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Patterns of cognitive change in elderly patients during and 6 months after hospitalisation: A prospective cohort study

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ABSTRACT

Background: The extent and patterns of cognitive change regularly occurring in elderly patients who experience prolonged hospitalisation have not been well examined.
Objective: To describe patterns of cognitive change during and 6 months after hospitalisation and to identify prognostic factors associated with different patterns of changes.
Design: A prospective cohort study.
Setting: Five med-surgical units at a tertiary hospital in Taipei, Taiwan.
Participants: Patients ≥65 years old without preexisting profound cognitive impairment (Mini-Mental State Examination score ≥20) and with an expected hospital length of stay >5 days were drawn from consecutive admissions. Of 351 patients, 82.9% (138 women, 153 men, mean age = 71.6 years) completed all four scheduled assessments.
Methods: Cognition was measured by the Mini-Mental State Examination at 4 times: admission, discharge, and 3 and 6 months post-discharge. Possible prognostic factors at admission included demographics, comorbidities, number of medications, serum haemoglobin, length of hospital stay, and surgery.
Results: Four cognitive-change patterns with a high prevalence of decline were identified by cluster analysis. The worsening then improve group ($n = 47$) had a deep V-shape with a mean fluctuation of 3.9 points on the Mini-Mental State Examination, and the low continuous group ($n = 83$) had little change. Both the start high and decline ($n = 66$) and start low and decline ($n = 95$) groups showed persistent and accelerated declines, with baseline cognitive scores of 29.1 and 25.5 points, respectively. Predictor variables at admission for different patterns of cognitive change were age, total education (years), cardiovascular comorbidities, number of medications, functional and nutritional status, depressive symptoms, surgical treatment, and haemoglobin level <12 g/dL.
Conclusions: Cognitive decline during and after hospitalisation shows four heterogeneous patterns of change. Different patterns of change were predicted by age, education, cardiovascular comorbidities, number of medications, functional and nutritional status, depressive symptoms, surgical treatment, and haemoglobin level <12 g/dL, most of which are potentially modifiable factors.

What is already known about the topic?

- Hospitalisation often initiates events leading to cognitive decline, particularly in elderly patients who experience prolonged hospitalisation.

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- Although cognitive decline is common, the patterns of decline might vary.
- Little is known about the extent and patterns of cognitive change regularly occurring during and 6 months after elderly patients are hospitalised for >5 days.

What this paper adds

- Elderly patients without preexisting profound cognitive impairment and hospitalised for >5 days experienced four cognitive-change patterns: *worsening then improve*, *low continuous*, *start high and decline*, and *start low and decline*.
- Over half the participants declined cognitively by 6 months post-discharge. Patients experienced long-term declines despite differences in baseline cognition and not experiencing acute decline during hospitalisation.
- Different patterns of change were predicted by age, education, cardiovascular comorbidities, number of medications, functional and nutritional status, depressive symptoms, surgical treatment, and haemoglobin level <12 g/dL, most of which are potentially modifiable factors.

1. Introduction

Acute hospitalisation often initiates events leading to cognitive decline culminating in hospital-acquired geriatric syndromes (Mecocci et al., 2005). About 30% of hospitalised elders whose cognitive status was assessed by the Mini-Mental State Examination (MMSE) declined more than 1 MMSE point (Huber and Kennard, 1991), and approximately 20% declined more than 2 MMSE points at discharge (Fitzpatrick et al., 2004). Such cognitive declines occurring during hospitalisation can have a substantial effect. For example, cognitive decline has been positively associated with increased risk of mortality (Schupf et al., 2005) and has been suggested to lead to dysfunction in performing activities of daily living (ADLs, Mehta et al., 2002). Similarly, elderly patients who developed cognitive decline during hospitalisation were about 16 times more likely to develop functional decline than those without cognitive decline (Pedone et al., 2005).

Whether these cognitive declines recover after hospitalisation remains uncertain as few studies have followed these changes over multiple time points after discharge. One of the first well-known studies showed that cognitive decline persisted in 24–42% of coronary artery bypass patients at 6 weeks to 5 years after hospital discharge (Newman et al., 2001). Similarly, 40% of elderly (≥65 years) patients admitted for hip fracture developed cognitive decline that persisted 2 and 12 months post-discharge (Gruber-Baldini et al., 2003). Those with cognitive decline persisting through 2 months had poor functional outcomes at 12 months (Gruber-Baldini et al., 2003). Cognitive decline is also likely to be more prevalent and severe among elderly patients who experience a longer course of hospitalisation (Monk et al., 2008). With rapid advances in medical care, increasing numbers of elderly patients with complex conditions necessitating leading to longer stay can be expected. In this context, understanding differences in patterns of cognitive change for elderly patients after prolonged hospitalisation and identifying prognostic factors are clinically important for designing effective interventions.

1.1. Aims

The aims of this prospective cohort study were to (1) examine the magnitude and patterns of cognitive change for elderly patients during and 6 months after prolonged hospitalisation (>5 days) and (2) identify whether different patterns of cognitive change are associated with demographic, medical, or psychosocial comorbidities. We looked at degree of cognitive change, as opposed to disease, i.e. delirium or dementia, to understand how global cognitive function changed during and 6 months following prolonged hospitalisation both for elderly medical and surgical patients.

2. Methods

2.1. Design and procedure

This prospective, longitudinal, interview-based study of hospitalised elderly patients used cluster sampling. Details of the study design have been reported elsewhere (Chen et al., 2008, 2009). Data were collected by two trained research nurses who used validated and standardised instruments. All participants were evaluated 4 times: within 48 h of admission, before discharge, 3 months, and 6 months after discharge. Global cognition was measured by the MMSE, a screening instrument that covers aspects of orientation, registration, attention, calculation, recall, and language (Folstein et al., 1975). Despite its limited value in identifying specific cognitive dysfunction, serial testing using the MMSE is of value in monitoring global cognitive changes. The study was approved by the Research Ethics Review Committee of National Taiwan University Hospital.

2.2. Sample

Five medical and surgical units were randomly selected from 24 units at a 2200-bed medical centre in northern Taiwan. Three units were proportionally selected from surgery and two from medicine. Patients aged 65 years and older consecutively admitted to one of the five units from August 2004 to May 2006 were screened for enrolment. Patients were excluded if they had preexisting cognitive impairment (MMSE score < 20 based on culturally adjusted norms [Shyu and Yip, 2001], $n = 43$), expected length of stay (LOS) less than or equal to 5 days ($n = 1091$), isolated within infection-control protocol ($n = 56$), intubated or unable to communicate due to profound sensory loss ($n = 140$). Of the 439 eligible patients, 351 (80.0%) were enrolled. The reasons given for not participating were not interested ($n = 57$), not feeling well ($n = 20$), and declined to consent ($n = 11$). In the follow-ups, 291 participants (82.9%) completed all assessments and are the focus of this report. Primary reasons for attrition were death ($n = 44$), intubation ($n = 3$), isolated for tuberculosis ($n = 1$), missed appointments ($n = 9$), and withdrew consent

($n = 3$). Participants not included in the analysis ($n = 60$) did not differ significantly from those in our analysis ($n = 291$) with respect to age ($p = .07$), education ($p = .32$) and baseline MMSE score ($p = .94$). However, the study sample included more females ($p = .01$).

2.3. Measures

We examined an array of prognostic factors: demographics, medical and psychosocial comorbidities. Medical comorbidities included number of current medications, serum haemoglobin, LOS, surgical treatment, and sensory, cardiovascular, neurological, and diabetic comorbidities (coded as prevalence, %). Sensory comorbidities included visual and hearing impairments; cardiovascular comorbidities included coronary heart disease, hypertension, congestive heart failure, and hyperlipidemia; and neurological comorbidities included stroke and parkinsonism. Diabetic comorbidity was studied as a known risk factor for cognition (Nguyen et al., 2002). Demographic information was collected in face-to-face patient interviews. Data on medical and psychosocial comorbidities (see below) were also obtained from interviews; data on surgical treatment and on serum haemoglobin were collected from patients' medical records; and data on LOS, as a proxy for disease severity, were obtained from the hospital computer system. Surgical treatment was coded as a dichotomous variable (yes/no).

Data on psychosocial comorbidities included functional status, nutritional status, and depressive symptoms. These data were collected using three instruments: the Chinese Barthel Index (BI), Chinese Mini-Nutritional Assessment (MNA), and Chinese Geriatric Depression Scale Short-Form (GDS-15). The BI measures independence in performing 10 ADLs, with higher scores indicating better functional status (Mahoney and Barthel, 1965). The 18-item MNA assesses nutritional status, defined as the assessment of the state of nourishment of a patient with scores ranging from 0 to 30 and higher scores indicating better nutritional status (Guigoz et al., 1996). The 15-item GDS-15 measures depressive symptoms, with higher scores indicating more depressive symptoms (Wong et al., 2002; Yesavage et al., 1983).

2.4. Data analysis

Data were analysed using statistical program R Language version 2.6.1(http://www.r-project.org/), with significance set at $p < .05$. Overall differences among identified patterns in demographics, clinical characteristics, and functional scores at each time point were tested by ANOVA, Kruskal–Wallis test, χ^2 test, and Fisher's exact test. To determine whether differences among patterns were significant, we performed post hoc comparisons. Significance of post hoc comparisons was judged at $p < .008$ (=.05/6), using the Bonferroni multiple-comparison adjustment (Rosner, 2005).

Given the exploratory nature of this study, cluster analyses were performed to identify naturally occurring subgroups of elderly patients with similar patterns of cognitive change (MMSE scores) over four time points. Cluster analysis is a statistical technique that sorts similar observations into clusters or groups. The grouping from this analysis is primitive in that no assumptions are made concerning the group structure (Johnson and Wichern, 2007). The identified patterns of cognitive change provide an informal means for suggesting interesting hypotheses about their relationships with potential risk factors. We used the k-means method (Everitt et al., 2001) as computed by the *kmeans* function in R. The optimal number of clusters to retain was determined by examining a plot of cluster number vs. the within-cluster sum of squares.

Relationships between patterns of cognitive change and various characteristics were examined by multinomial logistic regression, using the *multinom* function in R. Individual membership within different cognitive patterns was modelled as depending on age; gender; total education; prevalence of cardiovascular, neurological, sensory, and diabetic comorbidities; number of current medications; admission scores for the BI, MNA, and GDS-15; serum haemoglobin level; LOS; and surgical treatment. The model fitness was evaluated using the -2 log-likelihood ratio comparing the fitted model with the saturated model (residual deviance) and degrees of freedom for the fitted model. Model fitness was judged by the naïve criterion of whether (residual deviance)/(degrees of freedom) was less than 3.8 (the upper 5.0% quantile of the $\chi^2(1)$ distribution).

3. Results

Our sample was diverse in gender, educational background, and income level. Their mean age was 71.6 years. Detailed demographics are shown in Table 1. Naturally occurring subgroups of patients with similar patterns of cognitive change (clusters of MMSE scores) were identified by plotting number of clusters vs. the within-cluster sum of squares (data not shown). Since this plot showed an elbow at the four-cluster solution, participants were classified into four cognitive subgroups. These four groups showed cognitive changes that varied significantly in pattern and magnitude of decline over the 6-month study period (Fig. 1a). These characteristic changes were used to name the four groups: *low continuous* ($n = 83$), *worsening then improve* ($n = 47$), *start low and decline* ($n = 95$), and *start high and decline* ($n = 66$). The *low continuous* group was characterised by little cognitive change, while the *worsening then improve* group was characterised by a substantial acute decline (3.8 MMSE points) at discharge, which bounced back after discharge. The other two groups were both characterised by continuous declines in cognition, but were differentiated by MMSE baseline scores and rates of decline. The *start high and decline* group was characterised by an accelerated decline over time (mean reductions of 0.8, 1.2, and 1.6 MMSE points at discharge, 3 months, and 6 months after discharge, respectively), and a higher MMSE baseline score (29.1) than that of the *start low and decline* group (25.5).

Overall, participants in the *worsening then improve* and *start high and decline* groups were younger, better

Table 1
Sample demographics ($n = 291$).

Variable	Low continuous ($n = 83$)	Worsening then improve ($n = 47$)	Start high and decline ($n = 66$)	Start low and decline ($n = 95$)	Total ($n = 291$)	Significant post hoc comparisons
Age, mean (SD)[a,**]	73.10 (5.66)	69.98 (4.95)	70.17 (4.74)	72.2 (5.95)	71.64 (5.58)	1≠2, 1≠3, 2≠4, 3≠4
Gender, %[b,***]						1≠2, 1≠3, 2≠4, 3≠4
Female	60.24	27.66	28.79	58.95	47.42	
Marital status, %[c,*]						
Married	63.86	78.72	80.30	61.05	69.07	
Widowed	34.94	21.28	16.67	33.68	28.18	
Living with others, %[c]	96.39	100	95.45	92.63	95.53	
Total education(years), mean (SD)[a,***]	4.18 (4.57)	8.15 (5.49)	10.55 (4.92)	5.71 (5.15)	6.76 (5.52)	1≠2, 1≠3, 3≠4
Monthly income (NTD[d]), %[b,***]						2≠4, 3≠4
≤10,000	62.65	36.17	46.97	74.74	58.76	
>10,000	37.35	63.83	53.03	25.26	41.24	

Notes: All percentage results are the percentage of the trajectory groups. Significant post hoc comparisons were significant at $p < 0.008$ with Bonferroni correction. 1 = low continuous; 2 = worsening then improve; 3 = start high and decline; 4 = start low and decline.

[a] ANOVA.
[b] Based on chi-square test.
[c] Based on Fisher's exact test.
[d] New Taiwan dollar, 32 NTD = 1USD.
[*] $p < .05$.
[**] $p < .01$.
[***] $p < .001$.

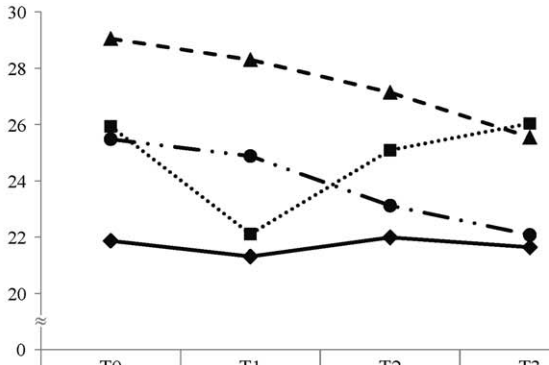
educated, more likely to be male, and reported higher incomes than participants in the other groups (Table 1). In terms of medical and psychosocial comorbidities, participants in the *worsening then improve* group reported significantly fewer cardiovascular and sensory comorbidities than low-staring groups, and the majority underwent surgical treatment with the longest LOS of all four groups (Table 2). As shown in the last column of Tables 1 and 2, all post hoc comparisons were confirmed by Bonferroni correction. Although cognitive decline persisted in both *decline* groups, nutritional status, ADL functional status, and depressive symptoms all gradually bounced back after discharge, suggesting that the progress in cognitive decline was effectively separate from declines in other variables (Fig. 1).

Different patterns of cognitive change were found by multinomial logistic regression to be independently and significantly associated with several factors measured at admission: age, total education, cardiovascular comorbidities, surgical treatment, number of medications, BI, MNA, and GDS scores, and haemoglobin level <12 g/dL (Table 3). Specifically, older patients were more likely to belong to the *low continuous* group and more educated participants were more likely to present the *start high and decline* pattern. Participants with cardiovascular comorbidities upon admission were least likely to be in the *worsening then improve* group. Participants taking fewer medications were most likely to show the *start slow and decline* pattern. Although the effect size seems to be small, patients with better ADL function were most likely to be in the *start low and decline* group. Depressive participants (at admission) were most likely to be in the *low continuous* or *start low and decline* group. Participants who were anaemic upon admission were most likely to be in *decline* groups and surgical treatment was most related to the *worsening then improve* pattern. Notably, all observations in Table 3 reflect pair-wise comparison and therefore care is needed with interpretation.

This final model was adjusted for gender, marital status, income, neurological morbidities, sensory morbidities, diabetic morbidities, and length of stay. The overall model had residual deviance = 595.49 and 274 degrees of freedom, thus meeting the goodness-of-fit test ([595.49/274] = 2.17 < 3.84).

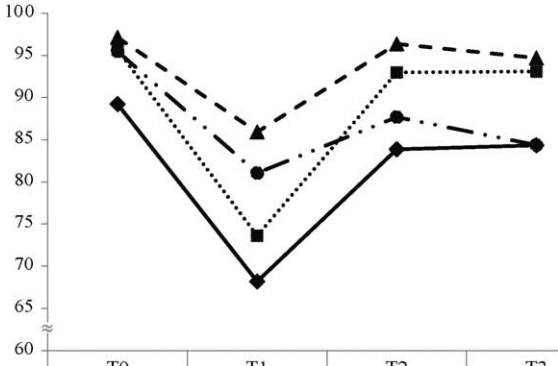
4. Discussion

Our analysis of cognitive changes in elderly patients from admission to 6 months post-discharge after prolonged hospitalisation revealed four phenotypically distinct subgroups: *low continuous*, *worsening then improve*, *start low and decline*, and *start high and decline*. The *low continuous* group was characterised by a flat cognitive trajectory, whereas the trajectory of the *worsening then improve* group had a deep V-shape (Fig. 1a). The shape of the latter trajectory may reflect the participants' experience of delirium from which they later recover (O'Keeffe et al., 2005). Given that the *worsening then improve* group had the highest percentage of patients who underwent surgical treatment, postoperative cognitive dysfunction likely played a role in this observation. Cognitive dysfunction at 1 week after surgery is reported to be common at any age, but the rates of cognitive dysfunction at 3 months after surgery were much higher for the elderly (9.9–14.3%) than for younger groups (1.8–2.8%) (Seymour and Severn, 2009). Such cognitive dysfunction persisting after discharge is likely to lead to poor outcomes. In this study, the high prevalence of cognitive decline over time after discharge is a matter of concern, particularly in the *start high and decline* and *start low and decline* groups, which showed little acute decline during hospitalisation. Therefore, such elderly patients may not have the



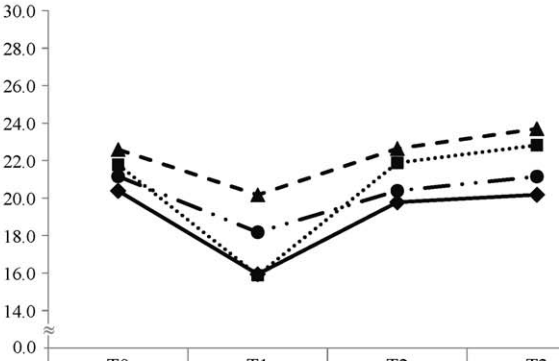
	T0	T1	T2	T3
Low Continuous	21.87	21.31	21.99	21.64
Worsening then Improve	25.94	22.11	25.09	26.04
Start High and Declines	29.05	28.30	27.14	25.55
Start Low and Declines	25.48	24.88	23.12	22.08

(a) Cognition



	T0	T1	T2	T3
Low Continuous	89.22	68.19	83.86	84.34
Worsening then Improve	95.64	73.62	92.98	93.09
Start High and Declines	97.12	85.91	96.36	94.70
Start Low and Declines	95.47	81.05	87.68	84.37

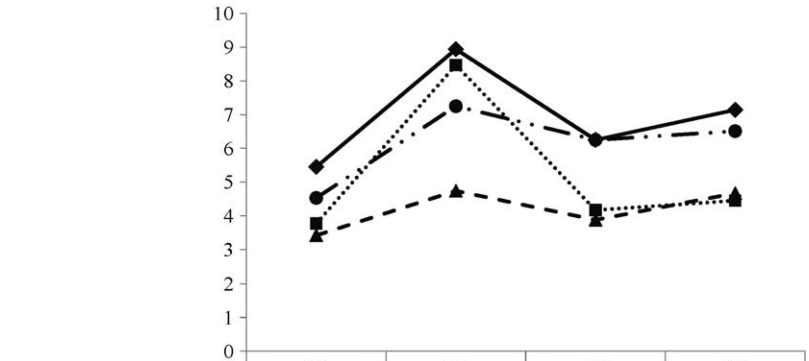
(b) Function



	T0	T1	T2	T3
Low Continuous	20.39	15.94	19.78	20.18
Worsening then Improve	21.78	15.89	21.88	22.82
Start High and Declines	22.59	20.17	22.64	23.70
Start Low and Declines	21.16	18.18	20.39	21.15

(c) Nutrition

Fig. 1. Changes in cognition and psychosocial comorbidities for four cognitive subgroups: low continuous ($n = 83$), worsening then improve ($n = 47$), start high and decline ($n = 66$), and start low and decline ($n = 95$).



	T0	T1	T2	T3
Low Continuous	5.45	8.94	6.25	7.14
Worsening then Improve	3.77	8.47	4.17	4.45
Start High and Declines	3.42	4.74	3.88	4.67
Start Low and Declines	4.53	7.25	6.25	6.51

(d) Depression

Fig. 1. (*Continued*).

opportunity to receive prompt medical attention and treatment. The predictors identified in this study should alert clinicians to pay closer attention to at-risk groups during post-discharge follow-ups.

Specifically, our study showed that different patterns of cognitive change were significantly associated with several factors measurable at admission: age, total education, cardiovascular comorbidities, number of medications, functional and nutritional scores, depressive symptoms, surgical treatment, and haemoglobin level <12 g/dL. Education plays a key role in cognitive functioning. However, we found that better educated participants were more likely to experience more dramatic cognitive changes, and more education did not ensure recovery of cognition (Tables 1 and 3). These findings contradict a previous report that a higher education level predicted recoverable cognitive dysfunction, defined as an admission MMSE score that improved 3 or more points by discharge (Inouye et al., 2006). A possible explanation, in line with the cognitive reserve hypothesis (Stern, 2002), is that education may delay the onset of observable cognitive decline, but once the decline begins, the rate may be faster. Although demographic characteristics such as age and education are untreatable, they can alert nurses and clinicians to at-risk groups.

In the present study, participants with fewer cardiovascular morbidities were more likely to recover cognition as more of them belonged to the *worsening then improve* group. This finding emphasises prior reports that cardiovascular morbidities, including hypertension and coronary heart disease, have negative effects on cognition (Selnes et al., 2008). Preventing and raising awareness of the cognitive effect from this comorbid condition are important for clinicians and the lay public.

Furthermore, participants in the *worsening then improve* and *start high and decline* groups were 0.84 and 0.82 times less likely, respectively, to present with depressive symptoms at admission than those in the *low continuous*

Table 2
Participants' medical comorbidities at admission ($n = 291$).

Variable	Low continuous ($n = 83$)	Worsening then improve ($n = 47$)	Start high and decline ($n = 66$)	Start low and decline ($n = 95$)	Total ($n = 291$)	Significant post hoc comparisons
Cardiovascular morbidities, %[a,*]	71.08	44.68	65.15	68.42	64.60	1≠2, 2≠4
Neurological morbidities, %[a]	10.84	12.77	6.06	9.47	9.62	
Sensory morbidities, %[a,**]	68.67	46.81	63.64	76.84	66.67	2≠4
Diabetic morbidity, %[a]	31.33	25.53	28.79	35.79	31.27	
# meds taken, mean (SD)[b]	3.71 (2.06)	3.32 (2.80)	3.47 (2.46)	3.00 (2.63)	3.36 (2.47)	
Haemoglobin, mean (SD)[b,***]	12.28 (2.38)	12.41 (1.97)	11.51 (2.28)	10.70 (2.55)	11.62 (2.45)	1≠4, 2≠4
Surgical treatment, %[c,***]	63.86	85.11	63.64	49.47	62.54	2≠4
Length of stay, mean (SD)[d,**]	16.89 (9.25)	17.21 (7.56)	12.89 (7.26)	15.83 (12.15)	15.69 (9.77)	1≠3, 2≠3

All percentage results are the percentage of the trajectory groups. Significant post hoc comparisons were significant at $p < 0.008$ with Bonferroni correction.
1 = low continuous; 2 = worsening then improve; 3 = start high and decline; 4 = start low and decline.
[a] Based on Fisher's exact test.
[b] ANOVA.
[c] Based on chi-square test.
[d] Based on Kruskal–Wallis test.
[*] $p < .05$.
[**] $p < .01$.
[***] $p < .001$.

Table 3
Baseline factors associated with four cognitive subgroups ($n = 291$).

Predictor[a]	Worsening then improve vs. low continuous	Start high and decline vs. low continuous	Start low and decline vs. low continuous	Start high and decline vs. worsening then improve	Start low and decline vs. worsening then improve	Start low and decline vs. start high and decline
	OR[b] (CI[b])	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Age (years)	0.89* (0.81, 0.97)	0.89* (0.82, 0.97)	0.95 (0.89, 1.01)	1.00 (0.91, 1.09)	1.07 (0.98, 1.16)	1.07 (0.99, 1.15)
Education (years)	1.17* (1.07, 1.29)	1.32* (1.20, 1.45)	1.11* (1.03, 1.20)	1.13* (1.03, 1.23)	0.95 (0.87, 1.04)	0.84* (0.78, 0.92)
Cardiovascular morbidities	0.25* (0.10, 0.65)	0.58 (0.22, 1.52)	0.79 (0.36, 1.76)	2.33 (0.89, 6.12)	3.19* (1.26, 8.12)	1.37 (0.57, 3.29)
# meds taken	1.10 (0.89, 1.35)	1.03 (0.84, 1.25)	0.81* (0.69, 0.95)	0.94 (0.76, 1.15)	0.74* (0.60, 0.90)	0.79* (0.65, 0.95)
Function	1.01 (0.97, 1.06)	1.02 (0.97, 1.07)	1.05* (1.01, 1.09)	1.01 (0.95, 1.07)	1.04 (0.99, 1.09)	1.03 (0.98, 1.08)
Depression	0.84* (0.72, 0.98)	0.86 (0.74, 1.00)	0.96 (0.86, 1.08)	1.02 (0.87, 1.21)	1.14 (0.98, 1.33)	1.12 (0.97, 1.29)
Nutrition	1.01 (0.86, 1.20)	1.20* (1.01, 1.42)	1.04 (0.92, 1.18)	1.18 (0.99, 1.41)	1.03 (0.88, 1.20)	0.87 (0.74, 1.02)
Haemoglobin < 12 g/dL	2.60 (0.96, 7.02)	8.37* (3.09, 22.70)	5.15* (2.31, 11.51)	3.22* (1.18, 8.78)	1.98 (0.78, 5.06)	0.62 (0.25, 1.52)
Surgical treatment	3.56* (1.10, 11.48)	1.57 (0.58, 4.27)	0.76 (0.33, 1.74)	0.44 (0.13, 1.45)	0.21* (0.07, 0.67)	0.48 (0.20, 1.20)

Notes: Function measured by Barthel Index; cognition measured by Mini-Mental State Examination; nutrition measured by Mini-Nutritional Assessment; depression measured by Geriatric Depression Scale-Short Form. The final model was adjusted for gender, marital status, income, neurological morbidities, sensory morbidities, diabetic morbidities, and length of stay.

[a] Odds ratios were calculated for 1 unit increase in predictors.

[b] OR, odds ratio; CI, 95% confidence interval of OR.

* $p < .05$.

group. This finding is inconsistent with reports suggesting that depressive symptoms are a risk factor for cognitive decline and dementia (Geerlings et al., 2000; Wilson et al., 2002). This negative finding may be explained by growing evidence that baseline depressive symptoms predict cognitive decline in individuals with persistent, but not episodic depressive symptoms (Paterniti et al., 2002) and that persistent depressive symptoms may have a greater effect on cognition than transient symptoms (Dotson et al., 2008).

The finding that participants in the *worsening then improve*, *start high and decline*, and *start low and decline* groups were more likely to have had haemoglobin level <12 g/dL at admission adds to the literature by suggesting that anaemia upon admission is associated with future cognitive decline, up to 6 months after hospitalisation. The relationship between anaemia and subsequent cognitive changes in hospitalised elderly patients has been evaluated in few cohort studies, although an increased odds of association between anaemia and cognition was found in prior retrospective case–control and cross-sectional studies (Ng et al., 2008; Zamboni et al., 2006). A direct relationship between anaemia and cognitive changes is supported by a prospective study showing that cognition significantly improved in 8 of 10 elderly cancer patients after 4 weeks of erythropoietin treatment (Massa et al., 2006). Future studies should examine whether correcting low haemoglobin status during hospitalisation could delay or ameliorate onset of cognitive decline for elderly patients experiencing a prolonged hospitalisation.

This study had limitations. First, we were not able to obtain DSM-based (American Psychiatric Association, 1994) psychiatric diagnoses for delirium and dementia in this large-scale epidemiologic study. Second, attrition was 17.1% ($n = 60$), which included 44 deaths. Since deaths were excluded from the analysis, the predictive ability is therefore conditional on survival. Third, our study was observational, limiting the ability for causal interpretations. Fourth, subjects were recruited from one medical centre, limiting the generalizability of findings. Repeated administration of cognitive test leads to improved performance and might bias study results toward an underestimation of cognitive decline. Lastly, cluster analysis is an exploratory method. These patterns of change and their relationships with predictors might be sample-specific and needs to be cross-validated in future studies. It is also important to note that MMSE is a screening measure of global function, so we cannot rule out the possibility that different cognitive domains such as attention and memory might have different patterns of cognitive change.

Nevertheless, this study used a prospective design to examine cognitive changes in both medical and surgical inpatients over multiple time points. We purposely limited our sample to patients with a length of stay > 5 days to study those most vulnerable for cognitive decline. Our findings extend those of previous studies by indicating that elderly patients with a prolonged hospital stay are frequently discharged with a worse-than-baseline cognitive status and many decline further after hospitalisation. Not only did the elderly patients in our study not

experience any apparent learning effect from repeated MMSE tests, but over half the participants declined over the 6-month period. Patients experienced long-term declines despite differences in baseline cognition and not experiencing acute decline during hospitalisation. This finding draws attention to the need for further research to determine the cause of cognitive decline and potentially slow its progression.

Finding distinct patterns in cognitive decline is highly important, particularly if the identified prognostic factors are potentially modifiable, to mitigate cognitive declines during hospital stay or after. Nurses, who have intimate and ongoing contact with elderly patients, have the opportunity and obligation to assess and educate patients and caregivers regarding strategies to promote patients' cognitive function. Hospitalised elderly patients will be cared for by more nurses without specific gerontological background and their practice needs to be guided by an awareness of patterns of cognitive changes. Since age, education, cardiovascular morbidities, number of medications, functional and nutritional status, depressive symptoms, surgical treatment, and haemoglobin <12 g/dL have been identified as predictors, nurses and clinicians could be alerted to diverse patterns of cognitive decline so a timely work-up could be initiated.

Cognitive decline is costly. Declining MMSE scores have also been shown to predict mortality, even after adjusting for dementia and specific diseases (Lavery et al., 2009). Evidence suggests that cognitive status can be maintained by nursing measures such as reality orientation, cognitive stimulation, therapeutic activities, or enriched environment (Inouye et al., 2000). Given the length of hospitalisation among these vulnerable elderly patients, it is feasible and clinically indicated to organise some group-specific, hospital-initiated strategies to prevent and ameliorate cognitive decline during and after hospitalisation.

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References

American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). American Psychiatric Association, Washington, DC.

Chen, C.C.-H., Wang, C., Huang, G.H., 2008. Functional trajectory six months post hospitalization: a cohort study of older hospitalized patients in Taiwan. Nursing Research 57 (2), 93–100.

Chen, C.C.-H., Tang, S.T., Wang, C., Huang, G.-H., 2009. Trajectory and determinants of nutritional health in older hospitalized patients during and six-month post hospitalisation. Journal of Clinical Nursing 18, 3299–3307.

Dotson, V.M., Resnick, S.M., Zonderman, A.B., 2008. Differential association of concurrent, baseline, and average depressive symptoms with cognitive decline in older adults. American Journal of Geriatric Psychiatry 16 (4), 318–330.

Everitt, B.S., Landau, S., Leese, M., 2001. Cluster Analysis, 4th ed. Hodder Headline Group, London.

Fitzpatrick, J.J., Stier, L., Eichorn, A., Dlugacz, Y.D., O'Connor, L.J., Salinas, T.K., Smith, T., White, M.T., 2004. Hospitalized elders: changes in functional and mental status. Outcomes Management 8 (1), 52–56.

Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research 12 (3), 189–198.

Geerlings, M.I., Schoevers, R.A., Beekman, A.T.F., Jonker, C., Deeg, D.J.H., Schmand, B., Ader, H.J., Bouter, L.M., van Tilburg, W., 2000. Depression and risk of cognitive decline and Alzheimer's disease: results of two prospective community-based studies in the Netherlands. The British Journal of Psychiatry 176 (6), 568–575.

Gruber-Baldini, A.L., Zimmerman, S., Morrison, R.S., Grattan, J., Hebel, J.R., Dolan, M.M., Hawkes, W., Magaziner, J., 2003. Cognitive impairment in hip fracture patients: timing of detection and longitudinal follow-up. Journal of the American Geriatrics Society 51 (9), 1227–1236.

Guigoz, Y., Vellas, B., Garry, P.J., 1996. Assessing the nutritional status of the elderly: the mini nutritional assessment as part of the geriatric evaluation. Nutrition Reviews 54 (1), S59–65.

Huber, M., Kennard, A., 1991. Functional and mental status outcomes of clients discharged from acute gerontological versus medical/surgical units. Journal of Gerontological Nursing 17 (7), 20–24.

Inouye, S.K., Bogardus, S.T., Baker, D.I., Leo-Summers, L., Cooney, L.M., 2000. The hospital elder life program: a model of care to prevent cognitive and functional decline in older hospitalized patients. Journal of the American Geriatrics Society 48 (12), 1697–1706.

Inouye, S.K., Zhang, Y., Han, L., Leo-Summers, L., Jones, R., 2006. Recoverable cognitive dysfunction at hospital admission in older persons during acute illness. Journal of General Internal Medicine 21 (12), 1276–1281.

Johnson, R.A., Wichern, D.W., 2007. Applied Multivariate Statistical Analysis, 6th ed. Pearson Prentice Hall, Upper Saddle River.

Lavery, L.L., Dodge, H.H., Snitz, B., Ganguli, M., 2009. Cognitive decline and mortality in community-based cohort: the Monongahela valley independent elders survey. Journal of the American Geriatrics Society 57 (1), 94–100.

Mahoney, F.I., Barthel, D.W., 1965. Functional evaluation: the Barthel Index. Maryland State Medical Journal 14, 61–65.

Massa, E., Madeddu, C., Lusso, M.R., Gramignano, G., Mantovani, G., 2006. Evaluation of the effectiveness of treatment with erythropoietin on anemia, cognitive functioning and function studied by comprehensive geriatric assessment in elderly cancer patients with anemia related to cancer chemotherapy. Critical Reviews in Oncology Hematology 57 (2), 175–182.

Mecocci, P., von Strauss, E., Cherubini, A., Ercolani, S., Mariani, E., Senin, U., Winblad, B., Fratiglioni, L., 2005. Cognitive impairment is the major risk factor for development of geriatric syndromes during hospitalization: results from the GIFA study. Dementia and Geriatric Cognitive Disorders 20 (4), 262–269.

Mehta, K.M., Yaffe, K., Covinsky, K.E., 2002. Cognitive impairment, depressive symptoms, and functional decline in older people. Journal of American Geriatrics Society 50 (6), 1045–1050.

Monk, T.G., Weldon, B.C., Garvan, C.W., Dede, D.E., van der Aa, M.T., Heilman, K.M., Gravenstein, J.S., 2008. Predictors of cognitive dysfunction after major noncardiac surgery. Anesthesiology 108, 18–30.

Ng, T.P., Feng, L., Niti, M., Yap, K.B., 2008. Albumin, haemoglobin, BMI and cognitive performance in older adults. Age and Ageing 37, 423–429.

Nguyen, H.T., Black, S.A., Ray, L.A., Espino, D.V., Markides, K.S., 2002. Predictors of decline in MMSE scores among older Mexican Americans. Journals of Gerontology Series A: Biological Sciences and Medical Sciences 57A (3), M181–185.

Newman, M.F., Kirchner, J.L., Phillips-Bute, B., Gaver, V., Grocott, H., Jones, R.H., Mark, D.B., Reves, J.G., Blumenthal, J.A., 2001. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. New England Journal of Medicine 344, 395–402.

O'Keeffe, S.T., Mulkerrin, E.C., Nayeem, K., Varughese, M., Pillay, I., 2005. Use of serial mini-mental state examinations to diagnose and monitor delirium in elderly hospital patients. Journal of the American Geriatrics Society 53 (5), 867–870.

Paterniti, S., Verdier-Taillefer, M.H., Dufouil, C., Alperovitch, A., 2002. Depressive symptoms and cognitive decline in elderly people: longitudinal study. The British Journal of Psychiatry 181 (5), 406–410.

Pedone, C., Ercolani, S., Catani, M., Maggio, D., Ruggiero, C., Quartesan, R., Senin, U., Mecocci, P., Cherubini, A., 2005. Elderly patients with cognitive impairment have a high risk for functional decline during hospitalization: the GIFA Study. Journals of Gerontology Series A: Biological Sciences Medical Sciences 60A (12), 1576–1580.

Rosner, B., 2005. Fundamentals of Biostatistics, 6th ed. Duxbury Press, Belmont.

Schupf, N., Tang, M.X., Albert, S.M., Costa, R., Andrews, H., Lee, J.H., Mayeux, R., 2005. Decline in cognitive and functional skills increases mortality risk in nondemented elderly. Neurology 65 (8), 1218–1226.

Selnes, O.A., Grega, M.A., Bailey, M.M., Pham, L.D., Zeger, S.L., Baumgartner, W.A., McKhann, G.M., 2008. Cognition 6 years after surgical or medical therapy for coronary artery disease. Annals of Neurology 63, 581–590.

Seymour, D.G., Severn, A.M., 2009. Cognitive dysfunction after surgery and anaesthesia: what can we tell the grandparents. Age and Ageing 38 (2), 147–150.

Shyu, Y.I., Yip, P.K., 2001. Factor structure and explanatory variables of the Mini-Mental State Examination (MMSE) for elderly persons in Taiwan. Journal of the Formosan Medical Association 100 (10), 676–683.

Stern, Y., 2002. What is cognitive reserve? Theory and research application of the reserve concept. Journal of the International Neuropsychological Society 8, 448–460.

Wong, M.T.P., Ho, T.P., Ho, M.Y., Yu, C.S., Wong, Y.H., Lee, S.Y., 2002. Development and inter-rater reliability of a standardized verbal instruction manual for the Chinese Geriatric Depression Scale-Short Form. International Journal of Geriatric Psychiatry 17 (5), 459–463.

Yesavage, J.A., Brink, T.L., Rose, T.L., Lum, O., Adey, M., Leirer, V.O., 1983. Development and validation of a geriatric depression scale. Journal of Psychiatric Research 17 (1), 31–49.

Wilson, C.J., Finch, C.E., Cohen, H.J., 2002. Cytokines and cognition: the case for a head-to-toe inflammatory paradigm. Journal of American Geriatrics Society 50 (12), 2041–2056.

Zamboni, V., Cesari, M., Zuccala, G., Onder, G., Woodman, R.C., Maraldi, C., Ranzini, M., Volpato, S., Pzhor, M., Bernabei, R., 2006. Anemia and cognitive performance in hospitalized older patients: results from the GIFA study. International Journal of Geriatric Psychiatry 21 (6), 529–534.