Title

Outcomes in Patients With Heart Failure Using Cocaine



Authors

Garry, Jonah D

Thakkar, Anjali B

Durstenfeld, Matthew S

et al.

Publication Date

2022-08-01

DOI

10.1016/j.amjcard.2022.04.028

Peer reviewed

HHS Public Access

Author manuscript

*Am J Cardiol*. Author manuscript; available in PMC 2023 August 01.

Published in final edited form as:

*Am J Cardiol*. 2022 August 01; 176: 66–72. doi:10.1016/j.amjcard.2022.04.028.

# Outcomes in Patients With Heart Failure Using Cocaine

**Jonah D. Garry, MD**[a,*], **Anjali B. Thakkar, MD, MBA**[b], **Matthew S. Durstenfeld, MD**[b], **Yifei Ma, PhD**[b], **Sithu Win, MD, MPH**[b], **Priscilla Y. Hsue, MD**[b]

[a]Division of Cardiovascular Medicine, Vanderbilt University Medical Center, Nashville, Tennessee

[b]Division of Cardiology, San Francisco General Hospital, Department of Medicine, University of California, San Francisco, California.

## Abstract

Cocaine is an established cardiovascular toxin, but the impact of cocaine use on clinical outcomes in heart failure (HF) remains unknown. Although nonselective β-blocker use in cocaine users with HF and reduced ejection fraction (HFrEF) appears to be safely tolerated, selective β-blockers have not been evaluated. This study aimed to assess whether cocaine use is associated with worse clinical outcomes in patients with HF and evaluate the safety of β-blocker prescription upon discharge in cocaine users with HFrEF. This was a single-center retrospective cohort study of patients with incident HF hospitalization at a safety-net hospital. Primary outcomes included all-cause mortality and readmissions, including HF. Cocaine users were compared with nonusers matched by age, gender, and year of index admission. In cocaine users with HFrEF, outcomes were compared according to β-blocker prescription at discharge. From 2001 to 2019, 738 cocaine users were identified and compared with 738 matched nonusers. Cocaine use was associated with increased mortality (adjusted hazard ratio [HR] 1.21; 95% confidence interval [CI] 1.00 to 1.48) and 90-day readmission (all-cause: adjusted HR 1.49; 95% CI 1.20 to 1.85; HF: adjusted HR 1.49; 95% CI 1.10 to 2.01), persisting at 1 year. In cocaine users who were prescribed metoprolol, carvedilol, or no β-blocker at discharge, the rates of 1-year mortality and 30-day readmission were similar. In conclusion, cocaine use is associated with increased all-cause mortality, HF readmission, and all-cause readmission. Both nonselective and selective β-blocker may be safe in managing patients with HFrEF and cocaine use.

## Introduction

Cocaine is theorized to worsen cardiomyopathy through catecholamine surge, endothelial dysfunction, prothrombotic effects, and impaired calcium handling.[1] However, the clinical impact of cocaine use in patients with heart failure (HF) remains poorly described. Only 1 small cohort study has examined cocaine as a risk factor for readmission and mortality in patients with HF, failing to detect a significant difference in these outcomes.[2] Although

*Corresponding author: Tel: (615) 936-1720; fax: (615) 936-1872. Jonah.garry@vumc.org (J.D. Garry).

Disclosures

The authors have no conflicts of interest to declare.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2022.04.028.

β-blockers are a class I recommendation for patients with HF with reduced ejection fraction (HFrEF) stage C,[3] there have been concerns around efficacy and safety in cocaine users.[4–7] These concerns have since been challenged by overall reassuring clinical outcomes in ever larger cohorts with acute cocaine-related chest pain and HF.[2,8–14] Whether selective β-blockers (i.e., metoprolol) are equally safe to nonselective β-blockers (i.e., carvedilol) in the patients with HFrEF who use cocaine remains unknown.[13] Therefore, this study was designed to evaluate whether or not cocaine use is independently associated with poor outcomes in patients with incident HF, and whether nonselective and selective β-blockers are equally safe to use in active cocaine users with HFrEF.

## Methods

This was a single-center retrospective cohort study conducted at an academic safety-net hospital (Zuckerberg San Francisco General Hospital, San Francisco, California). Approval for this study was obtained through the University of California, San Francisco Committee on Human Research. The electronic health record was queried between January 2001 and July 2019 for patients admitted with a diagnosis of HF as indicated by the International Classification of Diseases (ICD), ninth or tenth revision coding. For patients found to have multiple hospitalizations, only data from the first admission (assumed to be incident HF hospitalization) was included. The predictor variables analyzed in this study were (1) cocaine use as indicated by ICD code or urine toxicology positivity and (2) β-blocker prescription at the time of index hospitalization discharge. The cocaine using population was matched 1:1 with noncocaine using patients based on age (within 5 years), gender, and year of index HF admission (within 2 years).

ICD coding from the index hospitalization was used to identify relevant co-morbid diagnoses, including all previously attached diagnoses in the local electronic health record (EHR). For the case of substance use disorders, urine toxicology results were also used to identify patients with ongoing use. Demographic data, including age, gender, race, insurance status, medication prescription, and details of index hospitalization, including the level of care, length of stay, and discharge disposition, were obtained through EHR abstraction. Regarding HF medications, all prescriptions from the time of discharge forward were obtained after January 2015. Echocardiographic left ventricular ejection fraction (LVEF) was abstracted from the exam conducted closest to the HF diagnosis date, up to 1 year after diagnosis. LVEF ≤ 50% was used to define HFrEF.

Follow-up began on the date of index HF hospital admission. The outcomes assessed were all-cause mortality, HF readmission, and all-cause readmission. For the overall cohort, mortality was assessed at 1, 5, 10 years, and at study end, whereas readmission was assessed at 30 days, 90 days, and 1 year. For the β-blocker analysis, the same outcomes were employed; however, only the earliest time point was assessed. The Social Security Death Index, National Death Index, and local hospital records were used to determine patient mortality. Follow-up data and readmission at Zuckerberg San Francisco General Hospital were obtained for all patients through EHR abstraction.

Categorical variables were described by number of patients and percentage, with chi-square or Fisher's exact testing employed to evaluate statistical differences. Continuous variables were described by mean and SD, or median and interquartile range, with unpaired Student *t* test or the Wilcoxon rank-sum test used to compare differences, as appropriate based on normality testing. Time-to-event analyses were plotted using Kaplan-Meier curves, and time-specific survival was described using Kaplan-Meier survival function. Cox proportional hazard regression was used to conduct univariate and multivariable regression analyses describing the association between covariates and mortality or readmission. Age, gender, race/ethnicity, coronary artery disease, hypertension, diabetes mellitus, HIV, chronic obstructive pulmonary disease, chronic kidney disease, opiate use, methamphetamine use, and alcohol use were selected as covariates for the multivariable analyses. Data on these variables were available for all patients. Echocardiographic data were available for 879 patients, with a significant difference in availability for cocaine users compared with nonusers. Therefore a sensitivity analysis was performed with LVEF included in the multivariable model. A 2-tailed p value <0.05 was considered statistically significant. All statistical analysis was completed using SAS Version 9.4M7 (SAS Institute Inc., Cary, North Carolina).

## Results

Of the 3,131 hospitalizations for HF between January 2001 and July 2019, 791 patients (25.3%) were found to concurrently use cocaine. Of these, 738 cocaine users were able to be matched 1:1 with cocaine nonusers by our matching criteria. The study flow diagram is displayed in Figure 1, and the baseline characteristics of each group are listed in Table 1. The groups notably differ by race, with a greater proportion of cocaine users identifying as African American (69.9% vs 29.5%, p <0.01). The prevalence of major co-morbidities is similar between groups, with the exception of hypertension more frequently found in cocaine users (88.5% vs 82.8%, p <0.01). Other substance use disorders, including alcohol (62.6% vs 25.7%, p <0.01), opiate (39.2% vs 9.5%, p <0.01), and methamphetamine use (50.7% vs 16.9%, p <0.01), are more prevalent in cocaine users.

The all-cause mortality rate at 1 year in cocaine users was not different from that of nonusers (13.2% vs 11.3%, p = 0.28). By 5 years, a higher proportion of cocaine users with HF had died (36.7% vs 29.2%, p <0.01), persisting at 10 years (45.5% vs 35.8%, p <0.01) and the overall study duration (56.8% vs 43.0%, p <0.01). After adjustment for demographics, co-morbidities, and concurrent substance use, cocaine was not found to significantly increase the risk of all-cause mortality at 1 year (adjusted hazard ratio [HR] 1.10; 95% confidence interval [CI] 0.78 to 1.55), 5 years (adjusted HR 1.13; 95% CI 0.91 to 1.40), or 10 years (adjusted HR 1.18; 95% CI 0.97 to 1.43), but did significantly increase risk over the complete follow-up period (adjusted HR 1.21; 95% CI 1.00 to 1.48). The Kaplan-Meier curve for all-cause mortality is displayed in Figure 2. Reduced LVEF was not found to interact with cocaine use and was not associated with mortality. When reduced LVEF was added to the multivariable model (excluding patients without an echocardiogram), there was no association between cocaine use and mortality at 1, 5, and 10 years or for the overall study (HR 1.18; 95% CI 0.97 to 1.43). The multivariable model of factors associated with

mortality is listed in Table 2, with reduced ejection added to the model in Supplementary Table 1.

Both HF and all-cause readmission rates in cocaine users were elevated in comparison to nonusers at 30 days, 90 days, and 1-year, as demonstrated in Figures 3 and 4. After multivariable adjustment, cocaine use was not associated with HF readmission at 30 days (adjusted HR 1.11; 95% CI 0.73 to 1.69) but was associated with a higher risk of readmission at 90 days (adjusted HR 1.49; 95% CI 1.10 to 2.01), and 1 year (adjusted HR 1.48; 95% CI 1.17 to 1.87). Similarly, cocaine use was not associated with all-cause readmission at 30 days (adjusted HR 1.18; 95% CI 0.88 to 1.59) but was associated with an increased risk of all-cause readmission at 90 days (adjusted HR 1.49; 95% CI 1.20 to 1.85) and 1 year (adjusted HR 1.48; 95% CI 1.24 to 1.77). These results were unchanged with reduced LVEF added to the multivariable model (data not shown).

There were 133 patients with HF concurrently using cocaine who had a reduced LVEF (≤ 50%) for whom data on medication prescription at discharge were available (admission in 2015 or later), with 79 prescribed metoprolol succinate, 25 prescribed carvedilol, and 29 without a $\beta$-blocker prescription. Baseline characteristics between each group were similar, listed in Supplementary Table 2. Medical therapies and primary outcomes comparing those patients prescribed a $\beta$-blocker at discharge to no $\beta$-blocker are listed in Table 3. In age and gender-adjusted analysis, there was no association between $\beta$-blocker prescription and 30-day readmission (adjusted HR 0.89; 95% CI 0.40 to 1.98), HF readmission (adjusted HR 0.61; 95% CI 0.23 to 1.58), or 1-year mortality (adjusted HR 0.39; 95% CI 0.13 to 1.16).

At 1 year postdischarge, 41 patients (52%) prescribed metoprolol were still receiving a $\beta$-blocker, whereas 17 patients (68%) prescribed carvedilol were still receiving a $\beta$-blocker ($p = 0.16$). Patients prescribed carvedilol were more likely to switch to metoprolol, with 7 patients (28.0%) transitioning, whereas 9 patients (11.4%) transitioned from metoprolol to carvedilol ($p = 0.04$). The median dose achieved by 3 months postdischarge was 6.25 mg twice per day (IQR 3.125 to 12.5 mg) in the carvedilol group and 56.25 mg daily (IQR 25 to 100 mg) in the metoprolol group. At 1 year, 5 patients (18.5%) died in the no $\beta$-blocker group, 9 patients (11.4%) in the metoprolol group, and 5 patients (18.5%) in the carvedilol group. After adjustment for age and gender, point estimates for the effect of metoprolol and carvedilol suggested benefit with wide confidence intervals (adjusted HR 0.31; 95% CI 0.09 to 1.04 and adjusted HR 0.62; 95% CI 0.16 to 2.39, respectively), without significant difference between metoprolol and carvedilol (adjusted HR 0.50; 95% CI 0.14 to 1.78). Similarly, there were no differences in the risk of 30-day all-cause or HF readmission (Supplementary Table 3).

## Discussion

We found that patients with HF using cocaine had a higher risk of all-cause mortality compared with age and gender-matched noncocaine users. Cocaine use was associated with increased HF and all-cause readmission at 90 days and 1 year. To our knowledge, this is the largest study to date to explore the effect of cocaine use on clinical outcomes in patients with HF. One previous study has compared outcomes between 90 cocaine users

with HF and 177 nonusers, finding no significant differences in all-cause readmission or all-cause mortality.[2] Matching, cohort size, and inclusion of ischemic cardiomyopathy in our study may account for the discrepant findings. There was also a significant proportion of methamphetamine users in our cohort (34%), whereas the proportion of methamphetamine users was not reported by Nguyen et al.[2] There was a substantially higher prevalence of cocaine use in our cohort (25.3%) compared with the prevalence in patients with HF in the national inpatient sample from 2008 to 2017 (1.4% of hospitalizations associated with cocaine or methamphetamine).[15] However, outcomes in our cohort were similar to those of patients with HF with cocaine use in the national inpatient sample for in-hospital mortality (0.8% vs 0.7%), length of stay (3 vs 4.5 days), and against medical advice discharge (6.8% vs 7.2%).[15] This would suggest that results from our cohort may be generalizable.

The mechanisms by which cocaine might precipitate worsening HF are only partially understood. Cocaine use has been associated with diastolic dysfunction, increased ventricular wall thickness, increased heart weight, and decreased left ventricular end-diastolic volume.[16] The sympathomimetic effects of cocaine increase myocardial demand through increased contractility, heart rate, and vasoconstriction, whereas worsening atherosclerotic disease precipitating chronic ischemia.[1] There is insufficient evidence to conclude that cocaine is directly associated with reduced LVEF. However, magnetic resonance imaging findings of decreased systolic strain in cocaine users suggest sub-clinical left ventricular dysfunction.[17] Through the mechanisms described, β-blockers may become indicated in cocaine users that develop coronary disease or HFrEF, and the question of β-blocker safety and efficacy becomes vitally important.

Although the confidence intervals are wide, HR point estimates for mortality in patients with HFrEF prescribed metoprolol and carvedilol compared with no β-blocker suggest a benefit, and the possibility of a greater effect from metoprolol cannot be excluded. Our findings add to the existing evidence supporting the safety of β-blocker therapy in patients with HFrEF who use cocaine. Thus far, β-blockers have been shown to improve LVEF, reduce readmissions, improve symptoms, and reduce major adverse cardiovascular events in patients with HFrEF using cocaine, with stronger evidence for carvedilol than metoprolol.[10–12,14] Theoretically, carvedilol would be preferred over metoprolol for its alpha-blockade effect, but this may not translate into clinical outcomes. The advantages of once-a-day dosing and decreased blood pressure effect, allowing for ease of titration and compliance, may outweigh the hypothesized pharmacologic benefit. This hypothesis would be supported by our finding of more transitions from carvedilol to metoprolol (compared with the converse). It is important to note that the risk of unopposed alpha-receptor agonism in selective β-blocker use may be significant in patients with higher cumulative cocaine use, higher doses of cocaine, or increased dosage of β-blocker, however, our study was not equipped to evaluate these questions.

Clinicians caring for patients with HF who use cocaine should be aware of the elevated rates of readmission and mortality in this high-risk patient population. These patients may benefit from coronary artery disease screening, aggressive use of antihypertensives, and early employment of guideline-directed therapies. Further research directed toward elucidating the mechanisms of cocaine-induced cardiovascular toxicity may be useful in devising

management strategies. Although not assessed in this study, psycho-socio-economic factors may play a significant role in adverse outcomes and warrant further investigation.

There are several limitations of the present analysis. Laboratory data were not able to be accurately abstracted and were not included. Data on patient follow-up and readmission were only available for Zuckerberg San Francisco General Hospital; therefore, follow-up percentages and readmission rates likely represent an underestimation. Beta-blocker prescription does not equate to compliance; however, this was mitigated by providing information on ongoing filled prescriptions. Co-morbidities and HF diagnosis were derived from ICD coding, which varies in sensitivity and specificity for a given diagnosis. Although this study was designed to examine incident HF, it is possible that previous admissions at outside institutions or under different medical record numbers were not identified and mistakenly included. Data on prescriptions were available from 2015 onwards. As a result, there was a small population available for the $\beta$-blocker analyses, which were conducted with limited power preventing strong conclusions. Information on cocaine usage duration, route, frequency, and amount was not available. Cross-over in the form of cocaine cessation or initiation during the study period after initial hospitalization could not be accounted for in our study.

In conclusion, cocaine use in patients with HF is a risk factor for readmissions and identifies patients at increased risk of mortality compared with nonusers. Selective $\beta$-blockers such as metoprolol may be safe in patients with HF who use cocaine.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

Dr. Hsue received funding provided by a National Institutes of Health grant, number NIH 2 K24 AI112393–06.

## References

1. Havakuk O, Rezkalla SH, Kloner RA. The cardiovascular effects of cocaine. J Am Coll Cardiol 2017;70:101–113. [PubMed: 28662796]
2. Nguyen P, Kamran H, Nasir S, Chan W, Shah T, Deswal A, Bozkurt B. Comparison of frequency of cardiovascular events and mortality in patients with heart failure using versus not using cocaine. Am J Cardiol 2017;119:2030–2034. [PubMed: 28456314]
3. Writing Committee, Maddox TM Januzzi JL, Allen LA, Breathett K, Butler J, Davis LL, Fonarow GC, Ibrahim NE, Lindenfeld J, Masoudi FA, Motiwala SR, Oliveros E, Patterson JH, Walsh MN, Wasserman A, Yancy CW, Youmans QR. 2021 update to the 2017 ACC expert consensus decision pathway for optimization of heart failure treatment: answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2021;77:772–810. [PubMed: 33446410]
4. Fareed FN, Chan GM, Hoffman RS. Death temporally related to the use of a beta adrenergic receptor antagonist in cocaine associated myocardial infarction. J Med Toxicol 2007;3:169–172. [PubMed: 18072171]
5. Rappolt RT Sr, Gray GR, Inaba DS. Letter: Propranolol in the treatment of cardiopressor effects of cocaine. N Engl J Med 1976;295:448. [PubMed: 934248]

6. Vargas R, Gillis RA, Ramwell PW. Propranolol promotes cocaine-induced spasm of porcine coronary artery. J Pharmacol Exp Ther 1991;257:644–646. [PubMed: 2033510]
7. Lange RA, Cigarroa RG, Flores ED, McBride W, Kim AS, Wells PJ, Bedotto JB, Danziger RS, Hillis LD. Potentiation of cocaine-induced coronary vasoconstriction by beta-adrenergic blockade. Ann Intern Med 1990;112:897–903. [PubMed: 1971166]
8. Rangel C, Shu RG, Lazar LD, Vittinghoff E, Hsue PY, Marcus GM. Beta-blockers for chest pain associated with recent cocaine use. Arch Intern Med 2010;170:874–879. [PubMed: 20498415]
9. Lo KB, Virk HUH, Lakhter V, Ram P, Gongora C, Pressman G, Figueredo V. Clinical outcomes after treatment of cocaine-induced chest pain with beta-blockers: a systematic review and meta-analysis. Am J Med 2019;132:505–509. [PubMed: 30562494]
10. Egbuche O, Ekechukwu I, Effoe V, Maduabum N, Millard HR, Maihemuti A, Cross JA, Adedinsewo D, Onwuanyi AE. Effect of $\beta$-blocker therapy on hospital readmission and mortality in heart failure patients with concurrent cocaine use. J Cardiovasc Pharmacol Ther 2018;23:518–523. [PubMed: 29793347]
11. Lopez PD, Akinlonu A, Mene-Afejuku TO, Dumancas C, Saeed M, Cativo EH, Visco F, Mushiyev S, Pekler G. Clinical outcomes of B-blocker therapy in cocaine-associated heart failure. Int J Cardiol 2019;277:153–158. [PubMed: 30146248]
12. Banerji D, Alvi RM, Afshar M, Tariq N, Rokicki A, Mulligan CP, Zhang L, Hassan MO, Awadalla M, Groarke JD, Neilan TG. Carvedilol among patients with heart failure with a cocaine-use disorder. JACC Heart Fail 2019;7:771–778. [PubMed: 31466673]
13. Mann BK, Bhandohal JS, Saeed M, Pekler G. Beta blocker therapy in heart failure patients with active cocaine use: a systematic review. Cardiol Res Pract 2020;2020:1985379. [PubMed: 32454995]
14. Lopez PD, Akinlonu A, Mene-Afejuku TO, Dumancas C, Saeed M, Cativo EH, Visco F, Mushiyev S, Pekler G. Improvement in clinical outcomes of patients with heart failure and active cocaine use after $\beta$-blocker therapy. Clin Cardiol 2018;41:465–469. [PubMed: 29663434]
15. Shetty S, Malik AH, Ali A, Yang YC, Briasoulis A, Alvarez P. Characteristics, trends, outcomes, and costs of stimulant-related acute heart failure hospitalizations in the United States. Int J Cardiol 2021;331:158–163. [PubMed: 33535075]
16. Arenas DJ, Beltran S, Zhou S, Goldberg LR. Cocaine, cardiomyopathy, and heart failure: a systematic review and meta-analysis. Sci Rep 2020;10:19795. [PubMed: 33188223]
17. Maceira AM, Guardiola S, Ripoll C, Cosin-Sales J, Belloch V, Salazar J. Detection of subclinical myocardial dysfunction in cocaine addicts with feature tracking cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2020;22:70. [PubMed: 32981526]

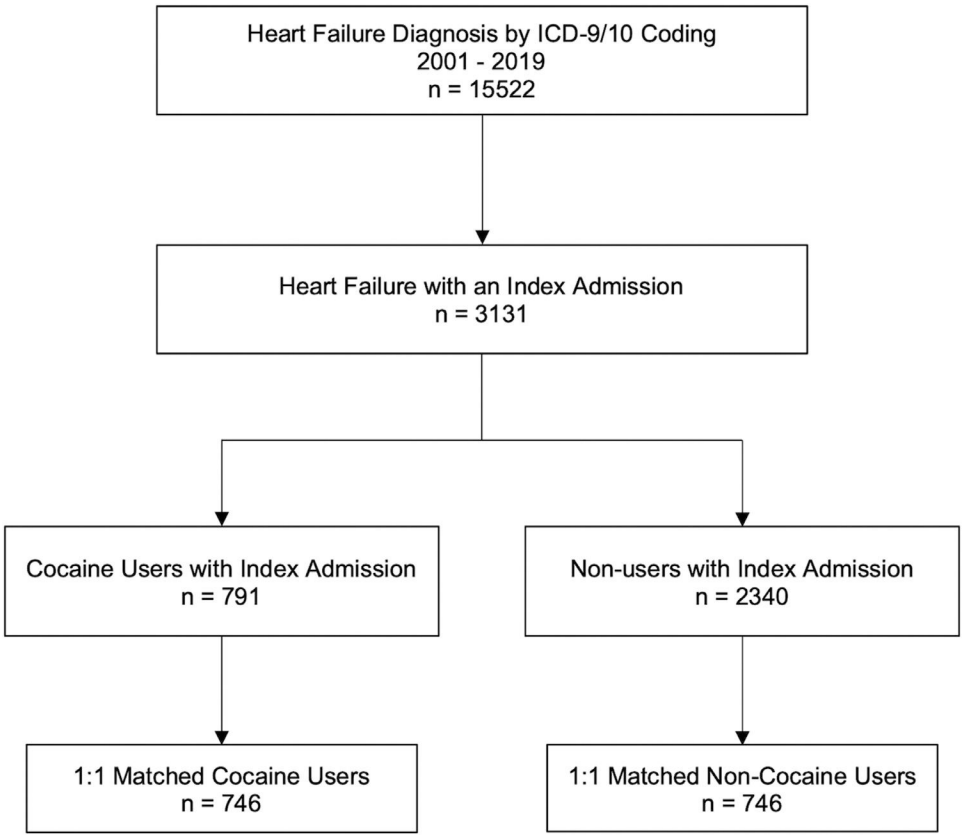


**Figure 1.**
Cohort diagram displaying the process of cohort identification and matching.

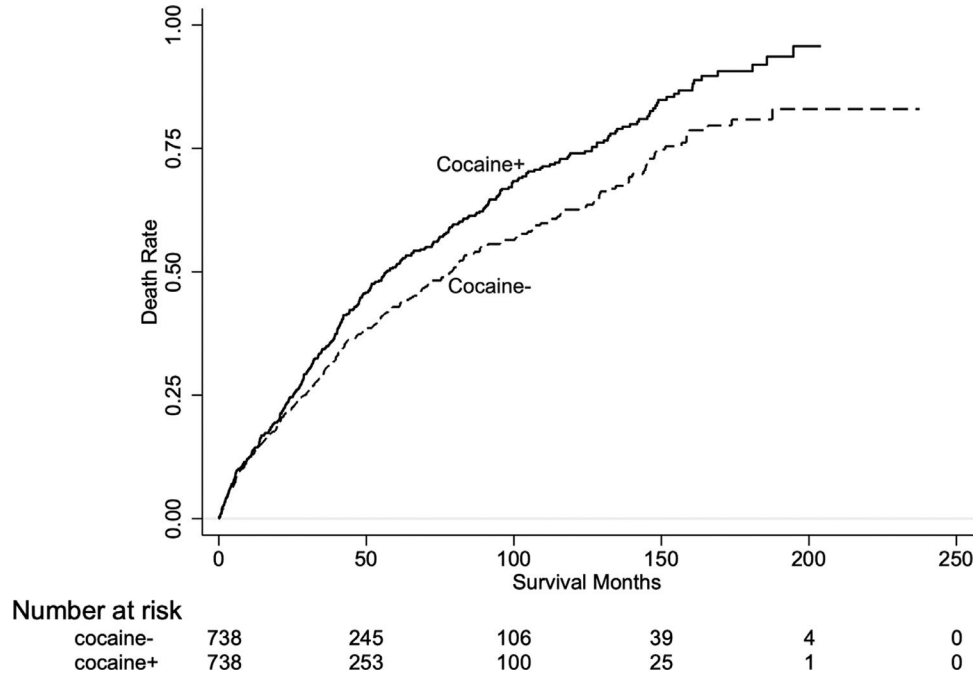


**Figure 2.**

Kaplan-Meier curve of mortality by cocaine. Displays Kaplan-Meier curves of survival over the full duration of follow-up, with separate curves for cocaine users (cocaine+) and nonusers (cocaine−).

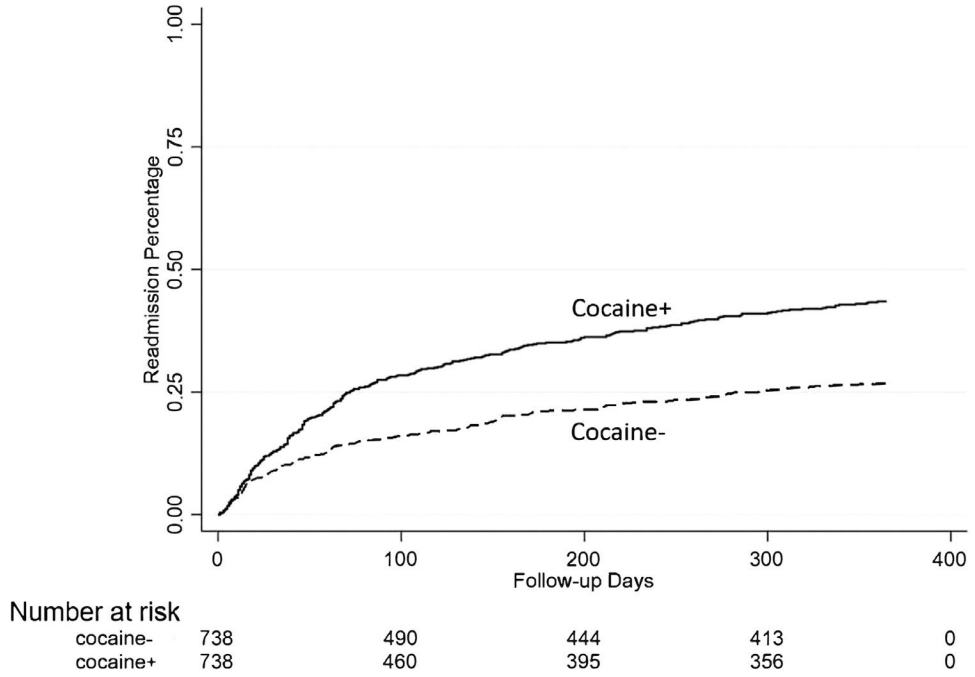


**Figure 3.**

Heart failure readmission by cocaine use. Displays the percentage of patients with a hospital readmission for a primary diagnosis of heart failure up to 1-year of follow-up, with separate curves for cocaine users (cocaine+) and nonusers (cocaine−).

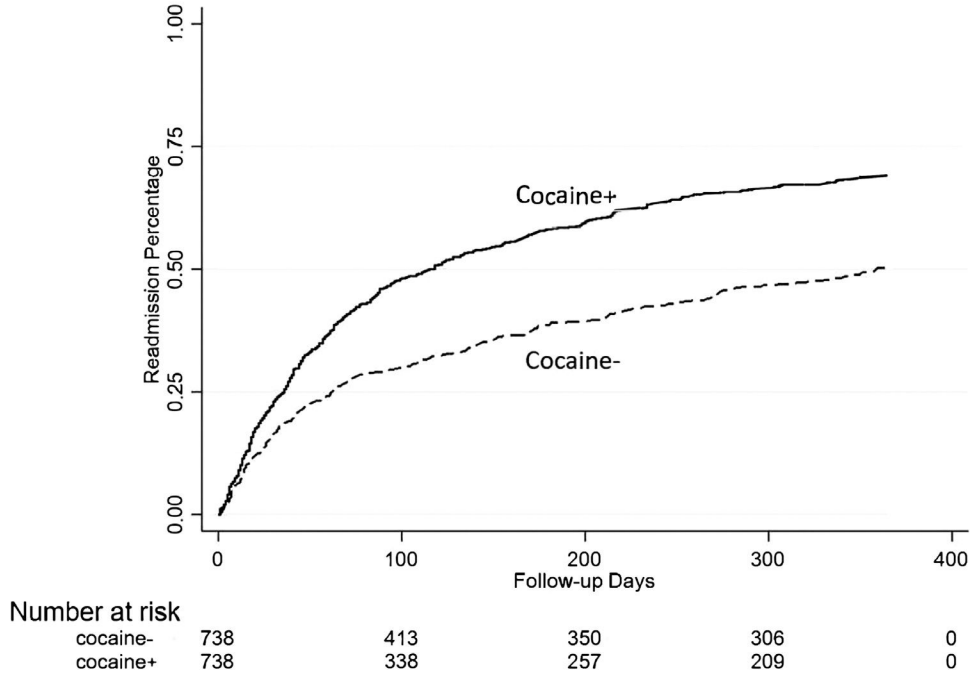


**Figure 4.**

All-cause readmission by cocaine use. Displays the percentage of patients with hospital readmission for any cause up to 1-year of follow-up, with separate curves for cocaine users (cocaine+) and nonusers (cocaine−).

## Table 1

Characteristics of matched cocaine using and nonusing patients with heart failure

| Variable | Cocaine use | | p Value |
|---|---|---|---|
| | Yes | No | |
| | (n=738) | (n=738) | |
| Age | 53.1 (47.4, 59.1) | 53.2 (47.5, 59.1) | 0.976 |
| Men | 579 (78.5%) | 579 (78.5%) | 1.000 |
| Race/Ethnicity | | | |
| Non-Hispanic White | 106(14.4%) | 183 (24.8%) | <0.001 |
| Black | 516 (69.9%) | 218(29.5%) | |
| Hispanic/Latinx | 15 (2.0%) | 37 (5.0%) | |
| Asian/Pacific Islander | 42 (5.7%) | 180 (24.4%) | |
| Other | 59 (8.0%) | 120 (16.3%) | |
| Insurance status | | | |
| Medicare | 243 (32.9%) | 251 (34.0%) | <0.001 |
| Medi-Cal | 407 (55.1%) | 336 (45.5%) | |
| Private | 2 (0.3%) | 11 (1.5%) | |
| Uninsured | 36 (4.9%) | 47 (6.4%) | |
| Other | 50 (6.8%) | 93 (12.6%) | |
| Coronary Artery Disease | 181 (24.5%) | 195 (26.4%) | 0.403 |
| Prior Myocardial Infarction | 137(18.6%) | 120 (16.3%) | 0.243 |
| Hypertension | 653 (88.5%) | 607 (82.2%) | 0.001 |
| Diabetes | 45 (6.1%) | 60 (8.1%) | 0.129 |
| Chronic Obstructive Pulmonary Disease | 8(1.1%) | 6 (0.8%) | 0.591 |
| Chronic Kidney Disease | 102(13.8%) | 91 (12.3%) | 0.396 |
| Human Immunodeficiency Virus | 43 (5.8%) | 28 (3.8%) | 0.068 |
| Atrial fibrillation or flutter | 132(17.9%) | 163 (22.1%) | 0.044 |
| Substance Use | | | |
| Alcohol use disorder | 462 (62.6%) | 190 (25.7%) | <0.001 |
| Opiate use disorder | 289 (39.2%) | 70 (9.5%) | <0.001 |
| Methamphetamine use | 374 (50.7%) | 125 (16.9%) | <0.001 |
| Ejection fraction * | | | |
| Preserved (>50%) | 121 (23.8%) | 95 (25.7%) | 0.503 |
| Reduced (<=50%) | 389 (76.2%) | 274 (74.3%) | 0.503 |
| Missing Echocardiogram | 228 (30.9%) | 369 (50.0%) | <0.001 |
| Medical Therapies † | | | |
| β-blocker | 327 (44.3%) | 315 (42.7%) | 0.529 |
| ACE Inhibitor | 331 (44.9%) | 319(43.2%) | 0.529 |
| Angiotensin Receptor Blocker | 70 (9.5%) | 90 (12.2%) | 0.094 |
| Spironolactone | 150 (20.3%) | 139(18.8%) | 0.471 |
| Sacubitril/Valsartan | 6 (0.8%) | 20 (2.7%) | 0.006 |

| | Cocaine use | | |
|---|---|---|---|
| **Variable** | **Yes** | **No** | **p Value** |
| Hydralazine | 74 (10.0%) | 65 (8.8%) | 0.423 |
| Index Hospitalization: | | | |
| Length of Stay | 3 [2–5] | 4 [2–6] | <0.0001 |
| Intensive Care | 282 (38.2%) | 299 (40.5%) | 0.365 |
| Against Medical Advice Discharge | 50 (6.8%) | 31 (4.2%) | 0.030 |
| Death | 6 (0.8%) | 6 (0.8%) | 1.000 |
| Home Health Referral | 26 (3.5%) | 32 (4.3%) | 0.422 |
| Follow Up (in months) | 28.7 (9.6, 60.6) | 23.7 (5.5, 56.6) | 0.001 |

*Ever prescribed to patient during study period.

†Proportion of patients who were determined to have reduced or preserved ejection fraction, in the patients who received a Transthoracic Echocardiogram (TTE).

**Table 2**

Univariate and multivariate analysis of factors associated with mortality

| | Univariate | | | Multivariate (n=1,476) | | |
|---|---|---|---|---|---|---|
| **Variable** | **HR** | **95% CI** | **p Value** | **HR** | **95% CI** | **p Value** |
| Cocaine use | 1.28 | 1.11–1.49 | 0.001 | 1.21 | 1.00–1.45 | 0.047 |
| Age | 1.01 | 1.00–1.02 | 0.007 | 1.01 | 1.00–1.02 | 0.014 |
| Male | 0.99 | 0.83–1.18 | 0.934 | 1.00 | 0.83–1.20 | 0.996 |
| Black/African American | 1.03 | 0.85–1.24 | 0.784 | 0.99 | 0.81–1.21 | 0.913 |
| Hispanic/Latinx | 1.81 | 1.21–2.72 | 0.004 | 1.80 | 1.19–2.71 | 0.005 |
| Asian Pacific Islander | 0.53 | 0.40–0.70 | <0.001 | 0.59 | 0.44–0.79 | <0.001 |
| Other Race | 0.64 | 0.48–0.87 | 0.004 | 0.64 | 0.47–0.87 | 0.004 |
| Coronary Artery Disease | 0.98 | 0.82–1.17 | 0.817 | 1.04 | 0.86–1.24 | 0.696 |
| Hypertension | 0.96 | 0.78–1.19 | 0.739 | 0.87 | 0.70–1.08 | 0.209 |
| Diabetes Mellitus | 0.85 | 0.54–1.35 | 0.487 | 0.87 | 0.54–1.39 | 0.560 |
| HIV | 1.39 | 1.02–1.89 | 0.036 | 1.31 | 0.95–1.80 | 0.101 |
| COPD | 1.03 | 0.51–2.07 | 0.927 | 1.20 | 0.59–2.41 | 0.618 |
| Chronic Kidney Disease | 1.41 | 1.15–1.73 | 0.001 | 1.46 | 1.18–1.81 | <0.001 |
| Ejection Fraction ≤ 50% | 0.96 | 0.77–1.20 | 0.739 | | | |
| Opiate use | 1.12 | 0.95–1.32 | 0.167 | 1.05 | 0.87–1.26 | 0.609 |
| Methamphetamine use | 0.87 | 0.75–1.02 | 0.092 | 0.76 | 0.64–0.91 | 0.003 |
| Alcohol use | 1.24 | 1.07–1.44 | 0.004 | 1.14 | 0.96–1.34 | 0.126 |

**Table 3**

Medical therapy and outcomes in patients with HFrEF with cocaine use

| Number of patients | β-Blocker 104 | No β-Blocker 29 | p Value |
|---|---|---|---|
| Medical Therapies | | | |
| Loop Diuretic | 99 (95.2%) | 10 (34.5%) | <0.0001 |
| ACE inhibitor/ARB | 99 (95.2%) | 13 (44.8%) | <0.0001 |
| Spironolactone | 44 (42.3%) | 1 (3.4%) | <0.0001 |
| Hydralazine | 14 (13.5%) | 1 (3.4%) | 0.189 |
| 30-d All-Cause Readmission | 30 (28.8%) | 8 (27.6%) | 0.894 |
| 30-d Heart Failure Readmission | 16 (15.4%) | 6 (20.7%) | 0.497 |
| 1-y Mortality | 15 (14.4%) | 5 (18.5%) | 0.598 |