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Use of Heart Failure Exacerbating Medications Among Adults with Heart Failure

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Optimal treatment regimens for adults with heart failure (HF) should include medications where the potential benefits outweigh the risks. However, the use of pharmacologic agents whose risks outweigh the potential benefits has received little attention, despite their potential to contribute to adverse outcomes among adults with HF. To help clinicians identify potentially-harmful agents, the American Heart Association (AHA)¹ released a list of medications that could exacerbate HF. To date, patterns of the use of these potentially-harmful agents are unknown. To address this knowledge gap, we examined a nationally-representative cohort of community-dwelling adults with HF using National Health And Nutrition Examination Survey (NHANES) data.

NHANES is a cross-sectional survey with a probability cluster sample design that produces national estimates of the non-institutionalized United States population.² We included participants aged ≥18 years with self-reported HF from NHANES cycles between 2003–2014. Self-reported HF has high specificity³, and is routinely used as a source for HF statistics by the AHA.⁴

We examined variables routinely collected from NHANES including: socio-demographics, 16 comorbid conditions, medications, geriatric conditions (cognitive impairment and functional impairment), and healthcare utilization (number of contacts with ambulatory healthcare and number of hospitalizations in the prior year). We classified medications as potentially HF-exacerbating according to their presence in the 2016 AHA statement on drugs that may induce or precipitate HF.¹ We included major HF-exacerbating agents,

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defined as agents whose effects could be life-threatening or could lead to hospitalization or emergency room visits.

For all statistical analyses, we accounted for NHANES' complex survey design, and reported weighted percentages and/or means for all variables. We used the t-test and Pearson's chi-square test to assess differences between groups. To identify factors independently associated with HF-exacerbating medication use, we performed a robust Poisson regression analysis that incorporated socio-demographics, comorbidity count, geriatric conditions, and healthcare utilization. To identify temporal trends, we performed a logistic regression with survey weights. For missing covariate values in our regression analysis, we employed multiple imputation using chained equations designed for complex survey data.⁵ All statistical tests were two-sided, with a p-value <0.05 indicating statistical significance. .

We examined 1069 survey respondents, which represented 5.3 million adults from the United States. Population characteristics, stratified by HF-exacerbating medication use, are shown in the Table. The prevalence of HF-exacerbating medications was 48%; 21% for agents with Level A evidence, 53% for Level B, and 35% for Level C. The most common classes included medications for diabetes, analgesia, and pulmonary conditions (Table). The prevalence of HF-exacerbating medication use was highest in 2013–2014 at 55%; p-for-trend for the study period did not reach statistical significance (2003–2004: 48%, 2005–2006: 48%, 2007–2008: 46%, 2009–2010: 44%, 2011–2012: 43%; p-for-trend=0.66). In multivariable regression analysis, comorbidity count (1.07 per condition, 95% CI[1.04–1.11], p<0.001) and functional impairment (1.23, 95% CI[1.01–1.49], p=0.04) were associated with HF-exacerbating medication use.

Our study showed that use of major HF-exacerbating medications, defined by the AHA, was common. These findings underscore the importance of performing a detailed review of all medications (not just for those related to HF) when caring for adults with HF. While expert medication review can reduce drug-related hospitalizations,^{6,7} few studies have focused on the HF population. Given the number of agents that can exacerbate HF¹ and their high prevalence as shown here, the utility of medication review tools that focus on adults with HF requires further evaluation.

Given the significant non-cardiovascular comorbidity burden experienced by adults with HF,⁸ there is a need for additional guidance on how to balance the risks and potential benefits of agents that treat non-cardiovascular conditions while worsening HF. For example, it is not clear how best to treat pulmonary conditions in the setting of HF, as commonly prescribed guideline-concordant agents like beta-agonists have few alternatives. Therapeutic competition, defined as a disease-drug interaction where treatment for one condition adversely affects another,⁹ represents just one example of how even seemingly-appropriate medications can potentially cause harm, underscoring the deficiencies of disease-specific recommendations, and lending support for developing patient-centered guidelines and approaches to managing common circumstances that arise in patients with multiple chronic conditions. Medication prioritization based on individual health goals may be a useful strategy to reconcile the competing risks and benefits of potentially appropriate medications,

but remains understudied. The role of deprescribing (discontinuing medication under medical supervision)¹⁰ in this context, especially among those with functional impairment—a key characteristic independently associated with HF-exacerbating medication use—is also understudied.

In summary, our data highlight the frequent use of HF-exacerbating medications among adults with HF, and suggest the need for strategies to mitigate their use in HF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

Disclosures:

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Table.
Population Characteristics and Medication Patterns According to the Use of HF-Exacerbating Medications

Variable	+ Use (n=503)	- Use (n=566)	p-value
Age, mean years (IQR)	66.1 (64.8–67.3)	66.5 (65.1–67.9)	0.59
Women, %	245 (52%)	245 (48%)	0.25
White Race, %	289 (75%)	321 (74%)	0.64
Medicare without Medicaid	233 (57%)	266 (60%)	0.009
Count of comorbidities, mean (95% CI)	5.1 (4.8–5.3)	4.1 (3.9–4.3)	<0.001
Cognitive impairment, %	153 (29%)	141 (20%)	0.005
Functional impairment, %	87 (15%)	50 (7%)	0.001
Use of Major HF-Exacerbating Medications	503 (100%)	--	
Level A evidence	93 (21%)	--	
Level B evidence	265 (53%)	--	
Level C evidence	187 (35%)	--	
Diabetes mellitus medications	184 (34%)	--	
Metformin (LOE C)	139 (25%)	--	
Thiazolidinediones (LOE A)	44 (9%)	--	
Staglipitan/Saxagliptan/(LOE B)	26 (5%)	--	
NSAIDS/COX-2 inhibitors (LOE B)	96 (20%)	--	
Albuterol (LOE B)	90 (17%)	--	
Diltiazem/Verapamil (LOE B)	60 (11%)	--	
Neurological and psychiatric medications	45 (10%)	--	
Citalopram (LOE A)	33 (7%)	--	
Clozapine (LOE C)	33 (7%)	--	
Other	12 (3%)		
Antiarrhythmic medications	23 (5%)	--	
Sotalol (LOE B)	19 (4%)	--	
Dronedarone (LOE A)	2 (0.7%)	--	
Flecainide (LOE B)	2 (0.3%)	--	

Variable	+ Use (n=503)	- Use (n=566)	p-value
Hematologic and Rheumatologic agents	9 (3%)	--	
Topical β -blockers (LOE C)	9 (2%)	--	

Numbers are unweighted. Percentages are weighted to represent the United States population.

Abbreviations: HF: Heart failure; IQR: Interquartile range; CI: confidence interval; NSAID: Non-Steroidal Anti-inflammatory Drug; COX-2: Cyclooxygenase-2 inhibitor; LOE: Level of evidence