

Dose of Beta-Blocker and Sinus Rate  
Achieved for Patients with Systolic Heart  
Failure without COPDTyler Trump<sup>1</sup>, John Robinson<sup>2</sup>, Qaisar Syed<sup>1</sup>, Phil Kostelic<sup>1</sup>, Kimberly Kerr<sup>2</sup>, Adil Memon<sup>3</sup>, Prerna Sharma<sup>3</sup>, Suzanne Kemper<sup>1</sup> and William Carter<sup>1\*</sup><sup>1</sup>Cardiology Specialist, West Virginia University School of Medicine, USA<sup>2</sup>Department of Cardiology, University of Charleston School of Pharmacy, USA<sup>3</sup>Department of Cardiology, Charleston Area Medical Center, USA

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## \*Corresponding author

William Carter, MD, West Virginia  
University Health Sciences Center,  
Charleston Division, 3110 MacCorkle  
Ave S.E, Charleston, WV 25304, USA,  
Tel: (304) 347-1358;  
Fax: (304) 347-1344;  
Email: williamcarterwv@gmail.com

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## Abstract

**Background:** All guidelines by experts agree that Beta-Blockers (BB) should be used for patients with systolic heart failure (SHF) to improve survival. Despite recommendations, the dosages of BBs prescribed are frequently less than 50% of target dose. Under dosing is suggested by doses <50% of target dose and/or Sinus Rate (SR) >70 bpm. Chronic Obstructive Pulmonary Disease (COPD) is the most common reason for omitting and under-dosing BB therapy. This led to the question how patients with SHF are without COPD being treated with BBs.

**Methods/Results:** A retrospective chart review of SHF patients without COPD was made at the time of admission to Charleston Area Medical Center from January 1, 2010 through September 30, 2016. Dosages of BBs on admission, SR on admission and discharge, other cardiac medications, echocardiogram ejection fraction, and EKG data were recorded. Of the 144 HF patients without COPD, 124 (86.1%) were taking BBs, 69 (55.6%) carvedilol; 40 (32.2%) metoprolol succinate; 12 (9.7%) metoprolol tartrate; 3 (2.4%) other and 18(12.5%) were not taking BBs. Mean dose of carvedilol at admission was 18.7±14.8 mg (target dose 50 mg); mean dose of metoprolol succinate was 52.8±43.8mg (target dose 200 mg). Mean sinus rate (not atrial paced or atrial fibrillation) at admission and discharge were 85.3±18.3 bpm and 76.0±16.6 bpm, respectively, for those whose BB dose did not change. 74% of patients had admission SR >70 bpm.

**Conclusion:** While almost all patients with diagnosed SHF are appropriately being prescribed BBs, a large percentage was not titrated up to the target doses established in the guidelines. Inappropriate dosing of BBs could potentially be responsible for worsening outcomes and overutilization of more expensive alternative treatments to adequately suppress SR.

## Introduction

Heart failure is an increasingly prevalent condition in the United States currently effecting approximately 5.7 million people with an estimated annual cost in the United States of \$31 billion in 2011 [1]. Overwhelming evidence from three landmark clinical trials between 1996 and 2000 demonstrated a reduction in morbidity and mortality in Systolic Heart Failure (SHF) patients who received Beta-Blocker (BB) therapy with either Metoprolol Succinate (MS), carvedilol (CV), or Bisoprolol (BS) [2]. This evidence led to these three medications becoming a class IA indication for SHF [3-5]. Current guidelines recommend a treatment goal of 200 mg/day for MS, 50 mg/day for CV, and 10 mg/day for BS [6].

Despite these recommendations, BBs are not being utilized appropriately in more than 50% of patients with SHF. The most common reason for omitting or under-dosing BB's is COPD [7]. Evidence suggests that under-dosing of BB's will not only lead to an increase in negative outcomes in patients with SHF but also increases healthcare costs both in those with and without COPD [8,9].

Under dosing of BB's is suggested by doses less than 50% of target dose and/or SR above 70 bpm. We recently reported under dosing of BB's in patients with COPD and SHF [10]. This led to the question of how SHF patients without COPD are being treated with BB's [11].

## Purpose

The purpose of this study is to determine for patients with SHF and no COPD:

- 1) The percentage receiving BB's
- 2) The BB dose as a percentage of target doses
- 3) The (SR) achieved on current BB therapy

**Table 1:** Data are numbers of patients (%) or mean (SD).

	Systolic Heart Failure Patients (n=144)
<b>Demographics</b>	
Age (years)	74.2±13.0
Sex (males)	87 (60%)
Race (white)	123 (85%)
Coronary artery disease	119 (83%)
Atrial fibrillation	45 (31%)
Myocardial infarction	48 (33%)
Hypertension	119 (83%)
Diabetes	59 (41%)
<b>Clinical factors</b>	
Admit SBP (mm Hg)	127.1±23.5
Admit DBP (mm Hg)	69.6±13.5
LVEF (%)	23.6±7.5
Admit HR (bpm)	80.7±15.8
BNP	1254.4±1061.5
Creatinine	1.6±1.2
<b>Medications</b>	
ACE/ARB	56 (39%)
Digoxin	20 (14%)
Loops	79 (55%)
Thiazides	5 (3%)
Spironolactone	29 (20%)

SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, LVEF = Left Ventricular Ejection Fraction, BPM= Beats Per Minute, BNP = Brain Natriuretic Peptide, ACE = Angiotensin Converting Enzyme, ARB = Angiotensin II Receptor Blocker.

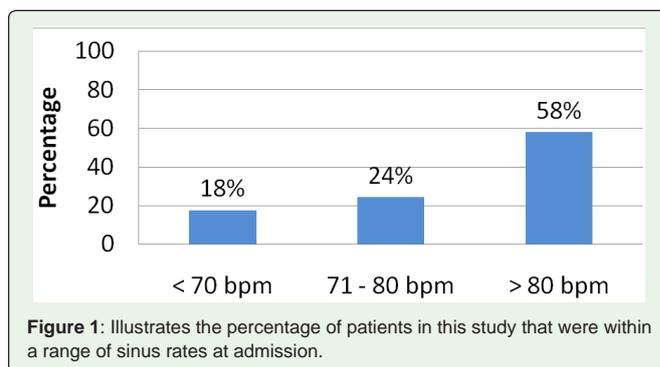
**Table 2:** Illustrates both the total number of patients and the percentage of patients in this study receiving a particular beta-blocker.

Beta-Blocker	Patients on beta-blockers (n=124) n (%)
carvedilol	69 (55.6)
metoprolol succinate	40 (32.3)
metoprolol tartrate	12 (9.7)
Other BBs	3 (2.4)
None	18 (12.5)

**Table 3:** Illustrates the percentage of patients receiving a range of doses with respect to target dose.

	0 - <25% target dose	25% - <50% target dose	50% - <75% target dose	75-100% target dose
<b>Carvedilol (50)</b>	30%	30%	25%	15%
<b>Metoprolol succinate (200)</b>	45%	40%	7.5%	7.5%

Each medications respective target dose is listed in parentheses in milligrams per day.



**Figure 1:** Illustrates the percentage of patients in this study that were within a range of sinus rates at admission.

**Methods**

A retrospective chart review was completed of adult SHF patients without COPD admitted to Charleston Area Medical Center from January 1, 2010 through September 30, 2016. Clinical data including: BB dose and type on admission, SR on admission and discharge, other cardiac medications, echocardiogram ejection fraction, and EKG data were recorded. Patients with acute heart failure, on BB treatment for less than two months, and/or an ejection fraction (EF) of greater than 40% were excluded from the study. SR was determined by careful evaluation of EKG and rhythm strips. Patients with atrial fibrillation (AF), atrial pacing, and other non-sinus atrial rhythms were excluded for the analysis of SR. Hospital Electronic Health Record (EHR) was the source of data collected. Summary statistics were analyzed using SAS Version 9.3 (SAS Institute, Inc.) software. Percentage, frequencies, means and standard deviations are reported. The Charleston Area Medical Center Institutional Review Board (IRB) reviewed and approved the protocol.

**Results**

Between January 1, 2010 and September 30, 2016 there were 144 eligible patients with SHF (mean age, 74 years [interquartile range, 61-87 years] 60% were male) (Table 1). Of the 144SHF patients without COPD, 124 (86.1%) were taking BBs, 69(55.6%) CV; 40(32.2%) MS; 12(9.7%) metoprolol tartrate; 3(2.4%) other BBs and 18 (12.5%) no BBs (Table 2). Mean dose of CV at admission was 18.7±14.8 mg (target dose 50 mg); mean dose of MS was 52.8±43.8mg (target dose 200 mg). Relative to target dose, 60% of patients treated with CV and 85% of patients treated with MS received less than 50% of recommended target dose (Table 3). Mean sinus rate (not atrial paced or AF) at admission was 85.3±18.3bpm. Mean sinus rate at time of hospital discharge was 76.0±16.6 bpm. 74% of patients had admission SR >70 bpm (Figure 1).

**Discussion**

Get with the Guidelines-Heart Failure was an initiative started by the American Heart Association in effort to close the treatment gap between guideline recommendations and real world clinical practice [12]. The goal of this initiative was to increase utilization of

treatments with proven mortality benefits. Hospitals were graded based on their compliance with guidelines and as a result there was an increase in the percentage of SHF patients being started on BB therapy [13]. Following up on dose obtained after the Get With The Guidelines initiative was logistically difficult and would have required close outpatient monitoring; thus, there is limited follow-up data on the dose of BB used [14].

This report is an evaluation of BB treatment at the time of hospital admission for patients with established SHF. This study demonstrates: 1) reasonable use of ACE inhibitors in SHF patients, 2) marked under-dosing of BB relative to target dose, and 3) inadequate SR slowing. These results are consistent with both clinical trials and registries evaluating SHF patients, specifically the SHIFT trial [15].

The SHIFT trial identified a reduction in hospitalization and mortality among SHF patients taking ivabradine. Only 56% of enrolled patients were receiving at least 50% of target dose for BBs [16]. Ivabradine is a selective, expensive sinus node rate depressor with a Class IIa indication for SHF in patients with a SR over 70 bpm. Patients often use ivabradine after failing therapy with BB or when considered an inappropriate candidate for BB therapy [17]. Comorbid COPD was the primary reason not to start a patient on BB therapy [9].

The average dose of BB used in the current study was well below the target dose stated in the MERIT-HF and COPERNICUS trials (37.4% of target dose for CV and 26.4% of target dose for MS). The target dose of BB's for SHF may be debated as SHF patients in the landmark trials achieved around 80% of target dose.

The European Society of Cardiology advises titrating upward BB dose as long as achieved SR does not drop below 50 bpm [18]. In this study, the average SR was 76 bpm at the time of hospital discharge. SR was evaluated both at hospital admission and at discharge in patients who remained on telemetry until day of discharge on the premise that acute illness may lead to an elevated SR at the time of admission. The validity of the SR was validated in this study by careful review of ECG and rhythm strips. Prior studies reported heart rate from recorded pulse including patients with paced rhythms. AF, atrial pacing, and other abnormal atrial rhythms were excluded from evaluation. Only one registry has documented SR previously while evaluating BB therapy for SHF [19].

Bradycardia, even when asymptomatic, frequently causes concern among both patients and care providers. Since many patients with low left ventricular ejection fraction have implantable defibrillators with pacemakers, bradycardia should be of less concern.

Hypotension is another common reason for under-dosing BB. Being a non-selective BB with alpha blocking activity as well, CV is the BB most commonly associated with hypotension in the treatment of SHF. One trial demonstrated that patients experiencing symptomatic hypotension could have their regimen successfully switched to a beta-1 selective blocker to relieve their symptoms and restore their pressures while maintaining BB therapy [20]. Additionally, there are many medications used in the treatment of SHF that cause hypotension. Careful review of a patient's medication list may reveal hypotensive medications that are no longer needed for remote hypertension and angina and can be discontinued or decreased.

Metoprolol tartrate, which is not approved for SHF, was used in 11.1% of patients in this study. There was no improvement in mortality demonstrated with MT in early studies or in the COMET trial, which had BB doses below the current guideline target dose for MS [21,22].

### Strengths/Weaknesses

Strengths of this study include evaluation of SR opposed to pulse rate, which could reflect paced or non-sinus rhythms, and exclusion of COPD, the most common reason for under-dosing BB in SHF. Having a board certified cardiologist carefully review each rhythm strip and ECG ensured accurate interpretation of SR.

Limitations include limited sample size and data collection from one hospital system, which could introduce selection bias, as well as the inherent biases that are associated with retrospective studies.

### Conclusion

Despite excluding COPD patients, inadequate dosing of BB's and inadequate rate slowing is common. The results of this study are consistent with the under-dosing of BB's demonstrated in our previous study of patients with COPD, limited registry data, and the SHIFT trial. Therefore, the results of this study most likely indicate that under-dosing of BBs is universal and not specific to this institution.

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