Original Article

Change in Cognitive Function in the Month After Hospitalization for Acute Coronary Syndromes

Findings From TRACE-CORE (Transition, Risks, and Actions in Coronary Events–Center for Outcomes Research and Education)

Jane S. Saczynski, PhD; David D. McManus, MD, MS; Molly E. Waring, PhD; Darleen Lessard, MS; Milena D. Anatchkova, PhD; Jerry H. Gurwitz, MD; Jeroan Allison, MD; Arlene S. Ash, PhD; Richard H. McManus, MPP, MSW; David C. Parish, MD; Robert J. Goldberg, PhD; Catarina I. Kiefe, PhD, MD

Background—Cognitive function is often impaired during hospitalization, but whether this impairment resolves or persists after discharge is unknown.

Methods and Results—We enrolled (April 2011–May 2013) and interviewed during hospitalization and 1-month post-discharge 1521 nondemented acute coronary syndrome survivors enrolled in TRACE (Transitions, Risks and Actions in Coronary Events). Cognitive function was assessed using the Telephone Interview of Cognitive Status (range: 0–41) at both time points. Patients reported demographic and psychosocial characteristics and medical records were abstracted. Using the Telephone Interview of Cognitive Status cut point of ≤28, we defined 4 groups of cognitive change based on cognitive status during hospitalization and 1 month later: consistently impaired, transiently impaired, newly impaired, and consistently nonimpaired. Characteristics associated with cognitive change categories were examined using multinomial logistic regression. Participants were 67% male, 84% non-Hispanic white, with mean age±SD 62±11 years; 16% (n=237) were cognitively impaired during hospitalization, and 11% (n=174) were impaired 1 month after discharge. Overall, 80% were consistently nonimpaired, 9% transiently impaired, 7% consistently impaired, and 4% newly impaired. Lower education level, minority status, low health literacy and numeracy, and higher severity of disease were independently associated with cognitive impairment during and after hospitalization. Male sex was associated with increased risk of cognitive impairment after hospital discharge.

Conclusions—Cognitive function changes during the transition from hospital to home after acute coronary syndrome are less favorable for men and those with psychosocial vulnerability. Assessing cognitive status both in hospital and post-discharge is important for detecting patients who could benefit from tailored transitional care including early follow-up and booster discharge instructions. (***Circ Cardiovasc Qual Outcomes*. 2017;10:e001669. DOI: 10.1161/CIRCOUTCOMES.115.001669.**)

Key Words: cognition ■ cognitive dysfunction ■ epidemiology ■ survivors

Cognitive impairment is highly prevalent and underdocumented in hospitalized patients, ≤40% who are cognitively impaired. Less than half of this impairment is documented in medical charts.[1–5] Cognitive impairment during hospitalization is associated with poor clinical outcomes including lack of functional recovery, rehospitalization, institutionalization, and mortality.[1,2,6–8]

Cognitive function may change around the time of a hospitalization, because of acute illness or the myriad insults associated with a hospitalization.[9,10] This, perhaps more subtle, hospital-associated cognitive impairment may pose less concern than persistent cognitive dysfunction, but may still signal a patient who is at elevated risk for adverse outcomes. In 1 study of elderly patients admitted to a general medicine ward, of those impaired at hospital admission, 39% had recovered to a nonimpaired state by discharge and an additional 41% were no longer impaired by 1 year after discharge.[10] However, patients who were transiently impaired (ie, impaired during hospitalization only) had a 2-fold risk of death in the year after discharge compared with nonimpaired patients. In addition, declines in cognitive status during the transition from hospital to home have recently been included in a hypothesized Post-Hospital Syndrome and may signify a patient at risk for poor self-management and, in turn, rehospitalization.[9]

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From the Department of Pharmacy and Health System Sciences, Northeastern University, Boston, MA (J.S.S.); Department of Medicine (D.D.M., J.H.G.) and Department of Quantitative Health Sciences (D.D.M., M.E.W., D.L., M.D.A., J.A., A.S.A., R.H.M., R.J.G., C.I.K.), University of Massachusetts Medical School, Worcester; Evidera, Lexington, MA (M.D.A.); Meyers Primary Care Institute, Worcester, MA (J.H.G.); and Department of Medicine, Mercer School of Medicine, Macon, GA (D.C.P.).

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Correspondence to Jane S. Saczynski, PhD, Department of Pharmacy and Health System Sciences, 140 The Fenway, R215x, 360 Huntington Ave, Boston, MA 02115. E-mail j.saczynski@northeastern.edu

WHAT IS KNOWN

- Acute illness often results in cognitive impairment.
- This impairment is temporary or transient in some patients.

WHAT THE STUDY ADDS

- During hospitalization, cognitive impairment is transiently impaired in ≈10% of acute coronary syndrome survivors and new impairments developed in nearly 5% in the month after discharge.
- Cognitive status fluctuates during the transition from hospital to home and serial assessments before and after discharge are important.

Despite increasing evidence for a strong association between cardiovascular disease and impaired cognition,[7,11] change in cognitive function during the transitional period after hospitalization for acute coronary syndrome (ACS) has not been described. In addition to understanding the proportion of patients whose cognitive function fluctuates after discharge, identifying factors associated with whether a patient's cognitive function may change could help in designing transitional care plans, aligning services with patient profiles, and informing content and timing of follow-up appointments. We hypothesized that person-level variables such as low educational level, low health numeracy, depressive symptoms, or living alone might be associated with cognitive impairment during hospitalization and lower likelihood of recovery. Thus, we examined change in cognitive function from ACS hospitalization to 1 month post-discharge and the clinical, demographic, and psychosocial factors associated with different trajectories of change. One month post-discharge was chosen as our first follow-up time point because it corresponds with a critical period for hospital readmission.

Methods

Data are drawn from TRACE-CORE (Transition, Risks, and Actions in Coronary Events-Center for Outcomes Research and Education), which is a large longitudinal observational study of ACS patients from 6 hospitals in Massachusetts and Georgia. Details of the study have been described elsewhere.[12] In brief, potentially eligible patients were identified by daily screening of ACS-related ICD-9 codes (410–412) in computerized hospital, cardiac catheterization laboratory, and emergency department records by trained reviewers from April 2011 to May 2013, approached in the hospital and further screened for eligibility. Eligibility criteria included a diagnosis of ACS consistent with the American College of Cardiology and American Heart Association criteria,[13,14] age 21 years or older, and ability to communicate in English or Spanish. Participants were excluded if they developed ACS secondary to another acute condition (eg, surgery), screened positive for delirium by the Confusion Assessment Method,[15] had documented dementia, were pregnant, imprisoned, expected to move out of the area within 18 months, or were admitted for palliative care only. Informed consent was obtained in writing from all participants, and the study was approved by institutional review boards at all study sites.

Information about patient's demographic characteristics, comorbidities, lifestyle changes, cognitive status, psychosocial measures, and experience of care during their hospitalization was collected by trained study staff via an in-person structured computer-assisted interview during hospitalization (baseline) and via telephone at 1 month after hospital discharge. Baseline assessments were conducted within a day of admission, and 1-month follow-up interviews were administered between day 24 and 35 post-discharge. Clinical characteristics and laboratory values were obtained via review of medical records for the index hospitalization.

Assessment of Cognitive Status

Patients' cognitive status was assessed during hospitalization (as part of the baseline in-person interview) and at 1 month post-discharge (as part of the follow-up telephone interview) using the Telephone Interview of Cognitive Status (TICS), a validated 11-item global cognitive screening instrument that can be administered in-person or over the phone.[16] The TICS is similar to the Mini-Mental State Examination in discriminating cognitive impairment from normal cognition[17] and has been used in other studies of patients with cardiovascular disease.[18] Cognitive status at both time points (in-hospital baseline and 1 month post-discharge) was dichotomized into nonimpaired and impaired using a cutoff score of ≤28 (range: 0–41, higher score indicates better cognition), consistent with previous epidemiological studies.[17,19]

Definition of Change in Cognitive Status

For our main analysis, change in cognitive status was defined based on the cut point for impairment of ≤28 and we created a 4-category variable of change groups. Participants were classified as follows: consistently nonimpaired (nonimpaired at baseline and 1 month), transiently impaired (impaired at baseline and nonimpaired at 1 month), consistently impaired (impaired at both baseline and 1 month), or newly impaired (nonimpaired at baseline and impaired at 1 month).

In a sensitivity analysis, we also examined an alternative definition of change defined as an absolute change of ≥4 points from hospitalization to 1 month. Four-point change was selected because practice/retest effects on tests of global cognitive function are 0.3 to 0.4 SDs[20] (corresponding to a 1.16–1.55 point change in the current TRACE-CORE sample); thus, a 4-point change represents improvement of ≈3× that expected by practice alone.

Other Study Variables

All other study variables were assessed as part of the baseline, in-hospital interview, or as part of the baseline medical record abstraction, which was conducted ≈4 weeks after discharge to capture clinical variables during the index hospitalization. Participants self-reported demographic data including race/ethnicity, education, and living status (with spouse, alone, or with others) and health-related quality of life was assessed using the Short Form-36 Survey.[21] Participants were asked "How confident are you in filling out medical forms by yourself?" Responses of not at all confident, a little confident, and somewhat confident indicated impaired health literacy; responses of quite a bit confident and extremely confident indicated adequate health literacy.[22] Participants were asked "which of the following numbers represents the biggest risk of getting a disease?", first with response options of 1 in 100, 1 in 1000, and 1 in 10 and then again with response options of 1%, 10%, and 5%. Participants were categorized as having impaired health numeracy if they did not answer both questions correctly.[23] Depressive and anxiety symptoms were assessed with the 9-item Patient Health Questionnaire (range: 0–27)[24] and 7-item Generalized Anxiety Disorder scale (range: 0–21),[25] using a score of ≥10 on both scales to signify high depressive or anxiety symptoms.[25] Perceived stress and social support were assessed with the 4-item Perceived Stress Scale and the Medical Outcomes Study Social Support Scale (range: 5–25),[26] with participants scoring ≤12 having low social support. Age, sex, comorbid conditions (eg, atrial fibrillation, stroke), other clinical characteristics, and laboratory values were abstracted from the medical record. ACS severity was calculated using the Global Registry of Acute Coronary Events (GRACE) 6-month mortality risk score.[27,28] The GRACE risk score includes the following components: age, heart rate, systolic blood pressure,

creatinine, troponin I, ST depression on ECG, history of myocardial infarction, history of congestive heart failure, and percutaneous coronary intervention during hospitalization.

Statistical Analysis

We estimated odds ratios (ORs) and 95% confidence intervals (CIs) for transient impairment, consistent impairment, and new impairment in relation to the common reference group of consistent nonimpairment using multinomial logistic regression models. In multinomial logistic regression, the outcome is 1 of 3 or more categories, and models are simultaneously fit using maximum likelihood to estimate ORs for each group compared with a common reference group.[29] We included factors in adjusted regression models if they differed significantly by categories of cognitive change in univariate analyses. The GRACE risk score was included in the adjusted models as a surrogate for severity of ACS and represented several clinical characteristics and laboratory values, including age and history of myocardial infarction and cognitive heart failure, which were not included in the model separately because they were included in the GRACE score. In sensitivity analyses, we used an absolute change of 4 points to examine improvement, decline, and stability of cognitive performance, modeled using multinomial logistic regression as described above. In secondary analyses, we restricted the sample to only those who were impaired in the hospital and examined characteristics associated with recovery of cognitive function. All analyses were performed using SAS version 9.2 (SAS Institute Inc, Cary, NC).

Missing Data

Because there was significant loss to follow-up (below), we reanalyzed our data with inverse probability weighting, using the probability that an originally hospitalized TRACE-CORE participant was interviewed at 1 month and therefore included in our study. We also reanalyzed our data in 5 multiply imputed data sets.

Results

Study Sample

TRACE-CORE included 2191 patients enrolled in hospital and 19 died before the 1-month follow-up interview resulting in 2172 patients eligible for follow-up. Of these, 1529 were interviewed at 1 month and had data on cognitive function at both time points. We further excluded 8 patients with hospital stays longer than 30 days for a final analytic sample of 1521 (Figure). Compared with those included in our analytic sample (n=1521), those excluded (n=651) were younger (60.1 versus 61.9 years), less likely to be non-Hispanic white (74% versus 84%), more likely to have high depressive symptoms (30% versus 19%), and had lower in-hospital mean TICS scores (30.3 versus 32.1; all $P<0.05$). GRACE risk scores did not differ in the 2 groups (95.6 versus 95.5).

Patients in the analytic sample had a mean age of 62 years (SD=11.1), had a mean 6-month mortality GRACE risk score of 95.5 (SD=27.3), and were predominantly male (67%) and non-Hispanic white (84%).

Change in Cognitive Function in the Month After Discharge

Sixteen percent (n=237) of participants were cognitively impaired during hospitalization, and 11% (n=174) were impaired 1 month after discharge. Overall, 80% of the sample was consistently nonimpaired, 9% transiently impaired, 7% consistently impaired, and 4% newly impaired. Among those who were transiently impaired (n=130), 3% (n=4) improved 1 point, 6% (n=8) improved 2 points, and 9% (n=12) improved 3 points. Among the group who became newly impaired at 1 month (N=67), 7% (n=5) declined 1 point and 15% (n=10) declined 2 points.

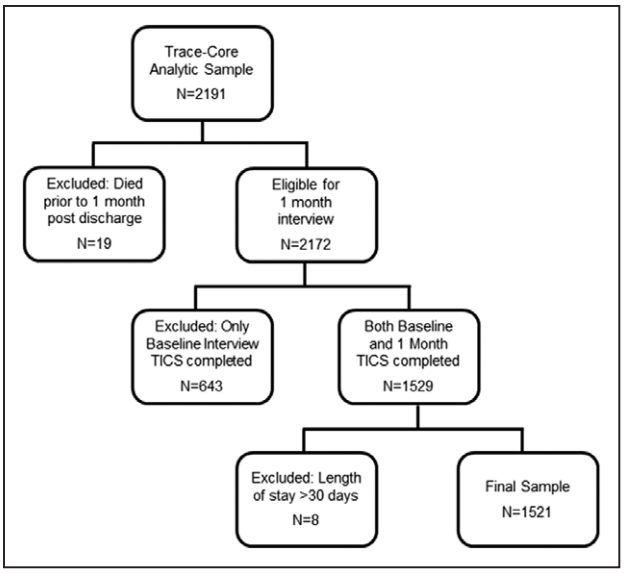

Figure. Flow diagram to final analysis sample. TICS indicates Telephone Interview of Cognitive Status.

All demographic and psychosocial characteristics examined varied by category of cognitive change (Table 1). Fewer clinical factors varied by cognitive change status (Table 2). For instance, although several comorbid diseases (eg, heart failure, stroke) varied by change status, with few exceptions (eg, percutaneous coronary intervention, acute renal failure), in-hospital complications and procedures did not. The risk of 6-month mortality as estimated using the GRACE risk score was higher among patients who were impaired cognitively during hospitalization mean (SD): 99 (25) in consistently impaired and 106 (31) in transiently impaired, compared with those who were not impaired: 95 (29) in consistently nonimpaired and 94 (27) in the newly impaired at 1 month. Average length of stay was longer in patients who were impaired during hospitalization, mean=4.5 days (4), irrespective of 1-month cognitive status compared with patients who were not impaired during hospitalization (mean=3.6–3.8 days; SD=3.5). Patients who were transiently impaired were more likely to be discharged to a location other than home (eg, nursing home or post-acute care setting) than were all other patients, with nearly 10% of transiently impaired patients discharged to a facility compared with 3% to 4% of all other patients.

Predictors of Change in Cognitive Status

After multivariable adjustment, several factors were associated with category of cognitive impairment change in the month after discharge, relative to patients who were consistently unimpaired (Table 3). Men had higher odds of becoming newly impaired (OR, 2.1; 95% CI, 1.2–4.0) than women (but were no more likely than women to be transiently or consistently impaired), and participants who lived alone were more likely to be transiently impaired than those living with a spouse (OR, 1.7; 95% CI, 1.0–2.8). Lower self-reported

Table 1. Demographic and Psychosocial Baseline Characteristics by Change Status From Baseline to 1-Month Follow-Up: TRACE-CORE, 2010 to 2013 (N=1521)

In-Hospital Through 1-Mo Cognitive Status	Consistently Impaired (n=107)	Transient Impairment (n=130)	New Impairment (n=67)	Consistently Nonimpaired (n=1217)	*P* Value
Age, mean (SD), y	62 (11)	65 (13)	60 (12)	62 (11)	<0.05
Sex, n (% female)	52 (49)	52 (40)	19 (28)	385 (32)	0.001
Education, n (%)					
High school or less	89 (84)	83 (64)	42 (63)	434 (36)	<0.001
Some college	15 (14)	26 (20)	18 (27)	402 (33)	
College or more	2 (2)	21 (16)	7 (10)	381 (31)	
Race/ethnicity, n (%)					
Non-Hispanic white	48 (45)	93 (72)	44 (67)	1085 (90)	<0.001
Non-Hispanic black	51 (48)	29 (22)	19 (29)	99 (8)	
Hispanic/Latino	8 (7)	8 (6)	3 (5)	26 (2)	
Living situation, n (%)					
Alone	28 (26)	40 (31)	10 (15)	232 (19)	<0.001
With spouse	36 (34)	46 (35)	24 (36)	642 (53)	
With others	43 (40)	44 (34)	33 (49)	343 (28)	
Low health literacy, n (%)	68 (64)	55 (42)	38 (57)	333 (27)	<0.001
Low health numeracy, n (%)	85 (79)	92 (71)	41 (61)	479 (39)	<0.001
Depression, n (%) moderate/severe	36 (34)	32 (25)	17 (25)	208 (17)	<0.001
Anxiety, n (%) moderate/severe	38 (36)	38 (29)	20 (30)	219 (18)	<0.001
Perceived stress, tertiles, n (%)					
Low	16 (15)	31 (25)	19 (29)	464 (38)	<0.001
Moderate	19 (18)	34 (28)	13 (20)	341 (28)	
High	68 (66)	58 (47)	34 (51)	401 (33)	
Low social support, n (%)	15 (14)	8 (6)	6 (9)	53 (4)	0.001
SF-36					
MCS	42 (13)	45 (14)	46 (14)	50 (12)	<0.001
PCS	38 (9)	39 (12)	38 (12)	43 (11)	<0.001
TICS at baseline	24.4 (3)	25.9 (2)	31.3 (2)	33.5 (2)	<0.001
TICS change, median (IQR; baseline to 1 mo)	0.00 (−2 to 2)	6.00 (4 to 8)	−4.00 (−6 to −3)	1.00 (−1 to 3)	<0.001

Missing data: race/ethnicity=9, perceived stress=24.

Depression ≥10 on the Patient Health Questionnaire 9[24]; anxiety ≥10 on the Generalized Anxiety Disorder 7[25]; low social support ≤12 (range 5–25) on the Medical Outcomes Study Social Support Scale[26]; for definitions of low Health Literacy and Numeracy, see Methods. IQR indicates interquartile range; TICS, Telephone Interview of Cognitive Status; and TRACE-CORE, Transition, Risks, and Actions in Coronary Events–Center for Outcomes Research and Education.

physical health-related quality of life was also associated with a lower odds of having new cognitive impairment (OR, 0.86; 95% CI, 0.76–0.99). Patients with low social support had 3× the odds of those with adequate social support to be consistently impaired (OR, 3.1; 95% CI, 1.4–6.8). Less than high school education, nonwhite race/ethnicity, and low health numeracy and literacy were associated with persistent, transient, and new impairment (Table 3). Only 2 clinical factors were significant predictors of change category in cognitive status: history of stroke and the GRACE risk score, both of which were associated with a higher odds of being both consistently and transiently impaired, but not newly impaired at 1 month (Table 3).

We conducted a secondary analysis restricted to those who were impaired during hospitalization and examined factors associated with transient, when compared with consistent impairment (data not shown). Patients with a college education or higher (OR, 8.3; 95% CI, 1.1, 41.6) and those who were non-Hispanic white (OR, 2.3; 95% CI, 1.3–4.5) had higher odds of transient impairment. For every point on the TICS from the in-hospital cognitive assessment, patients had 30% higher odds of transient versus consistent impairment (OR, 1.3; 95% CI, 1.1–1.4). The other patient characteristics associated with change in cognitive status in the main analyses (eg, health literacy and numeracy, history of stroke, and GRACE risk score) did not distinguish between improvement from baseline to 1 month among patients

Table 2. Clinical Baseline Characteristics by Change Status From Baseline to 1-Month Follow-Up: TRACE-CORE, 2010 to 2013 (N=1521)

In-Hospital Through 1-Mo Cognitive Status	Consistently Impaired (n=107)	Transient Impairment (n=130)	New Impairment (n=67)	Consistently Nonimpaired(n=1217)	*P* Value
Medical history, n (%)					
Coronary heart disease	53 (49)	62 (49)	29 (44)	453 (38)	0.008
Myocardial infarction	25 (24)	45 (35)	18 (27)	311 (26)	0.15
Heart failure	20 (19)	28 (22)	14 (21)	123 (10)	<0.001
Stroke	12 (12)	14 (11)	3 (5)	39 (3)	<0.001
Diabetes mellitus	47 (39)	37 (29)	27 (41)	349 (29)	<0.05
Hyperlipidemia	75 (72)	88 (69)	53 (80)	828 (69)	0.25
Atrial fibrillation	10 (10)	14 (11)	2 (3)	100 (8)	0.21
ACS type, n (%)					
STEMI	12 (12)	12 (10)	8 (12)	196 (17)	
NSTEMI	56 (54)	77 (61)	34 (52)	638 (54)	
UA	36 (35)	37 (29)	24 (36)	339 (29)	0.16
Laboratory values					
Creatinine, mean mg/dL (max)	1.8 (2.2)	1.6 (1.7)	1.2 (0.6)	1.2 (1.0)	<0.001
Troponin I, mean ng/mL (max)	10.6 (24)	14.0 (26)	12.8 (27)	19.1 (35)	0.05
Hemoglobin, mean mg/dL (min)	10.7 (2)	11.1 (2)	13.8 (16)	11.9 (2)	<0.001
Sodium, mmol/dL mean (min)	136 (3)	136 (3)	136 (3)	138 (5)	0.97
Physiological factors, mean at admission					
Heart rate, mean bpm	82 (24)	81 (19)	77 (17)	77 (19)	0.01
Systolic BP, mean mm Hg	146 (29)	142 (25)	144 (29)	142 (26)	0.51
Diastolic BP, mean mm Hg	80 (17)	85 (60)	80 (16)	80 (17)	0.15
Respiratory rate, mean	18 (4)	19 (6)	19 (9)	18 (4)	0.44
In-hospital procedures, n (%)					
Percutaneous coronary intervention	63 (61)	78 (62)	43 (65)	840 (70)	0.050
CABG	15 (14)	17 (13)	9 (14)	152 (13)	0.96
Cardioversion	1 (1)	1 (1)	2 (3)	28 (2)	0.43
IABP	2 (2)	6 (5)	3 (5)	32 (3)	0.48
Pacemaker/ICD	5 (5)	9 (7)	2 (3)	42 (4)	0.30
In-hospital complications, n (%)					
Atrial fibrillation	7 (7)	14 (11)	4 (6)	87 (7)	0.50
Heart failure	2 (2)	4 (3)	0 (0)	20 (2)	0.31
Acute renal failure	10 (10)	5 (4)	1 (2)	40 (3)	0.03
Stroke	0 (0)	0 (0)	1 (2)	3 (<1)	0.38
Recurrent MI	1 (1)	0 (0)	0 (0)	2 (<1)	0.49
Cardiogenic shock	1 (1)	3 (2)	0 (0)	9 (1)	0.31
Length of stay, mean d	4.5 (3.9)	4.5 (4.5)	3.8 (3.4)	3.6 (3.5)	0.01
GRACE risk score, mean (SD)	99 (25)	106 (31)	95 (29)	94 (27)	<0.001
Discharge disposition, n (%) facility	3 (3)	12 (9)	2 (3)	30 (4)	0.010

Missing data: PCI and CABG=4, cardioversion=10, ACS type=30–laboratory and physiological data >200. ACS indicates acute coronary syndrome; NSTEMI, non–ST-segment–elevation myocardial infarction; STEMI, ST-segment–elevation myocardial infarction; and TRACE-CORE, Transition, Risks, and Actions in Coronary Events–Center for Outcomes Research and Education.

impaired at baseline. These factors, though, were associated with in-hospital impairment, irrespective of 1-month status, in the full sample. Other factors, such as living situation and social support, were in the expected direction and were consistent with findings in the full sample, but were not statistically significant likely because of the restricted sample size and decreased power.

Table 3. Adjusted Odds Ratios (95% Confidence Intervals) for Change Status From Baseline to 1-Month, Relative to Consistent Cognitive Unimpairment, in Relation to Demographic, Psychosocial, and Clinical Characteristics: TRACE-CORE, 2010 to 2013 (N=1521)

	Consistent Impairment (n=107)	Transient Impairment (n=130)	New Impairment (n=67)
Demographics			
Male sex	0.95 (0.6–1.6)	1.2 (0.8–1.9)	2.1 (1.2–4.0)*
Education			
Less than high school	10.3 (3.0–35.1)*	2.2 (1.2–3.9)*	2.3 (1.0–5.6)*
Some college	2.9 (0.8–10.7)	0.97 (0.5–1.9)	1.5 (0.6–3.7)
College or more	Referent	Referent	Referent
Non-white race/ethnicity	7.4 (4.4–12.5)*	3.0 (1.8–4.9)*	3.8 (2.0–6.9)*
Living situation			
With spouse	Referent	Referent	Referent
Alone	1.2 (0.6–2.2)	1.7 (1.0–2.8)*	0.8 (0.4–1.9)
With others	1.1 (0.6–1.9)	1.5 (0.9–2.4)	2.0 (1.1–3.7)*
Psychosocial factors			
Low health literacy	2.8 (1.7–4.5)*	1.5 (1.0–2.3)*	2.5 (1.5–4.4)*
Low health numeracy	3.2 (1.9–5.6)*	2.8 (1.8–4.3)*	1.9 (1.1–3.3)*
Depression	0.7 (0.4–1.3)	0.7 (0.4–1.3)	0.7 (0.3–1.5)
Anxiety	1.4 (0.8–2.7)	1.6 (0.9–2.8)	1.5 (0.7–3.1)
Perceived stress			
Low	Referent	Referent	Referent
Moderate	1.2 (0.6–2.4)	1.0 (0.6–1.7)	0.7 (0.3–1.5)
High	1.6 (0.8–3.2)	0.9 (0.5–1.5)	0.9 (0.5–2.0)
Low social support	3.1 (1.4–6.8)*	1.1 (0.5–2.6)	1.8 (0.7–4.7)
SF-36 Mental subscore†	0.91 (0.81–1.0)	0.91 (0.82–1.0)	0.94 (0.83–1.1)
SF-36 Physical subscore†	0.95 (0.85–1.1)	0.90 (0.82–1.0)	0.86 (0.76–0.99)*
Clinical factors			
History of stroke	2.5 (1.0–5.8)*	2.1 (1.0–4.4)*	1.0 (0.3–3.5)
History of diabetes mellitus	0.8 (0.5–1.3)	0.7 (0.4–1.1)	1.1 (0.7–2.0)
ACS type			
STEMI	1.0 (0.5–2.2)	0.8 (0.4–1.6)	0.8 (0.3–1.8)
NSTEMI	0.8 (0.5–1.4)	1.1 (0.7–1.7)	0.8 (0.4–1.4)
Unstable angina	Referent	Referent	Referent
In-hospital renal failure	1.3 (0.5–3.3)	0.6 (0.2–1.7)	0.2 (0.1–1.7)
GRACE risk score‡	1.1 (1.0–1.02)*	1.2 (1.1–1.3)*	1.1 (0.95–1.2)

Referent group is those who are not impaired during hospitalization or at 1-mo post-discharge (n=1217). Missing data: race/ethnicity=9, perceived stress=24. ACS indicates acute coronary syndrome; GRACE, Global Registry of Acute Coronary Events; NSTEMI, non–ST-segment–elevation myocardial infarction; STEMI, ST-segment–elevation myocardial infarction; and TRACE-CORE, Transition, Risks, and Actions in Coronary Events–Center for Outcomes Research and Education.

*$P< 0.05$.

†SF-36 MCS and PCS scores are in 5-point units.

‡GRACE risk score is in 10-point units.

The reanalyses of our models with inverse probability sampling to account for differential dropout yielded point estimates of model coefficients very similar to those in Table 3, with the only changes occurring for a few variables whose *P* values are slightly above or slightly below the 0.05 level in each (highlighted in Table II in the Data Supplement). Similarly, there were no substantive changes in our findings about the relationships between patient characteristics and categories of cognitive status change after multiple imputations for missing data (data not shown).

Alternative Definition of Cognitive Change

In a sensitivity analysis, we examined an absolute change of 4 points from baseline, irrespective of impairment status at

baseline. This change represents ≈3× that which would be expected from practice effects.[20] On the basis of this definition of cognitive change, 23% of the sample (n=347) improved in the 1 month after discharge, 8% (n=130) declined, and 67% (n=1044) remained stable. In general, findings using the alternative definition of change were similar to findings in the main analysis. Sociodemographic (eg, race and education) and psychosocial factors (eg, health literacy and numeracy, cognitive status) were associated with change in cognitive function, but few (eg, history of stroke and GRACE risk score) clinical characteristics were associated with change (Table I in the Data Supplement).

Discussion

In one of the first studies with hospital and post-discharge measures of cognitive function in a diverse cohort of ACS survivors, we found that there is considerable change in cognitive function during the transition period from hospital to home. Over half of the patients who were impaired during hospitalization were only transiently impaired and recovered to normal cognitive function by 1 month. In addition, 5% of patients who were not impaired during hospitalization developed impairment in the month after discharge. Low health literacy, numeracy, educational attainment, and social support, as well as a history of stroke and higher GRACE risk sore, were associated with being cognitively impaired both during hospitalization and 1 month later. On the other hand, male sex, living with others, and low health literacy and numeracy were associated with the development of new cognitive impairment at 1 month.

Nearly 40% of hospitalized patients are cognitively impaired, although these rates are not specific to ACS patients.[1,3,30] To our knowledge, in-hospital rates of cognitive impairment have not been systematically assessed in a cohort of patients with ACS. Most studies examining cognitive function in ACS survivors only measure cognition after discharge and typically focus on long-term follow-up, 1 year or longer after the acute event. In general, these studies report that cognitive function is impaired after ACS. For example, in the TRIUMPH study (Transitional Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health), >50% of patients were cognitively impaired 1 month after hospital discharge.[18] The lower rates of impairment 1 month after hospital discharge observed in the current study (11%) may be because our sample was considerably younger than the subset of the TRIUMPH sample on which cognition was assessed (62 versus 73 years old). In the Health and Retirement Study, hospitalization for an acute myocardial infarction was associated with a 2.5-fold increased risk of developing mild, moderate, or severe cognitive impairment in the 1 to 3 years after discharge.[31] In several studies, cognitive change after ACS has also been compared with the impairment seen after stroke. One study found that ACS survivors were more than twice as likely than survivors of transient ischemic attacks to have moderate or severe cognitive impairment 1 year after the acute event.[32] In the Health and Retirement Study, cognitive decline accelerated in the years after stroke but not myocardial infarction,[33] suggesting that cognitive change in the transition from hospital to home may be important in understanding long-term trajectories of decline. Sixteen percent of our cohort were impaired during hospitalization, and 11% were impaired 1 month after discharge, but there was considerable change with remediation of cognitive function in patients who were impaired during hospitalization and development of new impairment. Also of note, we excluded demented, delirious, and palliative care patients from our study, suggesting that our sample was relatively high functioning relative to all patients hospitalized annually in the United States for ACS.

Our results highlight the importance of serial assessments of cognitive function during transition periods. With the aging of the US population and improvement in survival after hospitalization for ACS, clinicians and patients are increasingly concerned with factors associated with quality of life, including cognitive status, as important outcomes of an acute event.[34] Previous literature has focused on single assessments of cognitive function, either during hospitalization or after discharge, but few have measured cognitive function at multiple time points and thus we lack an understanding of how cognitive performance changes during the transitional period from hospital to home. Temporary cognitive impairment, particularly if not associated with an acute delirium, may signal a patient at risk for poor outcomes. For instance, in a study of all elderly patients on a general medicine service, cognitive impairment during hospitalization that resolved by discharge was associated with a 2-fold increased risk of death in the year after discharge.[10]

Cognitive impairment around the time of hospital discharge has been described as both a predictor and consequence of the proposed Post-Hospital Syndrome.[9] As such, cognitive ability may influence ability to comprehend and follow discharge instructions, to carry out disease self-management and to fully recover physical function after hospitalization. We found both improvement and decline in cognitive function after discharge for ACS, underscoring the importance of serial cognitive testing. Important questions remain including whether patients with the various cognitive trajectories we identified (eg, transiently impaired, consistently impaired) have different rates of long-term clinical outcomes. For instance, transient impairment may represent an intermediary risk category between nonimpaired and consistently impaired with respect to functional recovery, rehospitalization, or effective disease self-management.

Our findings are strengthened by the diversity of the sample and comprehensive assessment of the demographic, psychosocial, and clinical characteristics of the cohort. We had serial assessments of cognitive function, both in and out of the hospital, and we examined alternative definitions of change, including those linked to a cut point and absolute change, with similar overall results.

Several limitations of this study should be noted. The sample with baseline and 1-month data was predominately non-Hispanic white (84%) and slightly underrepresented women (67% male). We had attrition from baseline to 1-month follow-up, and those who did not complete 1-month interviews had significantly poorer cognitive function at baseline, and also higher psychosocial vulnerability; thus, the observed associations are likely to be stronger without this attrition. We excluded patients who were delirious or demented at the time

of enrollment, resulting in a higher functioning cohort that likely underestimates the prevalence of cognitive impairment during hospitalization. Although we screened for delirium, it is possible that we enrolled patients with subsyndromal delirium or those who developed delirium after our study interview. Similarly, because dementia is underdiagnosed in the medical record,[35] it is possible that we enrolled patients who were demented but did not have the diagnosis in their record. Unrecognized delirious or demented patients would be more likely to be cognitively impaired and to have poorer cognitive function after discharge. Like all cognitive screening tests, the TICS may be biased by education. In addition, we administered the TICS twice in a 1-month period, which could have resulted in some increase in scores because of practice effects because alternate forms of the TICS do not exist. However, in sensitivity analyses, we examined change in cognition that was ≈3× that which would be expected from practice effects and found similar results to our main model. Similarly, use of cut points, although conventional in cognitive impairment assessment, inevitably resulted in some participants with small absolute changes in TICS score moving between nonimpaired and impaired. However, the proportions of those who would have been reclassified if we had precluded a 1-point change from resulting in reclassification were small (3% for the transiently impaired and 7% for the newly impaired). The mode of administration of the TICS changed between the baseline (in-person) and follow-up (via telephone) assessments. Although the change in mode of administration may have resulted in a slight difference in test performance between the baseline and follow-up examination, it is unlikely to have impacted group membership (eg, being in the consistently impaired versus in the transiently impaired group) because the average change was 6 points (3 SDs) in the transiently impaired group and 4 points (2 SDs) in the newly impaired group. Health literacy and numeracy were assessed using brief (1 and 2 items, respectively) screening instruments, and future work should include more expanded assessments with greater validity and reliability. We did not have information on timing of in-hospital treatments or procedures relative to the timing of the cognitive assessments therefore cannot examine whether procedures impacted baseline cognitive performance.

Conclusions

In this diverse cohort of ACS survivors, we found considerable change, both improvement and decline, in cognitive function during the high-risk transitional period from hospital to home. We also found that markers of psychosocial vulnerability (eg, low health literacy and numeracy, poor social support) are generally associated with cognitive impairment and lower likelihood of recovery. Thus, assessing cognition both in hospital and post-discharge is important for detecting patients who could benefit from tailored transitional care, including early follow-up appointments with healthcare providers, increased surveillance, and booster post-discharge instructions.

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Disclosures

Dr Saczynski had full access to the data and takes responsibility for the integrity of the data and the accuracy of the data analysis. The other authors report no conflicts.

References

1. Sands LP, Yaffe K, Covinsky K, Chren MM, Counsell S, Palmer R, Fortinsky R, Landefeld CS. Cognitive screening predicts magnitude of functional recovery from admission to 3 months after discharge in hospitalized elders. *J Gerontol A Biol Sci Med Sci*. 2003;58:37–45.
2. Joray S, Wietlisbach V, Büla CJ. Cognitive impairment in elderly medical inpatients: detection and associated six-month outcomes. *Am J Geriatr Psychiatry*. 2004;12:639–647. doi: 10.1176/appi.ajgp.12.6.639.
3. Hickey A, Clinch D, Groarke EP. Prevalence of cognitive impairment in the hospitalized elderly. *Int J Geriatr Psychiatry*. 1997;12:27–33.
4. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, Cummings JL, Chertkow H. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53:695–699. doi: 10.1111/j.1532-5415.2005.53221.x.
5. Dodson JA, Truong TT, Towle VR, Kerins G, Chaudhry SI. Cognitive impairment in older adults with heart failure: prevalence, documentation, and impact on outcomes. *Am J Med*. 2013;126:120–126. doi: 10.1016/j.amjmed.2012.05.029.
6. Di Iorio A, Longo AL, Mitidieri Costanza A, Bandinelli S, Capasso S, Gigante M, Bavazzano A, Guizzardi G, Senin U, Ferrucci L, Abate G. Characteristics of geriatric patients related to early and late readmissions to hospital. *Aging (Milano)*. 1998;10:339–346.
7. Iadecola C, Yaffe K, Biller J, Bratzke LC, Faraci FM, Gorelick PB, Gulati M, Kamel H, Knopman DS, Launer LJ, Saczynski JS, Seshadri S, Zeki Al Hazzouri A; American Heart Association Council on Hypertension; Council on Clinical Cardiology; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Stroke Council. Impact of hypertension on cognitive function: a scientific statement from the American Heart Association. *Hypertension*. 2016;68:e67–e94. doi: 10.1161/HYP.0000000000000053.
8. Sanchis J, Bonanad C, Ruiz V, Fernández J, García-Blas S, Mainar L, Ventura S, Rodríguez-Borja E, Chorro FJ, Hermenegildo C, Bertomeu-González V, Núñez E, Núñez J. Frailty and other geriatric conditions for risk stratification of older patients with acute coronary syndrome. *Am Heart J*. 2014;168:784–791. doi: 10.1016/j.ahj.2014.07.022.
9. Krumholz HM. Post-hospital syndrome–an acquired, transient condition of generalized risk. *N Engl J Med*. 2013;368:100–102. doi: 10.1056/NEJMp1212324.
10. Inouye SK, Zhang Y, Han L, Leo-Summers L, Jones R, Marcantonio E. Recoverable cognitive dysfunction at hospital admission in older persons during acute illness. *J Gen Intern Med*. 2006;21:1276–1281. doi: 10.1111/j.1525-1497.2006.00613.x.
11. Joosten H, van Eersel ME, Gansevoort RT, Bilo HJ, Slaets JP, Izaks GJ. Cardiovascular risk profile and cognitive function in young, middle-aged, and elderly subjects. *Stroke*. 2013;44:1543–1549. doi: 10.1161/STROKEAHA.111.000496.
12. Waring ME, McManus RH, Saczynski JS, Anatchkova MD, McManus DD, Devereaux RS, Goldberg RJ, Allison JJ, Kiefe CI; TRACE-CORE Investigators. Transitions, Risks, and Actions in Coronary Events–Center for Outcomes Research and Education (TRACE-CORE): design and rationale. *Circ Cardiovasc Qual Outcomes*. 2012;5:e44–e50. doi: 10.1161/CIRCOUTCOMES.112.965418.
13. Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE, Jr, Chavey WE, 2nd, Fesmire FM, Hochman JS, Levin TN, Lincoff AM, Peterson ED, Theroux P, Wenger NK, Wright RS, Smith SC, Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Halperin JL, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura R, Ornato JP, Page RL, Riegel B. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-Elevation myocardial infarction. *Circulation*. 2007;116:e148–e304. doi: 10.1161/CIRCULATIONAHA.107.181940.

14. Kushner FG, Hand M, Smith SC Jr, King SB, 3rd, Anderson JL, Antman EM, Bailey SR, Bates ER, Blankenship JC, Casey DE, Jr, Green LA, Hochman JS, Jacobs AK, Krumholz HM, Morrison DA, Ornato JP, Pearle DL, Peterson ED, Sloan MA, Whitlow PL, Williams DO. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction. *Circulation*. 2009;120:2271–2306. doi: 10.1161/CIRCULATIONAHA.109.192663
15. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med*. 1990;113:941–948.
16. Brandt J, Spencer M, Folstein M. The telephone interview for cognitive status. *Neuropsychiatry Neuropsychol Behav Neurol*. 1988;1:111–117.
17. Seo EH, Lee DY, Kim SG, Kim KW, Kim DH, Kim BJ, Kim MD, Kim SY, Kim YH, Kim JL, Kim JW, Moon SW, Park JH, Ryu SH, Yoon JC, Lee NJ, Lee CU, Jhoo JH, Choo LH, Woo JI. Validity of the telephone interview for cognitive status (TICS) and modified TICS (TICSm) for mild cognitive impairment (MCI) and dementia screening. *Arch Gerontol Geriatr*. 2011;52:e26–e30. doi: 10.1016/j.archger.2010.04.008.
18. Gharacholou SM, Reid KJ, Arnold SV, Spertus J, Rich MW, Pellikka PA, Singh M, Holsinger T, Krumholz HM, Peterson ED, Alexander KP. Cognitive impairment and outcomes in older adult survivors of acute myocardial infarction: findings from the translational research investigating underlying disparities in acute myocardial infarction patients' health status registry. *Am Heart J*. 2011;162:860.e1–869.e1.
19. Manly JJ, Schupf N, Stern Y, Brickman AM, Tang MX, Mayeux R. Telephone-based identification of mild cognitive impairment and dementia in a multicultural cohort. *Arch Neurol*. 2011;68:607–614. doi: 10.1001/archneurol.2011.88.
20. Salthouse T. *Major Issues in Cognitive Aging*. New York, NY: Oxford University Press; 2010.
21. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30:473–483.
22. Powers BJ, Trinh JV, Bosworth HB. Can this patient read and understand written health information? *JAMA*. 2010;304:76–84. doi: 10.1001/jama.2010.896.
23. Lipkus IM, Samsa G, Rimer BK. General performance on a numeracy scale among highly educated samples. *Med Decis Making*. 2001;21:37–44. doi: 10.1177/0272989X0102100105.
24. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16:606–613.
25. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166:1092–1097. doi: 10.1001/archinte.166.10.1092.
26. Sherbourne CD, Stewart AL. The MOS social support survey. *Soc Sci Med*. 1991;32:705–714.
27. Eagle KA, Lim MJ, Dabbous OH, Pieper KS, Goldberg RJ, Van de Werf F, Goodman SG, Granger CB, Steg PG, Gore JM, Budaj A, Avezum A, Flather MD, Fox KA; GRACE Investigators. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. *JAMA*. 2004;291:2727–2733. doi: 10.1001/jama.291.22.2727.
28. Fox KA, Dabbous OH, Goldberg RJ, Pieper KS, Eagle KA, Van de Werf F, Avezum A, Goodman SG, Flather MD, Anderson FA Jr, Granger CB. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). *BMJ*. 2006;333:1091. doi: 10.1136/bmj.38985.646481.55.
29. Kutner MH, Nachtsheim CJ, Neter J, Li W. *Applied Linear Statistical Models*. New York, NY: McGraw-Hill Irwin; 2005:608–618.
30. Zuccalà G, Pedone C, Cesari M, Onder G, Pahor M, Marzetti E, Lo Monaco MR, Cocchi A, Carbonin P, Bernabei R. The effects of cognitive impairment on mortality among hospitalized patients with heart failure. *Am J Med*. 2003;115:97–103.
31. Davydow DS, Hough CL, Levine DA, Langa KM, Iwashyna TJ. Functional disability, cognitive impairment, and depression after hospitalization for pneumonia. *Am J Med*. 2013;126:615.e5–624.e5. doi: 10.1016/j.amjmed.2012.12.006.
32. Volonghi I, Pendlebury ST, Welch SJ, Mehta Z, Rothwell PM. Cognitive outcomes after acute coronary syndrome: a population based comparison with transient ischaemic attack and minor stroke. *Heart*. 2013;99:1509–1514. doi: 10.1136/heartjnl-2013-304207.
33. Levine D, Davydow DS, Hough CL, Langa KM, Rogers M, Iwashyna TJ. Functional disability and cognitive impairment for myocardial infarction and stroke. *Circ Cardiovasc Qual Outcomes*. 2014;7:863–871. doi: 10.1161/HCQ.0000000000000008.
34. Saczynski JS, Kiefe CI. Dawning of a new era: understanding the functional outcomes of cardiovascular disease. *Circ Cardiovasc Qual Outcomes*. 2014;7:812–814. doi: 10.1161/CIRCOUTCOMES.114.001427.
35. Boustani M, Peterson B, Hanson L, Harris R, Lohr KN; U.S. Preventive Services Task Force. Screening for dementia in primary care: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2003;138:927–937. doi: 10.7326/0003-4819-138-11-200306030-00015.

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Change in Cognitive Function in the Month After Hospitalization for Acute Coronary Syndromes: Findings From TRACE-CORE (Transition, Risks, and Actions in Coronary Events–Center for Outcomes Research and Education)

Jane S. Saczynski, David D. McManus, Molly E. Waring, Darleen Lessard, Milena D. Anatchkova, Jerry H. Gurwitz, Jeroan Allison, Arlene S. Ash, Richard H. McManus, David C. Parish, Robert J. Goldberg and Catarina I. Kiefe

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