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Gender Differences in Cognitive Test Performance in Adults with Heart Failure

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Abstract

Background—Cognitive deficits are found in up to 73% of persons with heart failure (HF) and are associated with increased mortality and other poor clinical outcomes. It is known that women have better memory test performance than men in healthy samples, but gender differences in cognitive performance in the context of HF are not well understood and may have important clinical implications.

Objective—The objective of this study was to examine possible gender differences in cognitive function in a sample of individuals with HF (98.9% NYHA class II and III).

Methods—A total of 183 adults with HF (116 men and 67 women) completed a neuropsychological test battery as part of a larger project. Measures were chosen to assess functioning in attention/executive function and memory.

Results—After controlling for demographic and medical factors, MANCOVA revealed that men and women differed on memory test performance [λ = 0.90, F(4, 169) = 4.76, p = .001]. Post-hoc comparisons revealed females performed better on CVLT Learning, Short Recall, and Delayed Recall. No differences emerged on tests of attention/executive function [λ = 0.97, F(5, 168) = 0.96, p = .44].

Conclusions—In this sample of persons with HF, men exhibited poorer performance on memory measures than women. Future studies are needed to determine the underlying mechanisms for this pattern and its possible influence on daily function.

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Keywords

heart failure; cognitive function; gender characteristics

INTRODUCTION

Heart failure (HF) is a significant public health problem, as an estimated 5.1 million Americans are currently living with the condition and this prevalence is expected to increase an additional 46% by 2030 [1]. HF is associated with many adverse health outcomes, including functional decline, reduced quality of life [2], recurring hospitalization and increased mortality [3]. In addition to these health consequences, HF is an established risk factor for cognitive impairment [4], particularly in domains of memory, attention, and executive function [5, 6]. Cognitive deficits are found in up to 73% of HF patients [4, 7, 8] and are independent predictors of premature mortality, re-hospitalization, and functional decline [9, 10].

Much research has been devoted to elucidating gender differences in the etiology, presentation and prognosis of HF. Data suggest that men are more likely to develop HF, do so at a younger age [11], and have poorer prognosis [12]. However, women are more likely to exhibit reduced quality of life [13], depression [14], higher pain levels, and sleep difficulties [15]. Less is known about possible gender differences in neurocognitive outcomes in HF.

Results from studies in healthy populations and other cognitively declining samples suggest that gender differences may exist in the context of HF. In healthy cohorts, gender differences in cognitive function are commonly reported, with women outperforming men on verbal learning and memory tasks [16–19]. However, no differences are consistently found on measures of attention and executive functioning [18, 19]. Other work has found that women maintain this cognitive advantage in a cognitively declining sample with atherosclerosis [20].

Despite these findings, few studies have directly examined possible gender differences in cognitive function in persons with HF. In one study of persons with HF (ejection fraction = 28.2 ± 10.3), men exhibited poorer test performance in multiple domains, including memory, psychomotor speed and visuospatial recall - despite having less severe HF [6]. Such findings encourage further examination, particularly in persons with milder forms of HF (e.g. New York Heart Association class II and III). Based on the above study, we hypothesized HF would be associated with poorer cognitive function in men relative to women.

METHODS

Participants

The current sample was comprised of 183 adults (116 men and 67 women) with HF that were enrolled in a larger project examining neurocognitive outcomes in HF [21]. All participants were stable ambulatory patients receiving routine clinical care at Summa Health System in Akron, OH. To be eligible for the study, persons must have been between the ages of 50–85 years of age at the time of enrollment, English-speaking, and have a NYHA class between II and IV (98.9% NYHA class II and III). Exclusion criteria included history of neurological disorder (e.g., dementia, stroke), head injury with > 10 minutes loss of consciousness, presence of a severe psychiatric disorder (e.g. schizophrenia, bipolar disorder), substance abuse and/or dependence, and renal failure. See Table 1 for baseline demographic and clinical characteristics.

Measures

Cognitive function—Commonly-used neuropsychological measures were used to quantify cognitive test performance. These measures are well-established, have strong psychometric properties, and have been recommended for use in persons with cardiovascular disease [22]. Raw scores for each measure were used in the primary analyses and were categorized into one of two neuropsychological domains. Specific measured included:

Attention/Executive Function—Trail Making Test A [23] has individuals rapidly draw a line connecting numbered circles and completion time is used as a measure of complex visual scanning and psychomotor speed. Trail Making Test B [24] asks individuals to quickly connect alternating numbers and letters in ascending order and completion time is used as a measure of ability to shift and maintain cognitive set.

The Frontal Assessment Battery [25] (FAB) is a short measure consisting of six subtests which assess frontal mediated abilities. The Word and Color Word trials from the Stroop Color Word Test [26, 27] were administered. The Word trial has individuals rapidly read the names of colors printed in black ink. The Color Word trial asks participants to indicate the color of ink a word is written in, ignoring the actual word, which spells out a different color. The number of words read aloud in 45 seconds for each trial is used as a measure of selective attention and mental flexibility.

Memory—The California Verbal Learning Test-II (CVLT-II) requires participants learn, recall, and recognize a 16-item word list. Four indices from the CVLT-II were used to quantify memory, namely: Sum of Learning Trials 1–5, Short Delay Free Recall, Long Delay Free Recall, and Total Recognition Hits [28].

Physical fitness—The 2-minute step test (2MST) asks individuals to lift their knees above a marked target during a two minute period [29]. This measure of physical fitness was included as a covariate, as research indicates that fitness levels are independently associated with cognitive function in people with HF [30]. This fitness estimate has been found to correlate with standard treadmill stress testing in persons with HF [30].

Demographic characteristics—Medical and demographic characteristics were ascertained through a combination of self-report and medical record review.

Procedures

Participants were informed of the research study by staff at Summa Health System. Interested participants then provided consent to be contacted by a research assistant. The local Institutional Review Board (IRB) approved the study procedures and all participants provided written informed consent prior to initiation of any activities. During a single assessment, participants completed the 2MST and demographic and psychosocial self-report measures. Participants were also administered the neuropsychological test battery. The visit occurred at a time convenient for the participant, typically in mid-morning or early afternoon. Medical records were later examined to supplement self-report and corroborate all available information. All procedures were performed in a hospital setting by trained research assistants and under the supervision of a licensed clinical neuropsychologist.

Statistical Analyses—Statistical differences in demographic and medical conditions between men and women were examined using t-tests and chi-squares. Prior to primary analyses, assumptions for inferential statistics were examined and met, including separately by gender. MANCOVA was used to compare cognitive test performance, adjusting for any demographic and medical characteristics that differed between groups. Raw scores from each neuropsychological test were used in the analyses. To further clarify gender differences in cognitive test performance, raw scores from each cognitive test were transferred to *T*-scores using existing norms and used to calculate prevalence of cognitive impairment in the sample. Cognitive impairment on a specific test was defined as a *T*-score ≤ 35. Chi-square analyses compared the prevalence rates of impairment on a specific task within one of the primary cognitive domains (i.e. attention/executive function, memory) or any impaired test performance.

RESULTS

Demographic and Medical Differences between Men and Women

Women had lower educational attainment [t(181) = 3.09, p = .002], were less likely to have a history of smoking [χ^2 (1) = 5.79, p = .02], had higher ejection fraction [t(181) = 2.46, p = .02], and poorer estimated fitness levels [2MST; t(1) = 2.06, p = .04] than men. See Table 1. Women also trended toward a higher likelihood of hypertension [χ^2 (1) = 3.77, p = .05], but were less likely to have history of bypass or valve surgery [χ^2 (1) = 3.01, p = .08] or history of myocardial infarction [χ^2 (1) = 3.26, p = .07]. Given these findings, between-group comparisons for cognitive test performance were adjusted for age, education, ejection fraction, 2MST, hypertension, history of bypass/valve surgery, history of myocardial infarction, and history of smoking.

No Gender Differences in Attention/Executive Function

A MANCOVA was conducted on tests of attention/executive function while adjusting for age, education, ejection fraction, 2MST, hypertension, history of bypass/valve surgery, history of myocardial infarction, and history of smoking. In terms of covariates, a significant influence of age [λ = 0.86, F(5, 168) = 5.38, p<.001], education [λ = 0.90, F(5, 168) = 3.90, p = .002], hypertension [λ = 0.92, F(5, 168) = 2.90, p = .02], and 2MST [λ = 0.87, F(5, 168) = 5.20, p<.001] emerged. However, analyses found no effect for gender, such that men and women with HF did not differ on tests of attention/executive function [λ = 0.97, F(5, 168) = 0.96, p = .44]. See Table 2.

Gender Differences in Memory Performance

A MANCOVA was then conducted on tests of memory while adjusting for age, education, ejection fraction, 2MST, hypertension, history of bypass/valve surgery, history of myocardial infarction, and history of smoking. In terms of these covariates, a significant influence of age [λ = 0.85, F(4, 169) = 7333, p<.001] emerged. This analysis also found an effect for gender, such that men and women with HF differed on tests of memory [λ = 0.90, F(4, 169) = 4.76, p = .001]. See Table 2. Bonferroni-corrected post-hoc tests showed that women performed better than men on Sum of Trials 1–5 (F (1,172) = 18.10, p<.001) Short Delay Free Recall (F (1,172) = 9.80, p = .002), and Long Delay Free Recall (F (1,172) = 12.89, p<.001). No differences emerged for Total Recognition Hits (F (1,172) = 1.92, p = .17).

No Gender Differences in Prevalence of Cognitive Impairment

Analyses indicated that men and women with HF did not differ in prevalence rates of cognitive impairment in attention/executive function, memory, or any impaired test performance (p>.05 for all; See Table 3).

DISCUSSION

Past research demonstrated that gender differences in cognitive functioning exist in persons with moderate to severe HF [6]. The current study sought to examine whether a similar pattern is found in a sample of HF patients with predominantly NYHA class II and III. After adjusting for possible confounds, results showed that women performed better than men on multiple memory indices, though no differences emerged on measures of attention/executive function.

As hypothesized, women performed better than men on tasks of memory in this sample of adults with HF. Women exhibit better memory test performance than men in healthy older populations [16, 19, 31] and APOE4 carriers [32], suggesting the current findings may reflect this premorbid advantage. However, it is also possible that specific aspects of HF might contribute to gender differences in cognitive functioning. For example, men develop HF at a younger age [33] and the cognitive effects of some medical conditions (e.g. Type 2 diabetes, obesity, hypertension) are known to increase over time [34–36]. Even though men and women were generally similar in their *current* HF status (and statistical adjustments were employed for all analyses), it is possible that *historical* aspects of HF that vary by gender may also influence cognitive outcomes (i.e. age of onset/duration, lowest ejection fraction, severity and number of myocardial infarctions, smoking history, combination of comorbid conditions, etc.). It is also possible that HF leads to differential structural and functional brain changes in men and women. A series of projects from Woo and Kumar have revealed that HF is associated with abnormalities on neuroimaging, including greater atrophy (including structures like the hippocampus and caudate, reduced cortical thickness, and changes in mean diffusivity [37–40]. Though gender differences have not yet been directly examined through these studies, preliminary findings suggested this possibility [40–41]. Data from large, epidemiological studies will help clarify possible mechanisms for the observed gender differences in cognitive function and the reason they are limited to memory test performance.

Despite these group differences in performance, follow-up analyses found no differences in the prevalence of cognitive impairment (*T*-score < 35) within domains. These findings suggest that men and women with HF are both susceptible to memory dysfunction, but men experience more severe levels of impairment. As above, the exact mechanism for this pattern is unclear and may involve novel risk factors for cognitive impairment in persons with HF. If confirmed, such findings may help to account for the increased mortality risk in men with HF [11], as cognitive impairment in HF populations is linked to diminished self-care behaviors and performance in instrumental activities of daily living [9, 42, 43], which are known to exacerbate HF symptoms and prognosis [44, 45]. Given that research suggests even mild cognitive dysfunction may impact self-care in this population [46] and the high prevalence of cognitive impairment in both genders in this sample, routine cognitive screening in HF should be explored as a means of improving functional outcomes.

The current study is limited in several important ways. First, all data used for this study were cross-sectional and a prospective study utilizing a closely-matched control group is needed to elucidate the pattern of cognitive decline in male and female HF patients. Results in this study may also be affected by methodological and statistical limitations of the current study, including unequal sample of men and women and inclusion/exclusion criteria. For example, this study excluded individuals with history of known neurological disorder and lacked information on other factors (e.g., HF duration, HF type, timing and specific severity of cardiac events) that should be accounted for in future studies, as they may help to clarify the cognitive profile in this sample.

In summary, the current study found gender differences in cognitive function in persons with HF. Specifically, women had better performance than men on measures of memory, though no differences were found in prevalence of cognitive impairment. The mechanisms underlying these findings are unclear and warrant further investigation. Better understanding the patterns of cognitive impairment in men and women with HF may help clarify the etiology of gender differences in the presentation and prognosis of HF. Elucidating these relationships is essential to improving clinical treatment and outcomes for both genders.

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Table 1

Differences in Demographic and Medical Characteristics of Men and Women with Heart Failure

	Men	**Women**	**t**	**p**
Age, mean ± SD	68.89 ± 9.40	68.52 ± 8.36	0.26	.79
Education, years ± SD	13.86 ± 2.99	12.60 ± 1.97	3.09	.002
Ejection Fraction, percent ± SD	38.46 ± 13.81	43.82 ± 14.93	2.46	.02
2 minute step test, mean ± SD	63.78 ± 23.64	56.51 ± 21.92	2.06	.04
	Men	Women	χ^2	p
NYHA class II, percent	89.7%	80.6%		
NYHA class III, percent	9.5%	17.9%		
NYHA class IV, percent	.9%	1.5%	2.96[a]	.23[a]
Hypertension[b]	65.5%	79.1%	3.77	.05
Bypass or valve surgery[b]	37.9%	25.3%	3.01	.08
Type 2 diabetes[b]	36.2%	35.8%	0.01	.96
Myocardial Infarction[b]	62.9%	49.3%	3.26	.07
History of Smoking[b]	68.7%	50.7%	5.79	.02

Abbreviations: NYHA, New York Heart Association; SD, Standard Deviation

[a]Represents chi-square analysis of differences for all NYHA classes

[b]Percentiles represent presence of condition

Table 2

Examination of Differences in Cognitive Test Performance in Men and Women with Heart Failure using MANCOVA

Domain	Men Raw Score ± SD	Women Raw Score ± SD	F	p
Attention/Executive Function				
Trail Making Test A	41.41 ± 14.86	42.45 ± 18.71	0.33	.57
Trail Making Test B	119.59 ± 67.40	146.33 ± 87.73	1.35	.25
Frontal Assessment Battery	15.78 ± 2.37	15.54 ± 2.78	0.07	.79
Stroop Color Word Test – Word	82.38 ± 16.02	83.49 ± 15.81	1.36	.25
Stroop Color Word Test – Color Word	27.84 ± 9.77	26.88 ± 9.93	0.13	.72
Memory				
California Verbal Learning Test-II – Sum 1–5	37.15 ± 10.30	43.55 ± 10.72	18.10	<.001
California Verbal Learning Test-II – Short Free Recall	6.83 ± 3.05	8.27 ± 3.37	9.80	.002
California Verbal Learning Test-II – Long Free Recall	7.14 ± 3.18	8.93 ± 3.54	12.89	<.001
California Verbal Learning Test-II – Total Recognition Hits	13.28 ± 2.26	13.85 ± 2.32	1.92	.17

Abbreviations: SD, Standard Deviation

Table 3

No Gender Differences in Prevalence of Cognitive Impairment

	Men (n=116)	Women (n=67)	Total (n=183)	χ^2	p
Any Impairment[a]	55.17%	58.21%	56.28%	0.16	0.69
Memory Impairment[b]	24.14%	29.85%	26.23%	0.72	0.40
Attn/EF Impairment[c]	41.38%	47.76%	43%	0.70	0.40

Abbreviations: Attn, Attention; EF, Executive Function

[a] Any impairment: *t* score ≤ 35 on 1+ test

[b] Memory Impairment: *t* score ≤ 35 on 1+ memory test

[c] Attn/EF Impairment: *t* score ≤ 35 on 1+ attention/executive function test