Cognitive performance in elderly patients: differences between prevalent and incident delirium.

A cross-sectional study.

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Abstract

Background: Delirium is present in some older patients at time of hospital admission (prevalent delirium) or develops during hospital stay in other elderly patients (incident delirium).

Objective: Our primary goal was to evaluate the effect of delirium on cognitive functioning one week prior to discharge and to determine which factors contribute the most to cognitive performance.

Methods: 105 participants were divided into three groups: prevalent delirium, incident delirium and controls. They completed The Dutch version of the Cambridge Cognitive Examination (Camcog-R).[1] Patients were only tested after their delirium had cleared up. ANCOVAs were performed to investigate group differences in cognitive performance. A stepwise linear regression was used to identify factors that contributed to impaired cognitive functioning.

Results: Both prevalent delirium and incident delirium had negative effects on cognitive performance one week prior to discharge, controlled for dementia, diabetes mellitus and history of delirium. There were no significant differences between prevalent and incident delirium groups on total Camcog-R and subscales. Prevalent delirium, incident delirium, dementia, epilepsy and gender were predictors of cognitive performance in the final regression model.

Conclusions: Delirium at admission and delirium developing during hospital stay both have a short-term negative effect on cognitive functioning. Prevalent delirium seems to be a more important predictor of cognitive performance compared to incident delirium. Prevalent delirium was significantly associated with pre-existing dementia. Patients with incident delirium stayed significantly longer at the hospital compared to the other groups. We recommend future studies to distinguish between prevalent and incident cases.

Keywords: prevalent delirium, incident delirium, cognitive functioning, Camcog-R, general geriatric population

Table of Contents

Introduction

While hospitalized, many older persons suffer from a delirium. This reversible neuropsychiatric syndrome is reported to be present in 10-31% of older patients at time of hospital admission (which we term prevalent delirium) and will develop in an additional 3-29% of patients during their hospital stay (termed incident delirium).[2] Prevalent delirium tends to be more common than incident cases.[2,3] A delirium is characterised by an altered level of consciousness, disorganized thinking, inattention, cognitive deficits and perceptual disturbances.[4] A disturbed sleep-wake cycle, altered psychomotor activity and emotional disturbances are also common.[5,6] The symptoms usually develop acutely and tend to fluctuate over time. They are classified according to their psychomotor activity, resulting in hypoactive, hyperactive and mixed subtypes.[6]

Delirium is thought to develop as a result of a complex interaction between underlying risk factors and exposure to precipitating factors. Predisposing factors are those that make older persons more vulnerable to development of delirium, such as: a history of delirium, coexisting medical conditions, cognitive impairment, dementia, visual and hearing impairment and low functional status. The factors that trigger pathophysiological mechanisms resulting in delirium are, among others, infection, use of physical restraints, urinary retention, polypharmacy, fever, metabolic deficiency, environmental issues, and pain. In vulnerable patients only one of these risk factors is necessary to trigger a delirium while in less vulnerable people more factors are required.[5-7]

Delirium is associated with a wide range of consequences, including prolonged hospital stay, increased health care costs, institutionalisation, functional and cognitive decline, and mortality.[8]

Cognitive functioning after a delirium

The existing literature suggests that delirium is significantly associated with long-term impaired cognitive functioning and some delirious patients may never recover to their baseline level of cognitive functioning.[8-10] Jackson et al[9] reviewed nine papers regarding relationships between first-onset delirium in non-demented patients and subsequent cognitive impairment. These studies included follow-up intervals ranging from 6 months to three years. Four out of nine studies used the MMSE[11] as the only cognitive measure, three used a brief test battery like the D-Test Battery[12], and two administered a comprehensive neuropsychological test battery. Evidence from the review suggests that patients who experience delirium during their hospital stay have greater cognitive decline and higher risks of dementia at follow-up compared to those who do not suffer from a delirium. Maclullich et al[10] conducted a further literature review, limiting their study to nine papers published after those covered by Jackson et al.[9] Seven of these studies assessed short cognitive

screening instruments similar to the MMSE, patient interviews or informant ratings and two studies used more extensive tests. follow-up ranged from three months to five years. Taken together, eight studies demonstrated a significant association between delirium and cognitive impairment. Wacker et al[13] assessed the CAMDEX[1] and its cognitive section the Camcog-R, in elderly persons with and without a delirium after a knee or hip replacement. Patients with delirium had significantly lower total Camcog-R scores compared to controls. The domains memory, orientation and abstract thinking were mostly affected. Recently, Van Rijsbergen et al[14] assessed a neuropsychological test battery covering multiple cognitive domains two years post-stroke in patients with or without a delirium in the acute phase after stroke. Elderly stroke patients with a previous delirium had significantly lower scores on verbal memory, attention, visual construction, language and executive functioning compared to stroke patients without delirium in the acute phase.

Evidence also exists to suggest that delirium accelerates the rate of deterioration in patients who already have been diagnosed with dementia.[10,15] In addition, delirium has an increased likelihood to occur in patients with dementia.[3-5,8] Some studies showed that patients with comorbid dementia and delirium had worse cognitive outcome than patients with dementia only.[8,10,16] In fact, several researchers stated that delirium may indicate an underlying neurodegenerative process.[10,14,17] Some implied that delirium and dementia are not completely distinguishable, but may represent two points along a continuum of cognitive impairment.[5]

According to Jackson et al[9] and Maclullich et al[10], studies focussing on delirium and cognition thus far had several methodological issues. For example, they used diverse study designs, widely different methods to identify delirium, relatively small sample sizes, selected patient groups and variable length of follow-up period. Moreover, measurement of cognitive impairment frequently relied on a cognitive screening instrument like the Mini-Mental State Examination (MMSE)[11] rather than a neuropsychological test battery. Remarkably, controlling for baseline cognitive impairment and other confounding variables did not always occur.

Prevalent and incident delirium

We found six papers that compared socio-demographic factors (i.e., age, gender, ethnicity), clinical factors (i.e., predisposing factors like dementia and precipitating factors like infection) and outcome variables (e.g., length of hospital stay, institutionalisation, mortality) between elderly patients with prevalent delirium and those with incident delirium.[18-23] Five of them were observational cohort studies, with sample sizes ranging from 193 to 461 participants. Lin et al[18], however, retrospectively analysed an administrative hospitalization database, including a sample size of nearly two million patients. The results of all papers are summarized in Table 1.

Table 1. Summary of six studies that compared patient groups with different onset of delirium

	Sample size	Study design	Findings	
	Prevalent *Incident* *Controls*		Prevalent delirium	Incident delirium
Lin et al[18], 2010	N= 1 968 527 *N=9617* *N=4368* *N=1 952 301*	Retrospective analysis of a hospitalization database	Greatest proportion in urinary tract/kidney infection category. Sig associated with adverse drug effects (OR=4.6, 95% CI= 4.3 –5.0). Stronger associated with dementia on admission (OR= 6.0, 95% CI= 5.8–6.3) compared to incident delirium Sig association with non-elective admission. Strongly associated with ↑age Sig adj. associations (in order of ↓ odds ratio) with caucasian ethnicity, not having Medicaid health program, male gender, and a more recent year of discharge.	Greatest proportion in lower extremity orthopaedic surgery category. Much stronger associated with adverse drug effects (OR= 22.2, 95% CI= 20.7–23.7). Associated with dementia on admission (adj. OR= 1.26 , 95% CI=1.12–1.42). Sig association with non-elective admission. Strongly associated with ↑ age. Sig. adj. associations with caucasian ethnicity, not having Medicaid health program and male gender. Modest relationship with diabetes.
Moschetta et al[19], 2009	N=261 *N=82* *N=29* *N=150*	Retrospective cohort study	↑ rates in patients with urinary infections, collateral medication effects, acute abdominal surgeries and respiratory infections. ↑ proportions of acute compared to elective hospitalizations (42.6% , 1.4 % respectively, p<0.001). ↑ rates with ↑ age (p=0.075).	Average length of hospital stay was 9.1 days > controls (p=0.002). Hospital mortality was 48% (2.7% in controls, p<0.001).
McCuster et al[20], 2003	N=193 *N=165*	Prospective cohort study	90.4% prevalence rate among demented older persons 73.3% among non-demented older persons..	9.6 % prevalence rate among demented older persons. 26.7% among non-demented older persons .

	N=28 *N=0* *(no controls)*			Non-demented elderly were more likely than demented elderly to have incident rather than prevalent delirium (p=0.04.)
Bourdel-Marchasson et al[21], 2004	N=427 *N=34* *N=15* *N=230*	Prospective observational cohort study	Independent predictor of institutionalisation (OR = 3.19 95% CI 1.33–7.64).	
McCusker et al[22], 2003	N=359 N=204 N=37 N=118	Prospective cohort study	No sig associations with length of hospital stay.	Sig associated with an excess length of stay of approximately 8 days, independent of dementia, diagnosis-related group, clinical severity and comorbidity (95% CI=3.59–12.51).
McCuster et al[23] , 2002	N=461 *Unknown* *Unknown* *N=118*	Prospective observational cohort study	Independent marker for ↑ mortality. No differences in 12-month mortality between prevalent and incident delirium, after adjusting for confounders like dementia and comorbidity.	

Although one study showed a trend toward higher frequencies of prevalent delirium with increasing age[19] , no further differences in socio-demographic factors between the two delirious groups have been found to date.

Other studies however do suggest that prevalent delirium and incident delirium have different underlying conditions. For example, Lin et al[18] found that patients with urinary tract or kidney infections had the greatest proportion of prevalent delirium, while incident delirium was more frequent in patients who had lower extremity orthopedic surgery. Diabetes had a modest relationship with incident delirium, but not with prevalent delirium.[18] The results of two studies indicate that prevalent delirium is more strongly associated with dementia on admission compared to incident delirium.[18,20] Moschetta et al[19] showed that prevalent delirium was more common in patients with urinary infections, those having acute abdominal surgery, respiratory infections and collateral medication effects . The latter finding is inconsistent with Lin et al[18], who showed that incident delirium was more strongly associated with adverse drug effects compared to prevalent delirium.

Three of the studies compared the prognosis between the two delirious patient groups. Bourdel-Marchasson et al[21] indicated delirium as an independent predictor of hospital discharge to an institution. Patients with prevalent delirium had a significantly higher risk of institutionalization compared to patients with incident delirium. However, Moschetta et al[19] showed that elderly patients with incident delirium stayed significantly longer at the hospital and had significantly higher mortality rates during hospitalization compared to hospitalized elderly without delirium. McCuster et al[22] indicated that incident delirium was significantly associated with an excess length of stay of approximately 8 days in elderly patients from the emergence department, independent of dementia, diagnosis-related group, clinical severity and comorbidity. Patients with prevalent delirium did not stay longer in hospital compared to patients without prevalent delirium.[22] McCuster et al[23] showed that postdischarge mortality did not differ between incident and prevalent delirium after adjusting for confounders like dementia and comorbidity.[23]

Although it has not been stated in the literature, the characteristics of delirium may differ between patients with prevalent and people with incident delirium. For patients with prevalent delirium, duration and severity of delirium before hospital admission are unrevealed. They have been delirious for an unknown period of time and probably without adequate treatment for the underlying cause of their state of confusion. These patients may represent a more vulnerable group compared to older persons with incident delirium.

The present study

To our knowledge, earlier studies that investigated cognitive impairment after a delirium have not taken into account the onset of delirium. Neither have they focused on cognitive functioning prior to hospital discharge and few have included a general geriatric patient group.[9,10] For example, several studies only investigated cognitive impairment after a delirium in elderly hip surgery patients, limiting the generalizability of their results.[9,10] The role of potential confounding factors should be reduced, for example by minimizing the time between cognitive assessment and hospital discharge. Thus, the current study investigated the effect of delirium on cognitive functioning in a general geriatric population in the week prior to hospital discharge. We distinguished three groups: (a) older patients with prevalent delirium, (b) elderly persons with incident delirium, and (c) an age-matched control group of patients. Our first goal was to compare socio-demographic factors and clinical characteristics between the three groups. The second aim was to evaluate their cognitive functioning assessed by the Camcog-R one week prior to discharge. The final purpose was to determine which factors (e.g socio-demographic and clinical factors) significantly contribute to their cognitive functioning. We hypothesized:

1. Patients with prevalent delirium to be the most vulnerable group, with higher average age[19], more comorbid conditions[19,21], higher functional dependency, higher prevalence of dementia[18,20], higher premorbid cognitive decline prior to hospitalisation[18,20] and higher prevalence of infections during hospital stay compared to the other groups.

2. Lower overall cognitive functioning in post-delirious patients compared to controls, with:
    a. Significantly worse performance of the delirious groups on the subscales memory, orientation and abstract thinking.[13]
    b. Lower scores on the overall Camcog-R and the subscales memory, orientation and abstract thinking in elderly persons with prevalent delirium compared to patients with incident delirium and controls, which remain after controlling for relevant covariates.

Methods

*Ethical considera*tions

The current cross-sectional study is part of a longitudinal study entitled: 'Delirium in elderly patients, risk factors and outcomes', and has been approved by the national Medical Ethics Committee (METOPP). Participating in this research is completely voluntary and all patients and their relatives have given informed written consent.

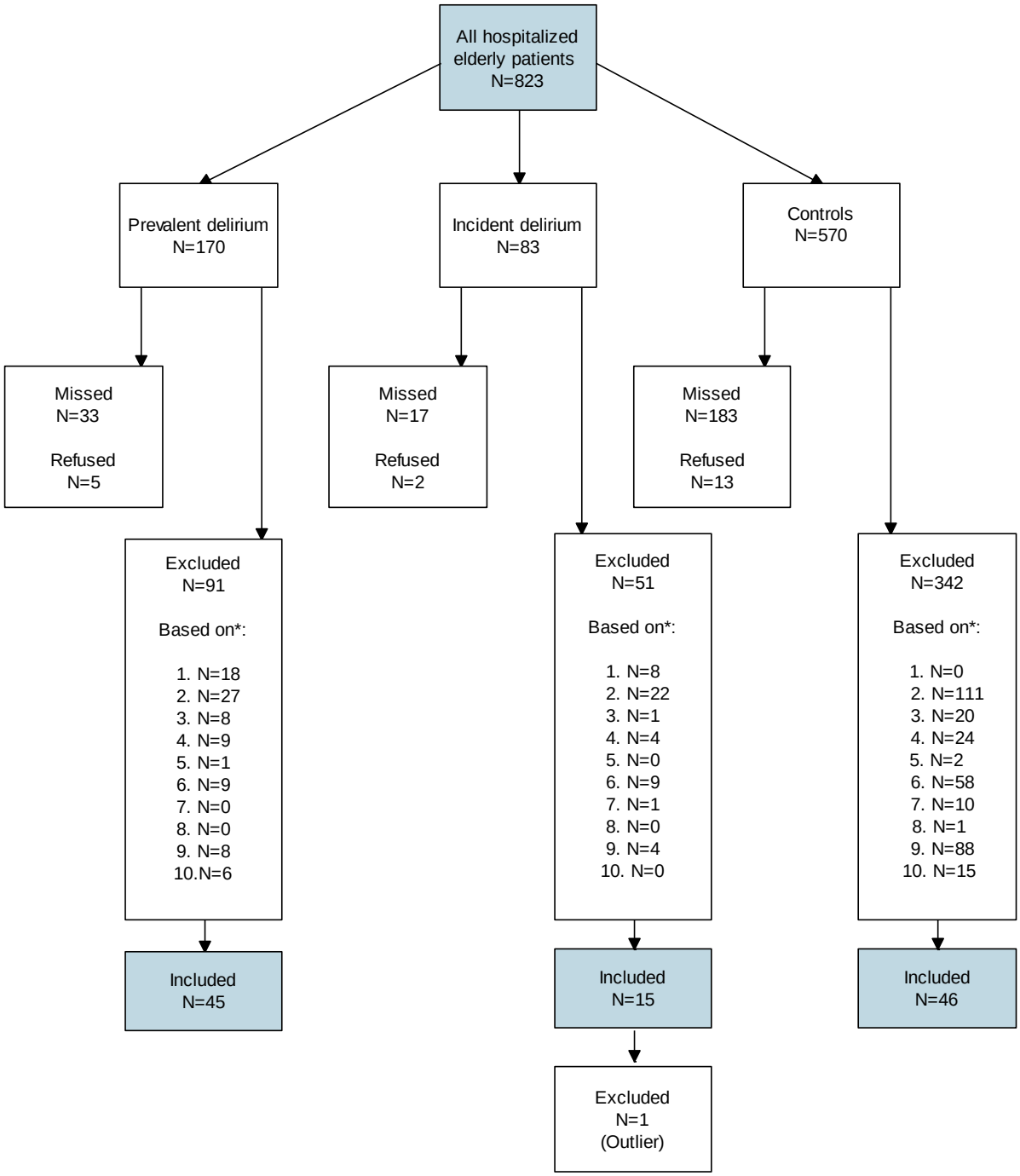
Participants

All patients admitted to the Department of Geriatrics at the Tweesteden Hospital (Tilburg, the Netherlands) were screened for this study. The geriatric hospitalized population is heterogenic including diverse medical conditions (i.e. anemia, fever, fractures, infections, dyspnea, etcetera). The inclusion and exclusion criteria for all patients, including controls are listed in Table 2. The total study population consisted of 105 patients. Participants were divided into three groups (1) patients with prevalent delirium (N=45) (2) patients with incident delirium (N=14) and (3) a gender and age-matched control group of non-delirious patients (N=46). Figure 1. depicts a flow-chart of the number of patients who were included and excluded in the present study. Most common reasons to exclude patients were; having severe cognitive problems, receiving palliative care, not being capable of giving informed consent or not testable according to physicians or nurses.

Table 2. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Delirium present at the time of admission	Delirium at time of cognitive assessment
Delirium developed during stay in hospital	MMSE<18, after ending of the delirium (indicating severe cognitive problems)
Acute admission, no delirium	Psychiatric comorbidity (except for affect disorders)
	Significant sight and/or hearing impairment
	Addictive disorder
	Palliative policy
	Inability to speak/write/read/understand Dutch
	Not capable of giving informed consent
	Not testable according to physicians/nurses (e.g somatic reasons or behavioural problems)
	Very recent neuropsychological assessment

Figure 1. Flow-chart of the current study



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1. Delirium at time of assessment
2. MMSE<18, indicating severe cognitive problems
3. Psychiatric comorbidity (except for affect disorders)
4. Significant sight and/or hearing impairment
5. Addictive disorder
6. Palliative policy
7. Inability to speak/write/read/understand Dutch
8. Patients not capable of giving informed consent
9. Patients not testable according to physicians/nurses
10. Recent neuropsychological assessment

Materials

Socio-demographic factors and clinical variables such as dementia status were retrospectively obtained from medical files.

The Dutch version of the Cambridge Cognitive Examination-Revised (Camcog-R)[24] was used to assess objective cognitive functioning. It contains 67 items and lower scores indicate poorer level of functioning. The items can be divided into eight subscales, namely; orientation, language, memory, attention, calculation, praxis, abstract thinking and perception. A score on executive functioning can be derived by combining the subscale abstract thinking and three additional items, namely: word fluency, ideational fluency and visual reasoning. [24] The Camcog-R can be used to differentiate between normal cognitive function and mild cognitive impairment. It has also been validated for the assessment of dementia.[25] Three cut-off scores are available according to the age and educational level of the patient. We did not use cut-off scores in the present study. Item 203 was omitted, because of the lack of a third person in the investigation room. The maximum total score was therefore 104 instead of 105.

A short form of the informant Questionnaire on Cognitive Decline in the elderly (IQCODE-N)[26] was chosen to estimate premorbid cognitive decline prior to hospitalisation. A relative or friend of each patient was called to examine his/her willingness to participate. They were asked to complete the IQ-CODE and sent the questionnaire and informed consent forms back by mail. Informants had to rate the change in the subjects' ability to handle 16 everyday situations over the past ten years. With a minimum score of 1 and maximum score of 5, average scores higher than 3.9 are assumed to indicate dementia. Since its introduction, the IQCODE has become one of the most widely used informant-based screening tools for cognitive decline.[27] Ehrensperger et al[27] found high reliability of the 16-item IQCODE (Cronbach's α= .914) and excellent screening properties for Mild Cognitive Impairment (MCI) and early Alzheimer's disease (AD) .

The Delirium Observation Scale (DOS) is a reliable and valid instrument, containing 25 items related to Diagnostic and Statistical Manual-IV (DSM-IV) criteria of delirium. It is based on nurses' observations during regular care. Recently, the study of Scheffer et al[28] indicated that the DOS is a reliable method to measure severity of delirium, although it was originally designed for early detection of delirium.

The modified Katz-ADL index score[29] was used to measure functional status. It is a validated 15-item scale that measures independence in basic and instrumental activities of daily living, for example bathing or dealing with money. Performance of patients can be graded into the number of disabilities. The modified Katz score range from 0 to 20 and a higher score indicates a poorer functional status. [29] In earlier phases of this study, the Barthel20 index (BI) [30] instead of the Katz-ADL

modified index[29] was used to measure independence. The BI scores range from 0 to 20 and a higher score shows better functional status.[30] We composed a variable named functional dependency, with value 0: no to mild limitations (BI score 15-20 or Katz Index score 0-3) and value 1: moderate to severe limitations (BI score 0-14 or Katz index score 4-15). [31,32]

Procedure

Physicians and nurses completed baseline screening and assessment for each new patient within two days after admission. This procedure is standard practice in the Tweesteden hospital and involves screening for (a) cognitive impairment with the Mini-Mental State Examination (MMSE) (b) delirium with the Delirium Observation Screening (DOS) three times a day and (c) functional status using the modified Katz-ADL index. If the DOS indicated that a patient was currently delirious, the geriatric physician evaluated the patient. The geriatric physician made the final diagnosis of delirium status according to the DSM-IV criteria. The researcher discussed each admitted patient according to the inclusion and exclusion criteria with a resident physician. Patients who met the inclusion criteria and did not show any of the exclusion criteria were asked to participate in the current study in the last week of their stay at the hospital. Patients with prevalent or incident delirium were only tested after their delirium had cleared up. The end of a delirious episode was determined by physicians, who used DOS scores of each patient to support their clinical experience. All participants received oral and written information about the study and its procedure. Both the researcher and the patient signed the informed consent form. All subjects received neuropsychological assessment in a quiet room at the geriatric ward. The answers to the questionnaire items were obtained by interview.

Design and statistical analyses

We used a cross-sectional design to compare the two delirious groups and non-delirious patients on potential factors contributing to the delirium as well as their cognitive functioning in the week of discharge. Prior to running the analyses, we checked for outliers and assumptions of normality, linearity, collinearity and homogeneity of variance. Differences in premorbid cognitive functioning, socio-demographic and clinical characteristics between the three groups were examined by Pearson Chi-square tests with pairwise comparisons for categorical variables and one-way between-groups ANOVAs for continuous variables. If the ANOVA showed a significant difference, post-hoc tests (Tukey HSD) were performed to see where the groups differences were located. For categorical data with small cell numbers (80% < 5), Fisher's exact probability tests were used.

Normality of the continuous variables was examined with the Shapiro-Wilk test and exploration of Q-Q plots. When the assumption of normality was violated, a Mann-Whitney U test was used for pairwise comparisons between groups. Boxplots were used to detect outliers. Scores were defined as outliers when they extended more than 1.5 box-lengths from the edge of the box.

Socio-demographic and clinical characteristics that significantly differed between the groups, were included as a covariate in the final ANCOVA analysis.

We performed separate one-way between group analyses of covariances (ANCOVAs) for eleven dependant variables to explore group differences in cognitive functioning. The independent variable was delirium status with three distinct categories: (1) prevalent delirium, (2) incident delirium and (3) control group. The dependant variables consisted of eleven continuous variables, specifically overall Camcog-R score, each Camcog-R subscale score (MMSE, orientation, language, memory, attention, calculation, praxis, abstract thinking, perception) and executive functioning. We included sociodemographic and clinical variables that significantly differed between the groups as covariates. We only included covariates that were complete for all participants. We checked for multicollinearity and observed no violations. Results of Shapiro Wilk statistics and exploration of Q-Q plots indicated normality of the total study population for al dependent variables except for orientation. The Camcog-R contained eleven missing values over all patients and items. Results of little MCAR test showed that these missing values were randomly distributed (p=0.065). We excluded one patient (#89) from the study, because his or her total Camcog-R score was an outlier (extremely low). Furthermore, we found three outliers in the subscale attention (patient number #104, #150 and #157), one outlier in memory (#88), two in language (#44 and #95) and one in orientation (#82). We excluded each of these patients from analyses of separate subscales. Levene's test of equality of error variances was violated for the praxis scale. However, the largest standard deviation was less than twice the smallest standard deviation.

Finally, we used a stepwise multiple regression analysis to identify factors that contributed to impaired cognitive functioning after a delirium. We included 12 independent variables suspected to influence cognition (e.g age, gender, delirium, mild cognitive impairment (MCI), dementia, Parkinson disease (PD), epilepsy, traumatic brain injury (TBI), stroke, diabetes mellitus, cardiovascular disease and history of delirium). Categorical variables were transcoded into dummy variables. We performed point-biserial correlations to evaluate whether prevalent delirium (yes or no) or incident delirium (yes or no) contributed the most to cognitive functioning.

All tests were two-tailed and a *p*-value of ≤0.05 was considered statistically significant. Statistical analyses were performed using the Predictive Analytics SoftWare Statistics, version 18.0 (SPSS inc., Chicago, Illinois, USA).

Results

Baseline characteristics

The socio-demographic of the patients who participated in this study are summarized in Table 3.1 for each group separately. The total study population consisted of 105 patients (N=45 prevalent delirium, N=14 incident delirium and N=46 controls). There were no significant differences between the delirious groups and controls regarding socio-demographic characteristics (e.g age, gender, marital status, institutionalisation, education level and functional dependency). Patients with incident delirium stayed significantly longer at the hospital compared to patients with prevalent delirium and controls.

The clinical variables are summarized in Table 3.2. Considering each clinical characteristic separately, both delirious groups and controls had similar frequencies of the following conditions: MCI, cardiovascular disease, cancer, epilepsy, TBI, stroke, Parkinson, depression in the past, hearing impairment, visual impairment and opiate use. Patients with prevalent delirium had significantly higher rates of dementia, history of delirium and psychotropic medication compared to controls. From the original sample of 105 patients, 47 family members completed the IQCODE questionnaire and 58 relatives did not send the forms back by mail. There was a tendency towards lower premorbid cognitive functioning in the prevalent delirium group compared to the control group. Patients with incident delirium were significantly more hospitalized in the last twelve months, compared to controls. Control patients had significantly higher rates of diabetes compared to patients with prevalent delirium mellitus, and a trend toward higher rates of diabetes mellitus compared to patients with incident delirium.

With regard to problems during hospital stay, the rates of electrolyte disturbance, thyroid disturbance, kidney disease, liver disturbance, urinary catheterization and pain were not significantly different between delirious patients and controls. Patients with prevalent delirium had higher rates of fever and infection compared to controls and there was a trend toward higher occurrence of urinary retention. The incident delirium group had significantly higher rates of fever, infection, urinary retention and dehydration compared to the control group. Clinical characteristics of the groups during hospital admission are summarized in Table 3.3.

Table 3.1 Sociodemographic differences between the delirious groups and controls

Sociodemographic variables	Prevalent delirium (N=45)	Incident delirium (N= 14)	Control group (N=46)	P-Value Omnibus tests
Age (mean ± sd)	81.9±6.2	85.4±6.9	81.7±6.2	ns
Gender				
(*male/female)*	(19/26)	(6/8)	(22/24)	ns
Marital status				
(*married/alone, widowed, divorced/missing*)	(11/33/1)	(4/10/0)	(15/31/0)	ns
Institutionalized (nursing home or residential care home)				
(yes/no/missing)	(7/37/1)	(2/12/0)	(8/38/0)	ns
Education level				
(very low- low/intermediate-high)	(12/17/16)	(2/6/6)	(10/27/9)	ns
Functional dependency				
(no to mild limitations/ moderate to severe limitations/missing)	(6/19/20)	(3/3/8)	(7/25/15)	ns
Length of stay *(days, mean ± sd)*	21.4±13.7**[1]	31.9 ±11.9**[2]	20.6±10.7	.009

Analyses are Chi-square analyses or Fisher's exact probability tests (categorical data) and ANOVAs with Tukey's HSD post-hoc or Mann-Whitney U-tests (continuous data).

*= $p < .05$, ** =$p < .01$

[1] Significant difference of length of stay between prevalent delirium and incident delirium (Mann-Whitney U), Z=-3.0, p=0.003

[2] Significant difference of length of stay between incident delirium and controls (Mann-Whitney U), Z=3.0, p=0.002

Table 3.2 Differences in clinical factors between the delirious groups and controls

Predisposing factors (yes/no)	Prevalent delirium (N=45)	Incident delirium (N= 14)	Control group (N=46)	P-value Omnibus tests
Dementia	(19/26) **[1]	(3/11)	(7/39)	X^2=8.6, p=0.14, ϕ=.286
Mild cognitive impairment (MCI)	(9/36)	(4/10)	(7/39)	ns
Premorbid cognitive decline (IQCODE, mean ± sd/missing)	(3.8± 0.7/24) ~[2]	(3.9 ± 0.35/6)	(3.5 ± 0.4/26)	Z=-1,9, p=0.064
Cardiovascular disease	(36/9)	(14/0)	(39/7)	ns
Cancer *(yes/no/missing)*	(9/32/4)	(5/9/0)	(16/29/1)	ns
Epilepsy	(2/43)	(0/14)	(2/44)	ns
Traumatic brain injury	(2/43)	(0/14)	(2/44)	ns
Diabetes	(9/36)***[3]	(4/10) ~[4]	(26/46)	X^2=13.5, p=0.001, ϕ=.359
Previous stroke	(10/35)	(1/13)	(14/32)	ns
Parkinson syndrome	(4/41)	(1/13)	(3/43)	ns
Depression in the past *(yes/no/missing)*	(8/37/0)	(2/12/0)	(5/40/1)	ns
History of delirium	(14/31)*[5]	(3/11)	(5/41)	X^2=5.6, p=0.06, ϕ=.232
Hearing impairment *(yes/no/missing)*	(15/30/0)	(3/11/0)	(13/32/1)	ns
Visual impairment *(yes/no/missing)*	(16/28/0)	(4/10/0)	(9/36/1)	ns
Hospitalization in last 12 months *(yes/no/missing)*	(10/10/25)	(8/1/5)*[6]	(16/20/10)	Fisher exact, p=0.025, ϕ=.356
Psychotropic medication *(yes/no/missing)*	(21/20/4)*[7]	(6/8/0)	(9/29/8)	ns
Opiate use *(yes/no/missing)*	(6/35/4)	(1/13/0)	(3/34/9)	X^2=6.4,p=0.04 , ϕ=.263

Analyses are Chi-square analyses or Fisher's exact probability tests (categorical data) and Mann-Whitney U-tests (continuous data). ~=p<0.10 (trend), *= *p* < .05, ** =*p* < .01, ***=p<0.001.

[1,2,3,5,7]= differences between prevalent delirium and controls, [4,6]=differences between incident delirium and controls.

[1.] X^2=8.1, p=0.004, ϕ=.299, [3.] X^2=12.8, p=0.000, ϕ=-.375, [4.]X^2=3.4, p=0.067, ϕ=-.236, [5.] X^2=5.6, p=0.018, ϕ=.249, [6.] p=0.025, ϕ=.356, [7.] X^2=6.3,p=0.012 , ϕ=.283

Table 3.3. Differences in clinical factors between the delirious groups and controls

Precipitating factors: *Problems during hospital stay (yes/no/missing)*	Prevalent delirium (N=45)	Incident delirium (N= 14)	Control group (N=46)	P-Value Omnibus tests
Fever	(16/28/1)**[1]	(6/8/0)**[2]	(3/41/2)	X^2=10.4, P=0.001, ϕ=.343
Infection	(32/12/1)**[3]	(10/4/0)*[4]	(17/27/2)	X^2=13.3, p=0.001, ϕ=.362
Electrolyte disturbance	(11/32/2)	(3/11/0)	(9/34/5)	ns
Thyroid disturbance	(3/41/1)	(0/14/0)	(2/41/3)	ns
Kidney disease	(10/34/1)	(4/10/0)	(13/30/3)	ns
Liver disturbance	(6/38/1)	(2/12/0)	(4/40/2)	ns
Urinary retention	(11/33/1) ~[5]	(5/9/0)*[6]	(4/39/3)	X^2=6.0, p=0.051, ϕ=.243
Urinary catheterization	(10/34/1)	(5/9/0)	(6/38/2)	ns
Dehydration	(5/39/1)	(4/10/0)*[7]	(2/42/2)	Fisher exact, p=0.026, ϕ=.338
Pain	(17/27/1)	(4/9/1)	(16/28/2)	ns

Analyses are Chi-square analyses or Fisher's exact probability tests (categorical data). ~=p<0.10 (trend), *= $p < .05$, ** =$p < .01$, ***=p<0.001

[1,3,5]= differences between prevalent delirium and controls, **[2,4,6,7]**=differences between incident delirium and controls.

[1.] X^2=10.4, p=0.001, ϕ=.359, [2.] X^2=10.5, p=0.001, ϕ=.426, [3.] X^2=10.4, p=0.001, ϕ=.343, [4.] X^2=4.6, p=0.032, ϕ=.281, [5.]X^2=3.8, p=0.053, ϕ=.208,

[6.]= X^2=5.5, p=0.019,ϕ=.312, [7.] p=0.026, ϕ=.338.

Cognitive functioning in post-delirious patients and controls

The results of the ANCOVA analyses are summarized in Figure 2 and Table 4.1. The ANCOVA showed significant main effects of delirium on the total Camcog-R, MMSE, orientation, language, memory and executive functioning. There was also a tendency towards a negative effect of delirium on attention, abstract thinking and perception. The groups did not differ significantly from each other on the subscales praxis and calculation.

Differences between prevalent delirium and controls

Pairwise comparisons indicated lower scores in patients with prevalent delirium on the total Camcog-R and the MMSE, memory and executive functioning subscales compared to controls. A tendency toward poorer performance in the prevalent delirium than the control group was found for orientation, language and abstract thinking.

Differences between incident delirium and controls

Patients with incident delirium had significantly lower scores on the total Camcog-R and MMSE, orientation and memory subscales compared to controls. A trend toward poorer performance in patients with incident delirium was found for attention and perception.

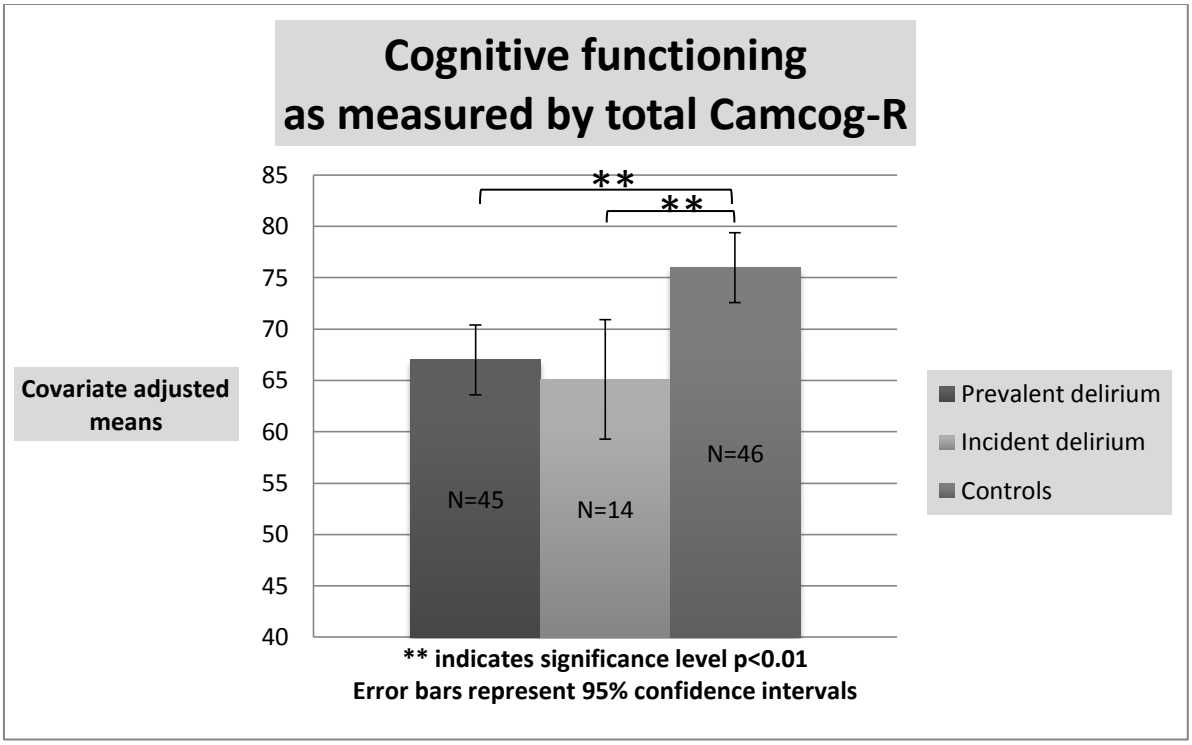
Differences between prevalent and incident delirium

The analyses showed no significant differences between prevalent and incident delirium on total Camcog-R or Camcog-R subscales.

Effects of covariates on cognitive performance

The ANCOVA showed a negative influence of an earlier diagnosis of dementia on the total Camcog-R scale, MMSE, orientation, language, memory, praxis, perception and executive functioning, as well as a tendency towards a negative effect on attention. The incidence of diabetes mellitus or a history of delirium did not significantly affect cognitive performance.

Figure 2. Cognitive functioning as measured by total Camcog-R



Differences between the three groups (prevalent delirium, incident delirium and controls) on general cognitive functioning, as measured by the total Camcog-R, adjusted for dementia, diabetes mellitus and history of delirium. Error bars represent 95% confidence intervals. Differences at 0.01 significance level are shown.

Table 4.1 Differences in total Camcog-R score and Camcog-R subtest scores.

Covariates: Dementia[1] Diabetes mellitus, History of delirium		Prevalent delirium (N=45)	Incident delirium (N=14)	Control-group (N=46)	Main Effect p-value, partial eta-squared
Total Camcog-R[2]	*M ± sd*	65.1 ± 13.1**	65.6 ± 13.1**	77.7 ± 9.9	p=.001, part η^2 =.141
	Adj. M	67.0 ± 1.7	65.1 ± 2.9	76.0 ± 1.7	
MMSE (Camcog-R)[3]	*M ± sd*	20.0 ± 5.3**	19.9 ± 5.3**	24.8 ± 3.4	p=.001, part η^2 =.132
	Adj. M	20.8 ± .7	19.8 ± 1.1	24.0 ± 0.7	
				8.5 ± 1.7	
Orientation[4]	*M ± sd*	7.1 ± 2.3~	6.9 ± 2.1*	± .3	p=.018, part η^2=.079
	Adj. M	7.3 ± .3	6.8 ± .5	24.1 ± 2.6	
				23.8 ± .5	
Language[5]	*M ± sd*	22.0 ± 3.0~	22.1 ± 3.5		p=.036, part η^2=.066
	Adj. M	22.3 ± .5	22.0 ± .8	18.7 ± 3.4	
				18.2 ± .6	
Memory[6]	*M ± sd*	14.4 ± 4.6**	15.3 ± 4.1*		p=.001, part η^2= .128
	Adj. M	14.9 ± .6	15.2 ± 1.0		

Analyses are ANCOVAs with Bonferroni's post-hoc comparisons. Outliers were removed. ~=p<0.10 (trend), *= $p < .05$, ** =$p < .01$

[1] Negative influence of dementia on total Camcog-R (p<0.001, part η^2=.161), MMSE (p<0.001, part η^2=.182), orientation (p<.001, part η^2=.149), language (p=.008, part η^2=.07) and memory (p=.003, part η^2=.084).

[2] Difference between prevalent delirium and controls (p=0.002). Difference between incident delirium and controls (p=.005).

[3] Difference between prevalent delirium and controls (p=.005). Difference between incident delirium and controls (p=.005).

[4] Difference between prevalent delirium and controls (p=0.087). Difference between incident delirium and controls (p=.035).

[5] Difference between prevalent delirium and controls (p=0.072).

[6] Difference between prevalent delirium and controls (p=0.002). Difference between incident delirium and controls (p=.042).

Table 4.1 Differences in total Camcog-R score and Camcog-R subtest scores. Continued

Covariates: Dementia[7], Diabetes mellitus, History of delirium		Prevalent delirium (N=45)	Incident delirium (N=14)	Control-group (N=46)	Main effect p-value, partial eta squared
Attention[8]	*M ± sd*	4.6 ± 1.9	4.0 ± 1.7~	5.4 ± 1.4	p=.054, part η^2= .059
	Adj. M	4.7 ± .3	4.0 ± .5	5.3 ± .3	
Calculation	*M ± sd*	1.5 ± .7	1.5 ± .7	1.7 ± .5	ns
	Adj. M	1.5 ± .1	1.5 ± .2	1.7 ± .1	
Praxis	*M ± sd*	7.7 ± 2.2	7.4 ± 2.9	8.9 ± 2.0	ns
	Adj. M	7.9 ± .4	7.3 ± .6	8.6 ± .3	
Abstract thinking[9]	*M ± sd*	3.4 ± 2.4~	4.2 ± 2.7	5.0 ± 2.4	p=.084, part η^2= .049
	Adj. M	3.5 ± .4	4.2 ± .7	4.9 ± .4	
Perception[10]	*M ± sd*	5.2 ± 1.6	4.5 ± 2.0~	5.7 ± 1.3	p=.084, part η^2= .049
	Adj. M	5.4 ± .2	4.5 ± .4	5.6 ± .2	
Executive functioning[11]	*M ± sd*	10.6 ± 3.8*	11.6 ± 3.6	14.0 ± 4.1	p=.003, part η^2= .112
	Adj. M	10.7 ± .6	11.4 ± 1.0	13.9 ± .6	

Analyses are ANCOVAs with Bonferroni's post-hoc comparisons. Outliers were removed. ~=p<0.10 (trend), *= $p < .05$

[7] Negative influence of dementia on attention(p=.058, part η^2=.037), praxis (p=.001, part η^2=.101), perception(p=.027, part η^2= .048) and executive functioning (p=.020, part η^2=.054).

[8] Difference between incident delirium and controls (p=.055).

[9] Difference between prevalent delirium and controls (p=.079).

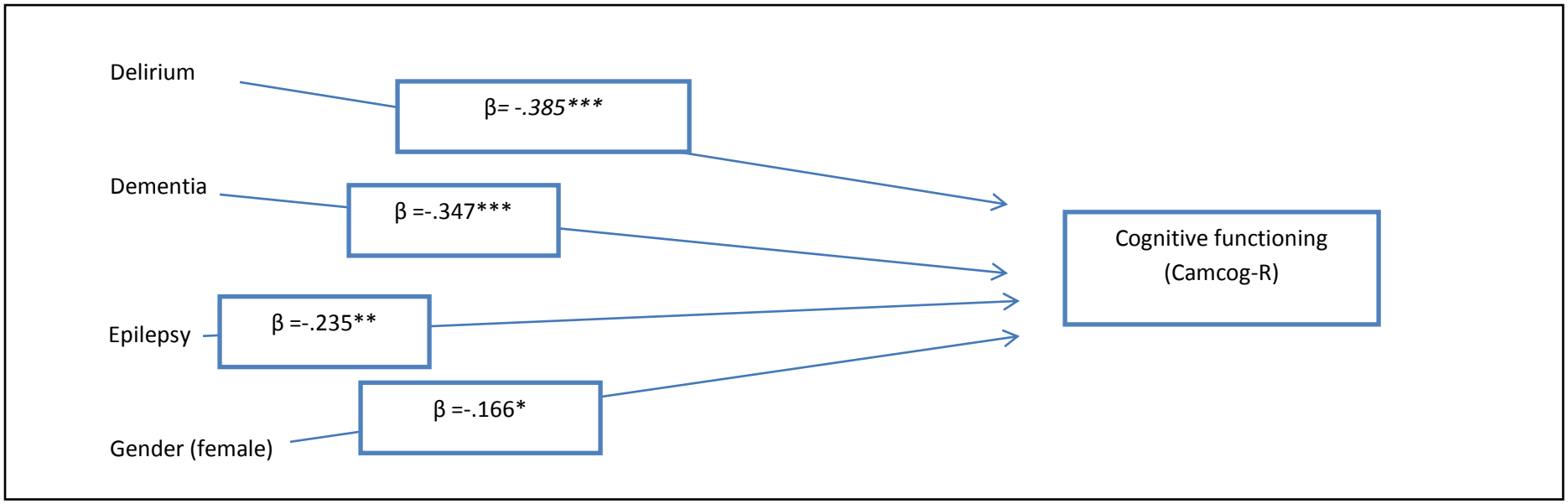
[10] Difference between incident delirium and controls (p=.082).

[11] Difference between prevalent delirium and controls (p=0.002).

Predictors of cognitive functioning

The final model in the stepwise multiple regression analysis (F=18.8, p=<0.001) indicated that delirium (β=-.385, p=<0.001), dementia (β=-.347, p=<0.001), epilepsy (β=-.235, p=<0.01) and gender (β=-.166, p=<0.05) made a significant negative contribution to cognitive outcome one week prior to hospital discharge, explaining nearly 43 per cent of the total variance (adjusted R^2=.41). The results of this regression analysis are summarized in Figure3 a. A stepwise multiple regression analysis including prevalent delirium and incident delirium separately (Figure 3b), indicated that prevalent delirium (β=-.360, p=<0.001), dementia (β=-.356, p=<0.001), incident delirium (β=-.310, p=<0.001), epilepsy (β=-.238, p=<0.01) and female gender (β=-.167, p=<0.05) added predictive value in the final regression model, explaining 43 per cent of the total variance (adjusted R^2=.40). The point-biserial correlation between prevalent delirium and total Camcog-R was -.37 (p=<0.01). The point-biserial correlation between incident delirium and total Camcog-R was -.152 (not significant).

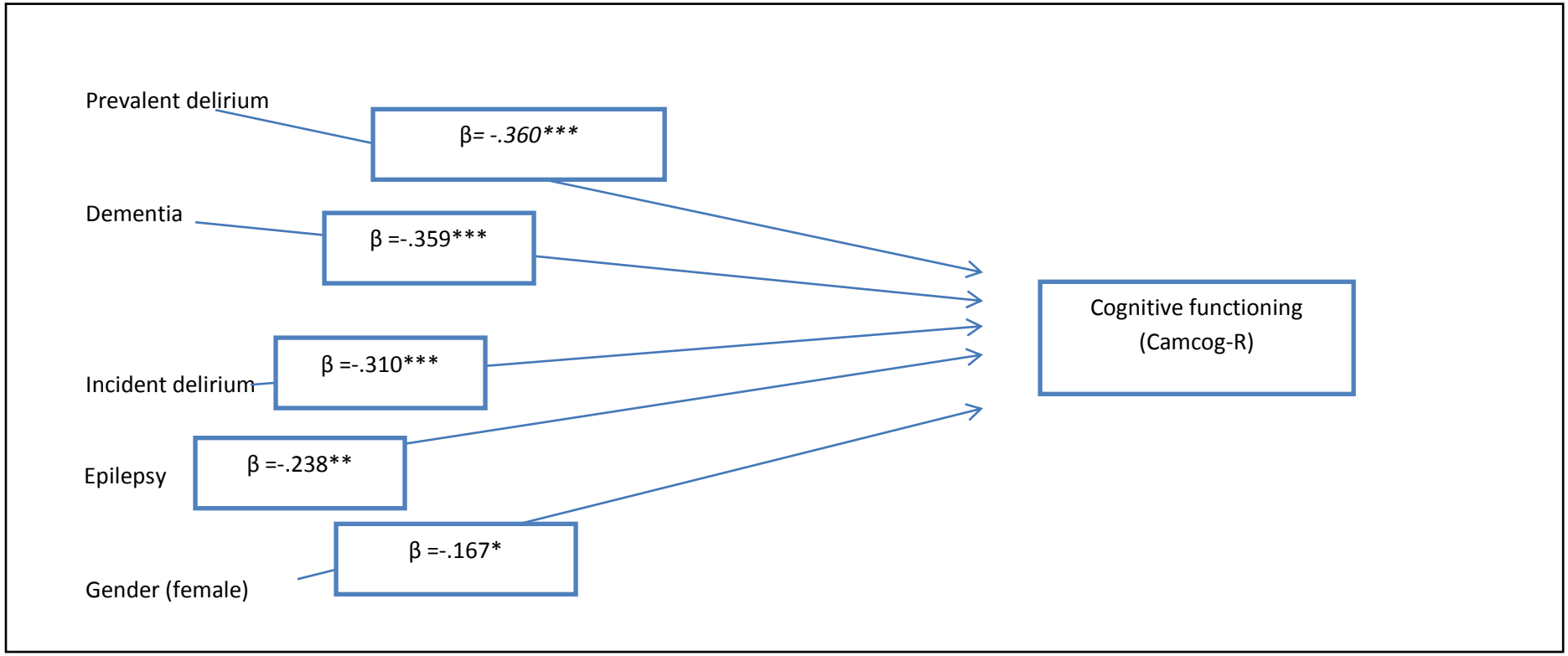
Figure 3a. Predictors of overall cognitive functioning (total Camcog-R score)



Final model in the stepwise multiple regression analysis. β indicates standardized coefficients. Note: *= $p < .05$, ** =$p < .01$, ***=p<0.001.

Note: *= $p < .05$, ** =$p < .01$, ***=p<0.001.

Figure 3b. Predictors of overall cognitive functioning (total Camcog-R score)



Final model in the stepwise multiple regression analysis. β indicates standardized coefficients. Note: *= $p < .05$, ** =$p < .01$, ***=p<0.001.

Discussion

Our study is an exploratory analysis of the short-term cognitive effects of delirium in a general geriatric population. The current study found lower performance in the two delirious groups on the total Camcog-R compared to controls, after adjustment for dementia, diabetes mellitus and history of delirium, which is evidence supporting our hypothesis of lower overall cognitive functioning in post-delirious patients. The clinical relevance of the effect is reflected by the large effect size. Wacker et al.[13] , as far as we know, were the only others that used the Camcog-R to examine cognitive performance in post-delirious patients. The study of Wacker and colleagues[13] differed from ours in a couple of ways. For example, they performed neuropsychological assessments on average two years after an orthopaedic intervention. Cognitive functions most affected in patients with post-operative delirium were memory, orientation and abstract thinking. We found moderate effects of delirium on MMSE , memory, orientation, language, attention and executive functioning and small effects on abstract thinking and perception. It is possible that the pattern of cognitive decline in our patients would change over a two-year period. Furthermore, Wacker et al.[13] did not made a distinction between prevalent and incident delirium. To the best of our knowledge, we were the first that took into account the onset of delirium in the evaluation of cognitive functioning.

We hypothesized that cognitive functioning would be worse in patients who had a delirium at admission compared to patients who developed a delirium during hospital stay and those who did not suffer from delirium. This hypothesis could not be confirmed. Instead, patients with prevalent and those with incident delirium did not differ on cognitive performance prior to hospital discharge. In comparison with patients who did not have a delirium, both delirious groups had (tendencies towards) lower scores on orientation and memory. Prevalent delirium was negatively associated with executive functioning and had a tendency towards lower performance on language and abstract thinking than the control group. Incident delirium, by contrast, had a tendency towards a significant negative effect on attention and perception. These findings may indicate differences in cognitive patterns between the two post-delirious groups.

Besides pre-existing differences in dementia, epilepsy and gender, both prevalent and incident delirium added predictive value to cognitive functioning. Prevalent delirium (yes or no) was the most important predictor of cognitive functioning in our regression model. This finding was in line with our expectations. We are aware that the contribution of each factor would change with a different set of independent variables.[33]Therefore, we also inspected the difference in the point-biserial correlation between prevalent and incident delirium. The point-biserial correlations indicated that prevalent delirium had a significant negative association with total Camcog-R performance, which was not the case for incident delirium. The same findings using different statistic methods

strengthen our conclusion that prevalent delirium is a more important predictor of cognitive functioning pre-hospital discharge in a general geriatric population compared to incident delirium.

The present study emphasizes the role of dementia, premorbid cognitive decline, history of delirium and psychotropic medication use as possible predisposing factors of prevalent delirium. Fever , infection and urinary retention may be potential precipitating factors. The association with pre-existing dementia and the tendency towards lower premorbid cognitive decline was consistent with earlier studies.[18,20] Our hypothesis that patients with prevalent delirium represent the most vulnerable group seemed to be partly confirmed. We have not detected predisposing factors of incident delirium, nonetheless fever, infection, urinary retention and dehydration may be precipitating factors. The fact that patients with incident delirium in the present study stayed significantly longer at the hospital compared to the other groups was consistent with the existing literature.[19-21] According to McCuster et al.[22], Incident delirium may result from illnesses or complications that are the underlying cause of the longer stay. Physicians will probably not discharge a patient until his or her clinical condition improves. McCuster et al.[22] also presume that a diagnosis of incident delirium may lead to additional evaluation and tests, which require longer stays.

The current study had several strengths. One of them was the use of a comprehensive neuropsychological test battery rather than a cognitive screening instrument like the MMSE . We studied a general geriatric population, increasing the generalizability of our findings. Furthermore, we minimized the potential effect of confounding variables by taking cognitive assessments prior to discharge. Another strength was the use of a comparable control group that consisted of age-matched patients without a delirium at admission or during hospital stay. Lastly, we adjusted for differences in pre-existing dementia.

Limitations of our study were the practical feasibility and the relatively small sample size which may have caused a lack of statistical power. The observed power in our analysis ranged from .286 (calculation), .469 (praxis) to .954 (total Camcog-R). We needed 27 subjects per patient group to detect an effect size of .5 and to get sufficient power (.80).[34] The relatively small sample size in the incident delirium group is consistent with earlier literature.[2,3] The flowchart in Figure 1 shows that it was challenging to let these patients participate in the current study. An alternative explanation for our results might have been the effect of fatigue on cognitive performance. We have not measured fatigue in our sample. On the other side, the physician excluded patients who were feeling too tired or sick .

The latter leads us to the final limitation. Even though physicians used their clinical experience and diagnostic criteria to detect ending of a delirium, we can never be sure whether a delirium was completely cleared up at the time of assessment. According to Cole, Ciampi, Belzi & Zhong[35] and Cole[36] , the partial recovery of delirium in a substantial minority of patients may account

for its adverse outcomes. We hope to evaluate the long-term effects with follow-up data from our longitudinal study in the future. Until then, our findings should be interpreted with caution.

We think that physicians and nurses should get more familiar with the possible risk factors and outcomes of delirium to improve prevention, diagnosis, treatment and follow-up care. Informing patients and their families of the risk factors and consequences of delirium should be standard clinical practice. Patients who suffered from delirium in the hospital, should get regular medical check-ups and follow-ups after hospital discharge. When these patients return home, they may face cognitive changes.

In summary, the current study suggests a short-term negative effect of both prevalent and incident delirium on cognitive functioning in elderly general hospital patients. Prevalent delirium seems to be a more important predictor of cognitive performance in the week prior to discharge compared to incident delirium. Prevalent delirium was also significantly associated with pre-existing dementia. Patients with incident delirium stayed significantly longer at the hospital compared to the other groups. We recommend future studies examining the risk factors and outcomes of delirium to distinguish between prevalent and incident cases. Future research is needed to confirm our results in a larger sample size, and to further explore the cognitive patterns in post-delirious patients.

References

1. Roth M TE, Mountjoy CQ, et al. CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. *Br J Psychiatry.* 1986;149:698–709.

2. Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: A systematic literature review. *Age and Ageing* 2006;35:350–364.

3. White S, Bayer A. Delirium – a clinical overview. *Rev. Clin. Gerontol.* 2007; 17:45–62.

4. Mittal V, Muralee S, Williamson D, et al. Delirium in the Elderly: A Comprehensive Review. *Am J Alzheimers Dis Other Demen.* 2011;26(2):97–109.

5. Inouye S. Delirium in Older Persons. *N Engl J Med.* 2006;354:1157–1165.

6. Saxena S, Lawley D. Delirium in the elderly: A clinical review. *Postgrad Med J* 2009;85:405–413.

7. Álvarez-fernandez B, Formiga F, Gomez R. Delirium in hospitalised older persons: Review. *J Nutr Health Aging.* 2008;12(4):246–251.

8. Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: diagnosis, prevention and treatment. *Nat. Rev. Neurol. .* 2009;5:210–220.

9. Jackson JC, Gordon SM, Hart RP, Hopkins RO, Ely EW. The Association Between Delirium and Cognitive Decline: A Review of the Empirical Literature. *Neuropsychol Rev.* 2004;14(2):87–98.

10. Maclullich AMJ, Beaglehole A, Hall R, Meagher DJ. Delirium and long-term cognitive impairment. *Int Rev Psychiatry.* 2009;21(1):30–42.

11. Folstein MF FS, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189–198.

12. Laaksonen R, Erkinjuntti T, Granberg M, Amberla K, Sulkava R. D-Test Battery-A comprehensive neuropsychological screening test. Preliminary results. *Psychiatria Fennica* 1985;63:87–94.

13. Wacker P, Nunes PV, Cabrita H, Forlenza OV. Post-Operative Delirium Is Associated with Poor Cognitive Outcome and Dementia. *Dement Geriatr Cogn Disord* 2006;21:221–227.

14. van Rijsbergen MWA, Oldenbeuving AW, Nieuwenhuis-Mark RE, et al. Delirium in acute stroke: A predictor of subsequent cognitive impairment? A two-year follow-up study. *J Neurol Sci.* 2011;306 138–142.

15. Fong TG, Jones RN, Shi P, et al. Delirium accelerates cognitive decline in Alzheimer disease. *Neurology* 2009;72 1570–1575.

16. McCusker J, Cole M, Dendukuri N, Belzile É, Primeau F. Delirium in older medical inpatients and subsequent cognitive and functional status: A prospective study. *CMAJ* 2001;165(5):575–583.

17. Kat MG, Vreeswijk R, de Jonghe JFM, et al. Long-term cognitive outcome of delirium in elderly hip-surgery patients. A 2.5 year prospective matched controlled study. *Dement Geriatr Cogn Disord.* 2008;26(1):1–8.

18. Lin RY, Heacock LC, Bhargave GA, Fogel JF. Clinical associations of delirium in hospitalized adult patients and the role of on admission presentation. *Int J Geriatr Psychiatry.* 2010;25:1022–1029.

19. Moschetta AL, Silveira CV, Dalacorte RR, Schneider RH, Gomes da Silva Filho I. Time of delirium onset and prognosis amongst Southern Brazilian hospitalized elderly patients. *Dement Neuropsychol.* 2009;3(4):303–307.

20. McCuster J, Cole M, Dendukuri N, Han L, Belzile É. The Course of Delirium in Older Medical Inpatients: A Prospective Study. *J Gen Intern Med.* 2003;18:696–704.

21. Bourdel-Marchasson I, Vincent S, Germain C, et al. Delirium Symptoms and Low Dietary Intake in Older Inpatients Are Independent Predictors of Institutionalization: A 1-Year Prospective Population-Based Study. *J Gerontol* 2004;59A(4):350–354.

22. McCusker J, Cole MG, Dendukuri N, Belzile E. Does Delirium Increase Hospital Stay? *J Am Geriatr Soc.* 2003; 51:1539–1546.

23. McCusker J, Cole M, Abrahamowicz M, Primeau F, Belzile E. Delirium Predicts 12-Month Mortality. *Arch Intern Med* 2002;162:457–463.

24. CAMDEX-R/N. third edition. Amsterdam: Harcourt Assessment B.V; 2005.

25. de Koning L, van Kooten F, Koudstaal PJ, DW D. Diagnostic value of the Rotterdam-CAMCOG in post-stroke dementia. *J Neurol Neurosurg Psychiatry.* 2005;76(2):263–265.

26. De Jonge J. Differentiating between demented and psychiatric patients with the Dutch version of the IQCODE. *Int J Geriatr Psychiatry.* 1997;12(4):462–465.

27. Ehrensperger MM, Berres M, Taylor KI, Monsch AU. Screening properties of the German IQCODE with a two-year time frame in MCI and early Alzheimer's disease. *Int Psychogeriatr.* 2010;22(1):91–100

28. Scheffer AC, van Munster BC, Schuurmans MJ, de Rooij SE. Assessing severity of delirium by the Delirium Observation Screening Scale. *Int J Geriatr Psychiatry.* 2011;26:284–291.

29. Weinberger M SG, Schmader K. Comparing proxy and patients' perceptions of patients' functional status: results from an outpatient geriatric clinic. *J Am Geriatr Soc* 1992;40(6):585–588.

30. Collin C, Wade DT, al. DSe. The Barthel ADL Index: a reliability study. *Int Disabil Stud. .* 1988;10:61-63.

31. de Rooij SEJA, Govers AC, Korevaar JC, Giesbers AW, Levi M, de Jonge E. Cognitive, Functional, and Quality-of-Life Outcomes of Patients Aged 80 and Older Who Survived at Least 1 Year After Planned or Unplanned Surgery or Medical Intensive Care Treatment *J Am Geriatr Soc.* 2008;56(5):816–822.

32. Haan Rd, Limburg M, Schuling J, Broeshart J, Jonkers L, Zuylen Pv. Klinische evaluatie van de Barthel-Index, een maat voor beperkingen in het dagelijks functioneren. *Ned Tijdschr Geneeskd.* 1993;137(18):917–921.

33. Pallant J. *SPSS survival manual*. Chicago: Open University Press; 2005.

34. Hinkle DE, Wiersma W, Jurs SG. *Applied statistics for the behavioral sciences.* Vol 663. Boston New York: Wadsworth Publishing; 2003.

35. MG Cole AC, E Belzile, L Zhong. Persistent delirium in older hospital patients: a systematic review of frequency and prognosis. *Age and Ageing.* 2009;38:19–26.

36. Cole MG. Persistent delirium in older hospital patients. *Curr Opin Psychiatry.* 2010;23:250–254.