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Clinical outcomes of B-blocker therapy in cocaine-associated heart failure

Persio D. Lopez [a,c,*,1], Adedoyin Akinlonu [a,c], Tuoyo O. Mene-Afejuku [a,c], Carissa Dumancas [a,c], Mohammed Saeed [a,c], Eder H. Cativo [a,c], Ferdinand Visco [b,c], Savi Mushiyev [b,c], Gerald Pekler [b,c]

[a] Department of Medicine, Health+Hospitals/Metropolitan Hospital Center, New York, NY, USA
[b] Division of Cardiology, Department of Medicine, Health+Hospitals/Metropolitan Hospital Center, New York, NY, USA
[c] New York Medical College, Valhalla, NY, USA

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ABSTRACT

Background: Cocaine is associated with deleterious effects in the heart, including HFrEF. Although β-blockers are recommended for this condition in other populations, their use is discouraged in cocaine users due to the possibility of exacerbating cocaine-related cardiovascular complications. This study was designed to determine if patients with heart failure and a reduced ejection fraction (HFrEF) who continue to use cocaine have better outcomes when they receive β-blocker therapy than when they do not.

Methods: We performed a retrospective analysis of 72 β-blocker-naïve patients with HFrEF and active cocaine use. Patients who were prescribed β-blockers as part of their therapy were compared to those who were not, and clinical and structural outcomes were compared after 12 months of treatment.

Results: When patients with HFrEF and active cocaine use received β-blocker therapy, they were more likely to have an improvement in their New York Heart Association functional class ($p = 0.0106$) and left ventricular ejection fraction ($p = 0.0031$) than when they did not receive β-antagonists. In addition, the risk of cocaine-related cardiovascular events ($p = 0.0086$) and of heart failure hospitalizations ($p = 0.0383$) was significantly lower in patients who received β-blockade than those who did not.

Conclusions: β-Blocker therapy is associated with improvement in the exercise tolerance and the left ventricular ejection fraction in patients with HFrEF and active cocaine use. They are also associated with a lower incidence of cocaine-related cardiovascular events and HFrEF-related readmissions.

1. Introduction

Illicit drug use is estimated to occur in 10% of individuals 12 years of age and older in the United States [1]. Cocaine use is not benign, as it contributes to different forms of heart disease, which can be found in up to 70% of asymptomatic users [2]. In particular, 5% of cases of acute decompensation in patients with heart failure and a reduced ejection fraction (HFrEF) are precipitated by illicit stimulant drug use [3]. The mechanism of cocaine's cardiotoxicity is complex, but it can be linked to β-adrenergic receptor hyperactivation, which may provide a therapeutic niche for β-blocker therapy [4]. However, β-blocker therapy in cocaine users is a controversial subject due to concerns regarding the risk-benefit ratio [5].

Current guidelines recommend caution when using β-blockers in the chronic setting [6,7], and it has been suggested they should be avoided altogether in patients with heart failure (HF) who use cocaine [8]. Recent research, however, suggests that the excessive α-stimulation phenomenon may be unrelated to β-blocker therapy [9]. In addition, clinical and echocardiographic improvement has been reported in patients with HF who use cocaine and received β-blocker therapy [5,10], without an increase in HF readmissions, cardiovascular events or mortality [11].

We hypothesized that patients with HFrEF and active cocaine use have better outcomes when treated with a therapeutic regimen that includes β-blockers. The purpose of this study was to determine the outcomes of patients with HFrEF and active cocaine use who received β-blocker therapy, compared with patients with HFrEF and active cocaine use who did not receive β-blocker therapy.

2. Methods

2.1. Study design and patient characteristics

A retrospective cohort study of adult patients (age ≥ 18 years) with newly-diagnosed HFrEF and active cocaine use was performed through a review of the echocardiogram database and the electronic medical records at Metropolitan Hospital Center, New York City, New York. The protocol was approved by the Biomedical Research Alliance of New York Institutional Review Board and the study was performed in accordance with

* Corresponding author at: 1901 1st Ave, Suite 704, New York, NY 10029, USA.
E-mail address: pd.research@icloud.com (P.D. Lopez).

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the Declaration of Helsinki. A full waiver of informed consent was obtained from the institutional review board to complete this retrospective study.

Active cocaine use was defined as either self-reported continued cocaine use or continued finding of cocaine in the patient's urine toxicology. HFrEF was defined as symptoms consistent with HF and left ventricular ejection fraction (LVEF) <40% on the index transthoracic echocardiogram (TTE) using the biplane method of disks, or N-terminal pro-brain natriuretic peptide levels >900 pg/mL and LVEF <40%. The subjects' first documentation of HFrEF and institution of therapy was the index point for this study. Patients were included in this study if they had been followed in our HF Clinic for a minimum of 12 months, had kept their scheduled appointments during this period, and had received a surveillance TTE at their 12-month appointment. We excluded patients with an identified etiology for transient HF, volume overload due to reasons other than HF, a life expectancy <12 months, active malignancy or presence of chronic kidney disease glomerular stages 4 or 5 (with or without fluid overload). In addition, patients were excluded if they were on β-blocker therapy for other indications at the time of diagnosis or if they were pregnant at or any time after the index point. The study group was comprised of patients whose HF regimen included β-antagonist medications; these patients received either carvedilol or metoprolol succinate. The control group included those who received guideline-directed medical therapy (GDMT) without β-blockers. There was no cross-over between groups.

2.2. Data collection

Clinical and demographic data were collected at the time of the index contact and included age, sex, ethnicity, body mass index, use of tobacco, abuse of alcohol, frequency of cocaine use, route of cocaine use, major comorbidities (i.e. hypertension, diabetes mellitus, dyslipidemia, pre-existing coronary artery disease (CAD), peripheral artery disease, atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary disease and liver disease) and HF-related medications prescribed. The first New York Heart Association functional class (NYHA-FC) documented at the moment of institution of GDMT was considered the patient's baseline. For patients in the study group, the type of β-blocker and the specific medication used were documented.

All notes for the duration of the patients' enrollment were reviewed to obtain information about the number of all-cause hospitalizations and HF-related hospitalizations (admission to other institutions is regularly inquired for and documented in our notes due to the urban location of our institution), as well as the occurrence of any acute coronary syndrome, stroke or hypertensive emergency. Information regarding the results from coronary angiography, percutaneous coronary intervention, coronary artery bypass grafting or cardiac resynchronization therapy was also collected; 20 patients did not undergo coronary angiography. Finally, the patients' NYHA-FC, LVEF and use of GDMT were documented from the follow-up note and TTE at 12-months from the index point.

2.3. Statistical methods

The primary outcomes for this study were improvement in the NYHA-FC and LVEF after 12 months of therapy. The secondary outcomes were the occurrence of a HF-readmission, and a composite of cocaine-related cardiovascular events (CRCE, defined as hypertensive emergency, acute coronary syndrome or stroke) during the 12 months of enrollment in the study.

Baseline characteristics were summarized according to variable type. Continuous variables are described as "mean ± standard deviation (SD)" if normal, or "median, interquartile range" if non-normal; categorical variables are described through frequencies and percentages. Balance of the baseline characteristics among the study groups was assessed using χ^2 or Fisher's exact tests for categorical variables, and Student's t or Mann-Whitney *U* tests for continuous variables. The unadjusted relationship between the use of β-blocker and the outcomes was assessed through χ^2 tests. Logistic regression analysis with stepwise selection was performed for the adjusted analysis. The following pre-specified predictors were selected based on published literature, while avoiding collinearity: age, sex, race, body mass index, frequency of cocaine use, tobacco use, alcohol abuse, CAD at baseline, atrial fibrillation at baseline, findings in the coronary angiography, β-blocker therapy, type of β-blocker and presence of GDMT at 12 months. Two pre-specified subgroup analyses comparing the primary outcomes were performed: (a) between patients who received a mixed α/β blocker and those who received no β-blockers, and (b) between patients who received a mixed α/β blocker and those who received a β-1 selective antagonist. All analyses were performed with SAS Studio (SAS Institute Inc., Cary, North Carolina) with $\alpha = 0.05$ and 95% confidence intervals.

3. Results

A total of 179 patients with HF who were actively using cocaine were identified. After the exclusion criteria were applied, 38 patients were included in the study group and 34 patients in the control group. Please see Fig. 1 for cohort selection details.

Baseline characteristics are summarized in Table 1. Overall, our patients were predominantly male (84.7%) and African American (64.9%); concomitant use of tobacco was common (76.4%). The mean age was 53.5 ± 8.0 years and most patients were overweight (mean body mass index 29.0 ± 7.3 kg/m^2). Hispanic patients were more likely to be prescribed β-blockers than African Americans ($p = 0.0355$). Tobacco users were less likely to be prescribed β-blockers than non-

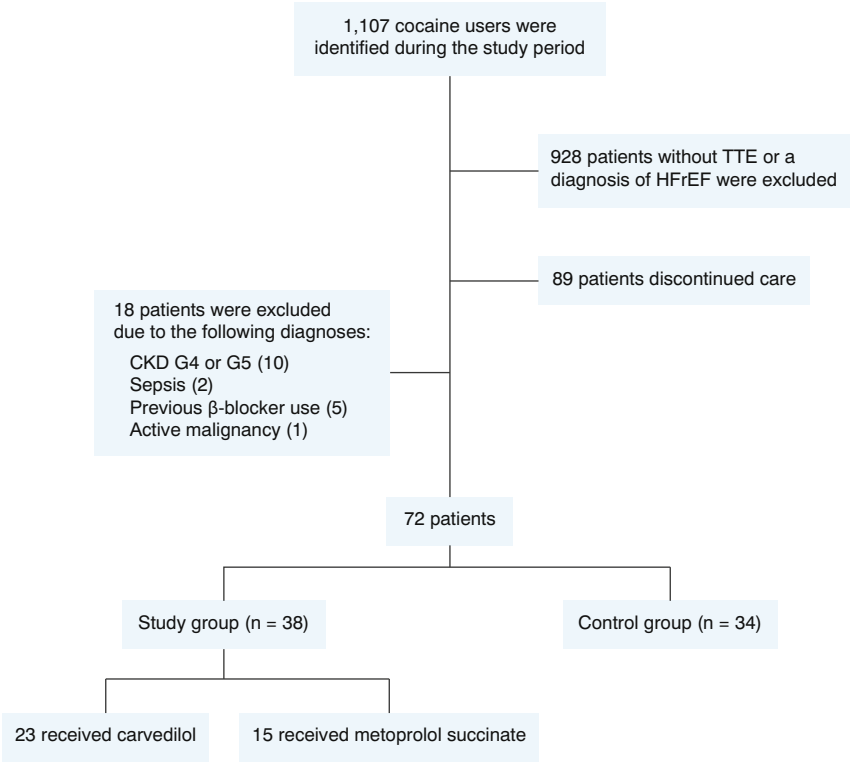

Fig. 1. Cohort selection details. CKD, chronic kidney disease; HFrEF, heart failure with a reduced ejection fraction; TTE, transthoracic echocardiogram.

smokers ($p = 0.0252$). No other differences in baseline characteristics were observed between the two groups; there was no difference in the baseline LVEF ($p = 0.1068$) or the baseline NYHA-FC ($p = 0.6466$) between patients who received β-blockers and those who did not. In the study group, 60.5% of patients received mixed α/β blockade and the rest, metoprolol.

3.1. Beneficial outcomes

Improvement in the NYHA-FC was seen in 20 (52.6%) patients who received β-blockers and in 8 (23.5%) patients in the control group ($p = 0.0106$; RR 2.24; CI 1.14–4.41). At baseline, 55.5% of patients in the study group and 55.9% of patients in the control group were NYHA-FC III or IV. After 12 months of therapy, nearly three fourths of the patients in the study group were classified as NYHA-FC I or II, while only 58.9% of the patients in the study group were on these categories. Further, 64.7% of the patients with a NYHA-FC I at the end of the study period had received a β-blocker as part of their therapy. See Table 2 for more details.

When LVEF is estimated by TTE at our institution, it is reported in the following categories: <25%, 25–35%, 35–40%, 40–50% and > 50%. Patients who had received a β-blocker were more likely to have an improvement in their LVEF than patients without β-blocker therapy ($p = 0.0031$; RR 2.46; CI 1.27–4.78; see Fig. 2). At the moment of enrollment, there was no difference in the LVEF between both groups, however, after a year of therapy, 57.9% of patients in the study group had had an improvement in their LVEF, compared with 23.5% of patients in the control group. In fact, 36.9% of patients who received β-blocker therapy had a LVEF above 40% at the end of the study period, compared to 20% of patients who did not; five patients in the study group and two patients in the control group had normalization of their LVEF. Table 2 provides further details.

Multivariate analysis was performed using the pre-specified predictors. Mixed α/β blockade (but not β1-selective blockade) was found to be significantly associated with improvement in the NYHA-FC at 12 months of therapy when compared to patients who did not receive β-blockers ($p = 0.0012$; OR 7.86; CI 2.20–32.89). In addition, the presence of obstructive CAD in the coronary angiography was associated with a lower likelihood of improvement in the NYHA-FC ($p = 0.0067$; OR 0.07; CI 0.03–0.52). On the other hand, improvement in the LVEF was associated with the status of receiving a β-blocker, regardless of the type ($p = 0.0027$; OR 4.47; CI 1.66–12.99).

3.2. Adverse outcomes

The rate of adverse events in our population was low. There were no CRCE in the group of patients receiving β-blockers and six CRCE in the control group. This represented a statistically significant difference ($p = 0.0086$) and the probability of not having a CRCE was 1.21 times higher in patients with β-blocker use than in those without a β-blocker (CI 1.04–1.42). Half of the patients who had CRCE were NYHA-FC II; the rest were NYHA-FC IV. All patients with a CRCE had a LVEF between 25% and 40%. Three out of the eight female participants in the study had a hypertensive emergency. The three male patients who had a CRCE had an acute coronary syndrome. Out of the nine patients who received the hydralazine and nitrate combination, one developed an acute coronary syndrome and two developed hypertensive

Table 1
Baseline characteristics of patients who received β-blockers, compared with those who did not.

Characteristics	GMDT + β-Blocker ($n = 38$)	GMDT alone ($n = 34$)	*p*-Values
Age, years ($\bar{x} \pm SD$)	54.0 ± 8.4	52.6 ± 7.6	0.4429
Male gender	33 (86.8)	28 (82.4)	0.5971
Race			**0.0355***
African American race	20 (52.6)	26 (76.5)	–
Hispanic race	17 (44.7)	8 (23.5)	–
BMI, kg/m2 ($\bar{x} \pm SD$)	29.9 ± 6.9	27.9 ± 7.7	0.2496
Tobacco use	25 (65.8)	30 (88.2)	**0.0252***
Alcohol abuse	17 (44.7)	13 (38.2)	0.5764
Frequency of cocaine use			0.4705
Several times per week	18 (47.4)	19 (55.9)	–
Weekly or less	20 (52.6)	15 (44.1)	–
Route of cocaine use			0.5191
Snorted	10 (26.3)	7 (20.6)	–
Inhaled	6 (15.8)	9 (26.5)	–
Unknown	22 (57.9)	18 (52.9)	–
Baseline HR, bpm ($\bar{x} \pm SD$)	84.8 ± 13.6	82.5 ± 16.1	0.532
Baseline SBP, mm Hg ($\bar{x} \pm SD$)	129.5 ± 22.4	138.5 ± 28.2	0.3505
Baseline DBP, mm Hg ($\bar{x} \pm SD$)	82.5 ± 12.1	82.4 ± 16.4	0.3575
Diastolic dysfunction			0.2851
None (normal function)	20 (52.6)	41 (41.2)	–
Grade I	14 (36.8)	5 (14.7)	–
Grade II	2 (5.3)	0 (0)	–
Grade III/IV	2 (5.3)	15 (44.1)	–
Hypertension	30 (79.0)	27 (79.4)	0.9614
Diabetes mellitus	14 (36.8)	10 (29.4)	0.5043
Dyslipidemia	14 (36.8)	11 (32.4)	0.6896
CAD	12 (31.6)	9 (26.5)	0.634
PAD	4 (10.5)	0 (0)	0.1168
AF	5 (13.2)	3 (8.8)	0.714
Mixed α/β blocker	23 (60.5)	–	–
Selective β1 blocker	15 (39.5)	–	–
ACEi/ARBs	35 (92.1)	30 (88.2)	0.7002
Spironolactone	6 (15.8)	7 (20.6)	0.7606
Eplerenone	0 (0)	0 (0)	–
Sacubitril-Valsartan	0 (0)	0 (0)	–
Hydralazine + Nitrates	5 (13.2)	7 (20.6)	0.5298
Loop diuretics	25 (65.8)	17 (50.0)	0.1749
Angiography findings			0.8329
Normal	11 (29.0)	13 (38.2)	–
Non-obstructive CAD	8 (21.0)	5 (14.7)	–
Obstructive CAD	8 (21.0)	7 (20.6)	–
Not done	11 (29.0)	9 (26.5)	
PCI	6 (15.8)	5 (14.7)	0.8985
CABG	1 (2.6)	2 (5.9)	0.5992
CRT	0 (0)	0 (0)	–
GDMT at 12 months	36 (94.7)	30 (88.2)	0.4119

All statistics are expressed as n (%) unless otherwise specified; asterisk and bold type indicate statistical significance. ACEi/ARBs, angiotensin converting enzyme inhibitors/angiotensin receptor blockers; AF, atrial fibrillation; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; DBP, diastolic blood pressure; GDMT, guideline directed medical therapy; HR, heart rate; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; SD, standard deviation; $\bar{x}$, mean.

Table 2
LVEF and NYHA functional class of patients who received β-blockers, compared with those who did not.

	GMDT + β-blocker (n = 38)		GMDT alone (n = 34)	
	Baseline	12-month	Baseline	12-month
LVEF				
<25%	10 (26.3)	7 (18.4)	5 (14.7)	8 (23.5)
25–35%	18 (47.4)	9 (23.7)	12 (35.3)	11 (32.4)
35–40%	10 (26.3)	8 (21.0)	17 (50.0)	8 (23.5)
40–50%	0 (0)	9 (23.7)	0 (0)	5 (14.7)
>50%	0 (0)	5 (13.2)	0 (0)	2 (5.9)
NYHA				
Class I	4 (10.5)	11 (29.0)	4 (11.8)	6 (17.6)
Class II	8 (21.0)	17 (44.7)	11 (32.3)	14 (41.2)
Class III	21 (55.3)	9 (23.7)	14 (41.2)	10 (29.4)
Class IV	5 (13.2)	1 (2.6)	5 (14.7)	4 (11.8)
NT-ProBNP				
Median; IQR	2038; 603–2835	1348; 816–7992	3235; 1482–10,379	3082; 1545–17,439

All statistics are expressed as n (%), unless otherwise specified. DD, diastolic dysfunction; GDMT, guideline directed medical therapy; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association.

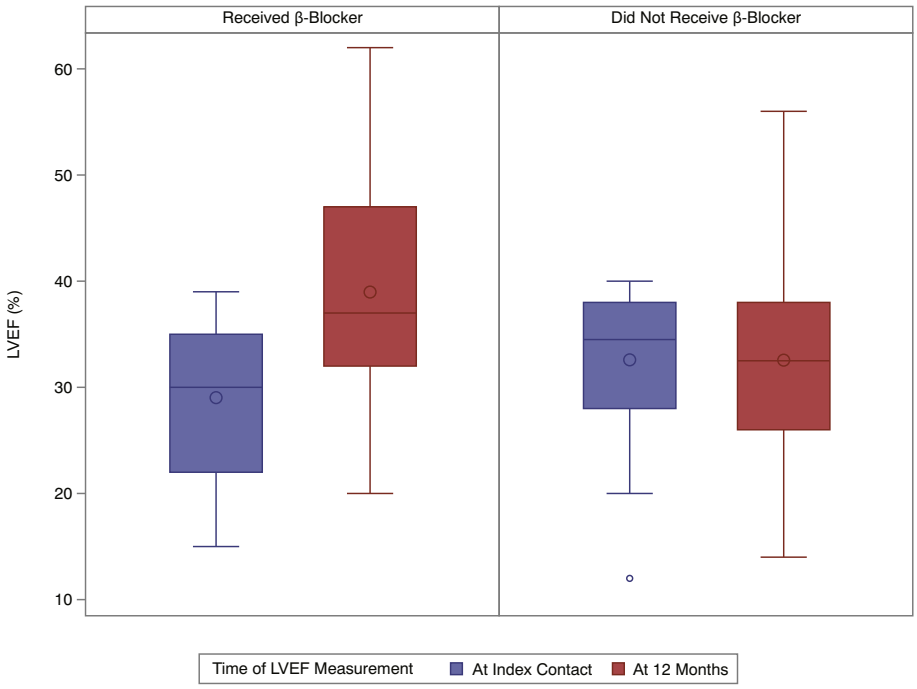

Fig. 2. LVEF improvement in patients with HF and active cocaine use who used β-blockers compared to those who did not. There was LVEF improvement in 57.9% of patients who received therapy with β-blockers after 1 year of therapy, compared with 23.5% of patients who did not receive β-blockers ($p = 0.0031$). In the group of patients who received β-blockers, the median LVEF improved from 30% (interquartile range [IQR] 22–35%) to 37% (IQR 32–47%). In comparison, the median LVEF did not change significantly in the group of patients who did not receive β-blockers (34.5% IQR 28–38% and 32.5% IQR 28–38%).

emergencies. There were no other significant differences in the baseline characteristics between patients who developed CRCE and those who did not.

One patient in the study group and six patients in the control group had a HF-related readmission ($p = 0.0383$; RR 0.15; CI 0.02–1.18). All of these patients were NYHA-FC III or IV and had been prescribed a loop diuretic as part of their medical therapy; most of them had a LVEF of 25–35%. Two female patients had a HF-related readmission. Six out of the seven patients with a HF-related readmission were African American. No other differences in the baseline characteristics were found between patients who had a HF-related readmission and those who did not.

3.3. Subgroup analyses

Subgroup analysis comparing patients whose therapy included carvedilol with those who had no β-blockade ($n = 57$) revealed a significant association between an improvement in the NYHA-FC and the use of carvedilol ($p = 0.0020$; RR 2.77; CI 1.41–5.45). A similar association was found between an improvement in the LVEF and the use of carvedilol ($p = 0.0051$; RR 2.59; CI 1.30–5.15). Patients who received carvedilol also had 1.21 times the probability of not having a CRCE ($p = 0.0371$; CI 1.04–1.42) as those who had no β-blockade, but there was no significant difference in the risk of having a HF-related readmission ($p = 0.1373$).

When we compared patients who received carvedilol with patients who received metoprolol succinate ($n = 38$), we did not find a significant difference in the number of patients who experienced LVEF improvement between the two groups ($p = 0.4494$). However, the number of patients who had improvement in their NYHA-FC was greater in the subgroup that received carvedilol, when compared to those who received metoprolol succinate; this represented a non-significant trend favoring carvedilol ($p = 0.0553$; RR 1.96; CI 0.90–4.25).

4. Discussion

Cocaine exerts significant cardiac toxicity through a variety of mechanisms, including increased sympathetic drive, increased synthesis of endothelin-1, inhibited nitric oxide synthesis, increased oxidative stress, interference with calsequestrin-mediated calcium storage, disruption of excitation-contraction coupling in myocardiocytes, as well as platelet and coagulation cascade activation [12,13]. This leads to microvascular flow dysfunction [13] and myocardial structural damage with fibrosis [14,15], which has been positively correlated with the duration of cocaine use [2,14]. The end result is significant myocardial dysfunction, with a higher incidence of ST-segment elevation myocardial infarctions in the acute setting [7,16], and a decrease in the systolic function of both ventricles in the chronic setting [2].

The possibility of potentiating the hemodynamic effects of cocaine led to concerns about the role of β-blockers in cocaine users [5]. Current guidelines discourage the use of these medications in the setting of a non-ST acute coronary syndrome with recent cocaine use [17,18]; it is unknown whether their long-term use in patients with HF who continue to use cocaine is either safe or efficacious [19]. Consequently, β-antagonists are used less commonly in patients who use cocaine than in those who do not [16]. At our center, active cocaine use usually precludes patients from β-blocker therapy. The patients in our study received β-antagonists for the following reasons: 24 patients initially denied cocaine use, but active use was subsequently uncovered through urine toxicology testing; 12 patients relapsed shortly after committing to quitting cocaine use; and 2 patients had an extensive discussion of the risks and benefits associated with concomitant β-blockade and active cocaine use, and decided to receive β-blocker therapy.

However, the "unopposed α phenomenon" that was originally seen with propranolol [20] may not be a class effect [9,21]. In fact, it is possible that β-blockers are beneficial in cocaine users [21]. β-blockers have been shown to reduce the incidence of myocardial infarction and in-hospital mortality in patients with cocaine use, regardless of the cause of admission [22]. In cocaine-positive patients presenting with

acute chest pain, early administration of β-antagonists resulted in greater decreases in the systolic blood pressure, compared to those who received β-blockers at a later time during the admission or who did not receive any at all, without an increase in adverse effects [23]. Moreover, these patients had a significant reduction in the cardiovascular mortality at 2.6 years when they were discharged on a β-blocker [23]. In patients admitted due to an acute coronary syndrome in the setting of cocaine, labetalol was non-inferior to diltiazem in controlling hemodynamic parameters, and provided a better anti-inflammatory profile, as determined by serum levels of CD40 ligand, interleukin 6 and choline [24].

The dramatic benefits of β-antagonists observed in patients whose HF is attributable to cocaine may be secondary to the fact that cocaine users with clinical heart disease are generally healthier than the prototypical patient with heart disease. An analysis of the Acute Coronary Treatment and Intervention Outcomes Network Registry—Get With The Guidelines (ACTION Registry-GWTG) program ($n = 102{,}952$) revealed that patients who use cocaine and have had a myocardial infarction are younger, have a lower body mass index, are more likely to be of African American race, and have less prevalence of hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, stroke and peripheral artery disease than their cocaine-negative counterparts [16]. Likewise, patients who use cocaine and develop HF are younger, have a lower body mass index, and have a lower prevalence of hypertension, chronic kidney disease and atrial fibrillation than patients with HF who do not use cocaine; however, they are more likely to develop coronary artery disease and use tobacco [11]. The findings in our population fall in line with these data, since our patients were predominantly male, African American and had a high prevalence of tobacco use. The mean age (53.5 ± 8.0 years) and the prevalence of coronary artery disease were lower in our patients than in a recent cohort of patients with HFrEF due to other causes [25], but they had a similar prevalence of hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, tobacco use, alcohol abuse and ACEi use.

The data are limited in cocaine users who develop HF. Dramatic improvement in the LVEF has been reported with the use of carvedilol in these patients [5,10]. Remarkably, a recent study comparing cocaine-positive and cocaine-negative patients with HF found no difference between them in HF-related readmissions, major adverse cardiovascular events, death or all combined endpoints when mixed α/β or β1-selective antagonists were used [11]. Our study reinforces that β-blockers are likely to be beneficial, not harmful, in patients with HF and active cocaine use. We found that cocaine-positive HF patients who received β-blockers (carvedilol or metoprolol succinate) were twice as likely to have an improvement in their NYHA-FC and their LVEF after 1 year of therapy as those who did not. In fact, many of these patients can have full or almost full recovery of their LVEF, particularly when receiving carvedilol. Multivariate analysis also revealed that symptomatic improvement is associated with mixed α/β blockade, especially in patients who have not developed obstructive CAD. Moreover, cocaine-positive patients with HF who received a β-blocker were significantly less likely to develop a CRCE or to have a HF-related readmission than their counterparts who did not receive β-antagonist therapy. Interestingly, despite a smaller sample size, these benefits were still evident when we compared patients who received carvedilol to those who did not receive β-blockade.

Carvedilol has several characteristics that make it a desirable β-blocker in cocaine users. It has a significantly higher affinity for β1 receptors than β2 receptors and also has α1-blocking qualities [26]; these characteristics blunt the β1-mediated cardiotoxic effects of cocaine without increasing the risk for the "unopposed α phenomenon". In addition, carvedilol has been shown to inhibit left ventricular remodeling and fibrosis [27,28], which is a hallmark of cocaine's cardiotoxicity. Carvedilol and its metabolite BM-910228 also have significant antioxidant properties [29,30], which could halt the oxidative stress caused by cocaine. Finally, carvedilol prevents ventricular tachyarrhythmias by restoring calcium homeostasis in myocardiocytes [31], thereby limiting the disturbances of cocaine on cardiac ion currents. This could serve as the biological basis for the findings in our study.

4.1. Study limitations

This is a single-centric, hospital based study, and our patients were exclusively of African American and Hispanic descent, which limits the generalization of our results. In addition, since most of our patients were male, our results may not be applicable to women. Because of the retrospective nature of this study and the lack of randomization, we cannot draw definitive conclusions regarding association between variables and we cannot fully rule out residual confounding factors; in particular, we cannot determine the presence and amount of cardiac fibrosis in each group. In addition, information about the adherence to therapy, and the amount and route of cocaine use is limited.

5. Conclusion

Patients with HF and active cocaine use should be considered as candidates for β-blocker therapy. Treatment with β-antagonists – carvedilol, in particular– may provide improvement in their exercise tolerance and LVEF. Further, it could help prevent CRCE and HF-related readmissions in these patients.

Conflicts of interest and funding source

The authors have no conflicts of interest or funding sources to declare.

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