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Mild cognitive impairment predicts death and readmission within 30 days of discharge for heart failure☆

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ABSTRACT

Background: Cognitive impairment is highly prevalent in heart failure (HF), and may be associated with short-term readmission. This study investigated the role of cognition, incremental to other clinical and non-clinical factors, independent of depression and anxiety, in predicting 30-day readmission or death in HF.

Methods: This study followed 565 patients from an Australia-wide HF longitudinal study. Cognitive function (MoCA score) together with standard clinical and non-clinical factors, mental health and 2D echocardiograms were collected before hospital discharge. The study outcomes were death and readmission within 30 days of discharge. Logistic regression, Harrell's C-statistic, integrated discrimination improvement (IDI) and net reclassification index were used for analysis.

Results: Among 565 patients, 255 (45%) had at least mild cognitive impairment (MoCA ≤ 22). Death (n = 43, 8%) and readmission (n = 122, 21%) within 30 days of discharge were more likely to occur among patients with mild cognitive impairment (OR = 2.00, p = 0.001). MoCA score was also negatively associated with 30-day readmission or death (OR = 0.91, p < 0.001) independent of other risk factors. Adding MoCA score to an existing prediction model of 30-day readmission significantly improved discrimination (C-statistic = 0.715 vs. 0.617, IDI estimate 0.077, p < 0.001). From prediction models developed from our study, adding MoCA score (C-statistic = 0.83) provided incremental value to that of standard clinical and non-clinical factors (C-statistic = 0.76) and echocardiogram parameters (C-statistic = 0.81) in predicting 30-day readmission or death. Reclassification analysis suggests that addition of MoCA score improved classification for a net of 12% of patients with 30-day readmission or death and of 6% of patients without (p = 0.002).

Conclusions: Mild cognitive impairment predicts short-term outcomes in HF, independent of clinical and non-clinical factors.

1. Introduction

Heart failure (HF) is the leading cause of hospitalization and rehospitalization in older adults [1,2], and short-term risks of readmission after a hospitalization with HF remain very high [3,4]. These events are costly and may be preventable [2], and HF has emerged as a priority condition in the current era of quality improvement and payment reform [5]. Although readmissions shortly after discharge are linked to quality of care [6], there are other individual patient factors – including the ability for self-care – that may contribute to early readmissions following an index admission of HF.

Cognitive impairment is very common among HF patients, and may involve different domains including learning memory, attention and working memory, executive functions and psychomotor speed. Cognitive function influences a patient's ability for self-care, which is a key to health maintenance and adherence to treatment. Perhaps as a consequence, cognitive impairment is associated with higher risk of cardiovascular events in HF patients [7]. HF patients with moderate to

Abbreviations: GAD-7, Generalized Anxiety Disorder scale; GWTG-HF, Get With The Guidelines-Heart Failure; HF, heart failure; IDI, integrated discrimination improvement; NYHA, New York Heart Association; LV, left ventricular; MARATHON, Multicentre Australian Risk Algorithm To predict Heart failure readmissiON; MoCA, Montreal Cognitive Assessment; PHQ-9, Patient Health Questionnaire.

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severe dementia have greater risks of readmission or death post-discharge [8]. Mild cognitive impairment is present in up to three quarters of the HF population [9,10], and our previous work has suggested it to be an independent risk for 30 day readmission [4]. However, whether it provides incremental information to widely-obtained correlates of HF readmission remains unclear, as indeed is which component of impaired cognition is important. We hypothesized that the association of components of mild cognitive impairment with short-term adverse outcomes in HF was primarily mediated by readmission (rather than mortality), that it was independent of depression and anxiety, and that it was incremental to other clinical and non-clinical factors for prediction of readmission or death within 30 days of discharge in HF.

2. Methods

2.1. Study population

In this prospective study, we followed 565 HF patients from the Multicentre Australian Risk Algorithm To predict Heart failure readmissiON (MARATHON) study, an Australia-wide longitudinal study of HF. Recruitment was carried out between January 2014 and June 2015 in most Australian States (Tasmania, Victoria, New South Wales, Queensland and South Australia). Patients were identified by the confirmed primary diagnosis of decompensated HF by their treating doctors. Exclusion criteria were: age < 18 years, inability to provide written consent, moderate or worse primary mitral or aortic valve disease, concomitant unstable angina or acute myocardial infarction, cardiac device malfunction, endocarditis, patients with LV assist device, potentially reversible LV dysfunction including post-partum, alcoholic cardiomyopathy and hyperthyroidism, and concomitant terminal non-cardiac illnesses that could influence 12-month prognosis. Baseline data from eligible patients who provided written consent were collected before hospital discharge. This study was approved by the Tasmanian Health and Medical Human Research Ethics Committee.

Table 1
Socio-demographic, cognitive function and mental health data at baseline.

Male sex	344	(61%)
Age at admission (years)	74	[63, 83]
Living alone	177	(31%)
Marital status		
Married/living as married	306	(54%)
Single/widowed	218	(39%)
Divorced/separated	41	(7%)
Education		
<High school	301	(53%)
High school	135	(24%)
College (grade 12)	73	(13%)
≥Bachelor degree	56	(10%)
Non-English speaking background	36	(6%)
Remoteness index		
Major cities	294	(52%)
Outer/inner regional Australia	271	(48%)
Length of hospital stay (day)	7	[4, 11]
Previous hospital admissions (last 12 months)		
0	238	(42%)
1	107	(19%)
≥2	220	(39%)
PHQ-9 score	9	[5, 15]
Depression		
No depression	168	(30%)
Mild	152	(27%)
Moderate	135	(24%)
Moderately severe/severe	110	(19%)
GAD-7 score	4	[1, 10]
Anxiety		
No anxiety	316	(56%)
Mild	113	(20%)
Moderate	79	(14%)
Severe	57	(10%)
MoCA score	23	[19, 26]
Classification of cognitive function		
No cognitive impairment (MoCA ≥ 23 points)	310	(55%)
Mild cognitive impairment (MoCA 17–22 points)	165	(29%)
Dementia (MoCA ≤ 16 points)	90	(16%)

Data are reported as n (%) or median [interquartile range].

2.2. Primary outcome

The primary outcome of this study was all-cause readmission or death within 30 days of discharge. Follow-up phone calls were performed at 30 days of discharge. Dates of readmissions or death were obtained from medical records.

2.3. Cognitive function and mental health data

Patients' cognitive function was assessed by trained personnel before discharge using the Montreal Cognitive Assessment (MoCA). This test has been widely validated and is recommended in HF [11]. The MoCA takes approximately 20 min to evaluate different domains of cognition including visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall and orientation. The MoCA was designed to detect mild cognitive impairment with excellent sensitivity (90%) and specificity (87%) [12]. MoCA cut-points of 23 and 17 were used to define mild cognitive impairment and dementia as previously suggested [13]. Patients who did not finish college/grade 12 had one point added to their MoCA score as instructed in the protocol.

Because many cognitively impaired patients may develop depression and/or anxiety disorder – which may confound the relationship between cognitive function and HF – we also assessed and investigated the patients using validated mental health questionnaires. Depression was assessed using the Patient Health Questionnaire (PHQ-9), with cut-points of 5, 10 and 15 used to define mild, moderate and moderately severe/severe depression respectively. Anxiety was assessed using the Generalized Anxiety Disorder scale (GAD-7), with cut-points of 5, 10 and 15 used to define mild, moderate and severe anxiety respectively.

Table 2
Clinical data at baseline.

Beta-blocker use	435	(77%)
ACEI/ARB use	458	(81%)
Diuretic use	525	(93%)
Aldosterone antagonist use	254	(45%)
Calcium antagonist use	68	(12%)
Antiarrhythmic medication use	102	(18%)
Digoxin use	136	(24%)
Statin use	300	(53%)
Antidepressant medication use	96	(17%)
Heart failure NYHA classification		
≤Class 2	271	(48%)
Class 3	203	(36%)
Class 4	91	(16%)
Left ventricular ejection fraction (%)	36	[25, 50]
Left ventricular volume index (ml/m^2)	58	[45, 80]
Left atrial volume index (ml/m^2)	42	[30, 60]
Left ventricular filling pressure E/e′	17	[13, 23]
Right atrial pressure (mm Hg)	8	[3, 15]
Pulmonary arterial systolic pressure (mm Hg)	37	[30, 47]
Hypertension	368	(65%)
Dyslipidaemia	300	(53%)
Angina	102	(18%)
Atrial fibrillation	282	(50%)
Life-threatening arrhythmia	52	(9%)
Cardiomyopathy	237	(42%)
Deep vein thrombosis	23	(4%)
Charlson comorbidity index	7	[5, 9]
Chronic lung disease	170	(30%)
Diabetes mellitus		
No	345	(61%)
Mild, without complications	152	(27%)
Complications and/or end-organ damage	68	(12%)
Chronic kidney disease	192	(34%)
Systolic blood pressure (mm Hg)	119	[107, 132]
Diastolic blood pressure (mm Hg)	67	[61, 73]
Heart rate (beats/min)	75	[68, 87]
Respiratory rate (respirations/min)	18	[18, 20]
Hematocrit (%)	37	[32, 42]
Hemoglobin (g/l)	124	[111, 140]
Sodium (mmol/l)	138	[135, 140]
Blood urea nitrogen (mg/dl)	10.5	[7.6, 16.1]
Serum creatinine (μmol/l)	116	[90, 153]
Serum albumin (g/dl)	34	[30, 37]
B-type natriuretic peptide (pg/ml)	1105	[698, 2450]
Abnormal troponin I (≥0.03 μg/l)	288	(51%)
C-reactive protein (mg/l)	12.0	[5.8, 28.0]

Data are reported as n (%) or median [interquartile range].