Usefulness of Cognitive Dysfunction in Heart Failure to Predict Cardiovascular Risk at 180 Days

Jill M. Gelow, MDa,*, James O. Mudd, MDa, Christopher V. Chien, MDa, and Christopher S. Lee, PhDb

Cognitive dysfunction is common in patients with heart failure (HF). Despite the high prevalence and the adverse associations of cognitive dysfunction in HF, the prognostic implications remain poorly understood. We sought to determine the influence of cognitive dysfunction, identified using the Montreal Cognitive Assessment (MoCA), on 180-day cardiovascular events. We analyzed data on 246 participants in an observational cohort study of adults with HF. The interview-format MoCA was administered to all participants. Time to first cardiovascular event was assessed as a cumulative end point during the 180 days after enrollment. Cox proportional hazards model was used for analysis of time to first event. The MoCA score was <26 for 91 patients (37%). Patients with a MoCA score <26 were more likely to have a cardiovascular event at 180 days. MoCA score <26 remained an independent predictor of cardiovascular event risk at 180 days when adjusted for the Seattle Heart Failure Model Score and the Charlson comorbidity index (hazard ratio 1.7, 95% confidence interval 1.1 to 2.6, p = 0.03). In conclusion, in patients with HF, cognitive dysfunction identified with a MoCA score of <26 is associated with increased risk of cardiovascular events at 180 days. © 2015 Elsevier Inc. All rights reserved. (Am J Cardiol 2015;115:778–782)

More than 650,000 patients are diagnosed with heart failure (HF) each year in the United States. Despite advances in medical therapy and device technology over the decades, about 50% of patients with HF will die within 5 years of their diagnosis.1,2 As many as half of the 5 million patients living with HF in the United States experience cognitive dysfunction.3,4 When identified in patients with HF, cognitive dysfunction is associated with increased risk of hospitalization, progressive physical disability, and higher mortality rate.5,6 Despite the high prevalence and the adverse associations of cognitive dysfunction in HF, the prognostic implications remain poorly understood. We sought to determine the influence of cognitive dysfunction, identified using the Montreal Cognitive Assessment (MoCA), on 180-day cardiovascular events and to identify subsets of MoCA items that are associated with cardiovascular risk.

Methods

We analyzed data on 246 participants in an observational cohort study of symptoms in adults with HF. All patients were recruited from 2010 to 2013 through a single HF outpatient clinic in the Pacific Northwest. Participants were approached for study participation immediately after an HF clinic visit. Participants were aged ≥21 years with the ability to read and understand English at a fifth-grade level and were able to provide informed consent. All patients had symptomatic (New York Heart Association functional classes II to IV) HF and were either on optimal HF therapy or undergoing optimization of medical therapy by a treating HF cardiologist. Patients were ineligible for inclusion in the study if they had a diagnosis of cognitive dysfunction in the medical record, had a major uncorrected visual impairment, or were unable to complete the study requirements.

Written informed consent and Health Insurance Portability and Accountability Act authorization were obtained from all participants by study staff not directly involved in patient care. The study was reviewed and approved by the Institutional Review Board at Oregon Health and Science University. There was a 3% refusal rate for study participation and a 94% completion rate.

Sociodemographic characteristics were assessed using questionnaire. An HF cardiologist determined each participant’s NYHA functional class immediately before enrollment. Clinical and treatment characteristics were collected during an in-depth electronic medical record (EMR) review. Co-morbidities were assessed with the Charlson Comorbidity Index. A list of 17 co-morbid diseases were evaluated during an in-depth electronic medical record (EMR) review. Co-morbidities were assessed with the Charlson Comorbidity Index. A list of 17 co-morbid diseases were evaluated and weighted, with possible scores ranging from 0 to 30. Greater Charlson comorbidity index scores indicate greater risk of mortality.7 Seattle Heart Failure Scores were calculated for each participant using available clinical data. The Seattle Heart Failure Model is a commonly used HF risk prediction tool that uses routinely available clinical information to estimate 1- and 5-year survival.8 Depression was measured with the 9-item Patient Health Questionnaire (PHQ9). The PHQ9 has an 88% sensitivity and specificity for major depression using a cut-off score of ≥10.9

Cognitive function was assessed using the MoCA. The MoCA is a 10-minute cognitive tool designed for use by

*Corresponding author: Tel: (503) 494-8750; fax: (503) 494-8550.
E-mail address: gelowj@ohsu.edu (J.M. Gelow).
The MoCA assesses 6 cognitive domains: visual-spatial ability, executive function, language, short-term memory, orientation, and attention, and working memory and concentration. The cognitive domains defined in this study and the MoCA tasks comprising each domain are provided in Table 1.

Time to first all-cause cardiovascular event (mortality, hospitalization, and emergency room visit) was assessed as a cumulative end point during the 180 days after enrollment. Clinical events and associated dates were extracted from the EMR and/or assessed by contacting participants by telephone. A second reviewer independently validated all clinical events, and 100% consensus was reached that the events were attributable to cardiovascular causes.

Means and standard deviations and proportions were used to describe the sample. Cox proportional hazards model was used for analysis of time to first event. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated to quantify the influence of the overall MoCA score and individual MoCA domains on 180-day event risk. The proportional hazards assumption was justified on the basis of Schoenfeld residuals. Model fit was assessed using the overall model chi-square test and by calculating Harrell’s C statistic. The influence of the overall MoCA score and individual MoCA domains on 180-day event-free survival was adjusted for the Seattle Heart Failure Score and the Charlson comorbidity index. Multiple other factors including body mass index, moderate or severe depression, and education were considered in Cox model but did not improve the model fit or remain independently associated with cardiovascular events when the Seattle Heart Failure Score and Charlson comorbidity index were included. All analyses were performed with Stata IC 13.0 (Stata Corp, College Station, Texas).

Results

The baseline characteristics of the study population are described in Table 2.

The mean MoCA score was 25.9 ± 2.6. Additional information regarding MoCA scores including scores for the individual MoCA domains is provided in Table 3. With more than 35,000 follow-up days (mean 145.9 ± 60.8 days), the cardiovascular event risk was 45.6%. At 180 days, 163 patients were alive without cardiovascular events and 6 patients were lost to follow-up. There were 4 deaths at 180 days, 14 emergency room visits for cardiovascular causes, and 59 cardiovascular hospitalizations. Patients with a MoCA score <26 were more likely to have a cardiovascular event at 180 days (Figure 1). MoCA score <26 remained an independent predictor of cardiovascular event risk at 180 days when adjusted for the Seattle Heart Failure Score and the Charlson comorbidity index (HR 1.7, 95% CI 1.1 to 2.6, p = 0.03, Harrell’s C = 0.65).

Of the 6 MoCA domains, the executive domain was most strongly associated with cardiovascular risk at 180 days. The executive domain score was nearly as predictive as total MoCA score for 180 cardiovascular events. Missing only 1 point of 4 possible on the MoCA executive domain was associated with increased 180-day cardiovascular event risk (Figure 2). The MoCA executive domain score remained independently associated with 180-day cardiovascular events after adjustment for Seattle Heart Failure Score and the Charlson comorbidity index (HR 1.6, 95% CI 1.02 to 2.6, p = 0.04, Harrell’s C = 0.66).

Discussion

Cognitive dysfunction is increasingly recognized as an important determinant of morbidity in patients with HF. Understanding cognitive dysfunction in the population with HF is challenging in part because HF is a heterogeneous clinical syndrome. Identifying uniform groups of patients with HF and controlling for differences among patients with HF is difficult. In addition, the risk of developing of cognitive dysfunction in HF is likely multifactorial. Hypoperfusion is postulated to contribute to cognitive dysfunction in patients with HF. Age, previous cardiopulmonary bypass, cardiovascular risk factors, vascular disease and stroke, chronic kidney disease and anemia, decreased physical activity, obesity, depression, and genetic risk factors, such as apolipoprotein E4, may also contribute to cognitive dysfunction in HF. Furthermore, there is no consensus in the studies regarding the definition of, or method used to identify, cognitive dysfunction in HF. The cumbersome method used in many research studies cannot readily be applied in HF clinical practice.

Table 1

<table>
<thead>
<tr>
<th>Cognitive Domain (Total points)</th>
<th>MoCA Tasks Included (Individual points assigned)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual-spatial ability (4 points)</td>
<td>Copy Cube (1 point)</td>
</tr>
<tr>
<td></td>
<td>Draw Clock (3 points)</td>
</tr>
<tr>
<td>Executive function (4 points)</td>
<td>Trail making (1 point)</td>
</tr>
<tr>
<td></td>
<td>Phonetic fluency (1 point)</td>
</tr>
<tr>
<td>Short-term memory (5 points)</td>
<td>Delayed recall at 5 minutes (5 points)</td>
</tr>
<tr>
<td>Language (5 points)</td>
<td>Naming animals (3 points)</td>
</tr>
<tr>
<td></td>
<td>Sentences repeated (2 points)</td>
</tr>
<tr>
<td></td>
<td>Phonetic fluency (1 point)</td>
</tr>
<tr>
<td>Orientation (6 points)</td>
<td>Date (1 point)</td>
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<tr>
<td></td>
<td>Month (1 point)</td>
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<td>Year (1 point)</td>
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<td></td>
<td>Place (1 point)</td>
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<tr>
<td></td>
<td>City (1 point)</td>
</tr>
<tr>
<td>Attention, working memory and concentration (6 points)</td>
<td>Tapping (1 point)</td>
</tr>
<tr>
<td></td>
<td>Serial subtraction (3 points)</td>
</tr>
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<td></td>
<td>Forward/backward numbers (2 points)</td>
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When it is identified, the implications of cognitive dysfunction are significant. We have previously shown that the presence of even mild cognitive dysfunction in patients with HF was associated with poor self-care maintenance (the ability of patients to adhere to medications, diet, and follow-up appointments) and management (the ability of patients to evaluate and respond to HF symptoms when they occur). Inability to engage in self-care is a well-known risk factor for hospital admission in patients with HF.

The presence of cognitive dysfunction in patients with HF has been associated with increased risk of morbidity and mortality. Pulignano et al prospectively followed 190 stable
outpatients aged 70 years with at least 1 previous admission for HF requiring intravenous diuretics, inotropes, or vaso- dilator therapies. Cognitive function was measured with age and education corrected Folstein Mini-Mental State examination (MMSE). In a multivariate analysis, moderate or severe cognitive impairment identified as an MMSE score <24 was associated with increased risk of hospitalization for worsening HF and the combination of all-cause mortality and HF hospitalizations. Zuccala et al identified 1,113 patients with a mean age of 78 years admitted to the hospital for HF. Cognitive dysfunction, assessed using the Hodkinson Abbreviated Mental Test, was associated with increased inhospital and 1-year mortality. In this study, we have shown that cognitive dysfunction is prevalent in a younger population with HF, largely because of nonischemic cardiomyopathy, with a 5-year predicted survival of 32% using the Seattle Heart Failure Score and relatively few co-morbid diseases. In this population, the presence of mild cognitive dysfunction, identified with a MoCA score of <26, is predictive of cardiovascular risk events even over a short follow-up duration of 180 days. Pertinent for the clinician with limited time, a subset of the MoCA focused on evaluation of the executive domain can be used to identify patients with mild and often subclinical cognitive dysfunction at increased risk for future events.

Although there are inherent limitations to an observational study, we had a low refusals rate and a high study completion rate. Our study population comprised patients referred to a tertiary care advanced HF clinic, which may limit generalization to other patient populations. We chose the MoCA as our screening instrument for cognitive dysfunction because of its ease of use and validation in populations with cardiovascular disease. Using multiple measures of cognitive dysfunction could have improved our ability to detect cognitive dysfunction. We did not measure cognitive function over time and therefore cannot comment on how changes in cognition over the study period may impact cardiovascular risk.

Disclosures

The authors have no conflicts of interest to report.


