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**RESEARCH ARTICLE**

**ASSESSING THE PATHOLOGIC EFFECT OF METHAMPHETAMINE COMPOUNDS ON HEART TISSUE OF CADAVERS OF FORENSIC MEDICINE CENTER IN 2014**

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**ABSTRACT**

**Objectives:** Methamphetamine is a powerful stimulant of the central nervous system that is widely used and the reports of its abuse is increasing day by day. Studies conducted on this subject have confirmed the potential relationship between methamphetamine and cardiomyopathy. The aim of this study is to show the relationship between methamphetamine and the incidence of cardiovascular pathologies.

**Methods:** This retrospective cross-sectional descriptive study has been conducted on cadavers undergoing autopsy in Tehran Forensic Medicine Center in 2014. After positive toxicology results for methamphetamine, heart samples were sent to pathology for examining the presence or absence of cardiomyopathy. Needed information about the deceased were obtained from the medical records.

**Results:** Among deceased who referred to Tehran Forensic Medicine Center in 2014, 58 cases had positive toxicology results for methamphetamine; of these, 22 (37.9%) had cardiomyopathy, and 36 patients (62.1%) did not. There was a significant relationship between age and the presence of cardiomyopathy and the mean heart weight was higher in individuals with cardiomyopathy.

**Conclusion:** It seems that methamphetamine abuse is associated with increased risk of cardiovascular pathologies. In young patients with cardiac symptoms, cardiac pathologies should not be neglected. Responsible organizations such as educational systems and media can warn society regarding the risk of abusing these materials by creating assembled program

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**INTRODUCTION**

Methamphetamine is an extremely addictive substance with different names, such as "speed", "crystal", "crank", "go", and "ice". Methamphetamine is the most important abused substance after cannabis in Western countries. World statistics show that about 1.9% of people, especially young people, had used it at least once. Particularly the age group 20-29 years, 20% of whom have experience it.

Methamphetamine and its chemical analogue, amphetamine, are artificial stimulants that affect through increasing catecholamine concentration in the central and peripheral nervous systems. Methamphetamine has more potent effects on the central nervous system and less effect on the peripheral nervous system than amphetamines, its main metabolite. This increase in catecholamine is the primary mechanism for the cardiotoxic effects of methamphetamine and amphetamine.

There are two isomers of methamphetamine. Isomer "d", and "l". The "d" form is more powerful and used for illegal purposes. The required or toxic dose to cause cardiac

symptoms is not known and is dissimilar in different people, but investigations have indicated that cardiac complications occur after the abuse in all means, including inhaled, injected, oral, and smoked methods. Since the active ingredient amount in the body is higher in injected and smoked forms, it is expected that these two methods induce more cardiovascular effects in long-term period than the other ways. (1,2) Doctor Kung-Kyung Yeo, from Davis Medical Center of the University of California suggests in the "The American Medical Journal" that methamphetamine abuse increases the risk of cardiomyopathy up to three times. (3, 4)

Other reports in this field indicate that 5% of people who refer to emergency department with heart failure were methamphetamine abusers and 40% of people under 45 years who visited doctor due to cardiomyopathy were chronic methamphetamine abusers. Studies have shown that chronic abuse of methamphetamine, in addition to cardiomyopathy, would also develop coronary artery disease. Various causes can be assumed for this relationship, including spasm or contraction of the arteries, thereby narrowing them, direct toxicity of methamphetamine on the heart, increase in blood

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pressure and heart rate during using this substance, severity of atherosclerosis (6), and acute aortic dissection, a known complication of methamphetamine, which have been confirmed in autopsies. In a study on deaths caused by aortic dissection, methamphetamine abuse was found to be the most important risk factor for incidence of aortic dissection after hypertension. In addition to the hypertensive effects of methamphetamine, methamphetamine itself can have direct degenerative effects on the aortic wall.

In autopsies of people who died of sudden cardiac death due to methamphetamine abuse, pathologies such as myocardial hypertrophy and fibrosis were found to make the person susceptible to sudden cardiac death. (7,8)

In one study, autopsies of people who have abused methamphetamine have been studied and 10% of them had average coronary artery changes and 6% had major changes. (9)

In a case series study by Witchunga on 21 cases of cardiomyopathy induced by methamphetamine, most of the patients were male; their most common usage method was inhaled; none had a history of previous heart disease; coronary arteries were normal in all subjects; and their most common type of cardiomyopathy was dilated type. (10)

In a retrospective study by Charlene and colleagues in 2008 in Australia on 371 cadavers, in which methamphetamine was reported as the cause of death, the mean age was 32.7, among which 77% were male and 23% were female, and most of them (89%) consumed injected methamphetamine; deaths were accidental and 14% were due to suicide. Cardiac pathology, mostly coronary atherosclerosis, was reported in 20% of cases. The researchers concluded that methamphetamine has caused enormous death rates in Australia and necessary warnings must be given to abusers about potential side effects. (11, 12)

In a study conducted in San Francisco by Karch and colleagues in 1999, 413 cases of people who died of methamphetamine were compared to 114 patients who had traumatic death and negative drug abuse in autopsy. Their mean age was 36.5 years, 11% over 50 years; most of them (85%) were male. Of 413 people with positive methamphetamine, 79 had mild to severe coronary artery disease, while only 6 in the control group of 114 patients had coronary heart diseases. Also the first group had greater heart size than the control group. Ten cases in the first group had subarachnoid hemorrhage; and hepatic (34%) and respiratory disorders (24%) was observed in 65% of patients in the first group. Finally, the researchers concluded that the abuse of methamphetamine is greatly associated with cardiac pathology. (13, 14)

A study in 2000 by Oritani S, Zhu BL in Osaka, Japan, carried out during a 5-year period among 646 cadavers, found amphetamine in 15 cases, 9 males and 6 females in the age range of 16 to 71 years. The cause of death has been determined to include the following: poisoning with amphetamine in 4 cases, suicide in 4 other cases, accident and aspiration following abuse in 4 cases, death due to fire in one

case, myocardial infarction in one case, and major brain hemorrhage due to drug abuse in one case. The most common complications found in autopsies of these people was cardiomyopathy, cerebral vasculitis, and cirrhosis. (15)

In a study in 1999 by Davis GG, Swalwell CI on 35 people who died of acute aortic dissection, 7 had positive toxicology tests for amphetamine and concluded that the most important risk factor for aortic dissection is high blood pressure and amphetamine abuse is the second risk factors and that their relationship is due to amphetamine effects on increasing blood pressure that causes aortic dissection secondarily. Although it seems that amphetamines have a more effective role in the development of aortic dissection than cocaine, both materials should be considered to cause such complications. (16)

A study in 1985 by R. Matoba and colleagues on histopathologic findings on 9 cases of sudden cardiac death in amphetamine abusers with a mean age of 32 years showed that hypertrophy and fibrosis of myocardial cells were dominant and only one case of atherosclerosis was observed. The observed cellular changes were typically similar to histopathologic changes of hypertrophic cardiomyopathy. It seems that increased release of catecholamines, especially nor epinephrine, which occurs due to amphetamine abuse, has caused hypertrophic cardiomyopathy in these individuals. (17) Given the prevalence of methamphetamine abuse in Iran in recent years, we decided to study the prevalence of cardiac complications of methamphetamine by assessing cardiac pathologic findings and cardiac complications in positive methamphetamine toxicology autopsies of Tehran Forensic Medicine Center.

## MATERIALS AND METHODS

### *Study type: Cross-sectional study*

**The studied population:** All the cadavers of Forensic Medicine Center in 2014, in which methamphetamine toxicology tests were positive, were pathologically assessed for heart complications.

**Sampling method:** All records of cadavers of Forensic Medicine Center in 2014, in which methamphetamine toxicology tests were positive, were pathologically assessed for heart complications.

**Place and time of the study:** Dissection hall of Tehran Forensic Medicine Center, 2014

**Ethical Considerations:** The results of autopsies, toxicology tests, pathologies, and medical records of this study will remain confidential.

**Data analysis method:** Data will be analyzed using descriptive and analytic statistics by SPSS version 15.

**Limitations:** Lack of clinical records and history in some cadavers, which were excluded from the study.

**Study method:** After referring to toxicology section of Tehran Forensic Medicine Center, all medical records of deceased cases whose toxicology test of amphetamine were positive were extracted and the raw data was analyzed by SPSS software.

**The definition of cardiomyopathy:** Hypertrophic myocytes, symptoms of myocarditis, edema in the heart tissue, and enlarged heart

**RESULTS**

**Table 1** Relative and absolute frequency of sex of the cadavers of Tehran Forensic Medicine Center in 2014

Relative and absolute frequency of sex		
	Frequency	Percent
Male	55	94.8%
Female	3	5.2%
Total	58	100

According to Table and Figure 2, age range was divided into seven categories with five-year intervals: 21-25 years, one case (7.1%); 26-30 years, twelve cases (7.20%); 31-35 years, six cases (3.10%); 36-40 years, 23 cases (7.39%); 41-45 years, three cases (2.5%); 46-50 years, nine cases (5.15%); 51-55 years, zero; and 56-60 years, four cases (9.6%).

**Table 2** Relative and absolute frequency of age range of the cadavers of Tehran Forensic Medicine Center in 2014

Relative and absolute frequency of age range		
	Frequency	Percent
21-25	1	1/7
26-30	12	20/7
31-35	6	10/3
36-40	23	39/7
41-45	3	5/2
46-50	9	15/5
51-55	0	0
56-60	4	6/9
Total	58	100

**Table 3.** Central index and distribution of the age of the cadavers of Tehran Forensic Medicine Center in 2014

Central indexes and distribution of the age	
Mean	37/7
Median	37
Mode	36
Standard deviation	8/16
Minimum	21
Maximum	58

According to Table 3, the mean age of the studied case was 37.7 years, median 37, mode 36, standard deviation 8.16, maximum age 58, and minimum age was 21 years.

**Table 4** Relative and absolute frequency of the presence of cardiomyopathy in the cadavers of Tehran Forensic Medicine Center in 2014

	Frequency	Percent
Presence of cardiomyopathy	22	37.9
No cardiomyopathy	36	62.1
Total	58	100

**Table 5** Relative and absolute frequency of methamphetamine abuse in the cadavers of Tehran Forensic Medicine Center in 2014

	Frequency	Percent
Inhaled	32	55/2
Injected	7	12/1
Taken orally	19	32/8
Total	58	100

According to Table 5, based on the history the relatives gave, 32 out of 58 deceased (55/2%) abused the drug by the inhaled, 7 (12/1%) injected, and 19 (32/8%) oral method.

**Table 6** Relative and absolute frequency of location of methamphetamine found in toxicology of the cadavers of Tehran Forensic Medicine Center in 2014

	Frequency	Percent
bile	1	1.7
Urine	44	75.9
Gastric contents	13	22.4
Total	58	100

Based on Table 6, of the total 58 toxicology tests, (1.7%) methamphetamine was found in one case in the deceased bile, in 44 cases (75/6% in urine, and in 13 cases (22.4%) in gastric contents.

**Table 7** Central index and distribution of heart weight of the cadavers of Tehran Forensic Medicine Center in 2014

Mean	377/51
Median	374/5
Mode	314
Standard deviation	63/39
Minimum	307
Maximum	661

According to Table 7, the mean heart weight of cadavers was 388 grams, median 374.5, mode 314, standard deviation 63/39, maximum weight 307, and minimum weight 661 grams. the two age ranges 21-25 and 26-30 years, all (100%) were without cardiomyopathy; one out of six cases (66.16%) in the age range 31-35 years had cardiomyopathy and 5 (33.83%) did not; of the 23 cases in the age range 36-40 years, 9 (13.39%) had cardiomyopathy and 14 (86.60%) did not; two out of three cases (66.66%) in the age range 41-45 years with cardiomyopathy and one (33.33%) did not; in the age range 46-50 year, 6 out of 9 (66.66%) had cardiomyopathy and three cases (33.33%) did not; and in the age range 56-60 years including four cases, all (100%) had cardiomyopathy. According to these results, there was a significant relationship between the presence or absence of cardiomyopathy in age ranges ( $p < 0.05$ ), 13 cases out of 32 (62.40%) who used the inhaled method had cardiomyopathy and 19 (37.59%) did not; two cases out of 7 (57.28%) who used the injected method had cardiomyopathy and five (42.71%) did not; and 7 out of 19 (84.36%) who have taken the drug orally had cardiomyopathy and 12 (15.63%) did not. There was no statistically significant relationship between the presence or absence of cardiomyopathy and methamphetamine abuse method, according to this study ( $p > 0.05$ ), seven of the 19 cases (84.36%) who had abused it for 1-5 years had cardiomyopathy and 12 (15.63%) did not; 9 of the 24 cases (5.37%) who had abused it for 5-10 years had cardiomyopathy and 15 (5.62%) did not; 5 of the 14 cases (71.35%) who had abused it for 10-15 years had cardiomyopathy and 9 (28.64%) did not; and the one person who had abused it for 15-20 years (100%) had cardiomyopathy. There was no statistically significant relationship between the presence or absence of cardiomyopathy and duration of methamphetamine abuse, according to this study ( $p > 0.05$ ).

**DISCUSSION AND CONCLUSION**

Sudden or natural death occurs due to heart problems in many cases. Thus, the aim of this study was to evaluate the prevalence of cardiomyopathy in the cadavers referred to

Forensic Medicine Center for autopsy with drug abuse, in order to be able to provide a more open view for the treatment group and abusers about the possible existence of cardiomyopathy along with methamphetamine abuse. Methamphetamine affects various organs including the cardiovascular system.

The present study on 58 deceased found cardiomyopathy in 22 cases (9.37%) in pathology testing, and 36 cases (1.62%) without cardiomyopathy and found no significant relationship between the presence or absence of cardiomyopathy with gender, place of death, place of the poison in toxicology, concomitant discovery of drugs in toxicology, the cause of death, methamphetamine abuse method and duration. But found a significant relationship between the presence or absence of cardiomyopathy with age range, mean age, and mean heart weight between individuals with and without cardiomyopathy.

In another study by Mewan Witchunga in 2003, the researchers concluded that methamphetamine causes cardiomyopathy in some abusers. (10)

In a retrospective study by Charlene and colleagues in 2008 in Australia, the researchers concluded that methamphetamine causes enormous death rates in Australia and necessary warnings must be given to abusers about its potential side effects. In the current study on 58 cases with mean age of 37.87 years, 55 (8.94%) were male and 3 (2.5%) were female. Thirty-two cases (2.55%) used the inhaled method, 7 (1.12%) the injected, and 19 (8.32%) the oral method. Karch and colleagues concluded in a study in 1999 that methamphetamine abuse is highly associated to cardiac pathology. In the current study, which was conducted on 58 cases, mean age was 37.87 years and 9.6% were over 50 years old and most of the studied cases (8/9%) were male. (11, 12)

In a study in 1991 by Matsuyama E and Hong R on two smoke amphetamine abusers, one had pulmonary edema and dilated cardiomyopathy and the other had diffused vasospasm leading to acute myocardial infarction following cardiogenic shock and death. Therefore, identifying the potentially fatal complications of smoke amphetamine abuse should be paid special attention. In the present study on 58 deceased cases, 22 (9.37%) had cardiomyopathy in pathology testing, and 36 (62.2%) had no cardiomyopathy. (13, 14)

A study in 1985 by R. Matoba and colleagues on cardiac histopathologic findings on 9 cases of sudden deaths due to amphetamine abuse with mean age of 32 years showed that hypertrophy of myocardial cells and fibrosis were dominant and coronary artery atherosclerosis was observed only in the case. The observed cellular changes were typically similar to histopathologic changes of hypertrophic cardiomyopathy. It seems that increased release of catecholamines, especially norepinephrine, which occurs due to amphetamine abuse, has caused hypertrophic cardiomyopathy in these individuals. In the current study on 58 deceased, 23 cases (39.7%) had fibrosis in the autopsy of and 35 (60.3%) did not. Of the 23 people who had fibrosis in the autopsy and pathology, 15 cases (65.21%) had cardiomyopathy and 8 (78/34%) did not. There was a

statistically significant correlation between the total absence or presence of cardiomyopathy and presence of fibrosis ( $p < 0.05$ ). The results obtained in the current study are consistent with other studies, including the results of the significant relationship between age and cardiomyopathy, which indicates that cardiac changes are associated with increase in the duration of methamphetamine abuse. Also, in cases with cardiomyopathy, fibrosis was significantly more than those without cardiomyopathy, which shows changes in heart over time following methamphetamine abuse. (15, 16)

Based on the Knight Pathology book, high heart weight reflects chronic diseases such as cardiomyopathy; in this study the mean heart weight of cases with cardiomyopathy was significantly higher than those without cardiomyopathy.

The sample size was limited in this study, which caused most of the results to be statistically insignificant.

Given the fact that toxicology tests strongly depend on technique and user, it is likely that the toxicology results of some deceased in 2014 were negative despite methamphetamine abuse, which has caused them not to be included in this study. (17)

### **Recommendations**

Concerning the current and previous studies, methamphetamine abuse is associated with increased risk of cardiac pathology. Thus, people who are occupationally in direct contact with the abusers should pay attention to this fact, especially in young patients referring with cardiac symptoms, the cardiac pathologies should not be neglected. Also, in rehab centers, it should be noted that methamphetamine-induced cardiac problem makes the person vulnerable to environmental stressors and stresses may flare the disease, incidence of sudden death, and other cardiac complications.

Responsible organizations such as educational systems and media can warn society about the risk of abusing these materials by creating assembled programs.

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