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The Impact of Substance Abuse on Heart Failure Hospitalizations

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Abstract

Background: The burden of substance abuse among patients with heart failure and its association with subsequent emergency department visits and hospital admissions are poorly characterized.

Methods: We evaluated the medical records of patients with a diagnosis of heart failure treated at the University of California, San Diego from 2005–16. We identified substance abuse via diagnosis codes and/or urine drug screens. We used Poisson regression to evaluate the incidence rate ratios (IRR) of substance abuse for emergency department visits and/or hospitalizations with a primary diagnosis of heart failure, adjusted for age, sex, race, medical insurance status, and medical diagnoses.

Results: We identified 11,268 patients with heart failure and 15,909 hospital encounters for heart failure over 49,712 person-years of follow-up. Substance abuse was diagnosed in 15.2% of patients. Disorders such as methamphetamine abuse (prevalence 5.2%, IRR 1.96, 95% confidence interval [CI] 1.85–2.07), opioid use/abuse (8.2%, IRR 1.54, 95% CI 1.47–1.61), and alcohol abuse (4.5%, IRR 1.51, 95% CI 1.42–1.60) were associated with a greater number of hospital encounters for heart failure, with associations that were comparable to diagnoses such as atrial fibrillation (37%, IRR 1.78, 95% CI 1.73–1.84), ischemic heart disease (24%, IRR 1.67, 95% CI 1.62–1.73), and chronic kidney disease (26%, IRR 1.57, 95% CI 1.51–1.62).

Conclusions: Although less prevalent than common medical co-morbidities in patients with heart failure, substance abuse disorders are significant sources of morbidity that are independently

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associated with emergency department visits and hospitalizations for heart failure. Greater recognition and treatment of substance abuse may improve outcomes among patients with heart failure.

Keywords

Heart failure; Substance abuse; Re-admission

Introduction

Heart failure is a growing epidemic in the United States. The lifetime risk of developing heart failure is approximately 1 in 5; with an aging population, the prevalence of heart failure is projected to increase swiftly over the next few decades.[1–3] Hospital encounters for acute decompensated heart failure are associated with high rates of morbidity and mortality, and are a significant burden on healthcare systems worldwide.[3] After being hospitalized for heart failure, approximately 1 in 4 patients are readmitted within 30 days of discharge,[4] and a history of hospitalization for heart failure is associated with higher cardiovascular mortality.[5] Hence, it is imperative to identify and treat patients with heart failure who are at risk for hospitalization in an effort to improve clinical outcomes.

Substance abuse is common and associated with substantial morbidity and mortality in the general population.[6,7] Many substances with high addiction potential, such as cocaine, alcohol, and methamphetamine, exert adverse effects on the cardiovascular system and may affect the disease course of patients with heart failure.[8–11] Thus, the diagnosis and management of substance abuse is an important consideration in patients with heart failure. However, the prevalence of substance abuse and its association with outcomes in heart failure has not been well described.

In this study, we aimed to better characterize substance abuse among patients with heart failure treated at a single institution between 2005 and 2016. We specifically sought to describe the prevalence of substance abuse and its independent association with hospital encounters and heart failure readmissions.

Methods

Study Sample

The study protocol was approved by the Institutional Review Board of the University of California, San Diego (UCSD). We retrospectively evaluated the electronic health record of the UCSD Healthcare System from January 1, 2005 through June 30, 2016. We abstracted International Classification of Diseases, 9th Revision (ICD-9) diagnosis codes to identify patients with heart failure based on ICD-9 code 428.xx, from both inpatient and outpatient encounters. Patients were excluded if they were less than 18 years of age at the time of identification. We abstracted data on substance abuse among patients with heart failure using ICD-9 codes for substance abuse and dependence along with urine drug toxicology where available. We also abstracted ICD-9 codes for common medical co-morbidities and

contributors to heart failure. A full list of ICD-9 codes utilized in this study is included in a supplementary table.

For each patient, the follow up period extended from the time of first diagnosis of heart failure to patient death or June 30th, 2016. We tallied the total number of hospital encounters (emergency department visits and hospital admissions) with a primary diagnosis of heart failure over the study period for each patient. When an emergency department visit was directly followed by a hospital admission, only the hospital admission was counted. In order to assess the association of substance abuse with heart failure readmissions, we identified patients with more than one recorded hospital admission with a primary admission diagnosis of heart failure, and determined the interval between the first and second hospital admissions.

Statistical Analysis

Baseline characteristics of patients with heart failure with evidence of any substance abuse were compared to heart failure patients without evidence of substance abuse. We compared continuous variables using the Student's t-test or the Mann-Whitney U test, and categorical variables using the chi-square test. We determined the annual incidence of substance abuse diagnoses among patients with heart failure starting in 2006, after excluding patients with heart failure and prevalent substance abuse diagnoses in 2005. In longitudinal analyses, we constructed multivariable models mutually-adjusting for substance abuse and medical diagnoses in addition to age, sex, race/ethnicity, and medical insurance status. We used Poisson regression to evaluate the associations of substance abuse and medical diagnoses with the count of hospital encounters for heart failure, and plotted incidence rate ratios (IRR) with 95% confidence intervals (CI) for each diagnosis. We used Cox proportional hazards regression to evaluate the associations of substance abuse and medical diagnoses with time to first hospital readmission for heart failure and time to all-cause mortality, and plotted hazard ratios and 95% CI for each diagnosis.

We performed statistical analyses using SPSS Statistics version 22.0 (IBM Corporation, Armonk, NY, USA). We considered a p-value of less than 0.05 statistically significant.

Results

From 2005 to 2016, 11,268 unique patients with heart failure were identified. Substance abuse was diagnosed in 15.2% of patients. Characteristics of patients with heart failure stratified by the presence or absence of a diagnosis of any substance abuse disorder are listed in Table 1. Patients with heart failure and substance abuse were younger (55 ±14 vs. 68 ±15 years, $p<0.01$), more often male (69% vs. 56%. $p<0.01$), African American (22% v. 9%), and without medical insurance (40% vs. 18%, $p<0.01$). Diagnoses of ischemic heart disease, cerebrovascular accident, and endocarditis were slightly more common among patients with heart failure and drug abuse, and atrial fibrillation/flutter was less common.

Table 2 lists the prevalence of substance abuse disorders among all patients with heart failure over the study period. Opioid use/abuse was the most common (8.4%), followed by methamphetamine abuse (5.2%), alcohol abuse (4.5%), and marijuana use/abuse (2.2%).

Figure 1 shows the annual incidence of substance abuse among patients with heart failure from 2006 to 2016. The annual incidence of any substance abuse diagnosis varied by year and ranged from 13.0% to 20.2%. Opioid use/abuse declined over the study period (9.6% to 4.1%), while methamphetamine (1.8% to 6.4%) and alcohol abuse (3.3% to 4.4%) rose.

Over a median follow up of 3.6 years (interquartile range [IQR] 1.6–6.9), 15,909 hospital encounters with a primary diagnosis of heart failure occurred. Duration of follow-up for patients with substance abuse (3.7 years, IQR 1.8–6.9) and without substance abuse (3.6 years, IQR 1.6–6.9) did not differ significantly (p=0.10). Figure 2 plots the incidence rate ratios (IRR) and 95% CI from the Poisson regression model evaluating the associations of substance abuse and medical diagnoses with the total number of heart failure hospital encounters over follow up. Red bars indicate substance abuse disorders and blue bars indicate medical diagnoses. Disorders such as methamphetamine abuse (period prevalence 5.2%, IRR 1.96, 95% CI 1.85–2.07), opioid use/abuse (8.2%, 1.54, 1.47–1.61), and alcohol abuse (4.5%, 1.51, 1.42–1.60) were significantly associated with hospital encounters for heart failure, with IRR that were comparable to diagnoses such as atrial fibrillation (37%, 1.78, 1.73–1.84), ischemic heart disease (24%, 1.67, 1.62–1.73), and chronic kidney disease (26%, 1.57, 1.51–1.62).

Of the patients with heart failure included in this study, 6,283 had a hospital admission with a primary diagnosis of heart failure, and 2,857 of these patients (45%) experienced a readmission with a primary diagnosis of heart failure over a median follow-up of 324 days (IQR 47–947). Figure 3 plots the hazard ratios (HR) and 95% CI from the Cox regression model evaluating the associations of substance abuse and medical diagnoses with time to first heart failure readmission. Methamphetamine abuse had the largest association (period prevalence 7.2%, HR 1.58, 95% CI 1.38–1.82), followed by atrial fibrillation (41%, 1.52, 1.41–1.64), hypertension (66%, 1.34, 1.23–1.47), and other medical diagnoses. Opioid use/abuse was also associated with higher risk (11%, 1.22, 1.08–1.37), while the remaining substance abuse disorders were not significantly associated with heart failure readmission.

Among the total sample, there were 2,094 deaths over follow-up. Figure 4 plots the hazard ratios and 95% confidence intervals from the Cox regression model evaluating the associations of substance abuse and medical diagnoses with time to all-cause mortality. Medical diagnoses were found to be significantly associated with all-cause mortality; chronic kidney disease with the largest association (HR 1.54, 95% CI 1.40–1.70), followed by endocarditis (1.37, 1.09–1.72) and diabetes mellitus (1.25, 1.14–1.38). Substance abuse disorders were not significantly associated with all-cause mortality.

Discussion

In this analysis of patients with heart failure, we found substance abuse to be independently associated with a greater risk of emergency department visits and hospitalizations for heart failure, as well as hospital readmission for heart failure. Methamphetamine abuse, alcohol abuse, and opioid use/abuse were independently associated with hospital encounters for heart failure, with incidence rate ratios that were comparable to comorbidities such as atrial fibrillation, ischemic heart disease, and chronic kidney disease. Methamphetamine and

opioid use/abuse were also independently associated with heart failure readmission. However, unlike medical diagnoses, the substance abuse diagnoses evaluated in this study were not significantly associated with heightened mortality.

Opioids were the most commonly used substance (8.4%) in our study, followed by methamphetamine (5.2%), alcohol (4.5%), marijuana (2.2%), and cocaine (0.6%). We observed a decrease in the annual incidence of opioid use (9.6% to 4.1%) over the study period, paralleling the recent reduction of opioid use/abuse observed in the general population.[12] Methamphetamine abuse, on the other hand, demonstrated a 4-fold increase between 2006 and 2016 (1.8% to 6.4%). In another study also conducted in San Diego, Sliman et al. reported an increase in the prevalence of methamphetamine associated heart failure from 1.8 to 5.6% between 2009 and 2014.[13] Methamphetamine abuse has grown increasingly common worldwide, and is a known cardiotoxin, implicated in the development of a severe form of dilated cardiomyopathy.[6,14] Importantly, we found that methamphetamine abuse is independently associated with heart failure hospital encounters and readmissions among patients with heart failure, with a magnitude of association that was as high or higher than any other medical and substance abuse comorbidity evaluated.

We found important demographic and clinical differences between patients with heart failure with and without a history of substance abuse. Patients with heart failure who had a history of substance abuse were younger, more likely to be male, to be African American, and to lack medical insurance. Despite being younger on average, patients with heart failure with substance abuse had similar or greater rates of comorbidities. Rates of hypertension, diabetes, and chronic kidney disease were similar between the two groups, whereas higher proportions of ischemic heart disease, cerebrovascular accidents, and endocarditis were observed in patients with substance abuse. Atrial fibrillation was the only comorbid condition examined which was more common in patients with heart failure without substance abuse. The differences in comorbidities between the groups are likely due to several factors, including socioeconomic barriers to care such as a lack of medical insurance. Moreover, many abused substances are known to exert toxic effects. For example, cocaine has been shown to cause a wide range of adverse cardiovascular effects including hypertension, myocardial ischemia, arrhythmia, aortic dissection, and stroke.[8,10] Alcohol has been associated with hypertension, atrial fibrillation, and development of alcoholic cardiomyopathy.[10] Cardiovascular complications of methamphetamine use are also increasingly recognized, including methamphetamine associated heart failure and pulmonary hypertension.[9,15] These factors make patients with concomitant heart failure and substance abuse a particularly vulnerable patient population.

Despite the strong association between substance abuse and hospital encounters and readmissions for heart failure, we did not find a similar association between substance abuse and mortality. It is likely that given relative youth of the patients with substance abuse, the baseline level of risk for mortality was lower among patients with substance abuse compared to without. Furthermore, although substance abuse can have multiple deleterious health effects, some may be dose dependent and even reversible with cessation of abuse[14].

Our study has several notable strengths. We examined a large population of patients with heart failure over an extended study period. Previous studies have demonstrated the association of comorbidities and demographic factors with hospital encounters and readmission.[16–18] Our study demonstrates that substance use is independently associated with future hospital encounters for heart failure at rates comparable to established medical comorbidities. These findings suggest the importance of consideration of substance abuse, especially methamphetamine use, in identifying high-risk patients with heart failure.

Our study also has several limitations. It had an observational design and was conducted using data from a single health care system. As with any observational study, we cannot exclude the possibility that residual confounding explains our results despite adjusting for several demographic and medical factors. Moreover, findings in our patient population may not be generalizable to all patients with heart failure. We relied on diagnosis codes for substance abuse during routine clinical care for inclusion in our study. As substance abuse may frequently go unrecognized among medical practitioners and underreported by patients, we likely underestimated the true frequency of substance abuse among these patients.

In conclusion, our study demonstrates that patients with heart failure often have concomitant substance abuse. Several substance abuse disorders are independently associated with heart failure related hospital encounters, to a degree comparable with traditional heart failure risk factors. Evaluation of substance abuse history, particularly methamphetamine abuse, opioid use/abuse, and alcohol abuse, may identify patients at a greater risk for heart failure morbidity. Greater recognition and treatment of substance abuse disorders may lead to improved outcomes among heart failure patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Clinical significance

- Substance abuse is common among patients with heart failure.
- Methamphetamine abuse, alcohol abuse, and opioid use/abuse were independently associated with hospital encounters for heart failure, with risks that were comparable to comorbidities such as atrial fibrillation and ischemic heart disease.
- Methamphetamine and opioid use/abuse were independently associated with heart failure readmission.

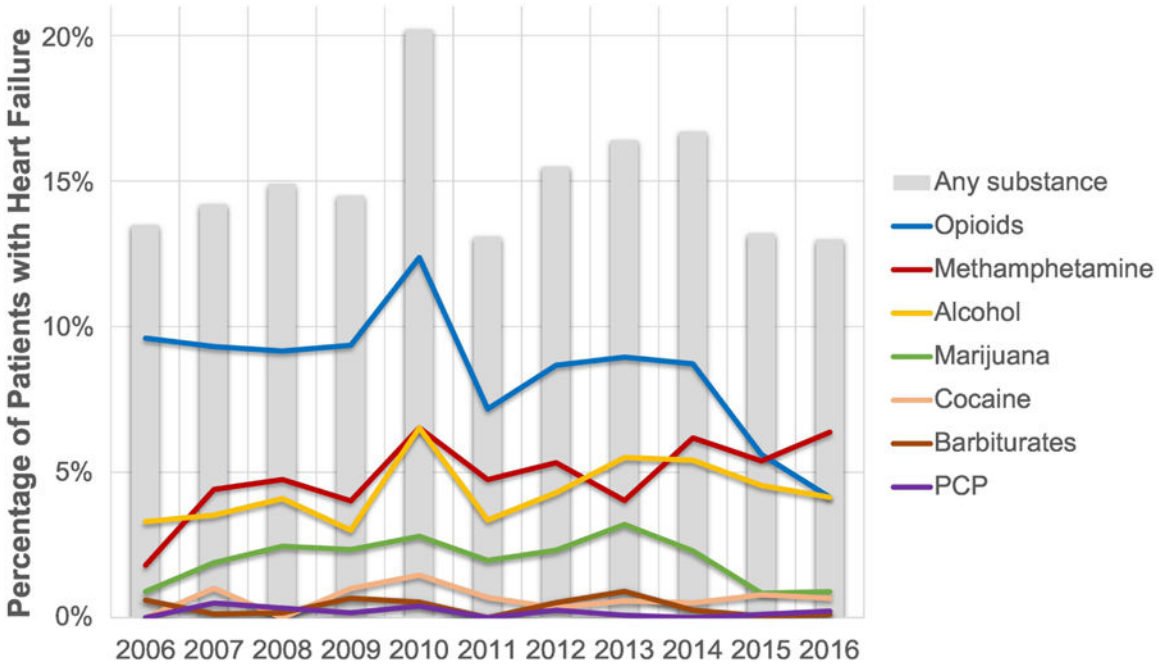

Figure 1: Trends in substance abuse among patients with heart failure, 2006–2016.

The annual incidence of substance use disorders among patients with heart failure treated at the University of California, San Diego are plotted. Patients with heart failure were identified based on ICD-9 diagnosis code 428.xx. Substance abuse was defined by a urine drug toxicology test positive for the given drug or the presence of the relevant ICD-9 code.

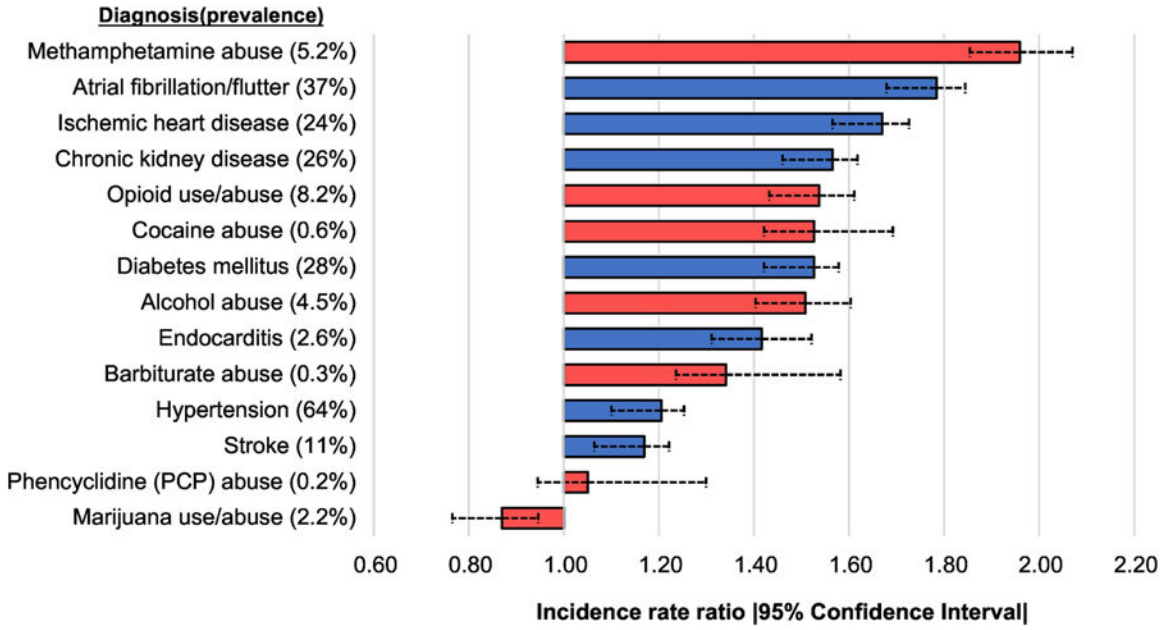

Figure 2: Risks of hospital encounter for heart failure associated with medical and drug abuse diagnoses.

Incidence rate ratios and 95% confidence intervals are plotted. 11,268 patients with a history of heart failure were evaluated in a multivariable Poisson regression model for the number of emergency department visits and/or hospitalizations with a primary encounter diagnosis of heart failure. Over a median follow-up of 3.6 years (interquartile range 1.6 to 6.9 years), 15,909 heart failure hospital encounters occurred. The multivariable model includes mutual adjustment for the variables listed above as well as age, sex, race/ethnicity, and medical insurance status. Red bars indicate substance abuse disorders and blue bars indicate medical diagnoses

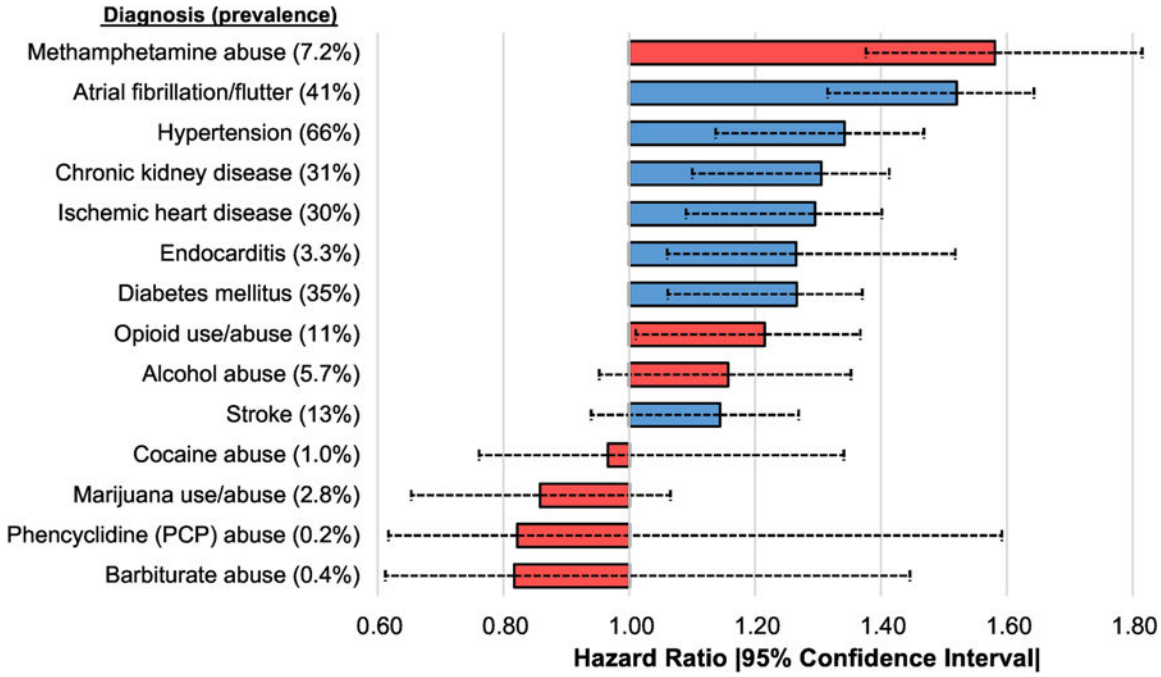

Figure 3: Risks of heart failure readmission associated with medical and drug abuse diagnoses.

Hazard ratios and 95% confidence intervals are plotted. 6,283 patients with a prior hospital admission with heart failure as the primary admission diagnosis were evaluated in a multivariable Cox regression model for time to first readmission with heart failure as the primary admission diagnosis. Over a median follow-up of 324 days (interquartile range 47 to 947 days), 2,857 heart failure readmissions occurred. Multivariable model includes mutual adjustment for the variables listed above as well age, sex, race/ethnicity, and medical insurance status. Red bars indicate substance abuse disorders and blue bars indicate medical diagnoses

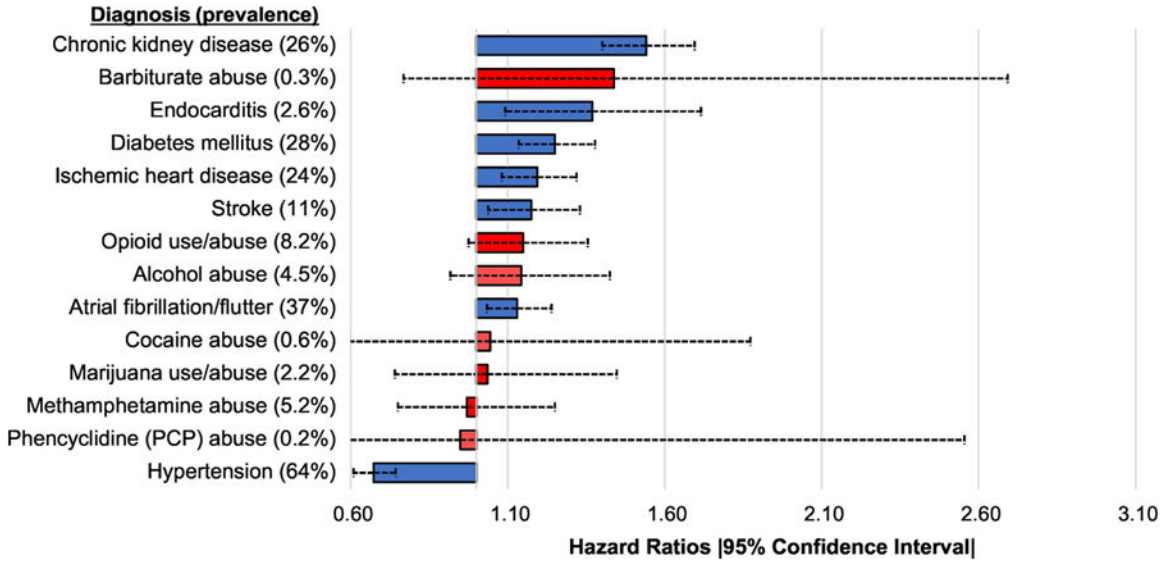

Figure 4: Risks of all-cause mortality associated with medical and drug abuse diagnoses.

Hazard ratios and 95% confidence intervals are plotted. 11,268 patients with a history of heart failure were evaluated in a multivariable Cox regression model for time to all-cause mortality. Over a median follow-up of 324 days (interquartile range 47 to 947 days), 2,094 deaths occurred. Multivariable model includes mutual adjustment for the variables listed above as well age, sex, race/ethnicity, and medical insurance status.

Table 1:
Patient characteristics stratified by diagnosis of any substance abuse.

Patients with heart failure treated at the University of California, San Diego between January 1, 2005 and June 30, 2016 were identified via International Classification of Diseases, 9th revision, diagnosis code 428.xx. Substance abuse was determined via urine drug toxicology and/or ICD-9 diagnosis codes. Substances evaluated were opioids, methamphetamines, alcohol, marijuana, cocaine, barbiturates, and phencyclidine. Medical diagnoses were determined via ICD-9 diagnosis codes.

	Patients with Heart Failure		
	Any substance abuse	**No substance abuse**	**p-value**
N (% of total)	1,718 (15.2%)	9,550 (84.8%)	
Age in years (standard deviation)	55 (14)	68 (15)	<0.01
Male sex	69.0%	55.5%	<0.01
Race/ethnicity			<0.01
Caucasian	56.5%	56.6%	
Hispanic	15.3%	18.9%	
African American	21.8%	8.9%	
Asian	2.9%	7.6%	
Other/mixed	3.5%	7.9%	
No medical insurance	40.0%	17.5%	<0.01
Hypertension	64.9%	64.6%	0.83
Atrial fibrillation/flutter	29.6%	38.4%	<0.01
Diabetes mellitus	28.3%	27.7%	0.59
Chronic kidney disease	24.5%	26.0%	0.19
Ischemic heart disease	29.3%	23.0%	<0.01
Cerebrovascular accident	12.9%	10.3%	<0.01
Endocarditis	3.7%	2.5%	<0.01
Median follow up in years (interquartile range)	3.7 (1.8, 6.9)	3.6 (1.6, 6.9)	0.10
Median heart failure emergency department and/or inpatient encounters (interquartile range)	1 (0, 3)	1 (0, 1)	<0.01
Mortality Rate	16.5%	19.0%	0.02

Table 2:

Period prevalence of substance abuse disorders among patients with heart failure, 2005 to 2016.

Patients with heart failure were identified at the University of California, San Diego using ICD-9 diagnosis code 428.xx. Substance abuse disorders were identified using ICD-9 diagnosis codes and urine drug toxicology.

	Prevalence
Opioid use/abuse	8.4%
Methamphetamine abuse	5.2%
Alcohol abuse	4.5%
Marijuana use/abuse	2.2%
Cocaine abuse	0.6%
Barbiturate abuse	0.3%
Phencyclidine (PCP) abuse	0.2%