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## Original Article

# *Substance Use Disorders and Cardiovascular Complications*

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## ABSTRACT

***Background:*** Substance use disorders (SUDs) constitute a serious medical problem. Information is scarce regarding the connection between SUDs and cardiovascular complications. We sought to examine the types of SUDs and their relationships with complications in patients with cardiovascular diseases.

***Methods:*** The present descriptive cross-sectional study evaluated 406 adult cardiovascular patients with 1 of the different types of SUDs according to eligibility criteria. Required data were extracted, recorded, and analyzed using the SPSS software, version 16.

***Results:*** The mean and standard deviation of the age of the participants was 59.7±11.92 years. Ninety percent of the participants used opium. Substance use had a significant relationship with age range, marital status, education level, and income ($P$<0.05). Opium use was more frequent in patients with hypertension than other illegal substances (73.8% vs 57.1%; $P$=0.035).

***Conclusions:*** Opium was the most frequent substance used by patients with cardiovascular disease. Moreover, our participants had little knowledge about the cardiovascular risks and complications related to SUDs. Therefore, stringent measures are recommended to prevent illegal substance use and raise public awareness in the country. ***(Iranian Heart Journal 2022; 23(4): 52-59)***

**KEYWORDS:** Substance-related disorders, Drug use disorders, Substance use disorders, Substance abuses, Cardiovascular complications

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Substance use disorders (SUDs) constitute a serious medical problem with significant psychological and psychiatric aspects, as well as economic and social consequences.[1] Substance use and alcohol consumption are ever-increasing problems in the United States of America. The main categories of abused substances include alcohol, stimulants, narcotics, cannabinoids, and hallucinogens. According to a national survey on drug use and health in America in 2012 with participants over 12 years old, 33.9 million Americans or 9.2% of the population used illegal substances. The number has increased significantly since 2008, however. Additionally, 52.1% of the

population consumed alcohol, 6.5% of which was reported as excessive drinking. Blood alcohol concentrations of over 0.20% signify considerable poisoning.[2] Overall, 5.8% of the individuals were considered to have a dependence disorder or substance abuse.[3] According to the United Nations, 450 000 people worldwide die each year from drug abuse. According to the Islamic Republic News Agency (IRNA), there are 300 million drug users around the globe: 29 million of these people live in the United States, equivalent to 11% of the country's population.[4]

Today, amphetamine stimulants are the second most frequent illegal substance in the world after cannabis. Substance users in Australia spend more than 1 billion dollars on methamphetamines annually, and the amount is increasing. The national concern about the amphetamine abuse epidemic has been put forward in Australia since March 2015. Furthermore, the mortality rate of using methamphetamines has doubled from 2001 to 2009. Cardiovascular complications related to methamphetamines play a crucial role in the mortality rate.[5]

Similarly, illegal substance use is one of the most significant social and medical problems and one of the central factors in causing other medical complications in individuals in Iran. According to a study in 2016, the rate of illegal substance use in Iran was 2.1% based on DSM-IV categories. Using opium derivatives and its use disorders comprise the most prevalent SUDs that have a higher risk of dependency than cannabis, which is the most frequent substance worldwide.[6]

The results of different studies have shown that statistics on addiction have fluctuated in the recent 4 decades in Iran. In 2011, a total of 1 325 000 people in the age range of 15 to 64 years were reported to have addiction.

According to the last and closest census, in 2006, the population of Iran was 50 million.[7] To the best of our knowledge, about 4000 people die due to drug abuse every year in Iran, and there were 2.8 million addicts in the country's population of 80 million in 2019.[4]

A high dose of methadone could result in QT prolongation, and when individuals are on a watchful dose of opioid for a long period of time, the question is raised as to whether or not this issue could clinically increase the risk of cardiovascular diseases (CVDs) in patients. If the answer is positive, appropriate treatments for substance users need to be developed.

In addition to opioids, several other substances are also suspected to cause CVDs. For instance, high doses of cocaine and amphetamine are related to acute vascular accidents, common arrhythmias, hypertension, increased risks of myocardial infarction, and prolonged corrected QT intervals.[8] Intravenous thrombi and clots in the left ventricle have been observed during echocardiography in several patients receiving treatment in Rajaie Cardiovascular Medical and Research Center.[9] Further, it has been shown that using benzodiazepine in patients with depression or anxiety disorders has a risk of CVDs.[10] Studies have also shown that cannabis use might be related to acute myocardial infarction.[11] Individuals with SUDs are exposed to premature death with a vast range of different causes, but there is no sufficient information about particular cardiovascular relationships. Knowing and identifying this issue could assist physicians in preventing and treating CVDs in this population. Therefore, the purpose of this research was to study the types of SUDs and their relationships with complications in patients with CVDs referred to one of the largest cardiovascular centers in Iran in 2019.

## METHODS

The present descriptive cross-sectional study enrolled patients via the convenience sampling method. All adult patients with 1 SUD referred to one of the largest cardiovascular

centers in the country were included in the study. The inclusion criteria consisted of age over 18 years old, 1 SUD based on the DSM-5 criteria, willingness to answer the study's questions, and the provision of consent for the use of information in the research. Incomplete and unreliable information was excluded from the study. When the code of ethics was acquired (IR.RHC.REC.1398.047), physicians were asked to provide the researcher with the names of patients with SUDs referred to their clinics. First, the researcher explained the objectives and the methods of the study to the participants and obtained their consent to participate. Then, the participants were informed that they could withdraw from the study without any problems in their treatment continuation. Data regarding SUDs were collected from the participants and recorded in a data collection form. With respect to the patients' physical and mental conditions, the forms were completed in minimum time and in a peaceful place by an experienced interviewer along with a psychologist in case any psychological consultation was necessary. The participants with SUDs were referred to addiction treatment centers if required. Additionally, the variables of awareness of risks of substance use and income sufficiency were evaluated and recorded by asking the patients.

### Statistical Analysis

Information regarding demographic characteristics and clinical variables, including diagnoses, chronic diseases, and underlying conditions like diabetes, hypertension, rheumatic diseases, musculoskeletal disorders, and cardiovascular pulmonary complications were extracted from the records of the patients. Next, the data were entered into the SPSS software, version 16, and analyzed using frequency distribution tables, central tendencies, indices of dispersion, and the $\chi^2$ test or the Fisher exact test.

## RESULTS

The study population was composed of 406 cardiovascular patients with SUDs. The mean and standard deviation of the age of the participants was 59.7±11.92 years. The minimum and maximum ages were 19 years and 94 years, respectively. The frequency of substance types and the amounts of use are shown in Table 1. Opium was used by 367 participants, with the remaining patients using other illegal substances. The mean and standard deviation of the years of substance use was 12.9±9.88 years (range =1–50 y). The mean and standard deviation of the daily cost of substance use was 68000±6200 IRR, equal to 1.62±0.15 USD. The minimum and maximum daily costs of substance use were 33 000 and 500 000 IRR, equal to 0.78 and 11.88 USD, respectively.

**Table 1:** Frequency distribution of the SUD type and amount in the subjects

| SUDs | N(%) |
|---|---|
| Opium (g/d)<br><1<br>1-4<br>5-8 | 371(91.40)<br>13(3.5)<br>332(89.5)<br>26(7.0) |
| Methadone (mg/d)<br>≤10<br>>10 | 23(5.66)<br>14(60.9)<br>9(39.1) |
| Heroin (g/d)<br>1-4 | 4(0.98) |
| Crystal (g/ wk)<br><1 | 4(0.98) |
| Naswār (g/d)<br><5 | 2(0.49) |
| Alcohol (mL/ d)<br>100 | 2(0.49) |
| Total | 406(100) |

SUD, Substance use disorder

The frequency distribution of SUDs based on demographic and socioeconomic variables is demonstrated in Table 2. SUDs had a significant relationship with age range, marital status, education level, and income. The rate of opium use was 6.2% in participants under 40 years old and 50.8% in those over 60 years. The rate of opium use in participants under 40 years old was less than

that of other illegal substances (6.2% vs 17.1%; *P*=0.004). The rate of the use of other illegal substances was higher than that of opium in single participants (14.7% vs 3%; *P*=0.036). The rate of opium use was higher than that of other illegal substances in participants without a high school diploma (85.9% vs 62.9%, *P*=0.001). The rate of the use of other illegal substances was higher than that of opium in participants with a sufficient income (57.1% vs 37.3%; *P*=0.02).

The frequency distribution of SUDs based on clinical variables is presented in Table 3. The rate of opium use was higher than other illegal substances in participants with hypertension (73.8% vs 57.1%; *P*=0.035).

The cardiovascular pulmonary complications observed in participants were endocarditis in 8 subjects (2%), dissection in 1 (0.2%), arteriovenous disease in 5 (1.2%), cardiomyopathy in 6 (1.5%), mediastinitis in 2 (0.5%), aspiration pneumonia in 8 (2%), pulmonary abscesses in 2 (0.5%), septic pulmonary emboli in 3 (0.7%), pericardial effusions in 2 (0.5%), pulmonary thromboembolism in 3 (0.7%), and deep vein thrombosis in 3 (0.7%).

No significant relationships were observed between SUDs and crucial cardiovascular complications such as myocardial infarction, pulmonary edema, and asthma (Table 4).

**Table 2:** Frequency distribution of SUDs by demographic and socioeconomic factors

| Variables | Total N(%) | Opium N (%) | Others N (%) | *P* value |
|---|---|---|---|---|
| Sex<br>male<br>female | <br>357(87.9)<br>49(12.1) | <br>326(88.1)<br>44(11.9) | <br>30(85.7)<br>5(14.3) | 0.79 |
| Marital Status<br>married<br>single<br>Divorced/ Widowed | <br>359(88.6)<br>16(4.0)<br>30(7.4) | <br>329(88.9)<br>11(3.0)<br>30(8.1) | <br>29(85.3)<br>5(14.7)<br>0(0.0) | 0.004 |
| Age Group (y)<br>≤40<br>41-60<br>>60 | <br>29(7.1)<br>175(43.1)<br>202(49.8) | <br>23(6.2)<br>159(43.0)<br>188(50.8) | <br>6(17.1)<br>15(42.9)<br>14(40.0) | 0.036[1] |
| Occupation<br>employee<br>retired<br>unemployed<br>housekeeper<br>self-employed | <br>27(6.7)<br>76(18.7)<br>88(21.7)<br>49(12.1)<br>165(40.6) | <br>25(6.8)<br>70(18.9)<br>81(21.9)<br>44(11.9)<br>150(40.5) | <br>2(5.9)<br>6(17.6)<br>6(17.6)<br>5(14.7)<br>15(44.1) | 0.97 |
| Education<br>under diploma<br>diploma<br>academic | <br>341(84.0)<br>46(11.3)<br>19(4.7) | <br>318(85.9)<br>35(9.5)<br>17(4.6) | <br>22(62.9)<br>11(31.4)<br>2(5.7) | 0.001 |
| Residency<br>capital city<br>other cities | <br>179(45.1)<br>218(54.9) | <br>165(45.5)<br>198(54.5) | <br>14(41.2)<br>20(58.8) | 0.63 |
| Income<br>Efficient<br>Inefficient | <br>158(39.0)<br>247(61.0) | <br>138(37.3)<br>232(62.7) | <br>20(57.1)<br>15(42.9) | 0.02 |
| CVD Risk Awareness<br>Yes<br>No | <br>55(13.6)<br>350(86.4) | <br>50(13.5)<br>320(86.5) | <br>5(14.3)<br>30(85.7) | 1.00 |
| Criminal History<br>Yes<br>No | <br>13(3.2)<br>391(96.8) | <br>10(2.7)<br>360(97.3) | <br>3(8.8)<br>31(91.2) | 0.087 |

[1] *P* for trend

CVDs, Cardiovascular diseases

**Table 3:** Frequency distribution of SUDs by clinical factors

| Variables | Total N(%) | Opium N (%) | Others N (%) | *P* value |
|---|---|---|---|---|
| Diabetes | | | | |
| Yes | 103(25.4) | 95(25.7) | 8(22.9) | 0.714 |
| No | 303(74.6) | 275(74.3) | 27(77.1) | |
| Hypertension | | | | |
| Yes | 293(72.2) | 273(73.8) | 20(57.1) | 0.035 |
| No | 113(27.8) | 97(26.2) | 15(42.9) | |
| Rheumatic Diseases | | | | |
| Yes | 5(1.2) | 3(0.8) | 2(5.7) | 0.062 |
| No | 401(98.8) | 367(99.2) | 33(94.3) | |
| Musculoskeletal Diseases | | | | |
| Yes | 10(2.5) | 9(2.4) | 1(2.9) | 1.00 |
| No | 396(97.5) | 361(97.6) | 34(97.1) | |
| Other Diseases | | | | |
| Yes | 38(9.4) | 35(9.5) | 3(8.6) | 1.00 |
| No | 368(90.6) | 335(90.5) | 32(91.4) | |
| Diagnosis | | | | |
| CAD | 244(61.9) | 224(62.4) | 20(58.8) | 0.829 |
| Valvular disease | 50(12.7) | 46(12.8) | 4(11.8) | |
| Heart failure | 79(20.1) | 71(19.8) | 7(20.6) | |
| Others | 21(5.3) | 18(5.0) | 3(8.8) | |
| Concurrent medication | | | | |
| Yes | 20(7.1) | 27(7.3) | 2(5.7) | 0.766 |
| No | 377(92.9) | 343(92.7) | 33(24.3) | |

SUDs, Substance abuse disorders; CAD, Coronary artery disease

**Table 4:** Association between SUDs and more important complications

| Variables | Total N(%) | Opium N (%) | Others N (%) | *P* value |
|---|---|---|---|---|
| Myocardial Infarction | | | | |
| Yes | 34(8.4) | 33(8.9) | 1(2.9) | 0.340 |
| No | 371(91.6) | 337(91.1) | 34(97.1) | |
| Pulmonary Edema | | | | |
| Yes | 13(3.2) | 13(3.5) | 0(0.0) | 0.396 |
| No | 392(96.8) | 357(96.5) | 35(100.0) | |
| Asthma | | | | |
| Yes | 10(2.5) | 10(2.7) | 0(0.0) | 0.612 |
| No | 395(97.5) | 360(97.3) | 35(100.0) | |
| Total Complications | | | | |
| Yes | 95(23.4) | 89(24.1) | 6(17.1) | 0.356 |
| No | 311(76.6) | 281(75.9) | 29(82.9) | |

SUDs, Substance abuse disorders

## DISCUSSION

The results of the present study showed a high percentage of opium use (≈91%) in cardiovascular patients with SUDs referred to one of the cardiovascular specialized centers in Tehran, Iran. Likewise, the frequency of opium use was high (84%) in patients with SUDs referred to Masih Daneshvari Hospital.[12]

Esmaeili et al[13] in 2016 stated opium as the most prevalent substance in their study. The average substance use years was 13, and the average age of participants was 60 in the present study. Nonetheless, the average age of participants was 37 years in a study by Hatamkhani et al[14] in 2015. The reason for

the disparity could be the difference in the most used substance: while opium was the most frequently used substance in our study, inhaling heroin fumes was reported to be the most frequent in the study by Hatamkhani and colleagues. Although the most frequent substance was opium in the present study with a higher age range, the use of other illegal substances was observed more in participants under 40 years old, which is congruent with the study by Hatamkhani and colleagues.[14]

Other studies have indicated that CVDs are more prevalent in young people with drug use disorders (DUDs). The frequency of CVDs in older cardiovascular patients is close to the prevalence in the general population.[15]

Heroin, crystal meth, naswār, and alcohol were other SUDs reported in the current study. Hatamkhani et al[14] in 2015 reported inhaling heroin fumes; using opium, crystal meth, and hashish; and consuming alcohol in their study. As other illegal substances were used less frequently by the participants of this study, there is no sufficient evidence as regards their relationship with CVDs. Other studies have reported the harmful effects of other substances on the cardiovascular system.[16] In contrast, Thylstrup et al[15] in 2015, unexpectedly, reported lower risks of CVDs associated with the use of amphetamines. Elsewhere, Paratz[5] in 2016 showed that the mortality rate of cardiovascular complications doubled from 2001 through 2009.

Moussas[1] in 2017 concluded that consuming more than 60 grams of pure alcohol for men and more than 40 grams for women was considered chronic heavy drinking. Although alcohol consumption was reported to be very low in this study, it is chronic heavy drinking.

The relationships between alcohol consumption and CVDs like hypertension, ischemic heart diseases, heart failure, cardiomyopathies, atrial flutter and fibrillation, ischemic and hemorrhagic strokes, and other diseases have been shown in different studies. Rehm[17] in 2017 reported that a higher amount of alcohol consumption was associated with a higher mortality rate caused by cancer. In our study, there were no significant results to examine the relationship between alcohol consumption and cardiovascular complications as only a small number of participants consumed alcohol.

A very small percentage of cardiovascular patients with SUDs used multiple medications concurrently, with the most frequent ones being benzodiazepines. Thylstrup et al[15] in 2015 recommended that the relationship between the use of benzodiazepines and the risk of CVDs be interpreted carefully. This relationship has been supported by a few investigations, indicating only gentle and potential effects because benzodiazepines act as a confounding factor on the effects of anxiety and depression, which are the risk factors of CVDs.[10,18] Consistent with our study, different studies have not reported much information on the exclusive mechanisms related to medication abuse, prescription methods, and their special conditions. Nonetheless, the concurrent use of medication and substances may exert effects on the cardiovascular system via systemic ways such as inflammatory, immunological, and hormonal responses.[15] The rate of opium use was higher than that of other illegal substances in participants with hypertension in the current study. Correspondingly, there was a significant relationship between long-term opium use and CVDs in the study by Thylstrup et al[15] in 2015. The patients referred to the center for DUD treatment had a high prevalence of CVDs in comparison with the general population. The involvement of the venous system was the most prevalent type of CVDs in DUDs,

which was observed in patients who used methadone. Evidence has shown that CVDs, particularly venous involvement and accidents, comprised one of the complications caused by long-term opium use with an early start.[15]

Whicker[19] in 2006 suggested that DUDs were positively accompanied by chronic obstructive pulmonary disease and back pain. Hossain[20] in 2018 reported that intravenous SUDs led to a vast specter of cardiovascular complications. Cocaine, cannabis, amphetamines, and heroin are related to myocardial infarction, which occurs because of vasospasm or vasculitis in young patients. Non-cardiogenic pulmonary edema and acute respiratory distress syndrome are other prevalent complications caused by intravenous SUDs, which are secondary to an increase in vascular permeability. Cocaine, heroin, and methamphetamine, which lead to myocardial infarction, are also related to pulmonary edema without previous heart function disorders.[20] No significant relationship was observed between SUDs and diabetes, rheumatic and musculoskeletal diseases, myocardial infarction, pulmonary edema, and asthma in our study. The reason could be the low number of participants who used illegal substances other than opium, which was not sufficient to properly examine the relationship.

## CONCLUSIONS

The results of the present study showed that opium was the most frequent substance used by our patients with CVDs. Moreover, our participants had little knowledge about the cardiovascular risks and complications related to SUDs. Therefore, stringent measures are recommended to prevent illegal substance use and raise awareness in the country.

One of the salient limitations of this research is that we studied cardiovascular patients with SUDs referred to a large specialized cardiovascular center. We, therefore, recommended that future research consider a variety of populations with larger samples to establish a significant relationship between illegal substance use and CVDs. Furthermore, this study probably overestimated high-risk behaviors (using illegal substances) because carrying and using these substances are prohibited strictly by law.

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## REFERENCES

1. Moussas GI, Papadopoulou AG. Substance abuse and cancer. Psychiatrike = Psychiatriki. 2017; 28(3):234-41.

2. Ghanbari B, Malakouti SK, Nojomi M, De Leo D, Saeed K. Alcohol abuse and suicide attempt in Iran: a case-crossover study. Global journal of health science. 2016; 8(7):58.

3. Moran S, Isa J, Steinemann S. Perioperative management in the patient with substance abuse. Surgical Clinics. 2015; 95(2):417-28.

4. www.aa.com.tr. Apr 28, 2020.

5. Paratz ED, Cunningham NJ, MacIsaac AI. The cardiac complications of methamphetamines. Heart, Lung and Circulation. 2016; 25(4):325-32.

6. Bagheri-Lankarani K, Sulmaz G, Rahmanian-Haghighi M-R, Bikineh P, mahzad R, Mohit M, et al. Social Studies Yearbook. 1th, editor. Ghom: Miras Mandeghar; 2018.

7. Mohammadi Zeydi I, Pakpour-Hagiagha A. Application of the theory of planned behavior for the prevention of substance

abuse among male adolescents. Iranian journal of health education and health promotion. 2016; 3(4):298-310.

8. Mooney LJ, Glasner-Edwards S, Marinelli-Casey P, Hillhouse M, Ang A, Hunter J, et al. Health conditions in methamphetamine-dependent adults 3 years after treatment. Journal of addiction medicine. 2009; 3(3):155-63.

9. Alizadehasl A, Zohrian F, Hashemimanesh M, Pouraliakbar H, Mohamadifar A, Azarfarin R, et al. Left Ventricular Thrombus as a Cause of Recurrent Episodes of Transient Ischemic Attack While on Rivaroxaban in a Patient with Hyperhomocysteinemia. Multidisciplinary Cardiovascular Annals. 2020; 11(1):e98698.

10. Seldenrijk A, Vogelzangs N, Batelaan NM, Wieman I, van Schaik DJ, Penninx BJ. Depression, anxiety and 6-year risk of cardiovascular disease. Journal of psychosomatic research. 2015; 78(2):123-9.

11. Desbois AC, Cacoub P. Cannabis-associated arterial disease. Annals of vascular surgery. 2013; 27(7):996-1005.

12. Safa M, Najafizadeh K, Talischi F, Ghasem-Broujerdi F, Khodami-Vishteh H. Determination of the severity and pattern of substance abuse in patients referring for lung and heart transplantation in Masih Daneshvari Hospital. Research in medicine. 2012; 36(4):193-9.

13. Amin-Esmaeili M, Rahimi-Movaghar A, Sharifi V, Hajebi A, Radgoodarzi R, Mojtabai R, et al. Epidemiology of illicit drug use disorders in Iran: prevalence, correlates, comorbidity and service utilization results from the Iranian Mental Health Survey. Addiction. 2016; 111(10):1836-47.

14. Hatamkhani S, Shiva A, Pouraghdam R, Nojavan N, Ghasempour M. Study of the pattern of drug use among clients referring to the compulsory maintenance, treatment and reducing the harm of addicts center in Urmia in 1394. Medical Journal of Mashhad University of Medical Sciences. 2015; 61(3):1050-60.

15. Thylstrup B, Clausen T, Hesse M. Cardiovascular disease among people with drug use disorders. International journal of public health. 2015;60(6):659-68.

16. Hawley LA, Auten JD, Matteucci MJ, Decker L, Hurst N, Beer W, et al. Cardiac complications of adult methamphetamine exposures. The Journal of Emergency Medicine. 2013; 45(6):821-7.

17. Rehm J, Roerecke M. Cardiovascular effects of alcohol consumption. Trends in cardiovascular medicine. 2017; 27(8):534-8.

18. Jaussent I, Ancelin M-L, Berr C, Pérès K, Scali J, Besset A, et al. Hypnotics and mortality in an elderly general population: a 12-year prospective study. BMC medicine. 2013; 11(1):212.

19. Whicker SD, Sayer G, Saltman D. Substance abuse and other comorbidities--management in Australian general practice. Aust Fam Physician. 2006; 35(3):169-71.

20. Hossain R, Almeida RR, Natcheva H, Hedgire S, Ghoshhajra B, Shepard J-A, et al. Complications of Intravenous Substance Use Disorders (SUDs). Journal of thoracic imaging. 2018;33(2):W1-W12.