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## Physician Perspectives on the Use of Beta-Blockers in Heart Failure With Preserved Ejection Fraction

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### Abstract

Beta-blockers are commonly used in heart failure with preserved ejection fraction (HFpEF) even in the absence of a compelling indication and despite the potential to cause harm. Identifying reasons for beta-blocker prescription in HFpEF could permit the development of strategies to reduce unnecessary use and potentially improve medication prescribing patterns in this vulnerable population. We administered an online survey regarding beta-blocker prescribing behavior to physicians trained in internal medicine or geriatrics (non-cardiology physicians) and to cardiologists at 2 large academic medical centers. The survey assessed reasons for beta-blocker initiation, agreement regarding initiation and/or continuation of beta-blocker by another clinician, and deprescribing behavior. The response rate was 28.2% (n=231). Among respondents, 68.2% reported initiating beta-blockers in patients with HFpEF. The most common reason for initiating a beta-blocker was for treatment of an atrial arrhythmia. Notably, 23.7% of physicians reported initiating a beta-blocker without an evidence-based indication. When a beta-blocker was considered as not necessary, 40.1% of physicians reported they were rarely or never willing to deprescribe. The most common reason for not deprescribing a beta-blocker when the physician felt

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Declaration of interests

The remaining authors have nothing to declare.

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that a beta-blocker was unnecessary was the concern about interfering with another physicians' treatment plan (76.6%). In conclusion, a significant proportion of non-cardiology physicians and cardiologists report prescribing beta-blockers to patients with HFpEF, even when evidence-based indications are absent; and rarely deprescribe beta-blockers in these scenarios.

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## Introduction

Heart failure with preserved ejection fraction (HFpEF) accounts for half of all heart failure patients and disproportionately affects older adults<sup>1</sup>. A major challenge in treating HFpEF is that the traditional neurohormonal antagonists recommended for heart failure with reduced ejection fraction (HFrEF) have not clearly demonstrated benefit in HFpEF.<sup>2-4, 5</sup> For example, beta-blockers have unfavorable effects on central blood pressure,<sup>6</sup> increase wall stress,<sup>6, 7</sup> and exacerbate chronotropic incompetence.<sup>7, 8</sup> Consequently, beta-blockers may have negative effects on symptoms such as fatigue and function especially in older adults. Despite this, up to 80% of patients with HFpEF are prescribed a beta-blocker,<sup>9</sup> many of whom lack a compelling indication for a beta-blocker.<sup>10</sup> These data suggest that beta-blockers may be overused in HFpEF. Understanding reasons for beta-blocker prescription in HFpEF could permit development of strategies to reduce overprescribing. We aimed to investigate physician-reported attitudes and behaviors regarding beta-blocker use in HFpEF by administering a survey to 2 dedicated programs for treating HFpEF. Given that approaches to diagnosis and treatment of HFpEF differ across specialties,<sup>11</sup> and that attitudes toward deprescribing differ across specialties,<sup>12</sup> we surveyed physicians with training in general internal medicine, geriatrics, and cardiology to understand attitudes and behaviors of the most common specialties that care for older adults with HFpEF.

## Methods

We conducted the study at Weill Cornell Medicine, a quaternary academic center in New York City, and the University of Michigan, a quaternary academic center in Ann Arbor Michigan. Of note, both institutions have dedicated HFpEF Programs. The study was exempted by the institutional review boards at both institutions. We sent the survey to physicians trained primarily in internal medicine or geriatrics (non-cardiology physicians) and to cardiologists at these academic centers. We included all levels of practicing clinicians including resident and fellow trainees in these specialties.

The 5 minute long survey included 12 questions assessing reasons for beta-blocker initiation, agreement regarding initiation and/or continuation of beta-blocker performed by another clinician, and deprescribing behavior. Survey questions and answer choices are shown in the Supplemental Appendix.

We used the Qualtrics online software platform to administer the survey and distributed it via email to 819 physicians (643 non-cardiology physicians; and 176 cardiologists). The physicians were identified via email listservs. Responses were anonymous. The survey was available online from September 21, 2020 through November 19, 2020; reminder emails with a link to the survey were sent every two weeks.

We examined descriptive characteristics of participants and compared responses across specialties using Fisher's exact test and Pearson's Chi-squared test as appropriate, using a threshold  $P < 0.05$ . We performed all analyses using R, version 4.1.0.

## Results

Of the 819 physicians contacted, the response rate was 28.2% ( $n=231$ ). Of these 231 respondents, we excluded 6 physicians who reported that they did not provide routine care to patients with HFpEF and excluded 2 respondents who did not provide their specialty. Among the 223 remaining respondents, 151 (67.7%) were non-cardiology physicians and 72 (32.3%) were cardiologists. Table 1 displays years of training, % of time in outpatient care, and institution of employment.

Among the 223 respondents, 152 (68.2%) reported that they have initiated a new beta-blocker prescription in patients with HFpEF. Cardiologists were more likely to initiate beta-blockers in patients with HFpEF compared to non-cardiology physicians (86.1 vs. 59.6%,  $p<0.001$ ). The most common reason for initiating a beta-blocker was for treatment of an atrial arrhythmia among both cardiologists (66.1%) and non-cardiology physicians (55.6%) (Figure 1). Notably, 23.7% of physicians (12.9% of cardiologists and 31.1% non-cardiology physicians) reported initiating a beta-blocker for an indication without a strong evidence base (e.g., treatment of HFpEF, treatment for underlying coronary artery disease without a history of myocardial infarction or angina, treatment for hypertension, or treatment without specific indication but the physician felt that the potential benefits of a beta-blocker outweighed its risks).

When asked how often a physician agreed that a beta-blocker was necessary when another physician prescribed it, 46.6% of physicians agreed all or most of the time; non-cardiologist physicians were more likely to agree than cardiologists (53.0% vs. 33.3%,  $p=0.006$ ) (Figure 2A). The two most common reasons for agreeing that a beta-blocker was necessary when another physician prescribed it (among both subgroups) was treatment for atrial arrhythmias and history of myocardial infarction (Figure 2B).

When a beta-blocker was not considered necessary, 40.1% of physicians reported they were rarely or never willing to deprescribe; non-cardiologist physicians were more likely to report rarely or never deprescribing compared to cardiologists (47.6% vs. 25%,  $p=0.001$ ) (Figure 3). The most common reason for not deprescribing a beta-blocker when the physician felt that a beta-blocker was unnecessary (among both specialties) was concern of interfering with another physicians' treatment plan (76.6%) (Table 2). Other reasons for not discontinuing beta-blocker when considered unnecessary among non-cardiology physicians included insufficient evidence on the potential benefits of discontinuing beta-blockers (30.3%) and not having time to discuss the risks and benefits of discontinuing beta-blockers with patients and/or caregivers (26.1%). Among cardiologists, other reasons for not discontinuing beta-blocker when they felt that a beta-blocker was unnecessary included patient and/or caregiver reluctance about discontinuing beta-blocker (37.5%) and concern about causing an arrhythmia (27.8%).

## Discussion

There are 2 key findings from this multisite survey. First, a significant proportion of non-cardiology physicians and cardiologists report prescribing beta-blockers to patients with HFpEF, even when evidence-based indications are absent. Second, although non-cardiology physicians and cardiologists report facing situations where they perceive beta-blockers lack an indication, they typically will not deprescribe beta-blockers.

In contrast to clinical trials of patients with HFrEF which demonstrate that beta-blockers are beneficial,<sup>13</sup> clinical trials of beta-blocker in HFpEF have been neutral.<sup>14 15</sup> Accordingly, HFpEF itself is not a compelling indication for beta-blocker use. In fact, there are data to suggest that beta-blockers may be harmful in HFpEF. In a post-hoc analysis of the Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist (TOPCAT) trial, beta-blocker use was associated with increased risk for HF hospitalizations.<sup>5</sup> Some have suggested that beta-blockers are frequently necessary for HFpEF given the presence of concomitant conditions like atrial arrhythmias and a history of myocardial infarction. However, our prior work has shown that these indications are not universal; and that up to 40% of patients with HFpEF who take beta-blockers may not have an indication, that in the case of atrial fibrillation and myocardial infarctions with preserved ejection fractions is expert opinion based.<sup>10</sup> Yet, beta-blocker use remains high, with prevalence exceeding 80% in a recently conducted clinical trial in HFpEF.<sup>16</sup> Our findings here provide unique insights on why this might be the case.

As we have shown here, many physicians prescribe beta-blockers for conditions where the evidence for benefit is weak. There are limited data demonstrating benefit of beta-blockers in patients with coronary artery disease but without prior myocardial infarction or angina;<sup>17</sup> and there are data suggesting that beta-blockers may be harmful in managing hypertension by increasing central aortic blood pressure<sup>18</sup> with increased risk of stroke<sup>19</sup> in comparison to other anti-hypertensive agents. We found that some physicians prescribe beta-blockers specifically to treat HFpEF despite lack of evidence. This may be a result of the common viewpoint that prolonged diastasis improves the pathophysiology of HFpEF. Contemporary understanding of the pathophysiology of HFpEF suggest that the opposite may be true — slow heart rate and resulting chronotropic incompetence may be a more important pathophysiologic feature.<sup>20</sup> In a recently published study of 52 patients with HFpEF and chronotropic incompetence, beta-blocker withdrawal led to improvements in exercise capacity which would be expected to translate into improved heart failure outcomes.<sup>8</sup> It even appears possible that a significant portion of patients enrolled into contemporary HFpEF trials are only enrolled because beta-blockers have elevated their NTproBNP levels above the required thresholds. Taken together, our data highlight gaps in clinician knowledge related to HFpEF and its management, and supports the need for improved education related to medication prescribing.

We additionally found that deprescribing was rarely considered even when clinicians recognized that prescribed beta-blockers lacked an indication. Prescribing any medication without a clear indication is obviously problematic; given that beta-blockers can cause untoward side effects like fatigue and blunted mood, additional attention toward this

issue is necessary. Although deprescribing has emerged as a patient-centered approach to optimizing medication regimens<sup>21</sup> that patients with HFpEF are amenable to,<sup>22</sup> it is not commonly employed.<sup>23</sup> In our study, the most common barrier to beta-blocker deprescribing among both cardiologists and non-cardiologists was concern for interfering with other physicians' treatment plans. These findings support the need for improved physician-to-physician communication when medications that lack an indication are present, as well as interventions that can address clinical inertia and diffusion of responsibility,<sup>24</sup> which may also be contributing to overutilization of beta-blockers in HFpEF.

There were also some important limitations to this study. First, the response rate for the survey was only 28.2%—since physicians who did not respond to the survey may have been systematically different from those that did respond, generalizability of this study is limited. Unfortunately, we did not have data on physicians who did not participate in the survey, so we could not quantify this concern. Second, similar to any study based on self-reported surveys, there is risk for social desirability bias; this risk was mitigated by the anonymity of the survey. Third, surveys were conducted at two large academic institutions where there are established HFpEF programs, which could have influenced attitudes. Findings here regarding knowledge and familiarity with HFpEF likely represent the best case scenario.

In conclusion, a significant proportion of non-cardiology physicians and cardiologists reported prescribing beta-blockers to patients with HFpEF, even when evidence-based indications are absent, and rarely deprescribe beta-blockers in these scenarios. Future work is needed to develop strategies that improve medication prescribing patterns in older adults with HFpEF.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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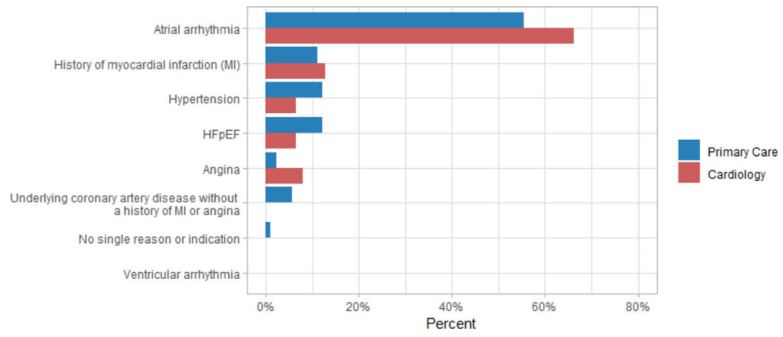
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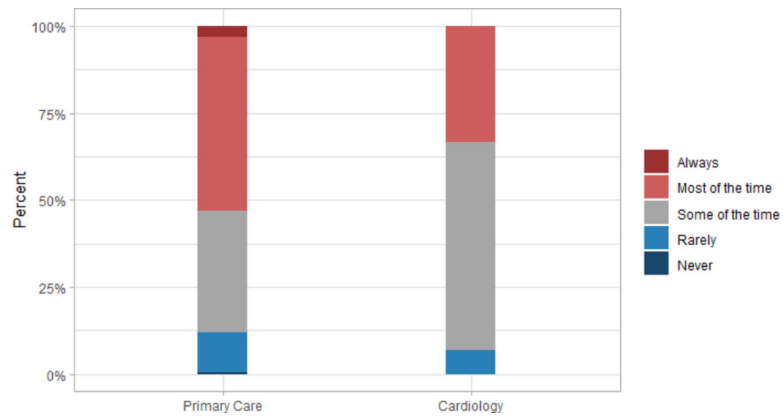
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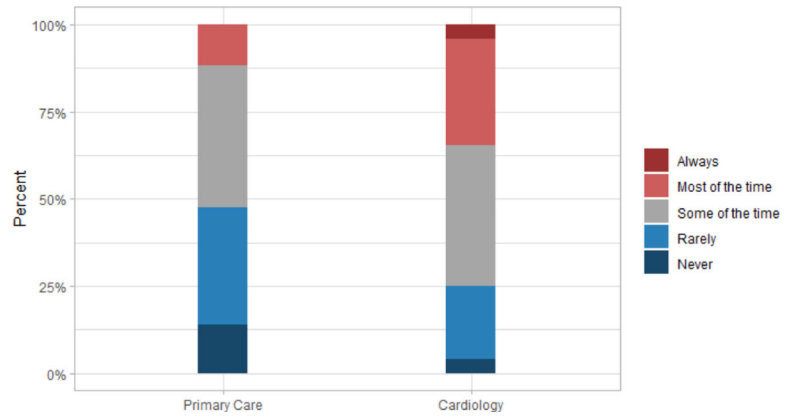
**Figure 1. Top reasons for initiating beta-blocker.**

Top reasons reported for initiating a beta-blocker for a patient with HFpEF (N=152). HFpEF = heart failure with preserved ejection fraction. \*P < 0.05.



**Figure 2. Frequency and reasons for agreement regarding the necessity of a beta-blocker prescribed by another physician.**

Frequency (A) and Reasons (B) that physicians report agreeing with the necessity of a beta-blocker prescribed by another physician for a patient with HFpEF (N=223). HFpEF = heart failure with preserved ejection fraction. \*P < 0.05.



**Figure 3. Frequency of discontinuing a beta-blocker when physician felt it was not necessary.** Reported frequency of discontinuing a beta-blocker when physician felt that the beta-blocker was not necessary for a patient with HFpEF (N=217). HFpEF = heart failure with preserved ejection fraction.

**Table 1:**

## Respondent characteristics by specialty

Variable	Overall (n=223)	Non-Cardiology (n=151)	Cardiology (n=72)	p value <sup>a</sup>
Years of training				<0.001
Still in training (Resident or Fellow)	37.7%	47.0%	18.1%	
<10 years	31.4%	29.8%	34.7%	
10–20 years	13.5%	10.6%	19.4%	
>20 years	17.5%	12.6%	27.8%	
Percent of time in outpatient care <sup>b</sup>				<0.001
0–20%	41.9%	51.3%	22.2%	
21–40%	16.7%	17.3%	15.3%	
41–60%	9.0%	4.0%	19.4%	
61–80%	14.9%	8.0%	29.2%	
81–100%	17.6%	19.3%	13.9%	
Institution of employment				0.60
University of Michigan	53.8%	55.0%	51.4%	
Weill Cornell Medicine	46.2%	45.0%	48.6%	

<sup>a</sup>Fisher's exact test; Pearson's Chi-squared test

<sup>b</sup>One trainee did not answer this question.

**Table 2:**

Barriers to deprescribing a beta-blocker when the physician felt that a beta-blocker was unnecessary

Variable	Overall (n=214)	Non-Cardiology (n=151)	Cardiology (n=72)	p value <sup>a</sup>
Concern about interfering with another physicians' treatment plans	76.6%	86.6%	56.9%	<b>&lt;0.001</b>
Insufficient evidence on the potential benefits of discontinuing beta-blockers	28.0%	30.3%	23.6%	0.305
Discussed discontinuing beta-blocker, but the patient and/or caregiver was reluctant to do so	23.8%	16.9%	37.5%	<b>&lt;0.001</b>
Concern about causing an arrhythmia	22.0%	19.0%	27.8%	0.14
Do not have time to discuss the risks and benefits of discontinuing beta-blockers with patients and/or caregivers	21.0%	26.1%	11.1%	<b>0.01</b>
Concern about worsening heart failure	15.9%	19.7%	8.3%	<b>0.03</b>
Do not know the safest way to discontinue beta-blockers	11.2%	15.5%	2.8%	<b>0.005</b>
Concern about the medico-legal implications of discontinuing medications	5.6%	4.9%	6.9%	0.54
Concern about upsetting the patient and/or caregiver through the implication that I had 'given up' on them	5.1%	5.6%	4.2%	0.75
Concern about precipitating a myocardial infarction	4.2%	5.6%	1.4%	0.28