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Care of Patients With Cardiovascular Disorders: Heart Failure

## Performance of the Automated Neuropsychological Assessment Metrics (ANAM) in detecting cognitive impairment in heart failure patients

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#### ABSTRACT

Objective:Evaluate capacity of the Automated Neuropsychological Assessment Metrics (ANAM) to detectcognitive impairment (CI) in heart failure (HF) patients.Background: CI is a key prognostic marker in HF. Though the most widely used cognitive screen in HF, theMini-Mental State Examination (MMSE) is insufficiently sensitive. The ANAM has demonstrated sensitivity to cognitive domains affected by HF, but has not been assessed in this population.Methods:Investigators administered the ANAM and MMSE to 57 HF patients, compared against a composite model of cognitive function.Results:ANAM efficiency (p < .05) and accuracy scores (p < .001) successfully differentiated CI and non-CI. ANAM efficiency and accuracy scores classified 97.7% and 93.0% of non-CI patients, and 14.3% and 21.4% with CI, respectively.

*Conclusions:* The ANAM is more effective than the MMSE for detecting CI, but further research is needed to develop a more optimal cognitive screen for routine use in HF patients.

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### Introduction

Over five million Americans suffer from congestive heart failure (HF), and an additional three million are projected to have HF by 2030.<sup>1.2</sup> HF results in reduced cerebral blood perfusion leading to gray matter loss, and is associated with mild cognitive impairment (CI) and difficulties with processing and executing demanding self-care regimens.<sup>3</sup> HF patients show two to four times the risk of CI compared to the general population and approximately a quarter of HF patients exhibit deficits in at least three cognitive domains.<sup>4–6</sup> Approximately 25–80% of patients experience cognitive deficits in at least a single domain.<sup>78</sup>

The most common domains of CI in HF are memory, attention, learning, psychomotor speed, language, and executive function; deficits in these domains impede self-care such as adherence to dietary and medication regimens.<sup>6–9</sup> Patients' decreased ability to carry out appropriate self-care due to CI leads to unsuccessful HF management, which is associated with increased mortality and disability, impaired quality of life, greater need for hospitalization, and higher health care costs.<sup>7,10,11</sup> Thus, CI is an essential prognostic marker in elderly HF patients.<sup>12</sup>

Although the prevalence and effects of CI have implications for HF management and outcomes, cognitive screening is not routinely performed in this population, and no sufficiently sensitive neuropsychological test is currently accepted for widespread use to screen for CI in HF.<sup>4,13</sup> Previous studies of HF and cognition commonly utilize the 30-point Mini-Mental State Examination (MMSE)<sup>14</sup>—which assesses orientation, registration, attention, language and comprehension, calculation, and immediate recall. Classification of CI in these studies is commonly based on a total



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MMSE score <24.<sup>15–19</sup> According to a review of screening instruments that are currently used to evaluate for CI in patients with HF, the MMSE has been the most frequently used neuropsy-chological test in this population, surpassing use of the Montreal Cognitive Assessment (MoCA), Six Item Screener, Abbreviated Mental Test (AMT), Clock Drawing Test (CDT), Short Portal Mental Status Questionnaire (SPMSQ), and Blessed Test of Orientation,Memory, and Concentration (BTOMC) in the clinical setting.<sup>13</sup>

However, despite its widespread usage in clinical contexts, the MMSE is inadequate for detecting CI in HF patients. The MMSE may not detect the subtler levels of cognitive deficits that HF patients experience, as this test was originally designed to assess for dementia and is insensitive to less severe impairments in executive function and memory.<sup>20–22</sup> Furthermore, there is no consensus on an appropriate MMSE cutoff score for determining CI in this population. The standard MMSE cutoff of <24 may be insensitive to milder forms of CI-especially among patients with higher educational levels or pre-morbid intelligence, who show a ceiling effect of higher MMSE scores and thus more false-negative results.<sup>23</sup> Although higher MMSE cutoffs have been suggested for detecting CI in various populations (e.g., 29 for individuals with nine or more years of schooling, 27 or 28 for HF patients, or 25 for individuals aged 80 or older),<sup>24–26</sup> the applicability of these various cutoff scores remains unclear for wider clinical applications. Although the MMSE may be quick to administer and therefore attractive as a screening measure, its insufficiency for detecting cognitive deficits in HF patients may create clinical obstacles for observing and treating cognitive problems in this population, making this issue important to care providers and patients alike.

The Research Committee of the American Neuropsychiatric Association has recommended that clinicians should use the MMSE only as a minimum screening measure, that scores should be corrected for age and education, and that when used, the MMSE should be supplemented with specific measures of memory, executive function, and visuospatial ability.<sup>27</sup> Despite recommendations against utilizing the MMSE for purposes beyond dementia screening, the MMSE is still regularly used to detect the milder types of CI in HF patients. It has even served as the sole test of cognitive function in a substantial number of recent studies evaluating HF patients, in both hospitals and outpatient settings.<sup>28–35</sup> Given that the MMSE is the most commonly used cognitive test for this population in the clinical setting, evaluation of other screening tools is needed to establish a more appropriately sensitive test for CI in patients with HF.

The Automated Neuropsychological Assessment Metrics  $(ANAM)^{36}$  is a computerized battery that has previously demonstrated capacity in testing the cognitive domains that are adversely affected by HF, but has not yet been evaluated specifically for the purpose of detecting CI in HF patients. The ANAM has already shown a wide range of utility in studies assessing the cognitive effects of concussions,<sup>37,38</sup> environmental stressors and exposures,<sup>39–42</sup> and medications and drugs of abuse.<sup>43,44</sup> It has served as an efficient tool for monitoring cognitive deficits in a range of patients, from screening military personnel for minor traumatic brain injuries and neuropsychological deficits,<sup>45–49</sup> to managing chronic medical conditions, including systemic lupus erythematosus<sup>50,51</sup> and multiple sclerosis.<sup>52</sup> Recently, in a mixed clinical sample, the ANAM significantly predicted CI status with a sensitivity of 81% and specificity of 89.1%.53 The ANAM has also demonstrated high sensitivity to CI among patients with Alzheimer's disease-correctly classifying 100% of the participants in a pilot study based on a discriminant function analysis of throughput scores-as well as the potential capacity to detect earlier, more subtle cognitive changes in the disease process.<sup>54</sup>

In particular, the ANAM consists of subtests that evaluate cognitive domains including attention, processing speed, learning, memory, and visuospatial ability-in which deficits often impede self-care in HF patients, leading to poor prognosis. Unlike most computerized cognitive batteries, the ANAM calculates a throughput score for each subtest (a corrected response rate ratio of accurate responses per minute), which measures cognitive efficiency. The throughput score is uniquely useful in increasing sensitivity to changes in a patient's cognitive performance over time, and facilitating comparisons across different tasks that measure accuracy and speed.<sup>55</sup> Another advantage of the ANAM is its configurability, as clinicians can select combinations of over 20 ANAM subtests to tailor a cognitive screening battery for specific populations and testing purposes.<sup>56,57</sup> Examinations of the construct validity of ANAM subtests compared to more traditional neuropsychological measures have already shown that ANAM scores can successfully measure processing efficiency, working memory, and recall.58

Despite its applications to various clinical populations and, importantly, demonstrations of its sensitivity to subtle cognitive changes, the ANAM has not been assessed as a screening tool for CI in patients with HF. Considering the insufficiency of the MMSE and lack of routine cognitive screening, evaluation of newer approaches is crucial to developing a sensitive, standardized measure to recognize CI and, in turn, improve HF patient care. The investigators aim to evaluate the extent to which the ANAM can better detect cognitive deficits in HF patients, compared to the widely used MMSE. The performance of the ANAM and MMSE in discerning CI among HF patients will be compared against a composite model of CI comprising a battery of neuropsychological tests—a more comprehensive reflection of the cognitive domains affected by HF, including attention, processing speed, learning, working memory, and delayed memory.

#### Method

#### Participants

The current study is a cross-sectional analysis of 57 systolic and diastolic HF outpatients recruited from Akron City Hospital (Summa Health System, Akron, OH). The investigators confirmed HF diagnosis by a review of the patients' medical charts. All participants were in an ongoing study examining HF self-management and completed a comprehensive battery of neuropsychological tests-including the ANAM and the individual tests comprising the composite model-to assess overall cognitive function. This investigation conformed to the principles outlined in the Declaration of Helsinki. A graduate student trained in neuropsychology tested participants at the Summa Center for Clinical Trials or in their respective homes between June 2011 and June 2012. The present analyses represent a sub-study of a trial aimed at examining medication adherence in heart failure patients using technology interventions. The sample size of that intervention was limited due to availability of the novel technologies: the investigators made all efforts to include participants' data from the parent study into this sub-study to maximize the sample size.

Inclusion criteria were: aged 45–90; English speaking; New York Heart Association class II or III for three or more months; history of HF managed by the patient for at least three months; systolic HF with LVEF  $\leq$ 40% documented using left ventricular angiography, nuclear wall motion study, echocardiography within 12 months of study enrollment, or diastolic HF confirmed by chart diagnosis; willing to allow a device attached to their telephone to be installed for the duration of the study; and reside within 30

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