

# Echocardiographic Parameters and Outcomes in Methamphetamine-Associated Heart Failure: A Propensity Score-Weighted Analysis

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## Abstract

**Background:** Methamphetamines are a common cause of systolic heart failure (HF). There are limited data on the prognosis associated with hospitalizations for decompensated HF in the setting of methamphetamine use. We aimed to evaluate patient characteristics and outcomes among patients admitted with decompensated HF who had positive drug screens for amphetamines as well as to determine whether any parameters from transthoracic echocardiogram (TTE) can predict outcomes in this population.

**Methods:** This was a retrospective cohort study of consecutive adult patients admitted to the Loma Linda Medical Center who had an active hospital problem of acute on chronic systolic (or systolic and diastolic) HF from 2013 to 2018. Electronic medical records were mined for relevant patient data. Methamphetamine-associated heart failure (MethHF) group was defined as those with an admission urine drug screen (UDS) that was positive for methamphetamines, whereas non-MethHF was defined by patients with negative methamphetamine on UDS or UDS was not done on physician's discretion. The primary outcomes of the study were 30-day composite outcome (defined as combined all-cause readmission and all-cause mortality), 365-day all-cause mortality, and length of stay (LOS). Propensity score weighting for these outcomes was performed using demographics, laboratory and clinical variables, and left ventricular ejection fraction (LVEF) as covariates. TTE parameters from presentation were also evaluated to determine if any had prognostic implications.

**Results:** A total of 1,655 patients were included (101 patients with positive urine methamphetamine and 1,554 patients without). Patients with MethHF were younger, more likely to be male, had fewer comorbidities, had lower LVEF, and were more likely to have right ven-

tricular systolic dysfunction. In propensity-weighted analyses, there were no significant differences in LOS, 30-day composite outcome, or 365-day mortality between the MethHF and non-MethHF group in ( $P > 0.05$  for all). Presence of at least moderate tricuspid valve regurgitation (TR) was the only TTE predictor of 30-day composite outcome (odds ratio (OR) = 4.67, 95% confidence interval (CI): 1.5 - 14.50,  $P < 0.01$ ) and 365-day mortality (OR = 4.67, 95% CI: 1.5 - 14.50,  $P < 0.01$ ) in the MethHF group.

**Conclusion:** Patients with MethHF admitted for decompensated HF had similar outcomes compared to non-MethHF after adjusting for baseline characteristics. TR is the only TTE value to predict outcomes in this population.

**Keywords:** Methamphetamine; Heart failure; Echocardiogram; Re-admission; Mortality

## Introduction

Heart failure (HF) prevalence and disease burden continue to grow and now affect more than 64 million people worldwide [1]. Methamphetamine use is a well-established cause of HF [2] and the prevalence of methamphetamine-associated heart failure (MethHF) has been continuously increasing in the past decade [3-5]. Prior publications on the association between methamphetamine use and outcomes have demonstrated inconsistent results [4-6], and there are limited outcome data which accounts for the demographic differences between methamphetamine users and non-users. Moreover, although cardiac structural changes assessed by a transthoracic echocardiogram (TTE) in methamphetamine users have been described, it remains unclear whether any TTE parameters can predict outcomes in this population [7-9].

In this study, we aimed to evaluate and compare baseline characteristics, TTE parameters, and outcomes between patients who were found to have positive urine methamphetamine during their HF hospitalization compared to non-positive patients. Additionally, we also sought to determine whether any parameters from the admission TTE can predict outcomes in the methamphetamine population.

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## Materials and Methods

This was a retrospective cohort study of consecutive adults (age  $\geq 18$  years old) admitted to the Loma Linda University Medical Center with an active problem of acute or chronic systolic (or systolic and diastolic) HF from 2013 to 2018 based on ICD-9 or ICD-10 codes. Patients who died during hospitalization were excluded. If a patient had multiple hospitalizations meeting criteria during the study period, only the first hospitalization and associated clinical and TTE data were used in these analyses.

Electronic medical records were searched for relevant patient data. Data collected included baseline demographics, comorbid conditions (based on ICD diagnoses), relevant laboratory values, admission and discharge vital signs, and relevant discharge medications, focusing specifically on HF-approved beta-blockers (carvedilol, bisoprolol, and metoprolol succinate), angiotensin system blockers, and mineralocorticoid receptor antagonist. Discharge doses were collected to determine where any dose of the given medication class and whether at least 50% of target dose for that medication were used. Data from the TTE performed only during the index hospitalization were collected, including left ventricular ejection fraction (LVEF), end-diastolic left ventricular internal diameter end diastole (LVIDd), left ventricular internal diameter end systole (LVIDs), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left atrium (LA) diameter, peak velocity blood flow from early diastole to peak velocity flow in late diastole caused by atrial contraction (E/A) ratio, tricuspid valve regurgitation (TR) velocity, right ventricular (RV) function, tricuspid valve function, and mitral valve function. Patients were divided into two groups: patients with admission urine drug screen (UDS) which was positive for methamphetamines were defined as MethHF, whereas non-MethHF was defined by patients with negative methamphetamine on UDS or if the UDS was not done due to physicians' discretion, regardless of history of methamphetamine use. While performed at the discretion of the treatment team, the UDS is standard of care at our institution.

The primary outcomes of the study were 30-day composite outcome (defined as combined all-cause readmission and all-cause mortality), 365-day all-cause mortality, and length of stay (LOS). Mortality data were obtained by matching with the National Death Index, while readmission only to our facility was included. We performed propensity score weighted log(relative risk) estimation to account for differences in baseline demographics and TTE parameters, and their relation to outcomes.

This retrospective study was approved by the hospital Institutional Review Board and follows the ethical standards of the institution.

## Statistical analysis

For comparison of baseline demographics, TTE characteristics, and outcomes, we used the  $\chi^2$  test to compare categorical variables and the Student's *t*-test to compare continuous variables. Propensity-weighted multivariate analyses (overlap weights)

were performed using generalized linear model with covariates including age, gender, diabetes mellitus, chronic kidney disease, admission systolic and diastolic blood pressure for the reduced model and adding variables electrolytes on admission, liver function tests on admission, weight on admission, and LVEF for the full model. These last analyses were used to predict log(relative risk) for the binary outcomes, and absolute difference for the LOS outcome. With overlap weighting, it is known that the covariance matching in the weighted samples is exact. This was demonstrated with Love plots in our data and analyses [10]. Univariate binary logistic regression was used to evaluate an association between TTE parameters and outcomes. We also aimed to evaluate independent effect of methamphetamine use on TTE variables adjusting for key demographic variables by using linear regression for continuous variables and logistic regression for the binary variable. In this last instance, relative risk was calculated from the logistic regression as  $[1 + \exp(-(b + B.CV))]/[1 + \exp(-B.CV)]$ , where *b* is the coefficient for the binary exposure, CV is a vector of covariates, and B is a vector of their coefficients. The bias-corrected and accelerated (BCa) 95% confidence interval (CI) and P value are found for this relative risk using a sandwich operator [11]. P-values  $< 0.05$  were considered statistically significant for all analyses. SPSS Statistics 22 (IBM Corp., Armonk, NY) was used for *t*-test, Chi-square and linear regression statistics, while RStudio 2021.09.0 Build 351 and the PSweight package [12] were used for bootstrap analysis and propensity-weighted analyses.

## Results

A total of 1,655 patients were included in the study (101 patients with MethHF and 1,554 patients with non-MethHF). Baseline characteristics of study participants are shown in Table 1. Patients with MethHF were younger ( $52.0 \pm 10.7$  vs.  $65.2 \pm 16.1$ ,  $P < 0.01$ ), more likely to be male (72.3% vs. 60.6%,  $P = 0.01$ ), and had fewer comorbidities including diabetes mellitus (14.9% vs. 27.3%,  $P < 0.01$ ), chronic kidney disease (10.9% vs. 22.4%,  $P < 0.01$ ), and coronary artery disease (13.9% vs. 31.9%,  $P < 0.01$ ). On admission, the MethHF group had lower creatinine level ( $1.3 \pm 0.7$  vs.  $1.7 \pm 1.6$ ,  $P < 0.01$ ) and N-terminal-pro-B-type natriuretic peptide (NT-proBNP) level ( $9,248 \pm 10,256$  vs.  $12,558 \pm 16,632$ ,  $P < 0.01$ ). Regarding TTE variables, the MethHF group had significantly lower mean LVEF ( $20.6 \pm 13.1\%$  vs.  $30.3 \pm 18.1\%$ ,  $P < 0.01$ ), larger indexed LVIDs ( $2.60 \pm 0.69$  vs.  $2.37 \pm 0.73$ ,  $P < 0.01$ ), larger indexed LVEDV ( $82.7 \pm 29.4$  vs.  $73.1 \pm 28.5$ ,  $P < 0.01$ ) and indexed LVESV ( $52.0 \pm 24.8$  vs.  $43.0 \pm 23.8$ ,  $P < 0.01$ ), and was more likely to have RV systolic dysfunction (62.2% vs. 37.8%,  $P < 0.01$ ). Differences in LVEF (mean difference 5.37, 95% CI: 2.81 - 7.64,  $P < 0.001$ ), indexed LVIDs (mean difference 0.17, 95% CI: 0.01 - 0.33,  $P = 0.04$ ), and RV systolic dysfunction (risk ratio (RR) = 1.41, 95% CI: 1.12 - 1.73,  $P = 0.005$ ) remained significant between the two groups after adjusting for key baseline characteristics (age, gender, chronic kidney disease, and coronary artery disease) (Table 2), while indexed LVEDV (mean difference 4.33, 95% CI: -1.86 - 10.33,

**Table 1.** Baseline Characteristics and Transthoracic Echocardiogram of Study Participants

Variables	MethHF (n = 101)	Non-MethHF (n = 1,554)	P-value
<b>Demographics</b>			
Male	73 (72.3%)	944 (60.7%)	0.01
Mean age	52.0 ± 10.7	65.2 ± 16.1	< 0.01
BSA	2.02 ± 0.29	1.95 ± 0.33	0.06
DM	15 (14.9%)	424 (27.3%)	< 0.01
CKD	11 (10.9%)	348 (22.4%)	< 0.01
CAD	14 (13.9%)	496 (31.9%)	< 0.01
COPD	10 (9.9%)	146 (9.4%)	0.49
Admission Na	137.5 ± 4.6	137.8 ± 5.1	0.61
Admission Cr	1.3 ± 0.7	1.7 ± 1.6	< 0.01
Mean admission SBP	136.8 ± 25.7	129.3 ± 25.8	< 0.01
Mean discharge SBP	118.1 ± 20.1	116.4 ± 18.7	0.36
<b>Echocardiogram variables</b>			
LVEF	20.6 ± 13.1	30.3 ± 18.1	< 0.01
IVSD	1.25 ± 0.30	1.22 ± 0.34	0.41
LVPWd	1.23 ± 0.26	1.13 ± 0.24	< 0.01
LVIDd/BSA	3.00 ± 0.65	2.87 ± 0.65	0.052
LVIDs/BSA	2.60 ± 0.69	2.37 ± 0.73	< 0.01
LVEDV/BSA	82.7 ± 29.4	73.1 ± 28.5	< 0.01
LVESV/BSA	52.0 ± 24.8	43.0 ± 23.8	< 0.01
LA diameter	5.92 ± 0.89	5.69 ± 1.1	0.06
E/A ratio	1.79 ± 0.92	1.58 ± 0.90	0.09
TR velocity	2.88 ± 0.58	2.91 ± 0.51	0.68
Greater or equal to moderate RV systolic dysfunction	56 (62.2%)	541 (37.8%)	< 0.01
Greater or equal to moderate MR	34 (36.6%)	462 (32.0%)	0.21
Greater or equal to moderate TR	30 (32.6%)	419 (29.0%)	0.26
<b>Discharge medication</b>			
<b>Any dose</b>			
ACEI/ARB	67 (66.3%)	858 (55.2%)	0.02
Beta-blocker	80 (79.2%)	1134 (73.0%)	0.10
Spirolactone	11 (10.9%)	217 (14.0%)	0.24
<b>Greater than 50% target dose</b>			
ACEI	16 (15.8%)	242 (15.6%)	0.52
Beta-blocker	26 (25.7%)	393 (25.3%)	0.50
Spirolactone	10 (9.9%)	171 (11.0%)	0.44

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; BSA: body surface area; DM: diabetes mellitus; CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; Cr: creatinine; E/A: peak velocity blood flow from early diastole to peak velocity flow in late diastole caused by atrial contraction; IVSD: interventricular septal diameter; LA: left atrium; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; LVIDd: left ventricular internal diameter end diastole; LVIDs: left ventricular internal diameter end systole; LVPWd: left ventricular posterior wall diameter; LVEF: left ventricular ejection fraction; MethHF: methamphetamine-associated heart failure; MR: mitral valve regurgitation; Na: sodium; SBP: systolic blood pressure; RV: right ventricle; TR: tricuspid valve regurgitation.

P = 0.17) and indexed LVESV (mean differences 4.33, 95% CI: -0.74 - 0.30, P = 0.09) were no longer statistically different between the groups.

At discharge, patients with MethHF were more likely to be

prescribed angiotensin system blockers (66.3% vs. 55.2%, P = 0.02). There were no differences in use of other goal-directed medical therapy (GDMT) at discharge.

Univariate outcomes are shown in Table 3. The MethHF

**Table 2.** Differences in Echocardiographic Adjusting for Demographics Using the Non-Methamphetamine-Associated Heart Failure as Reference

Variables	Mean differences (95% CI)	P-value
LVEF	5.37 (2.81 - 7.64)	< 0.001
LVIDd/BSA	0.11 (-0.03 - 0.26)	0.11
LVIDs/BSA	0.17 (0.01 - 0.33)	0.04
EDV/BSA	4.33 (-1.86 - 10.33)	0.17
ESV/BSA	4.33 (-0.74 - 9.39)	0.09
LA diameter	0.196 (-0.60 - 0.45)	0.13
E/A ratio	-0.95 (-0.32 - 0.13)	0.41
TR velocity	0.05 (-0.08 - 0.17)	0.44

  

Variables	Risk ratio (95% CI)	P-value
Greater or equal to moderate TR	1.26 (0.78 - 1.49)	0.47
Greater or equal to moderate MR	1.12 (0.78 - 1.52)	0.32
Greater or equal to moderate RV systolic dysfunction	1.41 (1.12 - 1.73)	0.005

BSA: body surface area; CI: confidence interval; E/A: peak velocity blood flow from early diastole to peak velocity flow in late diastole caused by atrial contraction; IVSD: interventricular septal diameter; LA: left atrium; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; LVIDd: left ventricular internal diameter end diastole; LVIDs: left ventricular internal diameter end systole; LVPWd: left ventricular posterior wall diameter; LVEF: left ventricular ejection fraction; MR: mitral valve regurgitation; RV: right ventricle; TR: tricuspid valve regurgitation.

group had significantly lower 30-day composite outcome (17.8% vs. 26.6%,  $P = 0.03$ ) and 365-day mortality (17.8% vs. 30.4%,  $P < 0.01$ ) than the non-MethHF group. Patients with MethHF also had shorter LOS ( $5.2 \pm 6.6$  vs.  $7.1 \pm 8.8$  days,  $P < 0.01$ ). Multivariate-adjusted outcomes with propensity score weighted models are also shown in Table 3. There were no significant differences in LOS, 30-day composite outcome and 365-day mortality between the MethHF and non-MethHF group in either full model or reduced multivariate models ( $P > 0.05$  for all).

Univariate analyses of TTE parameters predicting 30-day composite outcome and 365-day mortality in the MethHF group are shown in Table 4 (with similar data for the non-MethHF cohort shown in Supplementary Material 1, [www.cardiologyres.org](http://www.cardiologyres.org)). We found that moderate or greater TR was the only predictor of 30-day composite outcome (odds ratio (OR) = 4.67, 95% CI: 1.5 - 14.50,  $P < 0.01$ ) and 365-day mortality (OR = 4.67, 95% CI: 1.5 - 14.50,  $P < 0.01$ ).

## Discussion

This analysis of patients admitted with decompensated systolic HF categorized by the presence or absence of a positive UDS for methamphetamines on admission demonstrated several important findings. Patients with MethHF were younger, more likely to be male, and had a lower burden of comorbidities. On TTE, with adjustment for demographics data, the MethHF group had significantly lower LVEF and was more likely to have RV systolic dysfunction. After adjusting for baseline characteristics including age and LVEF, we could not detect significant differences in LOS of the index hospitalization, 30-day composite outcome, and 365-day mortality between the MethHF and non-MethHF groups. Only the presence of sig-

nificant TR during hospitalization was an echocardiographic predictor of outcomes in the MethHF population. These results have important implications for the care of patients admitted with decompensated HF in the setting of amphetamine use by highlighting demographic, echocardiographic, and outcome data associated with this population.

Methamphetamines are associated with significant cardiotoxicity, including direct myocardial toxicity, remodeling leading to dilatation and systolic dysfunction, arrhythmias, pulmonary hypertension, coronary vasospasm, accelerated coronary plaque formation, acute coronary syndrome, and sudden cardiac death [2]. Cardiovascular death is common in methamphetamine users and is reported to be the second leading cause of death in this population [13]. Autopsies obtained from chronic methamphetamine users showed cardiac fibrosis and necrosis findings that were directly proportional to the duration and frequency of drug use [2, 13]. Common structural changes include dilatation of both RV and LV with severe global hypokinesia, which then lead to bi-atrial enlargement from volume and pressure overload [14-16]. Mitral valve regurgitation (MR) and TR are frequently observed secondary to ventricular dilatation. Compared to cardiomyopathy from other causes, patients with methamphetamine use have been found to have worse biventricular systolic function, larger cardiac chambers, and more likely to develop significant regurgitation of atrioventricular valves [16]. The TTE findings of our MethHF cohort add to the prior literature [4, 9, 14], with demonstration of more prominent ventricular dilation and biventricular systolic dysfunction. However, when adjusting for differences in demographic data, we found that only the differences in LVEF, RV dysfunction, and LVIDs remained significant. Additionally, we did not find differences in prevalence of MR or TR, likely implying prominent heterogeneity in this population.

**Table 3.** Univariate Outcomes and Outcomes With Propensity Score Matching

	MethHF (n = 101)	Non-MethHF (n = 1,554)	P-value
Univariate outcomes			
Length of stay (days)	5.2 ± 6.6	7.1 ± 8.8	< 0.01
30-day combined	18 (17.8%)	413 (26.6%)	0.03
65-day mortality	18 (17.8%)	472 (30.4%)	< 0.01
Propensity score matching using non-MethHF as reference (full model)			
Length of stay (days)	6.0 (4.4 - 7.6)	7.1 <sup>a</sup>	0.18
30-day combined	19.9% (12.8-31.4%)	26.6% <sup>a</sup>	0.22
365-day mortality	28.3% (18.5-43.5%)	30.4% <sup>a</sup>	0.74
Propensity score matching using non-MethHF as reference (reduced model)			
Length of stay (days)	5.8 (4.3 - 7.4)	7.1 <sup>a</sup>	0.12
30-day combined	18.9% (12.0-29.8%)	26.6% <sup>a</sup>	0.14
365-day mortality	27.1% (17.6-42.6%)	30.4% <sup>a</sup>	0.63

<sup>a</sup>Reference group. Values for the MethHF group use absolute (length of stay) and relative (30-day and 365-day endpoints) differences compared with the reference group. MethHF: methamphetamine-associated heart failure.

Evidence regarding prognosis and outcomes in patients with MethHF is inconsistent. Recent data from National Inpatient Sample (NIS) showed that the MethHF group had lower in-hospital mortality despite having more complications such as acute kidney injury, ventricular tachycardia, and cardiogenic shock [17]. Readmission rate generally appeared to be higher in MethHF in several studies, although there was a discrepancy in mortality outcome [6, 18, 19]. In contrast, data from Veteran Affairs suggested that there were no differences in either short or long-term outcomes between MethHF and non-MethHF [5]. Our unadjusted outcomes showed that the MethHF group had a shorter LOS and lower 30-day composite outcome and 365-

day mortality than the non-MethHF group. However, given the major differences in age, baseline demographics and TTE variables, control for baseline variables is important to better clarify the association between methamphetamine use and outcomes. After incorporating a total of 14 variables in propensity score matching, we found that patients who were methamphetamine positive on admission had lengths of stay and prognoses that were not clearly different from other patients. It is also possible that the trend towards a decreased LOS observed in the MethHF group in propensity analyses, though not statistically significant, was due to a tendency to be discharged early relating to frequent hospital-related systematic difficulties or

**Table 4.** Binary Logistic Regression for 30-Day Combined Outcome and 365-Day Mortality of MethHF Group (n = 101)

Variables	30-day combined outcome		365-day mortality	
	OR (95% CI)	P-value	OR (95% CI)	p-value
LVEF (%)	1.01 (0.97 - 1.05)	0.68	0.99 (0.95 - 1.03)	0.72
LVIDd/BSA (cm/m <sup>2</sup> )	1.49 (0.64 - 3.44)	0.36	1.61 (0.71 - 3.68)	0.26
LVIDs/BSA (cm/m <sup>2</sup> )	1.38 (0.61 - 3.14)	0.44	1.27 (0.57 - 2.8)	0.56
EDV/BSA (mL/m <sup>2</sup> )	1.00 (0.98 - 1.02)	0.69	1.01 (0.99 - 1.03)	0.20
ESV/BSA (mL/m <sup>2</sup> )	1.00 (0.98 - 1.03)	0.70	1.01 (0.98 - 1.03)	0.39
LA diameter (cm)	1.37 (0.72 - 2.63)	0.34	0.73 (0.39 - 1.36)	0.32
E/A ratio	1.63 (0.76 - 3.50)	0.21	1.31 (0.59 - 2.9)	0.50
TR velocity (m/s)	1.13 (0.42 - 3.06)	0.81	1.18 (0.46 - 3.04)	0.73
Greater or equal to moderate TR	4.67 (1.5 - 14.50)	< 0.01	4.67 (1.5 - 14.50)	< 0.01
Greater or equal to moderate MR	2.67 (0.89 - 8.01)	0.08	1.96 (0.66 - 5.82)	0.23
Greater or equal to moderate RV systolic dysfunction	1.56 (0.51 - 4.76)	0.44	1.12 (0.36 - 3.48)	0.85

BSA: body surface area; CI: confidence interval; E/A: peak velocity blood flow from early diastole to peak velocity flow in late diastole caused by atrial contraction; IVSD: interventricular septal diameter; LA: left atrium; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; LVIDd: left ventricular internal diameter end diastole; LVIDs: left ventricular internal diameter end systole; LVPWd: left ventricular posterior wall diameter; LVEF: left ventricular ejection fraction; MethHF: methamphetamine-associated heart failure; MR: mitral valve regurgitation; Na: sodium; SBP: systolic blood pressure; OR: odds ratio; RV: right ventricle; TR: tricuspid valve regurgitation.

socioeconomic challenges in this population.

While complete cessation of methamphetamine is critical for LV recovery, evidence-based GDMT is also indicated in this population similarly as in the non-MethHF population [20]. However, given a high incidence of suboptimal compliance, optimization of GDMT in the MethHF population is challenging. Optimization of GDMT among hospitalized systolic HF patients has been shown to be feasible and associated with improved outcomes [21]. In this cohort, we found that patients with MethHF are discharged with overall similar GDMT to the non-MethHF patients, implying that the use of GDMT in this population appears feasible and may be an important step in improving outcomes, concurrent with substance cessation counseling.

### Study limitation

Our study has several limitations. This is a single-center, retrospective cohort study. MethHF was defined solely on admission UDS. While UDS can identify active user, patients who had cardiomyopathy secondary to methamphetamine or history or methamphetamine abuse but without recent use may have negative urine methamphetamine and are not included as MethHF in our cohort. Thus, this cohort more accurately represents patients with positive methamphetamine on UDS and may not reflect a specific etiology of HF. ICD codes entered by clinicians were used to identify subjects with acute on chronic systolic (or systolic and diastolic) HF as well as comorbidities, which can be heterogeneous and subjected to clinicians' discretion. The duration of systolic HF or other prior HF history, including whether HF with a preserved EF may have been present in the past, cannot be well evaluated from the current data. Moreover, we also excluded patients who died during the index hospitalized. Although we obtained mortality data from the National Death Index, readmission only to our facility was included for the outcome and could underestimate the true readmission rate. However, the readmission rates are close to the national average implying that most patients may return to our facility as the largest tertiary care provider in the geographic area. Additionally, we do not have the status of methamphetamine use during the follow-up periods, which is an essential factor affecting the outcomes. Several data were unavailable, including patient race and socioeconomic status, which may have important associations with substance use, and certain comorbidities commonly associated with methamphetamine use, such as endocarditis and chronic pulmonary hypertension. Other echocardiographic parameters, including those associated with filling pressure such as right atrial pressure or tissue Doppler velocities, were not included in this dataset. Finally, the number of outcome events at 30 days and 365 days was relatively small, providing adequate statistical power to detect only relatively large effects on such binary outcomes.

### Conclusion

In this single-center analysis of patients admitted with decompensated systolic HF, patients with MethHF were younger, had lower rates of comorbidities, and had more evidence of biventricular dysfunction. In propensity-weighted analyses, there were non-significant differences in LOS of the index hospitalization, 30-day composite outcome of mortality and readmission, and 365-day mortality between MethHF and non-MethHF. Among TTE parameters, moderate or severe TR is the only univariate predictor of short-term and long-term outcomes within the MethHF group. These results characterize patients admitted with decompensated systolic HF who test positive for methamphetamines as well as their outcomes, which can have important implication for the care of this growing population.

Suppl 1. Binary Logistic Regression for 30-Day Combined Outcome and 365-Day Mortality of Non-MethHF Group (n = 1,554).

### Supplementary Material

**Suppl 1.** Binary Logistic Regression for 30-Day Combined Outcome and 365-Day Mortality of Non-MethHF Group (n = 1,554).

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None to declare.

### Financial Disclosure

Authors have no relevant disclosures.

### Conflict of Interest

All authors declare no conflict of interest.

### Informed Consent

Not applicable.

### Author Contributions

Jakrin Kewcharoen and Dmitry Abramov: concept design, data collection, data analysis, and manuscript draft; Andrew K. Chang: concept design, data collection, and manuscript revision; Purvi Parwani: concept design, data analysis, data collection, and manuscript revision; Gary Fraser: data analysis and manuscript revision; Aditya Bhardwaj, Ahmed Seliem, Diane Tran, Liset Stoletniy, and Antoine Sakr: data collection and manuscript revision. All authors give final approval of the manuscript and agree to be accountable for all aspects of the work.

### Data Availability

The authors declare that data supporting the findings of this

study are available from the corresponding author on request.

## Abbreviations

CI: confidence interval; E/A: peak velocity blood flow from early diastole to peak velocity flow in late diastole caused by atrial contraction; HF: heart failure; LA: left atrium; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; LVIDd: left ventricular internal diameter at end diastole; LVIDs: left ventricular internal diameter at end systole; LVPWd: left ventricular posterior wall diameter; LVEF: left ventricular ejection fraction; MethHF: methamphetamine-associated heart failure; MR: mitral valve regurgitation; OR: odds ratio; RV: right ventricle; LV: left ventricle; RR: risk ratio; TR: tricuspid valve regurgitation; TTE: transthoracic echocardiogram

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