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Unappreciated Cognitive Dysfunction is Common among Patients Hospitalized with Cardiovascular Disease

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Authors' contributions

This work was carried out in collaboration between all authors. Authors RJ, MAD, JH and JG designed the study, selected and validated implementation of study instruments. Authors JVC and DL-S enrolled patients' data acquisition and literature review of the manuscript. Authors JVC, RJ and MAD analyzed results, drafted the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Better understanding of the prevalence of unappreciated cognitive dysfunction among patients with cardiovascular disease during hospitalization is integral to patient-centered care. We tested the hypothesis that there is a substantial prevalence of debilitating cognitive dysfunction in cardiac patients which health care providers do not appreciate.
Methods: This observational prospective study evaluated 51 patients on admission to a cardiac intensive care unit (CICU) who did not have a history of conditions known to adversely affect cognition and appeared cognitively intact to treating physicians and nursing staff. Patients

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underwent neuropsychological testing to assess the domains of global cognition, attention, memory, and executive function at important points during hospitalization.
Results: Twenty-six percent of participants were impaired globally based upon the Modified Mini Mental Status Examination. Of the study's participants, 46% were impaired in memory on short recall and 40% were impaired on long recall based upon Rey Auditory Verbal Learning, while 49% were impaired based upon Digit Span. Further, 38% of participants were impaired in attention based upon Trail Making Test Part A. Twenty-five percent of participants were impaired in executive function based upon Trail Making Test Part B, and 18% were impaired based upon Frontal Assessment Battery.
Conclusions: In patients hospitalized with cardiovascular disease, unappreciated cognitive dysfunction is common. The dysfunction involves multiple domains and likely impedes patient participation in longitudinal care and their comprehension of health education which ultimately hinders the transition from hospital to home care. This process creates a setting of poor self-management with significantly increased potential for rehospitalizations.

Keywords: Cardiovascular disease; cognition; executive function; memory.

1. INTRODUCTION

Cardiovascular disease (CVD) risk factors have been associated with cognitive decline in older populations [1,2]. These findings suggest that patients are in the middle of the vascular cognitive impairment continuum, performing worse than healthy age-matched peers, but substantially better than persons with dementia or other significant neurological disorders. This cognitive dysfunction can be subtle, and can go unrecognized by health care providers.

Patients with heart failure have been found to manifest difficulties with memory and concentration that are associated with poor health outcomes distinct from age-related memory and concentration abnormalities. Depending on the population under investigation, including inpatients and outpatients and the methodology used, it has been reported that 30% to 80% of patients with heart failure exhibit cognitive dysfunction [6], particularly on tests of memory and executive function. Several mechanisms have been implicated in this cognitive dysfunction including reduced cerebral perfusion [7] and cerebrovascular pathology [3-7].

Recent studies suggest that baseline cognitive dysfunction is associated with a five times greater risk of mortality and six times greater risk of functional decline in the future. [8-10] Cognitive dysfunction is associated with dependency in activities of daily living [11], which is further linked to disability and frequent rehospitalization. [12,13] One study found cognitive dysfunction to be associated with in-hospital mortality and decreased 1-year survival among older heart failure patients [13]. Cognitive dysfunction in attention, executive function, and memory can negatively impact patients' self-care behaviors such as taking medications, dietary compliance, and exercise. Such dysfunction also prevents patients from providing health care providers with accurate histories, which further reduces optimal medical care.

In hospitals, patient histories are often obtained on the first morning after admission and the patients' cognition plays a key role in providing an accurate history to health care providers. Furthermore, the majority of patient education regarding self-management occurs prior to discharge. As more and more patients are discharged from intensive care units, it is important to understand their cognitive status in order to ensure effective teaching related to discharge instructions.

We tested the hypothesis that there is a substantial prevalence of cognitive dysfunction in cardiac patients that is unappreciated by health care providers throughout the hospitalization course.

2. METHODOLOGY

2.1 Participants

A convenience sample of 51 patients being treated for acute cardiovascular conditions was recruited following their admissions to a cardiac intensive care unit at an academic tertiary care hospital. Patients were 18 years of age or older and were awake and conversant at the time of enrollment.

Inclusion criteria were chosen to maximize generalizability to other samples by selecting all comers to the CICU. Patients with conditions known to present cognitive dysfunction independent of their cardiac disease or its related conditions were excluded. Patients were excluded for a history of neurological disorder or injury (Alzheimer's disease, dementia, stroke, seizures) as well as moderate or severe head injury (defined as >10 minutes loss of consciousness). Patients with a past or current history of severe psychiatric illness, including psychotic disorders (schizophrenia and bipolar disorder), were excluded, but not those individuals with treated depression or anxiety disorders. Patients were also excluded if they had a history of alcohol or drug abuse within the last 5 years or a history of learning disorder or developmental disability. Patients were excluded for renal failure requiring dialysis, diagnosed untreated sleep apnea, and severely ill individuals, including those who were sedated, on a ventilator, or exhibiting acute hemodynamic changes. Furthermore, attending physicians and nurses were asked to exclude patients deemed inappropriate for the study due to clear cognitive dysfunction noted upon routine clinical examination. Thus, the study group represents a patient population that most health care providers would consider to have "normal" cognitive function.

2.2 Procedures

The local Human Subjects Institutional Review Board approved all study methods prior to conducting the study. Newly admitted patients were referred by nurse managers and physicians on the unit Prior to approaching the patient, the patient's nurse was asked if he/she noted any cognitive dysfunction. If not, the patient was approached and informed of the study, and written informed consent was obtained. A series of neuropsychological tests were administered to consented participants, and when logistically feasible, data collection was repeated prior to discharge. Testing sessions required approximately 1 hour.

2.3 Measures

2.3.1 Neuropsychological test battery

Participants completed a battery of well-established and validated neuropsychological measures assessing multiple domains. Researchers examined global cognitive functioning and cognitive performance in the domains of memory, language, and attention/ executive function [14,15]. The test battery was administered on the first morning following admission (Time 1) and again within three hours of anticipated discharge (Time 2). The order of neuropsychological testing was not random but rather the Modified Mini Mental Status Examination first, Rey Auditory Verbal Learning, Trails testing, followed by Digit Span Backwards, Rey Auditory Verbal Learning Long Delay and Recognition, and then finally Frontal Assessment Battery. Repeat testing prior to discharge was intended to confirm that the cognitive dysfunction noted at Time 1 was not transitory or unique to admission. The following neuropsychological tests were administered:

2.3.2 Global cognitive functioning

Modified Mini Mental Status Examination (3MS; Teng and Chui, 1987) provides a screening measure of global cognitive function. It is comprised of several short tasks, including orientation, similarities, animal fluency, learning, and brief and delayed recall of a short list of target words, and a copying a simple geometric figure. It is sensitive to a range of cognitive dysfunction including Alzheimer's disease and other forms of dementia.

2.3.3 Attention/executive function

Trail Making Test Parts A and B (Reitan), [16]. The Trail Making Test Part A requires participants to connect a series of 25 numbered dots in ascending order from 1 to 25 as quickly as possible. Trail Making Test Part B adds a set-shifting component, requiring participants to alternate between numbers and letters in ascending order (eg, 1, A, 2, B). The first part of this test assesses psychomotor speed and visual scanning, whereas the second part evaluates the ability to respond to shifting demands.

Frontal Assessment Battery [17]. The test includes subtests: (a) conceptualization and abstract reasoning (similarities test); (b) mental flexibility (verbal fluency test); (c) motor programming and executive control of action (Luris motor sequences); (d) resistance to interference (conflicting instructions); (e) inhibitory control (go-no go test); and (f) environmental autonomy (prehension behavior).

2.3.4 Memory

2.3.4.1 Rey auditory verbal learning test

Participants read a list of 15 words a total of 5 times followed by recalling as many words as possible. Following presentation and recall of a distraction list, participants are again asked to recall words from the original list. After a 30-minute delay, participants are again asked to recall target words from the original list. Finally, a recognition trial comprised of target words and foil (words not initially asked to learn) is completed.

2.3.4.2 Digit span backwards *test*

Participants hear a series of numerical digits read with one second intervals between digits. The participants are then asked to repeat the digits aloud in reverse order. Comprising each sequence gradually increases from 3 to 9 digits.

2.3.5 Neuropsychiatric normative data and validity

All neuropsychiatric assessments utilized for the study were well validated in age, socioeconomic, and education matched control populations alleviating the need to recruit normative data from a control population. The Modified Mini Mental Status Examination, Rey Auditory Verbal Learning Test, Digit Span Backward testing, and Trail Making testing have been validated across a variety of ages and educational backgrounds, thereby providing norms on the composite scores [18-22]. Furthermore, tests such as the Frontal Assessment Battery have demonstrated good interrater reliability, internal consistency, and discriminant validity [23]. The well-defined normative data allow the selected neuro-psychiatric assessments to detect clinically relevant cognitive dysfunction correlated to impairment in the tasks of daily living.

2.3.6 Analyses

Raw scores from each cognitive test were standardized to t- or z-scores using existing normative data based on age. Cutoffs for impairment were then created using these data, with scores falling greater than 1.5 standard deviations below normative values.

3. RESULTS AND DISCUSSION

3.1 Demographic Information

Table 1 shows the demographic characteristics of the study population. The median age was 62 with an even distribution of males and females. The majority of participants were Caucasian (82%) and 17.6% were African-American. The family structure and education backgrounds of the study's participants were comparable to CVD patients in a typical urban CICU in the United States.

3.2 Medical Conditions

Fig. 1 shows the primary admission diagnosis of participants, which was predominantly myocardial infarction followed by heart failure exacerbation and arrhythmia. A review of patient

Table 1. Patient demographics (N=51)

Variable		Total Sample N(%)
Age	Mean= 61.3 STD +/- 13.3	23 (48.4)/ 28 (51.9)
Gender	Women/ Men	
Current Living Arrangements	Live Alone	12 (25.5)
	With Spouse, Family, Friend	35 (74.5)
Marital Status	Single	7 (14)
	Married	27 (54)
	Widowed, Separated, Divorced	16 (32)
Race	Black	10 (19)
	Caucasian	41 (81)
Highest Education Level	Less than High School	6 (14.6)
	High School	15 (36.6)
	Advanced Degree or Training	20 (48.7)
Employment Status	Retired	21 (45.7)
	Work	18 (39.1)
	Unemployed	7 (15.2)

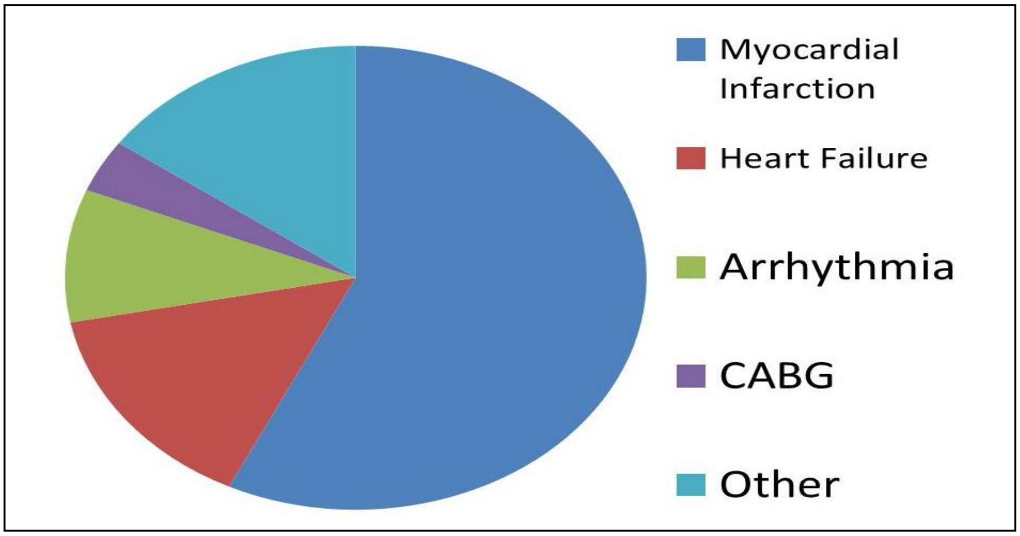

Fig 1. Primary admission diagnosis

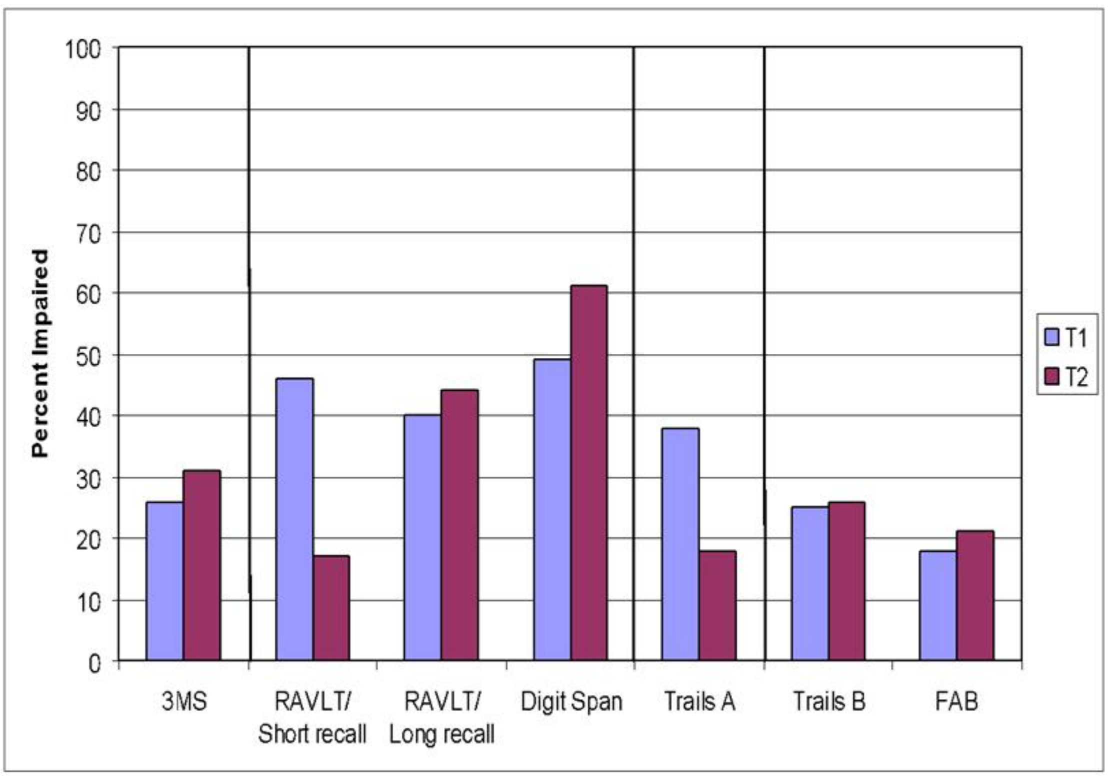

Fig. 2. Prevalence of cognitive dysfunction

comorbidities was used to calculate the Charlson Comorbidity Index, with 28.6% having a score of 0; 45.2% having a score of 1-2; 21.5% having a score of 3-4; and 4.8% having a score of 5 or greater. The patient sample selected is comparable to national CCU trends [24].

3.3 Invasive Procedures and Significant Medications Prior to Time 1 Testing

Patients underwent many invasive procedures between Time 1 and Time 2. 60.3% of participants underwent diagnostic cardiac catheterizations, 22.2% underwent percutaneous coronary intervention, and 4.7% underwent an electrophysiology study or pacemaker placement. To ensure that medications were not influencing cognitive testing, we collected data on the medication administration of all narcotic and sedatives and invasive procedures. Fewer than 3.1% of patients received opioids, benzodiazepines, antihistamines, or anti-cholinergic medications and no participants received medications during the 4 hours prior to cognitive testing. Therefore, medication side effects were unlikely to account for substantial cognitive dysfunction in this population.

3.4 Cognitive Dysfunction Prevalence

Fig. 2 and Supplemental Tables 1 and 2 indicate the prevalence of cognitive dysfunction in the CICU setting according to cognitive test and domains at Time 1. Among the participants at Time 1, 26 % had global impairment 45.5% demonstrated impairment on the short recall and 40.4% demonstrated impairment on the long recall in memory based upon Rey Auditory Verbal Learning Test, 49% were impaired in memory based upon Digit Span testing , 38% were impaired in attention based upon Trail Making Test A, 25% demonstrated impairment in executive function based upon Trail Making Test B and 18% had impairment in executive function based upon Frontal Assessment Battery.

3.5 Cognitive Dysfunction remains Prevalent prior to Discharge

Fig. 2 reveals the prevalence of cognitive dysfunction in the CICU setting at Time 2. Among particpants, 33% demonstrated impairment globally based upon the Modified Mini Mental Status Examination, 16.7% demonstrated impairment on the short recall and 43.8% demonstrated impairment on the long recall in memory based upon Rey Auditory Verbal Learning Test, 61% demonstrated impairment in memory based upon Digit Span testing, 18% demonstrated impairment in attention based upon Trail Making Test A, 26% of demonstrated impairment in executive function, and 29%demonstrated impairment in executive function based upon Frontal Assessment Battery testing.

3.6 Discussion

In this study, the prevalence of unappreciated cognitive dysfunction for patients hospitalized in the CICU, as evidenced by neurocognitive testing, was substantial. Nearly half of all patients manifested significant impairment in at least one measured domain. The most prevalent dysfunction appeared to occur in global cognition and memory. However, significant impairment in attention and executive function was also detected.

When logistically feasible, testing was repeated prior to discharge to confirm that prior findings of impairment at Time 1 were not an isolated or transient finding. In addition, the timing of the second test battery administration represents an important point when clinical staff often provides patient teaching. Reassessment before discharge indicated a high prevalence of cognitive dysfunction across multiple domains.

Strengths of the study include that the sample was chosen to represent the general CICU population. The distribution of demographics, admission diagnoses, comorbid conditions, medications administered, and invasive procedures performed are consistent with the majority of CICUs nationwide. Furthermore, patients were enrolled on the first morning of hospitalization, which is a critical time in patient care because history is often obtained by care providers at that time, particularly in a teaching environment. Moreover, both the first morning of hospitalization and the brief period of time prior to discharge are key points for patient disease orientation and self-care education. By conducting assessments at two time points during the hospitalization, this study indicates that the detected cognitive dysfunction is neither transient nor unique to a specific time point in hospitalization.

This study was designed to exclude participants with conditions that have been previously correlated to cognitive dysfunction, such as stroke and obstructive sleep apnea. We used care providers' clinical examinations to further eliminate from participating patients with clear cognitive dysfunction. Therefore, the study group represented what most physicians and nurses would consider "normal" cognitive function. This study also reveals the clear weaknesses of conventional clinical assessments currently being used, in which a large portion of cognitive dysfunction often passes unnoticed.

The cognitive function testing instruments used in this study have been validated in prior studies to measure other types of clinically significant dysfunctions. While these neurocognitive testing tools have been used extensively in other scientific fields, this study demonstrated the merits of these instruments in detecting cognitive dysfunction as well. As the public health costs of continuing to ignore cognitive dysfunction become more apparent, so too will the value of administration of these sensitive neurocognitive screening tests.

A notable barrier to implementation of neurocognitive testing in the broader health care system is the time resources required to appropriately perform these assessments. The study was impacted by the difficulty in completing the full battery of testing, which often required an uninterrupted hour. The majority of subjects were able to complete the Modified Mini Mental Status Examination (n = 51), but only 32 were able to complete the Trail Making Test Part B testing at Time 1. Patient refusal due to fatigue or anxiety, and interruption of medical procedures, sometimes prohibited the administration of the complete testing battery.

Research staff was not always available to perform Time 2 testing during evenings, weekends, or holidays. This resulted in fewer (n=24) patients undergoing testing at both time points. Although longitudinal reassessment of all patients would have been ideal, this was not feasible due to staff availability and a number of patient-related factors.

A clear limitation of this study is the modest sample size acquired as a convenience sample at a single institution. The representative nature of the hospital and patients mitigates this, but only in part. This data does establish the prevalence of clinically important unappreciated cognitive dysfunction in these patients and should serve as an stimulus for additional, larger investigations. This modest sample size precludes robust multivariate analyses, such as those of baseline demographics (e.g. age, gender), comorbidities (e.g common coronary or other vascular risk factors), or therapy (e.g. medication use). We anticipate future studies of these important factors.

4. CONCLUSION

Early in the hospital stay and prior to discharge, dysfunction in cognition is predictive of adversely affecting patient care by impairing the accuracy of the history provided and reducing a patient's ability to learn how to care for their illness, whether it is in the form of lifestyle modification, dietary changes, or medication compliance [25,26]. Further understanding of cognitive dysfunction in cardiac patients may reveal the underlying etiology of many of the difficulties and gaps in care associated with transitions from hospital to home.

Unappreciated cognitive dysfunction is common even in hospitalized CICU patients, who staff physicians and nurses considered to be cognitively intact. In this study's sample group, while cognitive dysfunction was more pronounced in the domains of memory and attention, significant impairment was also noted in global cognition and executive function.

Cognitive dysfunction likely impedes patients from participating in longitudinal care and comprehension of health education, with significantly increased potential for re hospitalizations. Future studies will address the determinants of cognitive dysfunction and better clarify the time course of the dysfunction, both in acute hospitalization and transition to outpatient care. Such studies will contribute to tailoring the delivery of education to optimize patient understanding, as well as offering a means of improving patient satisfaction. The implications for individual patients, caregivers, and the public health system are promising.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. This study received approval by the University Hospitals Institutional Review Board on March 22, 2013 (#05-09-25).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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