was registered at ClinicalTrials.gov (NCT05063097) and approved by the Committee for the Protection of Human Subjects, Ile de France-7, France (APHP190870). All patients provided written informed consent for participation. No patients were involved in the research design steps for the current study.

Assessment of drug detection

The following recreational drugs were evaluated for all consecutive patients by urine drug assay using a cartridge-based system (NarcoCheck, Kappa City Biotech SAS, Montluçon, France) as soon as possible, at most within 2 hours of admission to the ICCU: (1) cannabinoids (tetrahydrocannabinol (THC)), including cannabis and hashish; (2) cocaine and metabolites, including crack; (3) amphetamines; (4) MDMA; and (5) heroin and other opioids (online supplemental eFigure 1). The test was performed using a urine jar or a urinary catheter by nurses who were trained following a standardised protocol just before the recruitment period to ensure maintenance of clinical accuracy of the procedure. This urine drug assay was used for screening in other clinical trials[15] and provides detection of drug use within the last 2 to 6 days, depending on the drug. To assess its reliability, a comparative analysis between the NarcoCheck urine drug assay and the findings of the regional reference laboratory of biological toxicology was performed on a random sample of 60 patients. The sensitivity and specificity of the urine drug assay were excellent, at 91.7% and 97.9%, respectively (online supplemental eTable 2). To assess the rate of self-reported recreational drug use, a standardised questionnaire was used. Of note, morphine and other opioid administration for pain sedation during the initial management of patients before admission to the ICCU was recorded, and their urine tests for opioids were considered negative.

Outcome measures and definitions

The prevalence of recreational drugs detected was measured using systematic recreational drug detection screening. The clinical outcome was in-hospital major adverse events (MAEs), including in-hospital death, resuscitated cardiac arrest (severe ventricular arrhythmia requiring defibrillation or intravenous antiarrhythmic agents), and haemodynamic shock requiring medical or mechanical haemodynamic support. All events, including in-hospital MAEs, were adjudicated using standardised definitions[16] by an independent committee of experts who reviewed anonymised medical documents.

Statistical analysis

As already published,[14] the sample size calculation was performed to determine the minimum sample size for an expected prevalence of recreational drug use. Using an expected prevalence of use of 11%, with a level of precision of 2% and a confidence level of 95%, and with a 5% urine drug assay refusal or failure rate, we estimate a sample size of 990 patients to attain a specified confidence interval width of 4% and to assess this prevalence accurately. Regarding the calculation of the required number of patients in each group for the estimation of odds ratios (ORs), we assumed a rate of primary outcome of 9% among recreational drug users and 1% among those not using recreational drugs. With an α error of 5% and a β error of 20% (two-tailed), we needed 116 patients per group.

Patient characteristics are summarised as mean±SD for normally distributed data or as median and IQR for non-normally distributed data, as assessed with graphical methods for normality, and with counts and proportions for categorical variables. Group comparisons for quantitative and qualitative variables were carried out with the Student's t-test, Mann-Whitney test, or Pearson's χ^2 test, depending on the statistical distribution of the variables.

Clinical outcomes were analysed using logistic regression with the following covariables, based on clinical input[17]: comorbidities as known predictors of in-hospital outcome and the main admission diagnosis (model 1: age, sex, diabetes, current smoking status, history of cardiovascular disease before hospitalisation, known chronic kidney disease with a glomerular filtration rate <90 mL/min, history of cancer, and the main admission diagnosis) and the baseline clinical parameters as known predictors of in-hospital outcome and the main admission diagnosis

(model 2: age, sex, the main admission diagnosis, systolic blood pressure, Killip class, and heart rate). We performed two separate models to limit the number of covariates in each model to avoid overfitting the model given the number.

To confirm this main analysis using logistic regression, an additional analysis was conducted using propensity score matching (with versus without a recreational drug detected). A logistic regression analysis was used to create the propensity score to balance baseline characteristics in patients with versus without recreational drugs detected.[18] To minimise potential selection bias, the effects of the recreational drugs detected from in-hospital MAEs were assessed using a 2:1 propensity score matched population (with versus without recreational drugs detected, R package 'MatchIt', v3.0.2). The probit model with 2-to-1 nearest neighbour matching and without replacement was used to identify two patients without recreational drugs detected for each patient with recreational drugs detected. Variables used to calculate the propensity score included baseline characteristics and the main admission diagnosis. Imbalances between groups were considered using absolute standardised mean differences calculated using Yang and Dalton's method with <0.2 used as a proxy of covariate balance (online supplemental eMethod 3).[19]

Pre-specified sub-group analyses were performed according to the main admission diagnosis and recreational drugs detected. A two-tailed p value <0.05 was considered statistically significant. All data were analysed using R software, version 3.6.3 (R Project for Statistical Computing, R Foundation).

RESULTS

Study population

Between 7 and 22 April 2021, 1904 patients were admitted to ICCUs in the 39 participating centres. After exclusion criteria, of the 1575 patients recruited, 1499 (95.2%) were screened using a urine drug assay and constituted our study cohort to assess the prevalence of the recreational drugs detected (figure 1). The reasons for failure to perform a urine drug assay are presented in online supplemental eMethod 4. Of these 1499 screened patients (mean age 63.3±14.9 years, 69.6% male), 88 (5.9%) had some missing covariates in the models; additionally, 53.0% had hypertension, 38.8% had dyslipidaemia, 25.5% were current smokers, and 21.7% had diabetes mellitus (table 1 and online supplemental eTable 3). Regarding cardiovascular morbidities, more than one third of the overall study population had known coronary artery disease, and 5.2% had known cardiomyopathy. Concerning the main admission diagnosis, 761 (50.8%) patients had acute coronary syndromes (422 non-ST-elevation myocardial infarction (NSTEMI), 339 ST-elevation myocardial infarction (STEMI)), 202 (13.5%) had acute heart failure, 82 (5.5%) had severe cardiac conduction abnormalities, 98 (6.5%) had arrhythmia, 46 (3.1%) had pulmonary embolism, 71 (4.7%) had myocarditis or pericarditis, 16 (1.1%) had Takotsubo syndrome, 12 (0.8%) had coronary spasm, six (0.4%) had aortic dissection, six (0.4%) had spontaneous coronary dissection, 95 (6.3%) had chest pain without an identified cardiovascular cause, and 104 (6.9%) had other cardiovascular or non-cardiovascular diagnoses.

The median (IQR) duration of hospitalisation in the ICCU was 5.0 (3.0–7.0) days, and this was similar between patients with and without recreational drugs detected (online supplemental eTable 4).

Prevalence of detected recreational drugs

Of the 1499 patients screened with the urine drug assay, 161 (10.7%) had a positive urine test for at least one recreational drug, including 136 patients for cannabis (9.1%), 32 for heroin or other opioids (2.1%), 25 for cocaine (1.7%), 10 for amphetamines (0.7%), and nine for MDMA (0.6%) (figure 2). Of these 161 patients, 116 (72.0%) had used a single drug and 45 (28.0%) had used multiple recreational drugs. Of the recreational drug users, 91 (56.5%) patients admitted recreational drug use during the admission interview by physicians. The prevalence of recreational drugs detected with the distribution of final diagnosis based on the type of drug use is depicted in figure 3. The distribution of the prevalence of detected recreational drugs by age is shown in figure 4A. Interestingly, one-third of patients under 40 years had recreational drugs detected. Males used recreational drugs more frequently than females (11.9% vs 8.1%, p<0.001) (figure 4B).

Patients who used recreational drugs were younger (53.1±15.9 vs 64.6±14.3 years, p<0.001) and more frequently current smokers (56.3% vs 21.8%, p<0.001) and HIV positive (2.5% vs 0.6%, p<0.001) than those without recreational drugs detected. However, patients who used recreational drugs had a lower rate of diabetes (13.3% vs 22.7%, p=0.009), hypertension (32.3% vs 56.5%, p<0.001), dyslipidaemia (28.5% vs 39.9%, p=0.007), a lower N-terminal pro B-type natriuretic peptide (NT-proBNP) value (446 vs 789 pg/mL, p=0.015), and lower systolic blood pressure (124 vs 137 mm Hg, p<0.001). The baseline characteristics of patients according to use of each recreational drug are depicted in table 2.

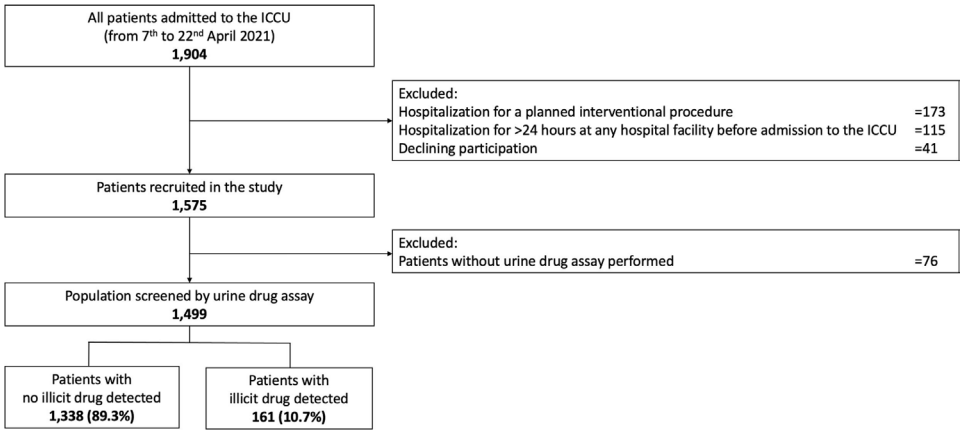

Figure 1 Flowchart of the ADDICT-ICCU study patients. ADDICT-ICCU, Addiction in Intensive Cardiac Care Units.

Table 1 Baseline characteristics of the overall population and the propensity matched population according to recreational drug detection (n=1411)

		Before propensity matching			After propensity matching 2:1		
	Overall population (n=1411)	Recreational drug use detected (n=158)	No recreational drug detected (n=1253)	P value	Recreational drug use detected (n=158)	No recreational drug detected (n=316)	P value
Age, years	63.3±14.9	53.1±15.9	64.6±14.3	**<0.001**	53.1±15.9	53.9±13.5	0.54
Men, n (%)	981 (69.5)	124 (78.5)	857 (68.4)	**<0.001**	124 (78.5)	236 (74.7)	0.43
BMI, kg/m²	27.2±5.5	26.3±5.4	27.3±5.5	**0.014**	26.3±5.4	26.6±4.5	0.50
CV risk factors, n (%)							
Diabetes	305 (21.6)	21 (13.3)	284 (22.7)	**0.009**	21 (13.3)	43 (13.6)	1.00
Hypertension	759 (53.8)	51 (32.3)	708 (56.5)	**<0.001**	51 (32.3)	115 (36.4)	0.43
Dyslipidaemia	545 (38.6)	45 (28.5)	500 (39.9)	**0.007**	45 (28.5)	93 (29.4)	0.92
Current or previous smoking	908 (64.4)	119 (75.3)	789 (63.0)	**<0.001**	119 (75.3)	256 (81.0)	0.09
Family history of CAD	235 (16.7)	29 (18.4)	206 (16.4)	0.62	29 (18.4)	66 (20.9)	0.60
Medical history of CV disease, n (%)							
Known MI	218 (15.5)	21 (13.3)	197 (15.7)	0.50	21 (13.3)	46 (14.6)	0.51
Previous PCI	459 (32.5)	60 (38.0)	399 (31.8)	0.14	60 (38.0)	124 (39.2)	0.72
Previous CABG	46 (3.3)	3 (1.9)	43 (3.4)	0.19	3 (1.9)	8 (2.5)	0.43
Stroke	3 (0.2)	0 (0)	3 (0.2)	1.00	0 (0)	0 (0)	1.00
Known chronic kidney disease*	145 (10.3)	12 (7.6)	133 (10.6)	0.30	12 (7.6)	26 (8.2)	0.56
History of HF hospitalisation	79 (5.6)	12 (7.6)	67 (5.3)	0.33	12 (7.6)	31 (9.8)	0.08
History of atrial fibrillation	166 (11.7)	11 (7.0)	155 (12.4)	0.063	11 (7.0)	15 (4.7)	0.43
Medical history of non-CV disease, n (%)							
Cancer	140 (9.9)	13 (8.2)	137 (10.9)	0.21	13 (8.2)	32 (10.1)	0.18
HIV	12 (0.9)	4 (2.5)	8 (0.6)	**0.036**	4 (2.5)	6 (1.9)	0.74
COPD or asthma	83 (5.9)	10 (6.3)	73 (5.8)	0.78	10 (6.3)	24 (7.6)	0.55
Psychiatric history	143 (10.1)	22 (13.9)	121 (9.7)	0.13	22 (13.9)	37 (11.7)	0.59
Chronic medications, n (%)							
Anticoagulant/anti-platelet aggregation	621 (44.0)	50 (31.6)	571 (45.6)	**0.001**	50 (31.7)	110 (34.8)	0.24
Antihypertensive treatment	769 (54.5)	61 (38.6)	708 (56.5)	**<0.001**	61 (38.6)	125 (39.6)	0.41
Statins	469 (33.2)	41 (25.9)	428 (34.2)	**0.048**	41 (26.0)	89 (28.2)	0.58
Alcohol use at least once a week, n (%)	766 (54.3)	94 (59.5)	672 (53.6)	0.19	94 (59.5)	210 (66.5)	0.07
Current smoker, n (%)	362 (25.7)	89 (56.3)	273 (21.8)	**<0.001**	89 (56.3)	204 (64.6)	0.06
Clinical data on admission							
Systolic blood pressure, mm Hg	136 (118–153)	124 (112–143)	137 (120–154)	**<0.001**	124 (112–143)	130 (114–146)	0.06
Heart rate, beats/min	79 (67–95)	80 (66–97)	78 (67–94)	0.39	80 (66–97)	79 (67–96)	0.66
Oxygen saturation, %	98 (96–99)	98 (97–99)	98 (96–99)	0.54	98 (97–99)	98 (96–99)	0.71
Killip class ≥2	235 (16.7)	26 (16.5)	209 (16.7)	0.40	26 (16.5)	57 (18.0)	0.08
Admission diagnosis, n (%)				**0.002**			0.096
STEMI	316 (22.4)	41 (25.9)	275 (21.9)		41 (26.0)	89 (28.2)	
NSTEMI	410 (29.1)	52 (32.9)	358 (28.6)		52 (39.1)	102 (32.3)	
Acute HF	194 (13.7)	18 (11.4)	176 (14.0)		18 (11.4)	29 (9.2)	
Arrhythmia	85 (6.0)	2 (1.3)	83 (6.6)		2 (1.2)	8 (2.5)	
Myocarditis or pericarditis	70 (5.0)	11 (7.0)	59 (4.7)		11 (7.0)	22 (7.0)	
Cardiac conduction abnormalities	82 (5.8)	5 (3.2)	77 (6.1)		5 (3.2)	11 (3.5)	
Pulmonary embolism	43 (3.0)	3 (1.9)	39 (3.1)		3 (1.9)	5 (1.6)	
Others	211 (15.0)	26 (16.5)	185 (14.8)		26 (16.5)	50 (15.8)	
Laboratory results							
Haemoglobin, g/dL	13.7 (12.5–14.9)	14.3 (13.0–15.3)	13.6 (12.3–14.8)	**<0.001**	14.3 (13.0–15.3)	14.1 (12.7–15.0)	0.58
Creatinine, µmol/L	80 (67–99)	79 (68–94)	80 (67–100)	0.43	79 (68–94)	80 (67–98)	0.73
High-sensitivity cardiac troponin peak	279 (40–4055)	492 (78–9166)	241 (37–3498)	**0.028**	492 (78–9166)	345 (56–5211)	0.42
NT-proBNP, pg/mL	700 (169–2675)	446 (136–1932)	789 (192–2851)	**0.015**	446 (136–1932)	512 (167–2055)	0.08
BNP, pg/mL	141 (39–453)	56 (28–273)	151 (40–462)	0.059	56 (28–273)	68 (30–298)	0.41
Echocardiography data							
LVEF, %	55 (45–60)	55 (45–60)	55 (45–60)	0.32	55 (45–60)	55 (45–60)	0.47

Values are n (%), mean±SD, or median (IQR). * glomerular filtration rate <90 ml/min

*glomerular filtration rate <90 ml/min

BMI, body mass index; BNP, brain natriuretic peptide; CABG, coronary artery bypass grafting; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; HF, heart failure; ICD, implantable cardioverter–defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; NT-proBNP, N-terminal pro B-type natriuretic peptide; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

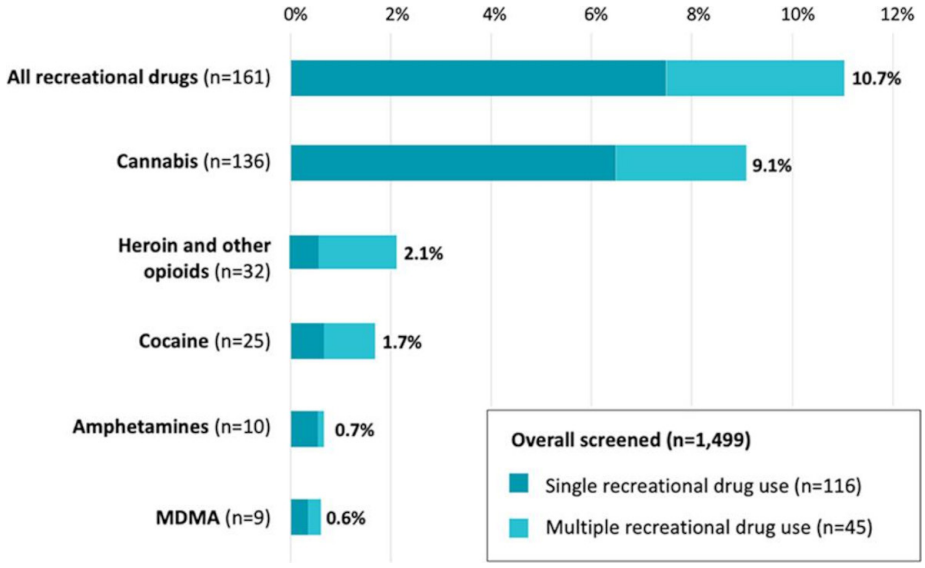

Figure 2 Prevalence of recreational drugs detected in patients hospitalised in intensive cardiac care units. MDMA, 3,4-methylenedioxymethamphetamine.

Impact of recreational drugs on in-hospital outcomes

For analysis, the final cohort was composed of 1411 patients, since 88 (5.9%) patients had missing covariates. Using a sensitivity analysis, there was no significant difference between the baseline characteristics of the 1499 screened patients and the final cohort of 1411 patients (online supplemental eTable 3). During the hospitalisation, there were 61 in-hospital MAEs (4.3%), including 25 (1.8%) in-hospital deaths, 10 (0.7%) cardiac arrests, and 26 (1.8%) haemodynamic shocks requiring medical and/or mechanical haemodynamic support. Of the 25 in-hospital deaths, 19 patients died due to ventricular arrhythmias. In univariable analysis, recreational drug detection was associated with the occurrence of in-hospital MAEs (OR 5.73, 95% CI 3.33 to 9.84, p<0.001) (online supplemental eTable 5).

In multivariable analysis (table 3), the detection of recreational drugs was independently associated with in-hospital MAEs after adjustment for comorbidities (model 1: adjusted OR 8.84, 95% CI 4.68 to 16.7, p<0.001) and for the known predictors of in-hospital outcome (model 2: adjusted OR 8.12, 95% CI 4.27 to 15.5, p<0.001).

For each component of in-hospital MAEs, the use of recreational drugs was associated with haemodynamic shock (OR 5.22, 95% CI 2.25 to 11.6, p<0.001) and resuscitated cardiac arrest (OR 33.4, 95% CI 8.27 to >100, p<0.001), but it was not significantly associated with in-hospital death (OR 2.01, 95% CI 0.66 to 5.06, p=0.167). The rate of ventricular arrhythmias was consistently higher among recreational drug users (0.063% vs 0.005%, respectively, p<0.001). With sensitivity analysis, the use of recreational drugs was also independently associated with another composite outcome including stroke (online supplemental eTable 6).

To confirm these results, an additional analysis was conducted using propensity score matching. The variables used for this (n=474; 316 without and 158 with recreational drugs detected) were age, sex, diabetes, history of cardiovascular disease before the hospitalisation, known chronic kidney disease, history of cancer, and the main admission diagnosis. The baseline characteristics of the propensity-matched population are presented in table 1. In this propensity-matched population, the use of recreational drugs was associated with a

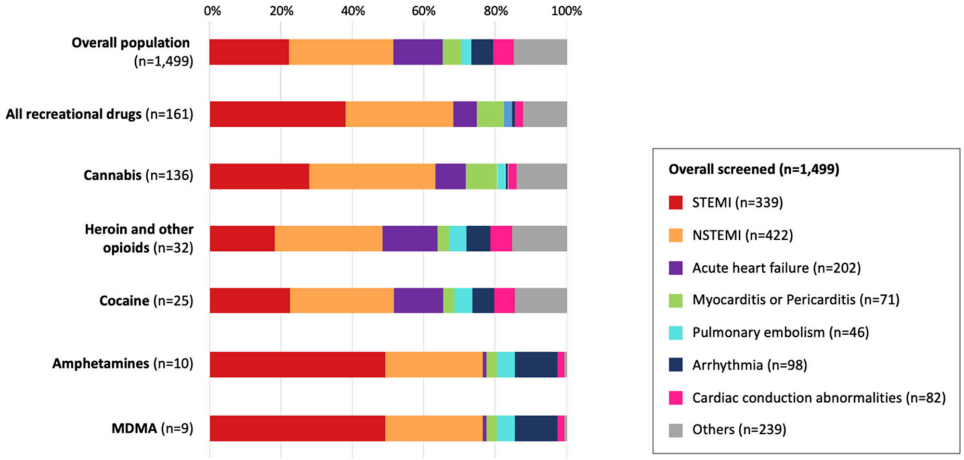

Figure 3 Prevalence of recreational drugs detected according to the main final diagnosis in the overall population screened (n=1499). Distribution of the main final diagnosis according to recreational drug detection. The top bar includes the overall population screened (n=1499). MDMA, 3,4-methylenedioxymethamphetamine; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.

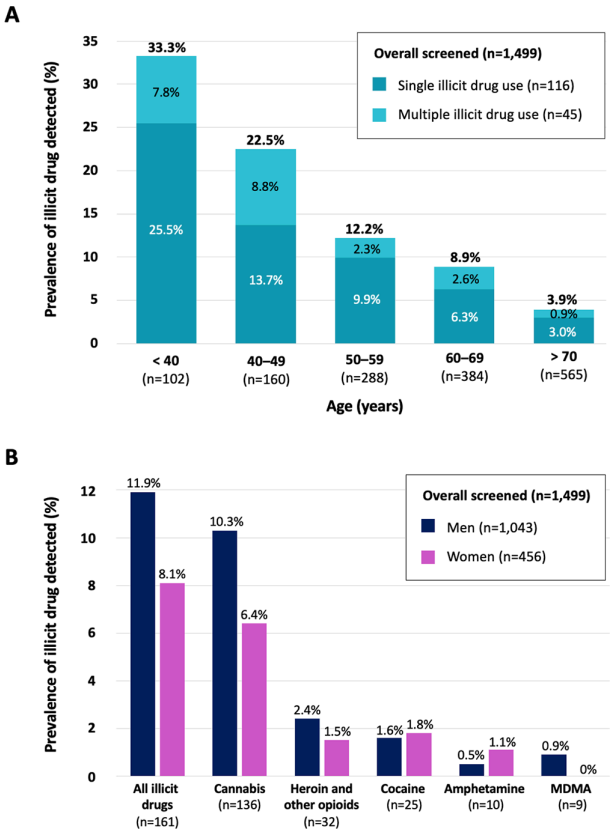

Figure 4 Prevalence of recreational drugs detected by age category and sex (n=1499). (A) Prevalence of recreational drugs detected according to age category (<40 years, 40–49 years, 50–59 years, 60–70 years, >70 years), stratified by single and multiple drugs detected. (B) Prevalence of each recreational drug detected according to patient sex. MDMA, 3,4-methylenedioxymethamphetamine.

higher incidence of in-hospital MAEs (OR 6.11, 95% CI 2.77 to 13.5, p<0.001).

In subgroup analysis, the use of recreational drugs remained significantly associated with in-hospital MAEs in patients with a main admission diagnosis of acute heart failure (OR 7.36, 95% CI 2.47 to 22.0, p<0.001) and STEMI (OR 5.07, 95% CI 1.70 to 15.1, p=0.004), but it was not significantly associated with MAEs among NSTEMI patients (OR 2.13, 95% CI 0.57 to 8.01, p=0.263) (online supplemental eFigure 2). Notably, there was no significant interaction between the effect of detected recreational drugs and smoking or alcohol use (online supplemental eFigure 3).

Association between single or multiple recreational drugs and in-hospital outcomes

After adjustment for model 1, the detection of cannabis, cocaine, and MDMA, assessed separately, was significantly associated with in-hospital MAEs (OR 3.53, 95% CI 1.25 to 9.95, p<0.001; OR 5.12, 95% CI 1.48 to 17.2, p=0.004; and OR 29.3, 95% CI 7.77 to >100, p<0.001, respectively) (online supplemental eFigure 4).

After adjustment for model 1, with drug-free patients as reference, the detection of multiple recreational drugs was associated with a higher rate of in-hospital MAEs (OR 12.7, 95% CI 4.80 to 35.6, p<0.001) than a single drug (OR 6.31, 95% CI 3.01 to 12.8, p<0.001) (online supplemental eTable 7).

DISCUSSION

In this prospective multicentre cohort of consecutive patients admitted for acute cardiovascular events in ICCUs with systematic urinary testing for recreational drug use, the main findings are as follows: (1) the prevalence of any detected recreational drug was 11% (72% single and 28% multiple recreational drugs); (2) of those patients with detected recreational drugs, only about half admitted recreational drug use during the physician admission interview; (3) the in-hospital MAE rate was 4.3%; (4) detection of recreational drugs was a strong predictor for in-hospital adverse outcomes, particularly among patients admitted for STEMI or acute heart failure; and (5) the use of multiple recreational drugs was common (28% of positive patients) and associated with a substantial increase in the risk of adverse outcomes, compared with single or no recreational drug use.

Prevalence of detected recreational drugs

The prevalence of recreational drug use observed in the general population younger than 65 years has been reported by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA).[5] In France, the prevalence of recreational drug use is 11.4%, ahead of Italy (10.6%), the UK (8.7%), and Germany (7.8%).[5] Of note, this prevalence is known to be higher in the USA, at approximately 16%.[4 20] In the current study, one in 10 patients admitted to ICCUs had used recreational drugs in the days before admission. Furthermore, in young patients

Table 2 Baseline characteristics of patients according to each recreational drug use

	No recreational drug detected (n=1253)	THC (n=136)	Cocaine (n=25)	Heroin (n=32)	Amphetamines (n=10)	MDMA (n=9)	P value
Age, mean±SD	65±14	51±15	53±14	61±14	47±12	41±12	**<0.001**
Men, n (%)	857 (68)	131 (81)	19 (76)	19 (59)	5 (50)	8 (89)	**<0.001**
Reason for hospitalisation, n (%)							**<0.001**
Chest pain	802 (64)	105 (77)	19 (76)	22 (69)	6 (60)	6 (67)	
Others	451 (36)	31 (23)	6 (24)	6 (31)	4 (40)	3 (33)	
Final diagnosis, n (%)							**<0.001**
Acute coronary syndrome	633 (50)	91 (67)	12 (48)	18 (56)	8 (80)	6 (67)	
Others	620 (50)	45 (33)	13 (52)	14 (44)	2 (20)	3 (33)	
Patients reporting recreational drug use during the medical interview, n (%)	0 (0)	78 (57)	7 (28)	3 (9)	1 (10)	2 (22)	**<0.001**
In-hospital MAE, n (%)	38 (3)	10 (7)	3 (12)	2 (6)	1 (10)	5 (56)	**<0.001**

MAE, major adverse event; MDMA, 3,4-methylenedioxymethamphetamine; THC, tetrahydrocannabinol.

Table 3 Univariable and multivariable analysis of recreational drug detected for in-hospital major adverse events (n=1411)

	Unadjusted		Model 1 (comorbidities)*		Model 2 (clinical severity)†	
Variables	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Recreational drug detected	5.73 (3.33 to 9.84)	**<0.001**	8.84 (4.68 to 16.7)	**<0.001**	8.12 (4.27 to 15.5)	**<0.001**
Age	1.02 (1.00 to 1.04)	0.076	1.02 (1.00 to 1.04)	0.093	1.03 (1.01 to 1.05)	**0.013**
Men	0.85 (0.50 to 1.46)	0.553	0.81 (0.45 to 1.45)	0.472	0.84 (0.46 to 1.52)	0.570
Diabetes mellitus	2.23 (1.31 to 3.80)	**0.003**	2.24 (1.22 to 4.12)	**0.010**	–	–
Current smoking status	0.74 (0.48 to 1.30)	0.812	0.72 (0.44 to 1.20)	0.781	–	–
History of CVD‡	1.07 (0.64 to 1.79)	0.783	0.93 (0.50 to 1.73)	0.826	–	–
Known CKD§	2.19 (1.14 to 4.22)	**0.019**	1.40 (0.67 to 2.93)	0.376	–	–
Cancer	2.55 (1.35 to 4.83)	**0.004**	2.36 (1.15 to 4.85)	**0.020**	–	–
Systolic blood pressure	0.97 (0.96 to 0.98)	**<0.001**	–	–	0.97 (0.95 to 0.99)	**<0.001**
Killip class	3.90 (2.10 to 7.27)	**<0.001**	–	–	3.68 (2.02 to 6.90)	**<0.001**
Heart rate	1.02 (1.01 to 1.02)	**0.002**	–	–	1.03 (1.01 to 1.05)	**0.001**
Admission cardiac diagnosis¶	2.86 (1.60 to 5.11)	**<0.001**	2.56 (1.30 to 5.05)	**0.007**	2.66 (1.34 to 5.28)	**0.005**

*Covariates in **model 1**: age, men, diabetes mellitus, current smoking status, history of CVD, admission cardiac diagnosis, known CKD with glomerular filtration rate <90 mL/min, history of cancer, and recreational drug detected.
†Covariates in **model 2**: age, men, admission cardiac diagnosis, systolic blood pressure, baseline Killip class, heart rate, and recreational drug detected.
‡CVD defined by the presence of: known MI, previous PCI, previous CABG, peripheral atheroma with revascularisation, stroke, history of heart failure, history of atrial fibrillation, history of surgery for valvular heart disease, pacemaker or ICD, and cardiomyopathies.
§Defined by history of CKD with glomerular filtration rate <90 mL/min.
¶Acute heart failure compared with others.
CABG, coronary artery bypass grafting; CKD, chronic kidney disease; CVD, cardiovascular disease; ICD, implantable cardioverter–defibrillator; MI, myocardial infarction; PCI, percutaneous coronary intervention.

under 40 years, the prevalence was 33%. To our knowledge, this study is the first to measure the prevalence of recreational drugs in admitted ICCU patients aged ≥65 years, which was found to be 6%. This result is consistent with the latest annual report of the International Narcotics Control Board,[21] which highlighted a global hidden epidemic among older individuals. Consistent with the latest EMCDDA report,[5] the prevalence of recreational drug use in our study was higher in males than in females. In our study, the rate of self-reporting current use of recreational drugs in patients with a positive urine assay was of 57%. This rate is consistent with the self-reporting rate of patients using recreational drugs (between 38% and 66% depending on the recreational drug) observed in previous studies using urinary drug assays.[22 23] These results highlight that declarative studies severely underestimate the actual prevalence of drug use.[24] In line with international surveys,[3 5] the prevalence of each recreational drug was 9.1% for cannabis, 2.1% for heroin or other opioids, 1.7% for cocaine, 0.7% for amphetamines, and 0.6% for MDMA. The description of the initial characteristics of these recreational drug users shows that they are younger and more frequently current smokers, but with fewer comorbidities (diabetes, hypertension, dyslipidaemia) and a lower NTproBNP value.

Association between recreational drug detection and in-hospital MAEs

The current study reports a strong and independent association between the use of recreational drugs and the occurrence of in-hospital MAEs, including haemodynamic shock, death, and cardiac arrest. Notably, this association was mainly driven by haemodynamic shock. Using a systematic urine assay, our study is the first to suggest a poorer in-hospital prognosis in those with detected recreational drugs in all consecutive patients admitted to ICCUs, which shows a potential interest in improving risk stratification of these patients. In addition, detection of drug use can also identify these drugs as risk factors for the acute cardiac event leading to hospitalisation, and therefore advise the patient to stop taking these drugs to reduce the risk of recurrent events, especially in patients with acute coronary syndromes. These current findings can be explained by several types of sympathomimetic effects of recreational drugs, which can increase blood pressure, heart rate, temperature, and consequently myocardial oxygen demand.[12 25 26] While the current guidelines recommend only a declarative survey to investigate recreational drug use,[12 13] these findings suggest the potential value of urine screening in selected patients with acute cardiovascular events to improve risk stratification in ICCUs.

Study limitations

This study has some limitations. First, the mean burden of missing data on all the variables collected was 2.5%. This relatively low rate of missing data does not warrant the use of a missing data imputation method. Second, urine tests at admission detected only recent recreational drug use with a risk of underestimating recreational drug use several days or weeks before hospitalisation. However, the urine drug assay that was used continues to be positive 2 to 6 days after substance use. As this study did not aim to assess the performance of the test used for drug detection, it may underestimate the prevalence of drug use compared with the reference assay of the toxicological laboratory. Notably, the detection of recreational drugs does not necessarily translate as a drug addiction which requires a more thorough clinical and psychological assessment. Moreover, the fact that the study was conducted in April limits the applicability of the results to other times as prevalence may be higher during holiday periods. Fourth, we cannot theoretically exclude the possibility that the knowledge of a positive recreational drug detection may have changed the medical management of patients, although such a possibility appears very hypothetical. Although several studies showed an association of socioeconomic status with recreational drug use and cardiovascular health, socioeconomic data were not collected in this study. Fifth, subgroup analyses and multiple comparisons introduces a risk of α risk inflation. Considering the sample size calculation for the estimation of the ORs, the results

of the subgroup analyses including the results for each of the drugs and for each of the admission diagnoses should be analysed with caution. Although the strong association between the use of recreational drugs and the occurrence of MAEs suggests an important prognostic role, the limited number of events requires caution in the clinical interpretation of these findings. Regarding the risk of selection bias, given that there were data on nationwide activity in ICCUs in France reporting an average ICCU admission rate of 45 patients per centre over the 15-day inclusion period of the study,[27] the theoretical recruitment would have been 1755 patients over 39 centres. Therefore, our recruitment of 1904 patients is consistent with a systematic and consecutive selection.

CONCLUSION

In this prospective, multicentre, observational study of consecutive patients admitted to ICCUs at 39 centres across France, recreational drugs were detected in more than one out of 10 patients, with a risk of underreporting by about one in two patients. The detection of recreational drug use was a strong and robust independent predictor of MAE. Moreover, the detection of cannabis, cocaine and MDMA, assessed separately, was also associated with a higher rate of in-hospital MAE after adjustment. Multiple recreational drugs users had the worst in-hospital prognosis, with a doubling of MAE risk, compared with single-drug users.

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