Cognitive impairment in older emergency department patients

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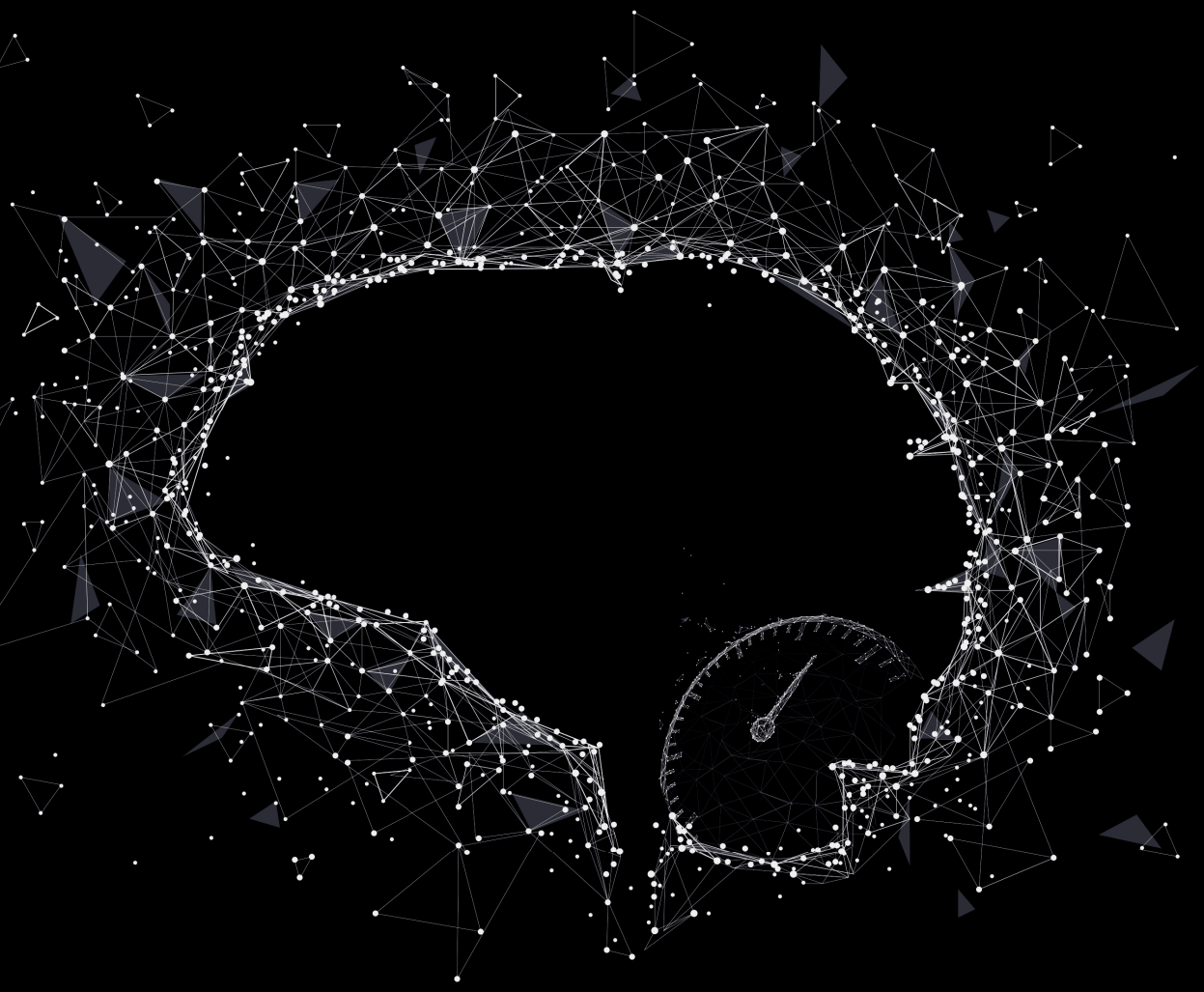
Part I

Cognitive impairment and adverse outcomes



Chapter 2

Cognitive impaired older patients and adverse outcomes after acute hospitalisation

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The Six-Item Cognitive Impairment Test (6-CIT) is associated with adverse outcomes in acutely hospitalised older patients; a prospective cohort study

ABSTRACT

Introduction: Cognitive impairment in older patients is a risk factor for functional decline and mortality. The aim of the present study was to investigate whether cognitive impairment, whichever the cause and measured by the Six-Item Cognitive Impairment Test (6-CIT), is an independent predictor of adverse outcomes in acutely hospitalised older patients.

Methods: For this secondary analysis of a prospective multicentre study, all acutely hospitalised patients aged 70-years and older were included during similar 4-month periods in 3 consecutive years. Multivariable logistic regression analyses were used to investigate whether impaired cognition (6-CIT ≥11 points) was an independent predictor of 90-day (long-term) adverse outcome, a composite measure of functional decline and 90-day mortality. Secondary (short-term) endpoints were hospital length of stay, new institutionalisation and in-hospital mortality.

Results: In total, 196 (15.6%) of 1252 included patients had a 6-CIT ≥11. Median age was 80 years (interquartile range 74-85). Patients with impaired cognition as assessed with the 6-CIT had a higher rate of 90-day adverse outcome (41.7% compared to 30.3% in 1056 not cognitively impaired patients, p=0.009). Impaired cognition was a predictor of 90-day adverse outcome with a crude odds ratio (OR) of 1.64 (95%CI 1.13-2.39), but statistical significance was lost when fully corrected for age, sex, living situation and specialism (OR 1.44, 95%CI 0.98-2.11). For all secondary outcomes (hospital length of stay, new institutionalisation and in-hospital mortality) impaired cognition was an independent predictor.

Conclusion: Acutely hospitalised older patients are frequently cognitively impaired. In the acute hospital setting the 6-CIT, a brief and easy to administer test for assessment of cognitive impairment, is associated with 90-day mortality and functional decline and is an independent predictor of hospital length of stay, new institutionalisation and in-hospital mortality. This emphasizes the importance of routinely screening for cognitive impairment in this vulnerable patient group.

INTRODUCTION

Acute hospitalised older patients have a high risk of adverse outcomes[1] and cognitively impaired older patients are at an even greater risk compared to patients with normal cognition[2]. Cognitive impairment can be caused by dementia, delirium, hypoperfusion of the brain or by a combination of these disorders. Impaired cognition is highly prevalent in acutely hospitalised older patients, but is frequently missed by doctors and nurses. Whichever the cause, professional caretakers should be vigilant for the presence of cognitive impairment as it calls for measures to prevent adverse events and to ensure safety when patients are hospitalised.

To date, in most studies investigating predictors of outcome among hospitalised older patients, the Mini Mental State Examination (MMSE)[3] was used to assess cognitive impairment, often in combination with pre-morbid ADL dependency[4-7]. However, a cognition test to be used in the acute hospital setting should be short, easy to administer and feasible when patients are unable to write. While the MMSE is considered the gold standard test, it has limitations due to the relatively lengthy time it takes to administer, its interaction with the level of education and the requirement to be able to write. In comparison with the MMSE, the Six-Item Cognitive Impairment Test (6-CIT) [8] takes only 2-3 minutes[9], is not influenced by educational level, can be used in bedbound patients who are unable to write and showed comparable test characteristics. If adverse outcome of acutely hospitalised older patients could be predicted by impaired cognition as assessed with the 6-CIT, it would be a suitable test to improve identification of older patients at risk for adverse events in the acute setting and to help identify their needs.

Therefore, the aim of the present study was to investigate the association of impaired cognition, as measured with the 6-CIT, and adverse outcomes in acutely hospitalised older patients. A cohort study among three hospitals in the Netherlands was conducted and a distinction was made in short-term adverse outcomes (in-hospital mortality, new institutionalisation and prolonged length of hospital stay) and long-term adverse outcomes (90-day functional decline and mortality).

METHODS

Study design and setting

This was a secondary analysis using the data of a prospective multicentre study the 'Recovery Care Programme' (*HerstelZorgProgramma*)[10]. A detailed description of the study design can be found in the article by Heim *et al.*[10]. In summary, this was an observational cohort study in which data were prospectively collected during 3 consecu-

tive years, in the same season. Three secondary care facilities (Alrijne Hospital, Leiden; Alrijne Hospital, Leiderdorp and HMC Bronovo Hospital, The Hague) and one tertiary care hospital (Leiden University Medical Center, Leiden) participated.
The medical ethics committee of the Leiden University Medical Center (LUMC) waived the need for ethical approval as data was collected to improve patient care. All patients provided written informed consent and data was treated anonymously.

Participants

Patients aged 70-years or older who were admitted to one of the four study hospitals were assessed for inclusion. Two secondary care hospitals and one tertiary care hospital included both acutely admitted and planned patients (wards of orthopaedics, neurology, urology and surgery). One secondary care hospital included only acutely admitted patients. For the analyses the wards of orthopaedics, urology and surgery were combined into 'surgery', and the departments of internal medicine, neurology and cardiology were combined into 'medical'.
Patients were excluded if they stayed in the hospital for less than 48 hours and if they were not able to perform the study interview within 72 hours after admission. Patients who had an MMSE of less than 19, indicating severe cognitive impairment, and had no caregiver present during the interview were also excluded because they could not provide informed consent. For the present secondary analysis only acutely admitted patients, from both medical and surgical departments, were included.

Data collection

Patients were interviewed on the wards by a trained nurse with a series of questionnaires. After 90-days, patients were sent follow-up questionnaires by mail, to be self-administered. Patients who did not respond were contacted by telephone.

Cognitive function

The Six-Item Cognitive Impairment Test (6-CIT)[8] contains items on orientation, attention and memory with a range from 0-28; a score ≥11 indicates cognitive impairment. The 6-CIT showed a good correlation with the MMSE and a cut-off point of eleven corresponded to a MMSE of ≤23[9]. The 6-CIT score was used to classify older people in those with (score ≥11) and without (score <11) cognitive impairment, a cut-off as has been recommended in literature.
Mini Mental State Examination (MMSE) evaluates overall cognitive functions, such as orientation, memory, attention, calculation[3], ranging from 0-30, and a score ≤23 indicating cognitive impairment. Scores <19 indicate severe cognitive impairment.

Functional status

The Katz Index of Independence in Activities of Daily Living[11] (Katz-ADL) was administered to quantify functional status. The Katz-ADL contains six yes/no items on whether a patient is independent in bathing, dressing, transferring from bed to chair, eating, going to the toilet and the use of incontinence products. A score ≥ 2 points means dependency in ADL[12].

Demographics

Data on age, sex and self-reported living situation were registered by the research nurse. Also the medical specialism and hospital were the patient was treated was registered.

Outcomes

Primary outcome

The primary outcome was defined as a composite end-point of adverse outcome, containing self-reported functional decline (by increasing one point in Katz-ADL) after 90-days and/or mortality within 90-days. Mortality was verified in the hospital files, by the healthcare insurer or was reported by family members. The cut-off point of ≥1 point increase in Katz-ADL was chosen because this results in a clinically relevant decrease in independency[12].

Secondary outcomes

Three secondary outcomes were investigated: in-hospital mortality, new institutionalisation directly after hospital admission and prolonged hospital length of stay (LOS). New institutionalisation was defined as moving from an independent living situation to assisted home care facilities directly after discharge from the hospital. Prolonged hospital LOS was defined as a length of stay of 7 days or longer.

Data analysis

Data are displayed as percentages, means and standard deviations for normally distributed variables or as medians with interquartile range for non-normally distributed variables. Independent T-tests and chi-square tests were used to assess equality of groups when variables were normally distributed and with Mann-Whitney-U tests for non-normally distributed variables. The association between 6-CIT and primary and secondary outcomes was calculated using crosstabs and chi-square tests. Patients were divided into two groups for analysis, using the 6-CIT (≤10, ≥11) at baseline. Univariable logistic regression was used to assess the crude association between 6-CIT and primary and secondary outcomes.

Two multivariable logistic regression models were used to assess whether 6-CIT was an independent predictor of adverse outcome. The first model was corrected for age

and sex. In the second model the association of interest was also corrected for living situation and specialism, to correct for baseline functional status and type of disease. The general rule of thumb that there should be a minimum of 10 events per possible variable in the model was used.

Statistical significance was defined by 95% confidence intervals excluding 1.0 or $p<0.05$. All statistical analyses were performed using IBM SPSS Statistics package (version 23, New York, USA).

RESULTS

Baseline characteristics

A total of 1252 patients was included in this study (figure 1), of which the baseline characteristics are shown in table 1. The majority of patients was female (n=710, 56.8%) and median age was 80 years (interquartile range 74-85). In 196 patients (15.6%), the 6-CIT score was ≥11, indicating cognitive impairment. In table 1, it is shown that patients with cognitive impairment were older, less frequently male and more often lived in an assisted living facility, compared to patients with a lower 6-CIT score.

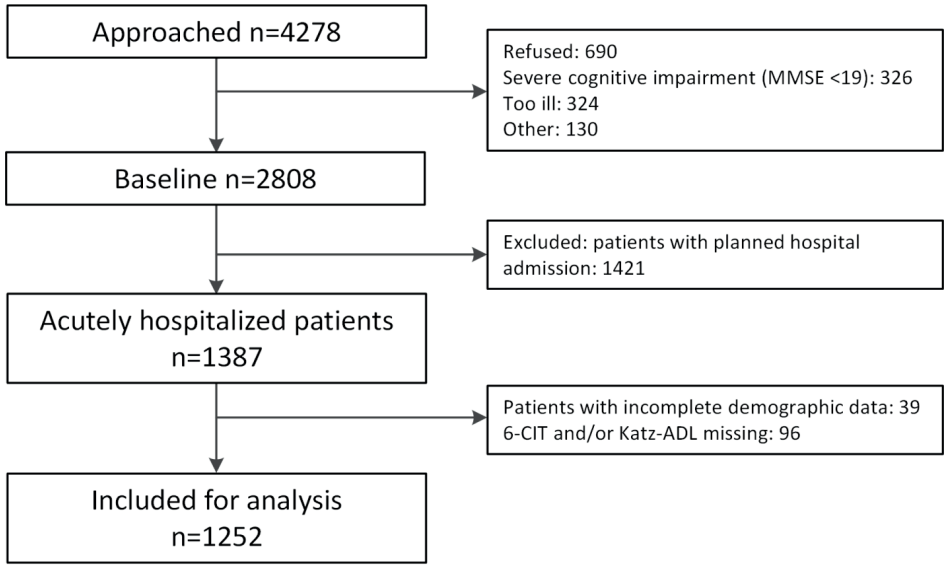

Figure 1: Flowchart of study population

Table 1: Baseline characteristics of the total study population, and stratified according to 6-CIT score

Characteristic	All patients n=1252	6-CIT ≤10 n=1056	6-CIT ≥11 n=196	p-value
Age	80 (74-85)	79 (74-84)	82 (78-87)	<0.001
Male n,%	542 (43.2)	476 (45.1)	66 (33.7)	0.003
Living situation[a] n,%				<0.001
Independent, with others	591 (47.5)	519 (49.4)	72 (36.9)	
Independent, alone	522 (41.9)	443 (42.2)	79 (40.5)	
Assisted living facility	132 (10.6)	88 (8.4)	44 (22.6)	
Specialism[b] n,%				0.740
Surgical	770 (61.7)	647 (61.5)	123 (62.8)	
Medical	478 (38.3)	405 (38.5)	73 (37.2)	
Hospital n,%				<0.001
LUMC	205 (16.4)	166 (15.7)	39 (19.9)	
Alrijne - Leiden	297 (23.7)	240 (22.7)	57 (29.1)	
Alrijne - Leiderdorp	375 (30.0)	308 (29.2)	67 (34.2)	
HMC Bronovo	375 (30.0)	342 (32.4)	33 (16.8)	
Katz-ADL[c]	1 (0-3)	0 (0-2)	1 (0-4)	<0.001
6-CIT	4 (0-8)	2 (0-5)	14 (12-18)	n.a
MMSE[d]	27 (24.3-29)	28 (26-29)	21 (19-24)	n.a.

Data are presented as median with interquartile range unless noted otherwise.
Abbreviations; n: number, 6-CIT: Six-Item Cognitive Impairment Test, Katz-ADL: Katz Index of Independence in Activities of Daily Living, IQR: interquartile range, n.a.: not applicable.
[a]number of values 1245; [b]number of values 1248; [c]number of values 1252; [d]number of values 892.

Primary and secondary outcomes

A total of 311 (31.8%) patients suffered from 90-day mortality or functional decline. Table 2 shows the incidence of various negative outcomes over strata of 6-CIT. More than 30% of patients with a 6-CIT ≤10 suffered from 90-days mortality or functional decline, in comparison to 41.7% patients with 6-CIT ≥11 (p=0.009). Patients with impaired cognition had a prolonged hospital stay of ≥7 days more frequently (n=455, 43.3% vs. n=108, 55.4%, respectively p=0.002) and were more often institutionalised after hospital admission, compared to those with a normal cognition. Also, in-hospital mortality was higher in cognitively impaired patients compared to cognitively normal patients (n=12, 1.2% vs. n=8, 4.1%, respectively p=0.003).

Table 2: Crude outcomes for total study population and according to 6-CIT-score

	Total n=1252	6-CIT ≤10 n=1056	6-CIT ≥11 n=196	p-value
Primary outcome				
90-day adverse outcome[a]	311 (31.8)	256 (30.3)	55 (41.7)	0.009
Secondary outcomes				
≥7 days LOS[b]	563 (45.1)	455 (43.3)	108 (55.4)	0.002
New institutionalisation[c]	67 (7.4)	46 (5.8)	21 (18.8)	<0.001
In-hospital mortality[d]	20 (1.6)	12 (1.2)	8 (4.1)	0.003

Data are presented as numbers and percentages.
Abbreviations: n: number, 6-CIT: Six-Item Cognitive Impairment Test, IQR: interquartile range, LOS: length of stay.
[a]number of values 977; [b]number of values 1247; [c]number of values 905; [d]number of values 1236.

Independent predictors

Patients with impaired cognition as assessed with the 6-CIT had a 1.6 times increased risk of mortality or functional decline after 90-days (OR 1.64, 95%CI 1.13-2.39). When corrected for age and sex this association was still observed but after correction for living situation and treating medical specialism, statistical significance was lost (table 3). Patients with impaired cognition were also at increased risk of prolonged hospital stay and of an 3-fold increased risk of being institutionalised, independent of age, sex, living situation, medical specialism. Finally, impaired cognition was independently associated with in-hospital mortality.

Table 3: The association between 6-CIT and adverse outcomes in older acutely hospitalised patients

	6-CIT ≤10	6-CIT ≥11	p-value
		OR (95%CI)	
Primary outcome – 90 day functional decline and mortality[a]			
Crude	1 (ref)	1.64 (1.13-2.39)	0.010
Model 1 – corrected for age and sex	1 (ref)	1.48 (1.01-2.17)	0.045
Model 2 - age, sex, living situation and specialism	1 (ref)	1.44 (0.98-2.11)	0.066
Secondary outcome - ≥7 days LOS[b]			
Crude	1 (ref)	1.63 (1.20-2.22)	0.002
Model 1 – corrected for age and sex	1 (ref)	1.51 (1.11-2.07)	0.009
Model 2 - age, sex, living situation and specialism	1 (ref)	1.54 (1.12-2.12)	0.008
Secondary outcome - New institutionalisation[c]			
Crude	1 (ref)	3.74 (2.14-6.56)	<0.001
Model 1 – corrected for age and sex	1 (ref)	2.94 (1.64-5.28)	<0.001
Model 2 - age, sex, living situation and specialism	1 (ref)	3.45 (1.89-6.31)	<0.001

Table 3: The association between 6-CIT and adverse outcomes in older acutely hospitalised patients (*continued*)

	6-CIT ≤10	6-CIT ≥11	p-value
		OR (95%CI)	
Secondary outcome – in-hospital mortality[d]			
Crude	1 (ref)	3.67 (1.48-9.10)	0.005
Model 1 – corrected for age and sex	1 (ref)	3.18 (1.26-8.05)	0.015
Model 2 - age, sex, living situation and specialism	1 (ref)	3.11 (1.21-7.99)	0.018

Abbreviations: OR=Odds Ratio, 95%CI= 95% Confidence Interval, 6-CIT= Six-Item Cognitive Impairment Test

[a]Patients included for analysis 977; [b]Patients included for analysis 1247; [c]Patients included for analysis 905; [d]Patients included for analysis 1236.

DISCUSSION

The present study shows that, in acutely hospitalised older patients with impaired cognition, as defined by a 6-CIT score ≥11, there is an association with increased risk 90-day adverse outcome (functional decline and mortality). We interpret the fact that statistical significance was lost after adjustment as a result of adding more variables in the model, as the estimate remained virtually unchanged. Further it is shown that impaired cognition is independently associated with a hospital LOS ≥7 days as well as increased in-hospital mortality and institutionalisation.

Our findings are in line with the literature, reporting an association between impaired cognition and functional decline, mortality and hospital length of stay[2, 6, 13-15]. Care providers often experience barriers in administering a cognition test in the acute setting. If such a test would be used on a regular basis, nurses and doctors could take instant tailor-made actions e.g. history taking, explaining treatment, involving relatives at an early stage and taking measures to prevent or treat delirium, which might prevent adverse outcomes in older patients. Several screening tools for measuring cognitive dysfunction have been proposed[14, 16]. The 6-CIT appears to be an instrument that can be easy and quickly applied, has a low chance of interpretation error and can also be administered in patients who are unable to read, write or perform lengthy tests[10, 16]. In this study, we further showed that the 6-CIT is an independent predictor of adverse outcomes, such as prolonged hospitalisation, institutionalisation and in-hospital mortality. Because of this combination of test characteristics and association with adverse outcomes, it might be a good tool to implement in daily practice.

In our study we used the 6-CIT for screening of cognitive impairment, irrespective of its cause, and showed that patients who are cognitively impaired have an increased risk of adverse outcomes. Dementia and delirium are the main causes of cognitive impairment

in older patients, but they can be difficult to diagnose and differentiate in the acute setting. As been recently proposed by Jackson *et al.*[17], cognitive impairment *per se* in acute hospital admissions is common and associated with poor health outcomes. Therefore, when managing acutely ill older patients, it is important to treat them based on their needs, rather than on a specific diagnosis. Therefore, medical staff needs to be vigilant and assess cognition on a routine basis. A short test such as the 6-CIT could facilitate this. In case of impaired cognition, the patient should be treated optimally in terms of optimizing the care process, providing environmental adjustments and minimizing harms[17]. The pro-active diagnosis of impaired cognition *per se*, whatever the specific underlying diagnosis, is likely to improve patient experience and outcomes, because the caregiver can focus on interventions, rather than on diagnostics. Furthermore, cognitive impairment should be considered when developing health care policies for improvement of outcomes such as hospital length of stay, new institutionalisation and in-hospital mortality.

We did not find an independent association of cognitive impairment and long term outcome, probably because adding more variables to the model borderline significance was lost. However, the estimates remained virtually unchanged.

The present study has several limitations. First, the exclusion of patients with a MMSE <19 points leads to an underestimation of the prevalence of cognitive impairment. However, in patients with more subtle cognitive impairment, the 6-CIT adds possibly unknown clinical information, while severely cognitive impaired patients are recognized relatively easily (e.g. nursing home patients with known dementia). Secondly, the 22% loss to follow-up after 90-days may have led to selection bias. However, the patients who were lost to follow-up were likely more cognitively impaired and frail, which leads to an underestimation of the association found in this study.

Major strengths of this study are the large sample size and multicentre design. Also, the duration of the study, in 3 consecutive years, during similar months renders the study more robust as temporary environmental effects are less likely to have influenced the data. The combination of both long and short term outcomes is another strength of this study.

In conclusion, cognitive impairment measured with the 6-CIT associates with 90-day adverse outcomes in acutely admitted older patients and is an independent predictor of prolonged hospital length of stay, institutionalisation and in-hospital mortality. This emphasizes the importance of routinely screening for cognitive impairment in this vulnerable patient group. Further research should focus on integrating cognition in risk-screening tools and investigate whether interventions for patients with impaired cognition improves clinically relevant outcomes.

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