Characteristics and Outcomes of Methamphetamine Abuse Among Veterans With Heart Failure

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Methamphetamine is one of the most commonly abused illicit substances worldwide. Chronic methamphetamine abuse (MA) is associated with the development of a dilated cardiomyopathy. MA in patients with heart failure (MethHF) is increasingly reported yet poorly characterized. This was a retrospective cohort study of veterans treated at the VA Medical Center in San Diego between 2005 and 2015 with a diagnosis of HF and a history of MA. The incidence of MA each year was calculated, and clinical characteristics and outcomes of veterans with HF with and without MA were compared. Among 9,491 veterans with HF, 429 were identified as having a history of MA. Between 2006 and 2015, the incidence of MA in veterans with HF doubled from 3.44% to 6.70%. Of the 429 identified, 106 veterans had a hospitalization for HF and they were compared with veterans with HF without evidence of MA (HF). Compared with veterans with HF, veterans with MethHF were significantly younger (60.7 ± 7.3 vs 71.6 ± 11.6 years, p <0.001), with more frequent co-morbid post-traumatic stress disorder (16.8% vs 4.4%, p = 0.006), depression (28.7% vs 11.0%, p = 0.002), homelessness (27.9% vs 8.9%, p = 0.001), and unemployment (55.8% vs 30.0%, p <0.001). Despite their younger age, veterans with MethHF had high rates of HF readmission or emergency room visit (49% vs 38% in MethHF vs HF, p = 0.34) and mortality at 6 months (27% vs 38% in MethHF vs HF, p = 0.10) compared with HF. In conclusion, MA in veterans with HF is on the rise. Certain demographic and clinical characteristics of veterans with MethHF may contribute to their poor outcomes. **(Am J Cardiol 2019;124:907−911)**

In recent years, methamphetamine has become one of the most commonly abused illegal drugs in the United States.[1,2] With increasing rates of methamphetamine abuse (MA), cardiovascular complications of MA are increasingly recognized, including methamphetamine associated heart failure (HF) and pulmonary hypertension.[3,4] Animal studies and human case series have demonstrated a strong association between MA and resulting cardiac dysfunction and HF.[5−9] However, methamphetamine associated HF remains poorly characterized. In this study, we sought to characterize patients with both MA and HF (MethHF) treated at the Veterans Affairs (VA) Medical Center in San Diego. We hypothesized that the incidence of MA in veterans with HF was on the rise, and that there would be important differences in demographic and clinical characteristics as well as outcomes between veterans with MethHF and those with HF that can lend insight into improving the management of these patients.

Methods

The VA electronic medical record maintains health information on all patients treated at the San Diego VA Medical Center. For this study, we retrospectively identified patients between January 1, 2005 and September 30, 2015 who had either an inpatient or outpatient encounter with a primary diagnosis of HF designated by International Classification of Diseases, 9th Revision (ICD-9) codes 425 (cardiomyopathy) or 428 (HF). We defined MA by the presence of any one of the following criteria: Presence of methamphetamine dependence ICD code 304.4 in the problem list, positive urine toxicology screen for methamphetamine, or hospitalization with primary diagnosis of methamphetamine dependence ICD code 304.4.

We then reviewed the medical records of 106 veterans with MethHF who had an inpatient encounter (hospitalization) associated with a primary diagnosis of HF or cardiomyopathy using the same ICD-9 codes and methamphetamine criteria above. Of the 106 veterans with MethHF identified, 57 met both ICD code and urine toxicology criteria, 33 met only the ICD criterion, and 16 met only the urine toxicology criterion. For patients with multiple admissions, data from the first visit was used for analysis. For a comparison sample, we performed chart review on 96 patients with an admission with a primary diagnosis of HF in the same year who did not have evidence of MA (HF cohort). Each patient's last date of follow-up was defined as the date of last patient encounter documented on electronic medical record of the patient's death. Outcomes of interest were all-cause mortality, emergency room visit, and HF readmission.

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Research involving human participants and/or animals: The VA HRPP Program at VASDHS approved analysis of the data from our institution for this study (protocol number H160103).

Informed consent: Owing to the retrospective and observational nature of this study, written informed consent was waived.

See page 910 for disclosure information.

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0002-9149/
https://doi.org/10.1016/j.amjcard.2019.05.068

The percentage of MA in inpatient and outpatient encounters with the primary diagnosis of HF or cardiomyopathy each year between 2006 and 2015 was calculated. Normally-distributed continuous variables were expressed as the mean ± SD, and compared by unpaired *t* Tests. Categorical variables were expressed as simple proportions and compared by chi-squared tests. To evaluate the association of MA with subsequent clinical outcomes, time-to-event analyses with Kaplan-Meier curves were constructed and evaluated with log-rank p values. The patient was censored at the last day of follow-up if no additional end points were met. Follow up was carried out to 180 days.

Analyses were performed using Stata Statistical Software Release 14 (Stata Corp 2015, College Station, Texas). The VA HRPP Program at VASDHS approved analysis of the data from our institution for this study (protocol number H160103).

Results

A total of 25,549 inpatient and outpatient encounters with the primary diagnosis of HF or cardiomyopathy were identified. The percentage of MA in inpatient and outpatient encounters with the primary diagnosis of HF each year is shown in Figure 1. In 2006, 3.44% had history of MA and this increased to 6.70% by 2015. Characteristics of veterans with MethHF compared with veterans with HF without MA (HF) are shown in Table 1. Compared with veterans with HF, veterans with MethHF were substantially younger (60.7 ± 7.3 vs 71.6 ± 11.6 years, p <0.001). Veterans with MethHF were more likely to have psychiatric co-morbidities including post-traumatic stress disorder (16.8% vs 4.4%, p = 0.006) and depression (28.7% vs 11.0%, p = 0.002). They were more likely to be homeless (27.9% vs 8.9%, p = 0.001) and unemployed (55.8% vs 30.0%, p <0.001). MethHF veterans were also more likely to have a history of co-morbid substance abuse, including opioid abuse (32.7% vs 7.7%, p <0.001), cocaine abuse (19.8% vs 1.1%, p <0.001), marijuana abuse (36.3% vs 6.6%, p <0.001), heroin abuse (10.8% vs 2.2%, p = 0.018), tobacco abuse (71.6% vs 38.5%, p <0.001), and alcohol abuse (42.6% vs 23.1%, p = 0.004). Veterans with MethHF were likely to have several co-morbidities including cerebral vascular accident (CVA) (7.8% vs 17.6%, p = 0.04), AF (4.0% vs 24.7%, p = 0.003), previous coronary artery bypass grafting (10.9% vs 22%, p = 0.04), and hyperlipidemia (46.6% vs 63.7%, p = 0.03). Echocardiographic measurements were similar between the two groups.

Over 6-months follow-up, emergency department (ED) visits or HF readmission occurred in 61 (37 in MethHF and 24 in HF). Death occurred in 61 (27 in MethHF and 34 in HF). Composite outcome of emergency room visits, HF readmission, or death occurred in 116 veterans (62 in MethHF and 54 in HF). Predictors of the composite outcome in the combined population included co-morbid chronic obstructive pulmonary disease, longer QRS duration on electrocardiogram, higher brain natriuretic peptide, and lower hemoglobin level. Kaplan-Meier curves for emergency room visits or HF readmission and mortality are shown in Figure 2. The rate of emergency room visit or HF readmission at 180 days was 49% versus 38% in MethHF versus HF. The rate of mortality was 27% versus 38% in MethHF versus HF. There were no significant differences in the risks of emergency room visits and HF readmission (log-rank p = 0.34) and mortality (log-rank p = 0.10) between patients with MethHF and HF.

Discussion

In this analysis of all veterans with HF treated at the VA San Diego, we found that the proportion of MA grew 2-fold

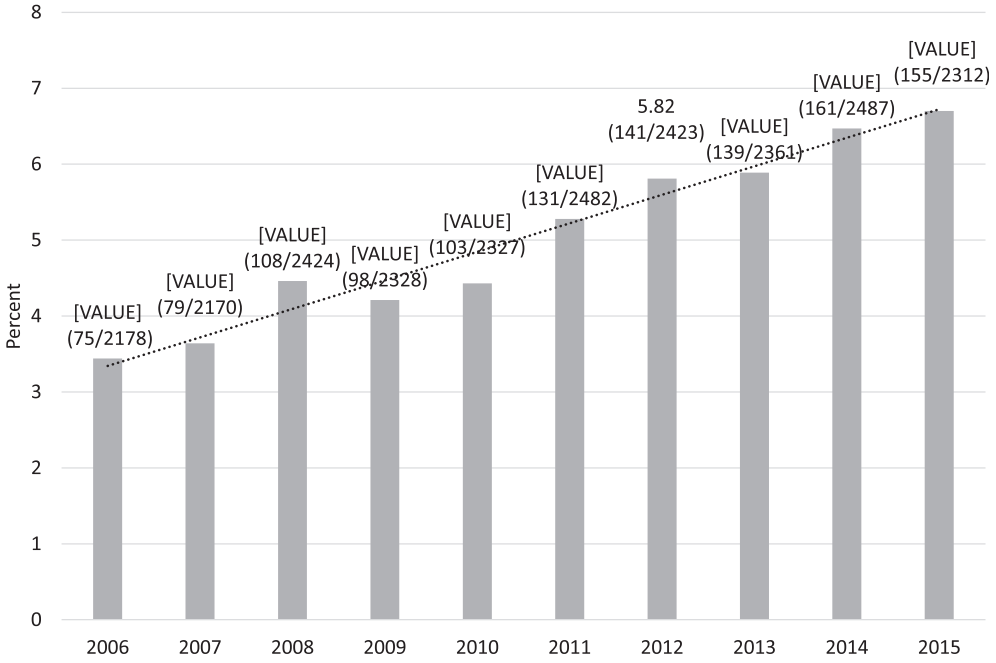

Figure 1. Percentage of MA in veterans with heart failure.
Percentage of MA in inpatient and outpatient encounters with the primary diagnosis of heart failure treated at VA San Diego each year. MA indicates methamphetamine abuse. Number of patients with MA/number of encounters with heart failure or cardiomyopathy within parenthesis. MA = methamphetamine abuse.

Table 1
Baseline characteristics, MethHF versus HF

	MethHF (n = 106)	HF (n = 96)	p Value
Age, mean (SD), y	60.7 (7.3)	71.0 (11.6)	<0.001
Weight, mean (SD), kg	93.0 (27.6)	92.4 (29.1)	0.90
Male gender	105 (99.1%)	93 (97.9%)	0.50
Homeless	29 (27.9%)	8 (8.9%)	<0.001
Unemployed	58 (55.8%)	27 (30.0%)	<0.001
Duration of hospitalization, mean (SD), days	6.7 (9.1) [n = 44]	7.9 (13.9) [n = 33]	0.48
Patient history and risk factors			
Heart failure with reduced ejection fraction (EF <50%)	44 (44.0%)	42 (44.7%)	0.92
Atrial fibrillation	7 (7.0%)	21 (24.7%)	0.003
Ventricular tachycardia	5 (4.9%)	2 (2.2%)	0.32
Previous myocardial infarction	19 (18.5%)	19 (21.1%)	0.64
Previous PCI	24 (23.5%)	21 (23.3%)	0.97
Previous CABG	11 (10.9%)	20 (22.0%)	0.04
Ischemic cardiomyopathy	31 (29.0%)	35 (36.8%)	0.23
Cerebrovascular disease	8 (7.8%)	16 (17.6%)	0.04
COPD	34 (33.0%)	22 (24.2%)	0.17
Diabetes	39 (37.9%)	41 (45.1%)	0.31
CKD	22 (21.6%)	24 (26.4%)	0.43
Hypertension	74 (72.6%)	74 (82.2%)	0.11
Hyperlipidemia	48 (46.6%)	58 (63.7%)	0.03
Alcohol abuse history	43 (42.6%)	21 (23.1%)	0.004
Cocaine use history	20 (19.8%)	1 (1.0%)	<0.001
Marijuana use	37 (36.3%)	6 (6.6%)	<0.001
Heroin use	11 (10.8%)	2 (2.2%)	0.02
PTSD	17 (16.8%)	4 (4.4%)	0.006
Depression	29 (28.7%)	10 (11.0%)	0.002
Schizophrenia	12 (11.9%)	6 (6.7%)	0.23
Patient diagnostic data			
LVEF, mean (SD) %	47.7% (20.5%)	50.8% (17.5%)	0.31
LVEDD, mean (SD) cm	5.1 (1.1) [n = 75]	5.8 (6.3) [n = 63]	0.31
LAVi, mean (SD) ml/m^2	38.0 (15.4) [n = 61]	39.1 (17.1) [n = 52]	0.72
Obstructive CAD	18 (64.3%) [n = 25]	22 (88.0%) [n = 24]	0.05
Nonobstructive CAD	3 (12.0%) [n = 25]	3 (12.5%) [n = 24]	0.53
QRS duration, mean (SD), milliseconds	104.6 (22.7)	114.0 (31.3)	0.02
Sinus rhythm (EKG)	81 (82.7%)	54 (63.5%)	0.006
eGFR, mean (SD), ml/min/1.73 m^2	74.5 (38.7)	65.3 (37.3)	0.10
Troponin-I, mean (SD), μg/L	0.49 (3.21)	0.14 (0.39)	0.37
BNP, mean (SD), pg/ml	833 (1283.3)	710 (1054.8)	0.50

MethHF = methamphetamine abuse among heart failure; HF = heart failure without evidence of methamphetamine abuse; SD = standard deviation; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; PTSD = post-traumatic stress disorder; LVEF = left ventricular ejection fraction; LVEDD = left ventricular end diastolic dimension; LAVi = left atrial volume index; CAD = coronary artery disease; EKG = electrocardiogram; eGFR = estimated glomerular filtration rate. Brackets include the denominator for the covariates with high rate of missing values (defined as greater than 25%).

between 2006 and 2015. We found several important differences between veterans with HF with and without a history of MA. Notably, the MethHF cohort was significantly younger and more likely to have co-morbid psychiatric conditions and substance abuse disorders. They were also less likely to have several medical co-morbidities. Despite their relative youth and lower burden of medical co-morbidities, veterans with MethHF had high risks of ED visit and/or admissions for HF and total mortality, with rates that were comparable to veterans with HF.

Methamphetamine is currently in the most commonly abused drugs and its use is on the rise.[1] Cardiovascular complication of MA is increasingly recognized, including hypertension, arrhythmia, methamphetamine associated cardiomyopathy, and pulmonary hypertension.[3,4] Hence, the prevalence of MA is particularly relevant in patients with HF. In our analysis, we observed that 6.7% of veterans with HF were diagnosed with MA in the final year of our analysis in 2015. Between 2005 and 2015, we observed a 2-fold increase in the proportion of methamphetamine abuse in line with a previous study also conducted in San Diego by Sliman et al.[10] Furthermore, we found that veterans with MethHF were significantly younger compared with veterans with HF, echoing previous studies that demonstrated high prevalence of MA in young patients with HF.[11,12]

Although the association of MA and HF is well-established in the medical literature, the natural history of methamphetamine associated HF is poorly understood. Animal models and case reports have suggested reversibility of methamphetamine associated HF with cessation of the drug.[6,13] Schürer et al also reported that discontinuation of methamphetamine together with medical therapy significantly improved cardiac

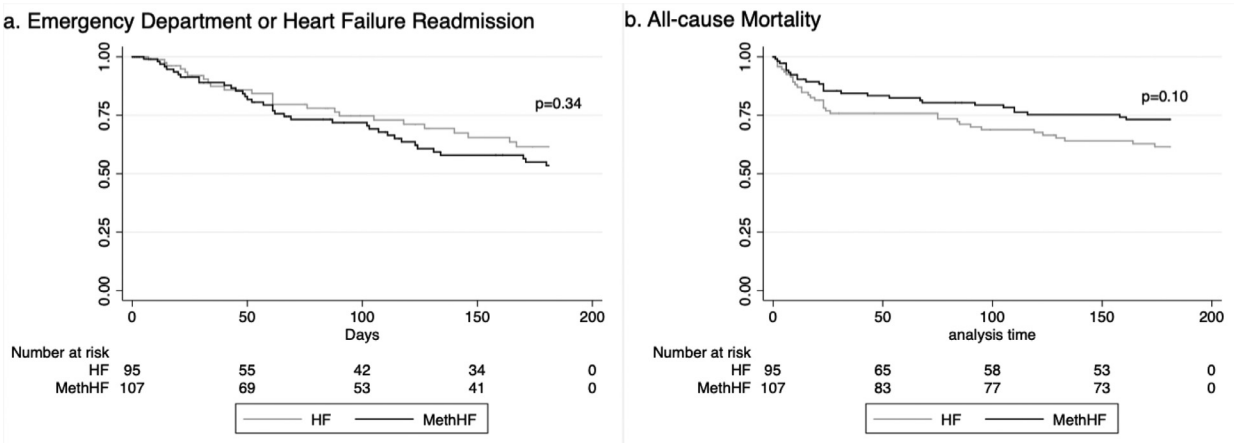

Figure 2. Kaplan-Meier curves for (a) emergency room visits or heart failure readmission and for (b) mortality as stratified by history of methamphetamine abuse.
HF = heart failure; MethHF = methamphetamine abuse among heart failure.

function (LVEF 19 vs 43 in those with continued methamphetamine use vs without, p <0.001), leading to improved clinical outcomes.[14] Nonetheless, there are significant barriers to cessation of MA in clinical practice. In our study, we found that Veterans with MethHF were significantly younger and more likely to carry psychiatric diagnoses of post-traumatic stress disorder and depression. They were also more likely to be homeless and unemployed, and use other substances including opioid, cocaine, marijuana, heroin, tobacco, and alcohol. Taken together, these specific demographic and socioeconomic characteristics of the MethHF cohort make them vulnerable to continued MA. Veterans, in particular, are vulnerable to mental health issues and substance abuse, and portend a worse outcome when they occur together.[15–17] The combat experience is also tied to subsequent unemployment and homelessness, which may further contribute to development of psychiatric co-morbidities and substance abuse in this patient population.[18]

We found that veterans with MethHF were substantially younger with similar or lesser rates of studied co-morbidities. MethHF and HF were noted to have similar rates of diabetes, chronic kidney disease, hypertension, history of ventricular tachycardia, or previous percutaneous coronary intervention, whereas rates of atrial fibrillation, cerebral vascular accidents, hyperlipidemia, and history of coronary artery bypass grafting were lower in MethHF. Lower rates of these co-morbidities seen in MethHF are likely attributable to the younger age. For example, age is major risk factor for atrial fibrillation and as such may explain higher prevalence of atrial fibrillation in HF.[19] Despite these differences, however, we found that veterans with MethHF had no significant differences in risks of ED visit, HF readmission, and mortality compared with veterans with HF. Studies have shown that hospital encounters for acute HF are associated with high rates of morbidity and mortality, and are a source of significant burden on healthcare systems worldwide.[20] Similar clinical outcomes of veterans with MethHF compared with HF despite the presence of protective factors such as younger age and lesser co-morbidity burden may highlight the importance of recognition of MA in veterans with HF.

Our study has several limitations. First, this was a single center observational study performed at a VA hospital. As with any observational study, we cannot exclude the possibility that residual confounding explains our results, and a VA hospital population may not be applicable to the general population of patients with HF. Second, our study is also limited by the small sample size and limited follow-up which decreased the statistical power of our study. We also relied upon the diagnosis and/or appropriate coding of MA during routine clinical care for inclusion in our study. As MA is frequently unrecognized in medical practitioners, the frequency of MA that we reported likely substantially underestimates the true prevalence of MA in these patients.

In conclusion, our study demonstrates a trend of increases in MA in veterans with HF. We found important differences between veterans with MethHF and those without a history of MA including more prevalent psychiatric co-morbidities, substance abuse history, and homelessness. Clinical outcomes were poor in veterans with MethH, despite a younger average age compared with veterans in the HF cohort. Given the rising prevalence of MA in Veteran's with HF, greater recognition of the complex underpinnings of this disease process may be needed to improve clinical outcomes in this patient population.

Disclosures

The authors have no conflicts of interests to disclose.

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