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Evidence-Based Heart Failure Medications and Cognition

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Abstract

Background—The etiology of cognitive impairment in heart failure (HF) is controversial and likely multifactorial. Physicians may hesitate to prescribe evidence-based HF medication because of concerns related to potential negative changes in cognition among a population that is already frequently impaired. We conducted a study to determine if prescription of evidence-based HF medications (specifically, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin-receptor blocking agents, diuretics, and aldosterone inhibitors) was associated with cognition in a large HF sample.

Methods—Six-hundred and twelve patients completed baseline data collection for the Rural Education to improve OuTcomEs in Heart Failure clinical trial (REMOTE-HF), including information about medications. Global cognition was evaluated using the Mini-Cog.

Results—The sample mean age was 66-years old (SD 13 years), 58% were male, 89% Caucasian. Global cognitive impairment was identified in 206 (34%) of the 612 patients. Prescription of evidence-based HF medications was not related to global cognitive impairment in this sample. This relationship was maintained even after adjusting for potential confounders (e.g. age, education, and comorbid burden).

Conclusion—Prescription of evidence-based HF medications is not related to low scores of a measure of global cognitive function in rural patients with HF.

Keywords

Cognition; heart failure; drug therapy

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None

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Introduction

Health care costs related to heart failure (HF) are approximately $31 billion per year in the United States[1]. According to current statistics, the number of hospital discharges for HF has remained unchanged since 2000 with 68% of HF costs directly related to medical care[1]. Inability to follow complex medication regimens and recognize worsening symptoms is frequently identified as a reason for re-admission[2–5]. Cognitive impairment, often described as difficulty with attention and memory among individuals with HF, likely contributes to the inability to follow complex medication regimens and recognize worsening symptom patterns.

Approximately 50% of individuals diagnosed with HF experience cognitive impairment[6–9]. The etiology of cognitive impairment in HF is controversial and most likely multifactorial. A leading hypothesis suggests that acute and chronic hypoperfusion related to the HF disease process may affect areas of the brain that are sensitive to changes in blood flow. These same areas of the brain that are sensitive to blood flow are also related to cognitive processes, such as memory and attention[10–14]. Evidence-based medications such as beta-blockers (BBs), angiotensin-converting enzyme inhibitors (ACEs), the newer generation angiotensin-receptor blocking agents (ARBs), aldosterone antagonists, and diuretics were created in part to improve cardiac output and blood flow to vital organs such as the brain. Several of the evidence-based medications used in HF have demonstrated positive effects on cognition, along with a decreased progression of dementia in non-HF samples[15–19].

The guidelines related to HF medications have been in place for over a decade and yet practitioners' prescription rates are still relatively low. Data from HF registries in the US, Asia/Pacific and Europe report low utilization rates of BBs (< 85%) and ACEs or ARBs (< 80%)[20–26]. Utilization is even lower for medications that have more contraindications, such as aldosterone inhibitors, with several authors reporting that fewer than 40% of eligible patients receive these agents[20–23,26]. Further, even though prescription rates among some evidence based medications are improving (e.g. BBs and ACE/ARB), the drugs are titrated to dosages that are associated with improved clinical outcomes less than 50% of the time[20,21,23,26,27]. Multiple factors contribute to low prescription rates, including patient age and comorbid conditions (e.g. asthma, depression or cognitive impairment)[22,23,28]

If data supporting minimal or even positive changes to cognition were available, prescription rates of evidence-based medication might improve. However, there is a dearth of information surrounding the impact of evidence-based HF medication on cognition among individuals with HF[29–32]. Consequently, physicians may hesitate to prescribe evidence-based HF medication because of concerns related to potential negative changes in cognition among a population that is already frequently impaired. Therefore, we conducted a study to determine if prescription of evidence-based HF medication (specifically BBs, ACEs, ARBs, aldosterone inhibitors, and diuretics) was associated with cognition in a large HF sample. In addition, we explored potential inconsistencies in the prescription of evidence-based HF medications based on the presence of cognitive impairment.

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Methods

Sample

This study was part of an ongoing multi-site randomized clinical trial, Rural Education to iMprove OuTcomEs in Heart Failure (REMOTE-HF), that was designed to test an education and counseling intervention to improve self-care in patients with HF who live in rural areas[33]. Rural areas were defined as towns of <2,500, living in open country or a metropolitan center of <50,000[33]. The methods used in the parent study have been described elsewhere[34]. The Institutional Review Boards at each site approved all activities. Briefly, inclusion criteria were age ≥ 18 years old with stable HF, hospitalized for HF within the last 12 months, able to read and write English, and living independently with primary decision-making ability (i.e., not institutionalized). Patients were excluded if they had a complicating serious co-morbidity (disease or illness predicted to cause death within the next 12 months), required dialysis, had a psychiatric illness or untreated malignancy, or were enrolled in a HF disease management program. Trained research nurses assessed 636 individuals with HF living in rural areas of California, Kentucky, and Nevada for eligibility and approached them about the study during a regularly scheduled clinic visit. Of the 636, 10 refused to participate and 12 were excluded for a score of <3 on the Mini-Cog assessment (scores <3 are indicative of severe global cognitive impairment). Two patients did not complete baseline data collection. All patients gave informed consent. The data reported here were collected on 612 patients at baseline prior to randomization.

Procedures

Demographic information (i.e. age, gender, race/ethnicity, education, and income) was collected through a simple self-administered form. Information pertaining to patients' medical history (i.e. medication use and dosage) was collected by medical chart review by trained study personnel. Co-morbidities were assessed using the Charlson Co-morbidity Index (CCI)[35].

Cognition was evaluated using the Mini-Cog which combines a three-item recall task (memory) with a clock drawing task (executive function). The Mini-Cog has good sensitivity and specificity across ethnically diverse populations and is not affected by education or language, as more traditional measures of cognition, such as the Mini Mental Status Exam[36–38]. Although the Mini-Cog was designed as a screening tool for dementia, Kaufer et al, (2008) reported that the Mini-Cog had a 90% positive predictive value of identifying cognitive impairment in a large sample of individuals residing in assisted living facilities[39]. Borson et al, (2005) documented that the Mini-Cog had an overall accuracy (true positives+true negatives/true positive+true negatives+false positives+false negatives) of 83% classifying participants as cognitively impaired or normal cognition in a sample of 371 community dwelling, ethnically diverse participants. Finally, the Mini-Cog has documented validity in HF samples[40,41]. Most recently, Patel et al. (2014) reported that among patients hospitalized with HF, Mini-Cog scores were associated with poor 30-day outcomes[40]. There are a variety of administration and scoring methods for the Mini-Cog assessment. For this study patients completed both the three-item recall and the clock draw task. The clock draw tests were independently scored by a single researcher according to a three point scoring

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criteria[38,42]. Based on the scoring system developed by Steenland et al, (2008), the Mini-Cog scores can range from 0 – 6 (3 points for the three-item recall and 3 points for the clock draw task; a score of 0 – 2 suggests dementia, a score of 3 – 4 suggests mild impairment, and a score > 4 suggests intact cognition). For this study cognitive impairment was defined as a Mini-Cog assessment score of 3 or 4.

Statistical Methods

Data were analyzed using SPSS® for Windows (version 19.0, SPSS, Inc., Chicago, IL). Descriptive statistics, Chi-square analyses and independent sample t-tests were used to characterize the samples and test for differences between those patients with cognitive impairment and those patients who were cognitively intact. Chi-Square analyses were also used to test for differences between the prescription of evidence-based medication (yes/no) and cognitive impairment. The demographic variables that varied significantly between the group of patients with cognitive impairment and those patients who were cognitively intact and all five HF medications (i.e. BBs, ACEs, ARBs, aldosterone inhibitors, and diuretics) were placed in a binary logistic regression with forced entry of all of the variables in a single step was used to explore the contribution of various sociodemographic and each the five HF medications to cognitive impairment with 2-sided significance set at 0.05.

Results

Patient characteristics and prescription of evidence-based HF medication

Six hundred and twelve HF patients completed baseline data collection and Mini-Cog assessments. Forty-nine percent of patients were diagnosed with heart failure with reduced ejection fraction (HFrEF). The patients had a mean age of 66 years old (SD 13 years), 58% were male and 89% were Caucasian. Forty-nine percent of the sample had completed high school, while only 17% had not. Complete demographic data are presented in Table 1.

Differences in age, gender, education, and LVEF among individuals who received medication prescriptions for the evidence-based medications studied and those who did not receive medication prescriptions were assessed by Chi-square analyses and independent sample t-tests. Individuals who were prescribed diuretics were older (66 years old vs. 65 years old, p=0.025). More males received prescriptions for BBs and ACE inhibitors compared to females (85% vs. 73%, p=0.001 and 59% vs. 51%, p=0.027, respectively). Individuals who received aldosterone inhibitor prescriptions were more likely to be male and to have a low LVEF than individuals who did not receive aldosterone inhibitors (27% vs. 19%, p=0.032 and 35% vs. 41%, p=0.041, respectively). There were no differences in gender, education, or LVEF between individuals who received prescriptions for ARBs compared to those who did not. Finally, there were no group differences in LVEF based on cognitive status.

Guideline-based medication usage and cognitive impairment

Cognitive impairment was identified in 34% of the sample. The cognitively impaired group was older, less likely to have completed high school, and had more comorbid illnesses. Other HF disease characteristics did not differ significantly between groups.

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Logistic regression modeling was conducted to examine the association between cognitive impairment and common HF medications. After adjusting for age, education and Charlson Comorbidity Index scores, none of the five commonly prescribed HF medications predicted cognitive impairment (Table 2). Diuretics and BBs were the most frequently prescribed medications, 84% and 80%, of the sample, respectively. ACE inhibitors or ARBSs were prescribed to 75% of patients in the sample. Alternatively, aldosterone inhibitors (23%) were prescribed less frequently. Cognitively impaired patients were more likely to have ARBs prescribed and less likely to have BBs and diuretics prescribed than those patients who were cognitively intact (Table 3). Prescription of evidence-based medications (i.e., BBs, ACE inhibitors, ARBs, diuretics, or aldosterone inhibitors) was not significantly related to cognitive impairment in this sample (Table 4). With the exception of the aldosterone inhibitors (p=0.019), the dose of medication did not differ significantly between the groups (p values range = 0.187 to 0.752).

Discussion

The results of this study demonstrate that prescription of evidence-based HF medication - specifically BBs, ACE-inhibitors, ARBs, aldosterone inhibitors, and diuretics is not related to cognitive impairment in a large sample of rural community dwelling HF patients (n=612). We found that approximately one-third of the patients met the criteria for cognitive impairment. However, contrary to our expectations, the prescription of evidence-based HF medication was not related to the presence of cognitive impairment. Further, among those patients classified as cognitively impaired, the dose of evidence-based HF medication was not significantly associated with cognitive impairment. Finally, our findings are the first to suggest that presence of cognitive impairment is not related to prescription of evidence-based HF medications regardless of HF classification (i.e. heart failure with preserved (HFpEF) versus reduced ejection fraction (HFrEF)).

Findings related to the relationship between ACEs and cognition are equivocal. Our findings extend the work of Hoth et al. (2008) who documented that 31 community-dwelling patients with HF who were taking ACEs did not perform differently than patients not taking ACEs. However, patients taking ACEs performed significantly worse on a measure of attention than patients not taking ACEs[43].

Our study contradicts the findings of Zuccala et al. (2005). They studied over 1,200 hospitalized patients with HF. They found that patients who were started on ACE-inhibitors experienced improved scores on measures of global cognitive function during their hospital stay. Further, they found that higher doses and longer duration of ACE-inhibitors were associated with greater improvement of cognition across hospitalization. The significant association between higher doses of ACE-inhibitors and improved global cognition remained even after controlling for multiple confounders in linear regression models[44]. Our findings suggest that if initiating ACE-inhibitor therapy leads to improved cognitive function, these improvements dissipate over time. A study by Sink et al. (2012) supports our hypothesis. They analyzed data from the Cardiovascular Health Study (CHS) and reported that individuals exposed to ACEs that did not cross the blood-brain barrier were at a 20% greater risk of dementia than individuals who used other anti-hypertension medications[30].

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Because our study was cross sectional in design it was not possible to explore the effects of ACEs over time, therefore prospective studies are needed to validate our findings.

Athilingam et al. (2012) also explored the effects of ACEs using a sample of community dwelling adults with HF. The authors noted that ACEs and dose of ACEs were associated with significantly higher cognitive scores using the Montreal Cognitive Assessment (MoCA) tool[29]. Our findings suggest that ACEs, regardless of dose were not associated with cognition. Reasons for this discrepancy may be related to sample size differences (Athilingam et al. n=90) and sample cognitive status. Mean cognitive scores for both groups (ACE-inhibitors vs. No ACE-inhibitors) in the Athilingam study were considered impaired (i.e. Montreal Cognitive Assessment score <26) whereas two-thirds of participants in our study were cognitively intact. More studies are needed to clarify the relationship between evidence-based medications and cognition in this population.

Age, education, and Charlson Comorbidity Index scores were significant predictors of cognitive impairment in our sample. It is widely accepted in neuropsychological literature that age and education affect measures of cognition. However, our findings extend the literature by exploring the effect of comorbid burden on cognition, as measured by the Charlson Comorbidity Index. The concept of comorbid burden has not been widely reported in the literature, but bears further exploration because individuals do not suffer from HF in isolation. Data related to comorbid burden is necessary In order to move forward with interventions to ameliorate or compensate for cognitive changes in the HF population. Therefore, findings related to comorbid burden from this study will need to be validated in future studies.

Decline in global cognition is a common precursor to dementia; therefore, the findings of our study may have long-term implications related to risk of dementia and Alzheimer's disease (AD). Specifically, taking evidence-based HF medications does not lead to dementia. In a community-based cohort study, Qui et al. (2006) examined the presence of HF as a risk for dementia and AD and found that the presence of HF was associated with a significantly higher risk of dementia and AD (OR 1.70, 95% CI 1.24 – 2.34 and OR 1.61, 95% CI 1.11 – 2.34, respectively). However, the use of antihypertensive medication (either BBs or ACE-inhibitors) was associated with a non-significant decrease in risk of dementia and AD (OR 1.38, 95% CI 0.99 – 1.94 and OR 1.39, 95% CI 0.93 – 2.07, respectively)[45]. A decreased risk of the incidence or progression of dementia related to BBs and ACE-inhibitors has also been documented in samples of older adults with hypertension[16,18,19,30,46,47]. It is possible that the use of evidence-based HF medication may decrease the risk of Mild Cognitive Impairment, dementia and AD. Prospectively designed studies that examine the use of evidence-based HF medications that utilize a comprehensive evaluation of Mild Cognitive Impairment and dementia are warranted. Such studies should include both individuals with HFpEF and HRrEF as the two groups differ in treatment regimens and cognitive impairment patterns[48].

Study Limitations

Several limitations of this study should be considered. First, the observational, cross-sectional study design does not allow extrapolation of cause and effect. However, it is not

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ethically feasible to carry out a randomized control trial that would withhold evidence-based HF medications from a control group. Second, we could not ascertain whether patients were taking their prescribed medications. Third, the sample was composed of rural individuals and 25% had less than a high school education; therefore the results we report may not apply to all patients with HF. Fourth, the Mini-Cog was designed as a screening instrument for dementia; therefore, its sensitivity to mild cognitive changes may be limited. Finally, the prescription numbers for this sample are low, with only 75% of patients being prescribed and ACE or ARB and only 80% of patients being prescribed a beta-blocker. These low rates of medication prescription may account for the negative findings. Nevertheless, in spite these methodological limitations, the evidence we present in this study supports the conclusion that there is no relationship between prescription of evidence-based HF medication and cognitive impairment.

Conclusions

In summary, our study presents evidence in a large sample of community dwelling, rural HF patients that prescription of evidence-based HF medication is not related to the presence of cognitive impairment in patients with HFpEF or HFrEF. These findings suggest that the use of evidence-based HF medications does not contribute to the cognitive decline commonly found in this population. The results warrant prospective cohort studies designed to document the incidence and progression of cognitive impairment and dementia over time among patients with HF.

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References

1. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics - 2014 update: a report from the American Heart Association. Circulation. 2014; 180:1–267.
2. Bennett SJ, Pressler ML, Hays L, Firestine LA, Huster GA. Psychosocial variables and hospitalization in persons with chronic heart failure. Progress in Cardiovascular Nursing. 1997; 12(4):4–11. [PubMed: 9433728]
3. Happ MB, Naylor MD, Roe-Prior P. Factors contributing to rehospitalization of elderly patients with heart failure. Journal of Cardiovascular Nursing. 1997; 11(4):75–84. [PubMed: 9200021]
4. Naylor MD, Stephens C, Bowles KH, Bixby MB. Cognitively impaired older adults: from hospital to home. American Journal of Nursing. 2005; 105(2):52–61. [PubMed: 15674058]
5. Pressler SJ, Therrien B, Riley PL, et al. Nurse-enhanced memory intervention in heart failure: The MEMOIR study. Journal of Cardiac Failure. 2011; 17(10):832–843. [PubMed: 21962422]
6. Bennett SJ, Sauve MJ. Cognitive deficits in patients with heart failure: a review of the literature. Journal of Cardiovascular Nursing. 2003; 18(3):219–242. [PubMed: 12837012]
7. Pressler SJ. Cognitive Functioning and Chronic Heart Failure: A Review of the Literature (2002-July 2007). Journal of Cardiovascular Nursing. 2008; 23(3):239–249. [PubMed: 18437066]

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8. Vogels RLC, Scheltens P, Schroeder-Tanka JM, Weinstein HC. Cognitive impairment in heart failure: a systematic review of the literature. European Journal of Heart Failure. 2007; 9:440–449. [PubMed: 17174152]

9. Bauer LC, Pozehl BJ, Hertzog M, Johnson JK, Zimmerman L, Filipi M. A brief neuropsychological battery for use in the chronic heart failure population. European Journal of Cardiovascular Nursing. 2012; 11(2):223–230. [PubMed: 21514892]

10. Alves TC, Rays J, Fraguas R, et al. Localized blood flow reductions in patients with heart failure: a study using Tc-HMPAO SPECT. Journal of Neuroimaging: The Official Journal of the American Society of Neuroimaging. 2005; 15(2):150–156.

11. Jennings JR, Muldoon MF, Price JC, Christie IC, Meltzer CC. Cerebrovascular support for cognitive processing in hypertensive patients is altered by blood pressure treatment. Hypertension. 2008; 52:65–71. [PubMed: 18519845]

12. Vogels RL, Oosterman JM, Laman DM, et al. Transcranial doppler blood flow assessment in patients with mild heart failure: correlates with neuroimaging and cognitive performance. Congestive Heart Failure (Greenwich, Conn.). 2008; 14(2):61–65.

13. Vogels RL, Oosterman JM, van Harten B, et al. Neuroimaging and correlates of cognitive function among patients with heart failure. Dementia & Geriatric Cognitive Disorders. 2007; 24(6):418–423. [PubMed: 17938570]

14. Woo MA, Kumar R, Macey PM, Fonarow GC, Harper RM. Brain injury in autonomic, emotional, and cognitive regulatory areas in patients with heart failure. Journal of Cardiac Failure. 2009; 15(3):214–223. [PubMed: 19327623]

15. Hajjar I, Catoe H, Sixta S, et al. Cross-sectional and longitudinal association between antihypertensive meidcations and cognitive impairment in an elderly population. Journal of Gerontology. 2005; 60A(1):67–73.

16. Jennings JR, Christie IC, Muldoon MF, Ryan CM, Price JC, Meltzer CC. Brain function, cognition, and the blood pressure response to pharmacological treatment. Psychosomatic Medicine. 2010; 72:702–711. [PubMed: 20639391]

17. Khachaturian AS, Zandi PP, Lyketsos CG, et al. Antihypertensive medication use and incident Alzheimer disease: the Cache County study. Archives of Neurology. 2006; 63:686–692. [PubMed: 16533956]

18. Rozzini L, Chilovi BV, Bertoletti E, et al. Angiotensin converting enzyme inhibitors modulate the rate of progression of amnestic mild cognitive impairment. International Journal of Geriatric Psychiatry. 2006; 21:550–555. [PubMed: 16642542]

19. Shah K, Qureshi SU, Johnson M, Parikh N, Schulz PE, Kunik ME. Does use of antihypertensive drugs affect the incidence or progression of dementia? A systematic review. American Journal of Geriatric Pharmacotherapy. 2009; 7:250–261. [PubMed: 19948301]

20. Atherton JJ, Hayward CS, Ahmad WAW, et al. Patient characteristics from a regional multicenter database of acute decompensated heart failure in Asia Pacific (ADHERE International - Asia Pacific). Journal of Cardiac Failure. 2012; 18(1):82–88. [PubMed: 22196846]

21. Fonarow GC, Albert NM, Curtis AB, et al. Improving evidence-based care for heart failure in outpatient cardiology practices. Circulation. 2010; 122:585–596. [PubMed: 20660805]

22. Juilliere Y, Suty-Selton C, Riant E, et al. Prescription of cardiovascular drugs in the French ODIN cohort of heart failure patients according to age and type of chronic heart failure. ARchives of Cardiovascular Disease. 2014; 107:21–32.

23. Krantz MJ, Ambardekar AV, Kaltenbach L, Hernandez AF, Heidenreich PA, Fonarow GC. Patterns and predictors of evidence-based medication continuation among hospitalized heart failure patients. The American journal of Cardiology. 2011; 107(12):1818–1823. [PubMed: 21482418]

24. Sato N, Kajimoto K, Asai K, et al. Acute decompensated heart failure syndromes (ATTEND) registry. A prospective observational multicenter cohort study: rationale, design, and preliminary data. American Heart Journal. 2010; 159:949–955. [PubMed: 20569705]

25. Scrutinio D, Passantino A, Ricci VA, Catanzaro R. Association between conformity with performance measures and 1-year postdischarge survival in patients with acute decompensated heart failure. American Journal of Medical Quality. 2013; 28(2):160–168. [PubMed: 22822168]

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26. Youn YJ, Yoo B, Lee J, et al. Treatment performance measures affect clinical outcomes in patients with acute systolic heart failure - a report from the Korean heart failure registry. Circulation Journal. 2012; 76:1151–1158. [PubMed: 22343195]
27. Kfoury AG, French TK, Horne BD, et al. Incremental survival benefit with adherence to standardized heart failure core measures: a performance evaluation study of 2958 patients. Journal of Cardiac Failure. 2008; 14(2):95–102. [PubMed: 18325454]
28. Calvin JE, Shanbhag S, Avery E, Kane J, Richardson D, Powell L. Adherence to evidence-based guidelines for heart failure in physicians and their patients: lessons from the heart failure adherence retention trial (HART). Congestive Heart Failure. 2012; 18:73–78. [PubMed: 22432552]
29. Athilingam P, Munro C, D'aoust R, Karch A, Chen L. Cognitive protection by angiotensin converting enzyme inhibitors in heart failure. International Journal of Nursing Science. 2012; 2(3): 14–22.
30. Sink KM, Leng X, Williamson J, et al. Angiotensin-converting enzyme inhibitors and cognitive decline in older adults with hypertension. Archives of Internal Medicine. 2009; 169(13):1195–1202. [PubMed: 19597068]
31. Torres A, Comin-Colet SR, Rizzo M, et al. Influence of chronic use of betablockers on cognitive function of chronic heart failure. European Journal of Heart Failure Supplements. 2008; 7(1):188.
32. Zuccala G, Onder G, Marzetti E, et al. Use of angiotensin-converting enzyme inhibitors and variations in cognitive performance among patients with heart failure. European Heart Journal. 2005; 26:226–233. [PubMed: 15618043]
33. Service ER. Measuring rurality: New definitions in 2003. United States Department of Agriculture. 2003
34. Robinson S, Moser D, Pelter MM, Nesbitt T, Paul SM, Dracup K. Assessing health literacy in heart failure patients. Journal of Cardiac Failure. 2011; 17(11):887–892. [PubMed: 22041324]
35. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. Journal of Chronic Disease. 1987; 40:373–383.
36. Borson S, Scanlan JM, Watanabe J, Tu S-P, Lessig M. Simplifying the detection of cognitive impairment: comparison of the Mini-Cog and Mini-Mental State Examination in a multiethnic sample. Journal of the American Geriatrics Society. 2005; 53:871–874. [PubMed: 15877567]
37. Borson S, Scanlan JM, Watanabe J, Tu S-P, Lessig M. Improving identification of cognitive impairment in primary care. International Journal of Geriatric Psychiatry. 2006; 21:349–355. [PubMed: 16534774]
38. Lessig M, Scanlan JM, Nazemi H, Borson S. Time that tells: critical clock-drawing errors for dementia screening. International Psychogeriatrics. 2008; 20(3):459–470. [PubMed: 17908348]
39. Kaufer DI, Williams CS, Braaten AJ, Zimmerman S, Sloane PD. Cognitive screening for dementia and mild cognitive impairment in assisted living: comparison of 3 tests. Journal of the American Medical Directors Association. 2008; 9(8):586–593. [PubMed: 19083293]
40. Patel A, Parikh R, Howell E, Hsich E. Mini-cog performance: a novel marker of risk among patients hospitalized for heart failure. Journal of the American College of Cardiology. 2014; 63(12 Supplement):A755.
41. Riegel B, Bennett JA, Davis A, et al. Cognitive Impairment in Heart Failure: Issues of Measurement and Etiology. American Journal of Critical Care. 2002; 11(6):520–529. [PubMed: 12425402]
42. Streenland NK, Auman CM, Patel PM, et al. Development of a rapid screening instrument for mild cognitive impairment and undiagnosed dementia. Journal of Alzheimer's Disease. 2008; 15:419–427.
43. Hoth K, Poppas A, Moser DJ, Paul RH, Cohen RA. Cardiac dysfunction and cognition in older adults with heart failure. Cognitive and Behavioral Neurology. 2008; 21(2):65–72. [PubMed: 18541980]
44. Zuccala G, Marzetti E, Cesari M, et al. Correlates of cognitive impairment among patients with heart failure: results of a multicenter survey. The American Journal of Medicine. 2005; 118:496–502. [PubMed: 15866252]

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45. Qui C, Winblad B, Marengoni A, Klarin I, Fastbom J, Fratiglioni L. Heart failure and risk of dementia and alzheimer disease: a population-based cohort study. Archives of Internal Medicine. 2006; 166:1003–1008. [PubMed: 16682574]

46. Anderson C, Teo K, Gao P, et al. Renin-angiotensin system blockade and cognitive function in patients at high risk of cardiovascular disease: analysis of data from the ONTARGET and TRANSCEND studies. Lancet Neurology. 2011; 10:43–53. [PubMed: 20980201]

47. Gliebus G, Lippa CF. The influence of beta-blockers on delayed memory function in people with cognitive impairment. American Journal of Alzheimer's Disease and Other Dementias. 2007; 22(1):57–61.

48. Bratzke LC, Pozehl BJ, Paul SM, Johnson JK. Neuropsychological patterns differ by type of left ventricular dysfunction in heart failure. Archives of Clinical Neuropsychology. 2013; 28(2):114–124. [PubMed: 23257366]

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What's New?

- Prescription of evidence-based heart failure medications does not contribute to cognitive impairment among individuals with heart failure, regardless of LV dysfunction type (i.e. HFpEF or HFrEF)
- Presence of cognitive impairment is not related to evidence-based heart failure medication dosage
- Comorbid burden contributes to cognitive impairment among individuals with HF

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Table 1

Comparison of Demographic Characteristics Based on Cognitive Status

Characteristic	Cognitive impairment (n = 207)	Cognitively intact (n = 405)	p
	Mean (SD)	Mean (SD)	
Age (years)	69 (13)	64 (13)	**<0.001**
LVEF (%)	38 (15)	40 (15)	0.155
BNP (pg/ml)	507 (1142)	363 (859)	0.090
Creatinine (mg/dl)	1.23 (0.700)	1.22 (0.563)	0.281
	Frequency (%)	Frequency (%)	
Gender			0.921
• Male	122 (59%)	237 (59%)	
• Female	85 (41%)	168 (41%)	
Education			**0.024**
• <HS	52 (25%)	65 (16%)	
• HS	94 (45%)	199 (49%)	
• >HS	61 (30%)	141 (35%)	
NYHA			0.054
• I	12 (6%)	52 (13%)	
• II	116 (56%)	216 (53%)	
• III	69 (33%)	121 (30%)	
• IV	10 (5%)	15 (4%)	
Charlson Comorbidity Index Score			**0.003**
• 1 – 2	56 (27%)	164 (41%)	
• 3 – 4	101 (49%)	151 (37%)	
• 5+	50 (24%)	90 (22%)	
Cause of HF			0.663
• Ischemic	107 (52%)	183 (45%)	
• Hypertension	47 (23%)	101 (25%)	
• Cardiomyopathy	37 (18%)	74 (18%)	
• Idiopathic	7 (3%)	18 (4%)	
• Other	9 (4%)	27 (8%)	

LVEF=left ventricular ejection fraction; BNP=brain natriuretic peptide; HS=high school; NYHA=New York Heart Association

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Table 2

Predictors of Cognitive Impairment among Rural HF Patients (n=611)

Variable	β	SE	p	OR	95% CI
Age	0.032	0.007	**0.000**	1.033	1.018, 1.048
Education	−0.271	0.124	**0.029**	0.762	0.598, 0.973
Charlson Comorbidity Index	0.260	0.118	**0.027**	1.297	1.030, 1.633
BB	0.242	0.229	0.290	1.274	0.814, 1.994
ACE Inhibitor	0.194	0.211	0.359	1.214	0.803, 1.835
ARB	0.187	0.255	0.464	1.206	0.731, 1.989
Diuretic	−0.045	0.246	0.854	0.956	0.591, 1.547

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Table 3

Comparison of Evidence-Based Medication Prescription Rates

Medication	Total Sample n=611	Cognitive Impairment n=206	Cognitively Intact n=405
BB	489 (80%)	38 (18%)	321 (79%)
ACE inhibitor	341 (56%)	92 (45%)	227 (56%)
ARB	116 (19%)	165 (80%)	75 (19%)
Diuretic	515 (84%)	31 (15%)	340 (84%)
Aldosterone Inhibitor	143 (23%)	53 (26%)	90 (22%)

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Table 4

Comparison of Cognitive Impairment and Medication Prescription Rates (n=206)

Medication	Medication prescribed (n)	Medication not prescribed (n)	χ^2	p
BB	38	168	0.450	0.502
ACE Inhibitor	92	114	0.070	0.791
ARB	165	41	0.170	0.680
Diuretic	31	175	0.103	0.748
Aldosterone Inhibitor	53	153	0.905	0.341