Research Letter

Use of Heart Failure–Exacerbating Medications Among Adults With Heart Failure

Optimal treatment regimens for adults with heart failure (HF) should include medications for which 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 National Health And Nutrition Examination Survey (NHANES) data, a nationally representative cohort of community-dwelling adults with HF.

NHANES is a cross-sectional survey with a probability-cluster sample design that produces national estimates of the noninstitutionalized United States population.[2] We included participants aged ≥18 years with self-reported HF in NHANES cycles from 2003 to 2014. Self-reported HF has high specificity[3] and is routinely used as a source for HF statistics by the AHA.[4]

We examined variables routinely collected from NHANES, including sociodemographics, 16 comorbid conditions, medications, geriatric conditions (cognitive impairment and functional impairment), and health care utilization (number of contacts with ambulatory health care and number of hospitalizations in the previous 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, 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 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 sociodemographics, comorbidity count, geriatric conditions, and health care utilization. To identify temporal trends, we performed a logistic regression with survey weights. For missing covariate values in our regression analysis, we used multiple imputation with the use of chained equations designed for complex survey data.[5] All statistical tests were 2 sided, with a P value of $<.05$ 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 presented in Table 1. 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 1). 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 = .66). In multivariable regression analysis, comorbidity count (1.07 per condition, 95% confidence interval [CI] 1.04–1.11; $P < .001$) and functional impairment (1.23, 95% CI 1.01–1.49; $P = .04$) 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. Although 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 HF[1] 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 noncardiovascular 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 noncardiovascular conditions while worsening HF. For example, it is not clear how best to treat pulmonary conditions in the setting of HF, because commonly prescribed guideline-concordant agents, such as 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 potentially appropriate medications can 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.

Table 1. Population Characteristics and Medication Patterns According to the Use of HF-Exacerbating Medications

Variable	Used (n = 503)	Not Used (n = 566)	*P* Value
Age, y, mean (IQR)	66.1 (64.8−67.3)	66.5 (65.1−67.9)	.59
Women, %	245 (52%)	245 (48%)	.25
White race, %	289 (75%)	321 (74%)	.64
Medicare without Medicaid	233 (57%)	266 (60%)	.009
Count of comorbidities, mean (95% CI)	5.1 (4.8−5.3)	4.1 (3.9−4.3)	<.001
Cognitive impairment, %	153 (29%)	141 (20%)	.005
Functional impairment,%	87 (15%)	50 (7%)	.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%)	–	
Sitagliptan/saxagliptan/ (LOE B)	26 (5%)	–	
NSAIDs/COX-2 inhibitors (LOE B)	96 (20%)	–	
Albuterol (LOE B)	90 (17%)	–	
Diltiazem/verapamil (LOE B)	60 (11%)	–	
Neurologic 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%)	–	
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; LOE, level of evidence; NSAID, nonsteroidal antiinflammatory drug; COX-2, cyclooxygenase-2 inhibitor.

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.

Disclosures

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Supplementary Data

Supplementary data related to this article can be found at doi:10.1016/j.cardfail.2018.10.014.

Jerard Kneifati-Hayek, MD[1]
Peter Kennel, MD[2]
Joanna Bryan, MPH[2]
Monika M Safford, MD[2]
Parag Goyal, MD, MSc, FACC[2,*]
[1]*Department of Medicine, Columbia University Irving Medical Center, New York, New York*
[2]*Department of Medicine, Weill Cornell Medicine, New York, New York*

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