Brief Report

The Prevalence of Cognitive Impairment Among Adults With Incident Heart Failure: The "Reasons for Geographic and Racial Differences in Stroke" (REGARDS) Study

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ABSTRACT

Background: Cognitive impairment (CI) is estimated to be present in 25%−80% of heart failure (HF) patients, but its prevalence at diagnosis is unclear. To improve our understanding of cognition in HF, we determined the prevalence of CI among adults with incident HF in the REGARDS study.

Methods and Results: REGARDS is a longitudinal cohort study of adults ≥45 years of age recruited in the years 2003−2007. Incident HF was expert adjudicated. Cognitive function was assessed with the Six-Item Screener. The prevalence of CI among those with incident HF was compared with the prevalence of CI among an age-, sex-, and race-matched cohort without HF. The 436 participants with incident HF had a mean age of 70.3 years (SD 8.9), 47% were female, and 39% were black. Old age, black race, female sex, less education, and anticoagulation use were associated with CI. The prevalence of CI among participants with incident HF (14.9% [95% CI 11.7%−18.6%]) was similar to the non-HF matched cohort (13.4% [11.6%−15.4%]; $P < .43$).

Conclusions: A total of 14.9% of the adults with incident HF had CI, suggesting that the majority of cognitive decline occurs after HF diagnosis. Increased awareness of CI among newly diagnosed patients and ways to mitigate it in the context of HF management are warranted. (*J Cardiac Fail 2019;25:130−136*)

Key Words: Heart failure, cognition, cohort study, hospitalization, prevalence.

Cognitive impairment (CI) is one of the most common comorbid conditions among adults with heart failure (HF)[1,2] and is associated with poor quality of life[3] and self-care[4] and increased morbidity and mortality.[5-7] Although previous studies agree that CI is highly prevalent in HF, prevalence estimates vary widely, ranging from 25% to 80%.[1,7,8] In addition, the underlying pathophysiology of CI and its trajectory in HF remain uncertain.[1,7]

Table 1. Baseline Characteristics of REGARDS Participants With Incident Heart Failure by Cognitive Status, n (%) or Mean ± SD

Characteristic	All Participants (n = 436)	No Cognitive Impairment (n = 371)	Cognitive Impairment (n = 65)	P Value
Prevalence of cognitive impairment: 14.9% (95% CI 11.7%−18.6%)				
Demographic characteristics				
Age, y	70.31 ± 8.98	69.81 ± 8.94	73.14 ± 8.73	.006*
Sex				.02*
Male	231 (53.0%)	188 (50.7%)	43 (66.2%)	
Female	205 (47.0%)	183 (49.3%)	22 (33.8%)	
Race				.14
White	264 (60.6%)	230 (62.0%)	34 (52.3%)	
Black	172 (39.4%)	141 (38.0%)	31 (47.7%)	
Education				.03*
Less than high school	78 (17.9%)	60 (16.2%)	18 (27.7%)	
High school or higher	358 (82.1%)	311 (83.8%)	47 (72.3%)	
Income				.87
<$35,000	234 (53.7%)	202 (54.4%)	32 (49.2%)	
≥$35,000	147 (33.7%)	126 (34.0%)	21 (32.3%)	
Region of residence				.79
Belt	166 (38.1%)	139 (37.5%)	27 (41.5%)	
Buckle	94 (21.6%)	80 (21.6%)	14 (21.5%)	
Nonbelt	176 (40.4%)	152 (41.0%)	24 (36.9%)	
Clinical characteristics				
Heart failure type				.76
HFrEF (<50%)	198 (45.4%)	168 (45.3%)	30 (46.2%)	
HfpEF (≥50%)	178 (40.8%)	153 (41.2%)	25 (38.5%)	
Coronary heart disease	139 (31.9%)	116 (31.3%)	23 (35.4%)	.51
Diabetes mellitus	168 (38.5%)	142 (38.3%)	26 (40.0%)	.93
Hypertension	339 (77.8%)	288 (77.6%)	51 (78.5%)	.91
Stroke	50 (11.5%)	41 (11.1%)	9 (13.8%)	.52
Atrial fibrillation	18 (4.1%)	15 (4.0%)	3 (4.6%)	.82
Chronic kidney disease	113 (25.9%)	93 (25.1%)	20 (30.8%)	.34
Depressive symptoms	60 (13.8%)	55 (14.8%)	5 (7.7%)	.12
General health				.68
Poor	23 (5.3%)	20 (5.4%)	3 (4.6%)	
Fair	112 (25.7%)	98 (26.4%)	14 (21.5%)	
Good	161 (36.9%)	136 (36.7%)	25 (38.5%)	
Very good	102 (23.4%)	83 (22.4%)	19 (29.2%)	
Excellent	38 (8.7%)	34 (9.2%)	4 (6.2%)	
Body mass index (kg/m^2)	30.2 ± 6.6	30.3 ± 6.7	29.8 ± 6.5	.56
Waist circumference (cm)	102.2 ± 16.7	101.91 ± 16.11	103.87 ± 19.8	.39
Systolic blood pressure (mm Hg), mean, (SD)	134.4 ± 19.0	133.9 ± 18.8	137.4 ± 19.5	.17
Total cholesterol (mg/dL)	184.8 ± 41.9	186.0 ± 41.9	177.9 ± 42.0	.15
HDL cholesterol (mg/dL)	47.1 ± 14.2	47.4 ± 14.4	45.8 ± 13.0	.43
Health behaviors				
Smoking history				.88
Never	182 (41.7%)	157 (42.3%)	25 (38.5%)	
Current	66 (15.1%)	56 (15.1%)	10 (15.4%)	
Former	186 (42.7%)	157 (42.3%)	29 (44.6%)	
Alcohol use				.84
Never	143 (32.8%)	122 (32.9%)	21 (32.3%)	
Current	191 (43.8%)	164 (44.2%)	27 (41.5%)	
Past	102 (23.4%)	85 (22.9%)	17 (26.2%)	
Medication use				
Antiplatelet[†]	239 (54.8%)	204 (55.0%)	35 (53.8%)	.86
Anticoagulation	17 (3.9%)	11 (3.0%)	6 (9.2%)	.02*
Statin	170 (39.0%)	147 (39.6%)	23 (35.4%)	.52
Antihypertensive	298 (68.3%)	255 (68.7%)	43 (66.2%)	.92
Insulin	52 (11.9%)	45 (12.1%)	7 (10.8%)	.75

Missing values included: income (n = 55), heart failure type (n = 60), coronary heart disease (n = 7), diabetes (n = 11), hypertension (n = 11), stroke(n = 1), atrial fibrillation (n = 3), chronic kidney disease (n = 15), depressive symptoms (n = 2), waist circumference (n = 3), systolic blood pressure (n = 1), total cholesterol (n = 15), HDL cholesterol (n = 17), smoking status (n = 2), aspirin (n = 1), antihypertensives (n = 10). HDL, high-density lipoprotein.
*Significant at $P < .05$.
[†]Includes aspirin and clopidogrel.

Some uncertainty could be attributed to a lack of understanding of the prevalence of CI among adults with newly diagnosed disease. For example, if CI is prevalent at disease onset, then providers need to screen for cognitive deficits early and advise patients accordingly. If, however, adults with incident HF have cognitive profiles similar to adults without HF, then more attention ought to be focused on mitigating cognitive decline among those with existing HF. Yet, few studies have investigated the prevalence of CI in incident HF.

To fill this gap, we determined the prevalence and correlates of CI among adults with incident HF in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, a national prospective cohort of 30,239 community-dwelling adults in the US aged ≥45 years.

Methods

REGARDS

Details of the REGARDS study have been described previously.[9] Briefly, REGARDS is a cohort study that evaluates racial and geographic disparities in cardiovascular disease. Recruitment occurred from 2003 to 2007. Blacks and residents of the "Stroke Belt" were oversampled by design.[9] Participants completed a telephone interview followed by an in-home examination. At 6-month intervals, participants are asked about hospitalizations and health status. The study was approved by the Institutional Review Boards of all participating institutions. All participants provided written informed consents.

Study Population. Adults with incident HF who underwent a cognitive assessment 1–18 months before their incident HF diagnosis were included. One month was selected as a cutoff because individuals may experience cognitive changes as HF worsens.

Incident Heart Failure. An incident HF diagnosis was defined as the participant's first hospitalization for HF without a history of HF. We included hospitalizations from 2004 to 2016. HF hospitalizations were adjudicated by 2 experts, and disagreements were resolved by committee with $\kappa \geq 0.80$.[10] Because hospitalizations for cardiac events can affect cognition, participants with hospitalizations for other cardiac etiologies known to REGARDS before their incident HF hospitalization were excluded.

Cognition. REGARDS participants undergo global cognitive function assessments annually with the Six-Item Screener (SIS), a validated measure that assesses 3-item recall and orientation to year, month, and day of the week.[11] The SIS, which can be administered easily by telephone, has a sensitivity of 74.2%–84.0% and specificity of 80.2%–85.3% in community and clinical samples for a diagnosis of cognitive impairment.[11] Scores for the SIS range from 0 to 6, and each correctly answered question receives 1 point.[12–15] Similarly to other studies, scores were dichotomized: scores of 5 and 6 were normal, and scores of ≤4 connoted CI.

Participant Characteristics. Demographic data included age, sex, race, education, annual household income, and region of residence. Clinical data included history of coronary heart disease (CHD) by self-report or electrocardiogram (ECG); diabetes, defined as fasting blood glucose ≥126 mL/dL, nonfasting glucose >200 mL/dL, or oral hypoglycemic or insulin use; history of hypertension, defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure of ≥90 mm Hg, or medication use for hypertension; history of atrial fibrillation by self-report or ECG; history of self-reported stroke; chronic kidney disease, defined as estimated glomerular filtration rate (eGFR) <60 mL·min^{-1}·1.73^{-2}; body mass index; cigarette smoking; and high–density lipoprotein and total cholesterol. Left ventricular ejection fraction was abstracted from the most recent echocardiogram. Depressive symptoms were assessed by means of the 4-item Center for Epidemiological Studies—Depression scale.[16] Medication use at baseline was ascertained.

Healthy Comparison Population. To contextualize our findings, we compared the prevalence of CI among adults with incident HF with that of an age-, sex-, and race-matched group of participants without HF. We matched participants (3:1 ratio) who did not have an adjudicated HF hospitalization or another adjudicated cardiovascular event in REGARDS and were similar in age (±5 years), sex, race, and year of SIS, to each HF participant. Matching was performed with SAS macro gmatch, which uses a "greedy" algorithm approach.[17,18]

Statistical Analysis. The prevalences of CI were determined among participants with incident HF and among the

Table 2. Association Between Baseline Characteristics of REGARDS Participants With Incident Heart Failure and the Odds of Cognitive Impairment, Odds Ratio (95% Confidence Interval)

Characteristic	Model 1 (Age Adjusted)	Model 2 (Fully Adjusted)
Age	1.04 (1.01–1.08)	1.05 (1.02–1.09)
Female	0.54 (0.31–0.94)	0.48 (0.27–0.85)
Black	1.88 (1.08–3.28)	1.83 (1.01–3.32)
Less than high school education	1.89 (1.02–3.51)	1.79 (0.92–3.46)
Region of residence		
Belt	reference	reference
Buckle	0.89 (0.44–1.81)	0.85 (0.41–1.76)
Nonbelt	0.72 (0.39–1.32)	0.62 (0.33–1.16)
Systolic blood pressure	1.01 (1.00–1.02)	1.01 (0.99–1.02)
Anticoagulation use	3.01 (1.05–8.63)	3.00 (1.00–8.99)

matched control group. First, we examined differences in participant characteristics according to CI. Next, we performed multivariable logistic regression to examine associations between participant characteristics and CI among those with incident HF. Multiple imputation with chained equations was used to account for missing data. Analyses were conducted with the use of Stata, and statistical significance for all analyses was set as $P < .05$ (2 sided).

Table 3. Baseline Characteristics of a Matched Cohort of REGARDS Participants Without Heart Failure, n (%) or Mean ± SD

Characteristic	All Participants (n = 1307)	Cognitively Intact (n = 1132)	Cognitively Impaired (n = 175)	P Value
Prevalence of cognitive impairment: 13.4% (95% CI 11.6–15.4%)				
Demographic characteristics				
Age, y	70.28 ± 8.94	69.56 ± 8.90	74.99 ± 7.67	<.001*
Sex				<.001*
Male	692 (52.9%)	575 (50.8%)	117 (66.9%)	
Female	615 (47.1%)	557 (49.2%)	58 (33.1%)	
Race				<.001*
White	791 (60.5%)	707 (62.5%)	84 (48.0%)	
Black	516 (39.5%)	425 (37.5%)	91 (52.0%)	
Education				<.001*
< High school	200 (15.3%)	145 (12.8%)	55 (31.4%)	
≥ High school	1106 (84.6%)	987 (87.2%)	119 (68.0%)	
Income				<.001*
<$35,000	619 (47.4%)	520 (45.9%)	99 (56.6%)	
≥$35,000	482 (36.9%)	439 (38.8%)	43 (24.6%)	
Region of residence				.03*
Belt	436 (33.4%)	372 (32.9%)	64 (36.6%)	
Buckle	303 (23.2%)	276 (24.4%)	27 (15.4%)	
Nonbelt	568 (43.5%)	484 (42.8%)	84 (48.0%)	
Clinical characteristics				
Heart disease	262 (20.0%)	212 (18.7%)	50 (28.6%)	.002*
Diabetes mellitus	261 (20.0%)	219 (19.3%)	42 (24.0%)	.14
Hypertension	817 (62.5%)	705 (62.3%)	112 (64.0%)	.68
Stroke	92 (7.0%)	75 (6.6%)	17 (9.7%)	.14
Atrial fibrillation	50 (3.8%)	42 (3.7%)	8 (4.6%)	.59
Chronic kidney disease	200 (15.3%)	154 (13.6%)	46 (26.3%)	<.001*
Depressive symptoms	139 (10.6%)	113 (10.0%)	26 (14.9%)	.05*
General health				.35
Poor	34 (2.6%)	29 (2.6%)	5 (2.9%)	
Fair	192 (14.7%)	158 (14.0%)	34 (19.4%)	
Good	462 (35.3%)	404 (35.7%)	58 (33.1%)	
Very good	417 (31.9%)	366 (32.3%)	51 (29.1%)	
Excellent	197 (15.1%)	174 (15.4%)	23 (13.1%)	
Body mass index (kg/m^2)	28.4 ± 5.4	28.5 ± 5.4	27.5 ± 4.9	.02*
Waist circumference (cm)	95.6 ± 13.9	95.5 ± 14.2	96.4 ± 12.7	.41
Systolic blood pressure (mm Hg)	129.7 ± 17.1	129.4 ± 17.1	131.9 ± 17.3	.06
Total cholesterol (mg/dL)	189.9 ± 40.4	190.7 ± 40.4	185.2 ± 40.2	.11
HDL cholesterol (mg/dL)	51.7 ± 16.7	52.2 ± 16.7	48.6 ± 16.4	.01*
Health behaviors				
Smoking history				.26
Never	568 (43.5%)	487 (43.0%)	81 (46.3%)	
Current	161 (12.3%)	146 (12.9%)	15 (8.6%)	
Former	566 (43.3%)	489 (43.2%)	77 (44.0%)	
Alcohol use				.02*
Never	405 (31.0%)	338 (29.9%)	67 (38.3%)	
Current	639 (48.9%)	570 (50.4%)	69 (39.4%)	
Former	263 (20.1%)	224 (19.8%)	39 (22.3%)	
Medication use				
Antiplatelet[†]	615 (47.1%)	537 (47.4%)	78 (44.6%)	.48
Anticoagulation	41 (3.1%)	34 (3.0%)	7 (4.0%)	.48
Statin	429 (32.8%)	367 (32.4%)	62 (35.4%)	.43
Antihypertensive	709 (54.2%)	616 (54.4%)	93 (53.1%)	.82
Insulin	33 (2.5%)	29 (2.6%)	4 (2.3%)	.83

Missing values included: education (n = 1), income (n = 206), coronary heart disease (n = 26), diabetes (n = 44), hypertension (n = 2), stroke (n = 3), atrial fibrillation (n = 18), chronic kidney disease (n = 52), depressive symptoms (n = 14), waist circumference (n = 6), systolic blood pressure (n = 2), total cholesterol (n = 58), HDL cholesterol (n = 58), smoking status (n = 12), aspirin (n = 2), antihypertensives (n = 37). HDL, high-density lipoprotein.
*Significant at $P < .05$.
[†]Includes aspirin and clopidogrel.

Results

Cognitive Impairment in Incident Heart Failure

A total of 539 participants were hospitalized for incident HF (Supplemental Fig. 1). Among them, 103 lacked an SIS, leaving 436 in the final analytic cohort. Of note, there were no clinical differences between this cohort and the 103 who were excluded.

Overall participants had a mean age of 70 (SD 8.9) years, 53.0% were male, 60.6% were white, the majority (82.1%) had at least a high school education, 77.8% had hypertension, 38.5% had diabetes, and 31.9% had CHD (Table 1). The prevalence of CI was 14.9% (95% confidence interval [CI] 11.7%−18.6%). Participants with CI were older, male, and less educated than those without CI. The majority of clinical characteristics did not differ by CI.

Among participants with incident HF, older age (1.04 [1.01−1.08]), black race (1.88 [1.08−3.28]), less education (1.89 [1.02−3.51]), higher SBP (1.01 [1.00−1.02]), and anticoagulant use (3.01 [1.05−8.63]) were associated with higher odds of CI, whereas female sex (0.54 [0.31−0.94]) was associated with lower odds of CI in an age-adjusted model (Table 2). In a fully adjusted model, age, sex, race, and anticoagulant use remained independently associated with CI.

Cognitive Impairment in Healthy Comparison Population

A total of 1,307 participants composed the healthy comparison population (Supplemental Fig. 2). Participants with CI were older, male, black, and with less education and income than those without CI (Table 3). Again, hypertension (62.5%), CHD (20%), and diabetes (20%) were prevalent. The overall prevalence of CI was 13.4% (11.6%−15.4%), which did not differ from the incident HF cohort ($P < .43$).

Discussion

Overall, 14.9% of adults with incident HF had CI, indicating that health care providers should consider assessing cognition at the time of HF diagnosis. Because the prevalence of CI among adults with existing HF ranges from 25% to 80%,[1,19] our results, alongside 2 recent studies in the Cardiovascular Health Study,[20,21] suggest that CI may develop during the course of the disease itself, rather than at the outset or due to CHD risk factors alone.[7,22]

Previous studies have attributed cognitive decline in HF to disease duration and severity.[23] Underlying mechanisms include cerebral hypoperfusion, multiple cardiogenic emboli, and impaired microcirculation.[1,23−26] Thus, among newly diagnosed HF patients, in addition to mitigating CHD risk factors, increased attention to interventions and medications that have the ability to affect these underlying processes may be most important to preserving cognitive function.[7]

Similarly to other studies,[27,28] we found older age, black race, and less education to be associated with CI, indicating that certain patient subgroups may require targeting at diagnosis. Interestingly, many clinical characteristics known to be associated with CI in HF were not associated with CI in incident HF. This may be due to our relatively small sample size and because the severity of some factors may be less at HF onset. In addition, index event bias may support these unanticipated observations.[29]

The prevalence of CI (13.4%) among a matched subcohort without HF did not differ significantly from the incident HF cohort and was similar to that among other populations of similar age and comorbidity status.[30,31] This finding supports our main finding, but also speaks to the accumulating evidence that has shown CHD and CHD risk factors to be associated with the development of CI.[15,30−33]

Strengths of our study include a geographically and racially diverse cohort, expert-adjudicated outcomes, and the measurement of cognition before an incident HF hospitalization, which minimizes the bias of clinical deterioration on cognition. Limitations include that cognition was assessed with the use of 1 screener; although the SIS is brief, reliable, and validated against the Mini Mental Status Examination,[11] it is less sensitive for the detection of mild CI.[34−36] In addition, we did not study other cognitive domains that are relevant to self-care.[34,36] Finally, incident HF diagnoses made in the ambulatory setting were not included, which limits the generalizability.[37]

Conclusion

A total of 14.9% of adults hospitalized for incident HF had CI in a range consistent with varying levels of CHD risk in a similarly aged group of adults. The majority of the cognitive decline previously reported in HF may occur over the course of the disease rather than before presentation. Increased awareness of the prevalence of CI among newly diagnosed HF patients and ways to mitigate cognitive decline in the context of HF management are warranted.

Acknowledgments

Disclosures

Previous Presentation

This study was presented at the American Heart Association Epidemiology/Lifestyle Meeting, March 21, 2018, New Orleans, Louisiana.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2018.12.006.

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