Original Article

Recovery after acute illness after hospital discharge - a prospective cohort study

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Abstract

Background: *Long-term outcomes after acute medical and surgical illness are largely unknown.*
Aim: *To describe cognitive and physical function, health-related quality of life and risk of anxiety and depression after acute illness.*
Design: *Prospective cohort study.*
Methods: *Home visit at three and twelve months measuring: Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Chelsea Critical Care Physical Assessment tool, Short Form Health Survey, Hospital Anxiety and Depression Scale and Trail Making Test.*
Results: *Of 101 included patients, 60 were visited at three and 36 at twelve months. The RBANS value was 84 (69-96) at three months and 88 (69-101) at twelve months.*
Conclusions: *We found a moderately reduced cognitive function three and twelve months after acute illness.*

Keywords

Cognition disorders, Quality of life, anxiety and depression, critical illness

Key Learning points

- Key learning points: Patients with acute illness have reduced cognitive function even long after discharge. This can impact capacity for receiving information and adherence to medication and rehabilitation plans.

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Background

There is insufficient knowledge regarding cognitive and functional status of patients after an acute hospital admission, which can make it difficult to plan the rehabilitative efforts after discharge. Studies on outcomes in the critically ill, treated in the intensive care unit (ICU) have demonstrated that both mental and physical impairments are common, and may persist for years.[1] Such impairments most likely have a multifactorial origin, including impact of both critical illness, and ICU therapy and stay.

Knowledge regarding acutely hospitalized medical and surgical patients is still sparse and we do not know if these patients face the same challenges as critically ill patients. Newer studies have suggested that postoperative cognitive dysfunction is common, however, these studies have primarily been performed in elective surgical populations.[2] Another recent study examined the cognitive function after hospitalization for pneumonia. In this study, hospitalization for pneumonia in older adults was associated with subsequent functional and cognitive impairment.[3] Therefore, as our knowledge is limited in this field, further studies evaluating longer term cognitive, mental and physical outcomes following acute medical and surgical conditions are warranted.

The aim of this study was to investigate the cognitive function and functional status three and twelve months after acute medical or surgical hospital admission. We hypothesized that due to the acute illness, the longer term health-related quality of life, cognitive and physical function would be impaired compared with population norms.

Methods

This is a prospective cohort study of cognitive function and physical status, health-related quality of life and risk of anxiety and depression in acutely ill patients at three and twelve months after emergency admission with either an acute medical or abdominal surgical condition at Zealand University Hospital, Køge, Denmark. We obtained oral and written informed consent from all patients. The local ethics committee was contacted before initiation, but no approval was needed. The study was conducted according to the principles in the Helsinki declaration.

This manuscript adheres to the Strengthening The Reporting of Observational studies in Epidemiology (STROBE) statement.[4] The study was registered at www.clinicaltrials.gov (NCT03286439). All individual, deidentified data are available by contact to corresponding author as well as the protocol.

Inclusion and exclusion criteria

Patients ≥18 years of age with an acute admission to a medical or surgical ward with at hospital stay of more than three days, were screened for inclusion if admitted with one of the following diagnoses: pneumonia, heart failure, pulmonary embolism, acute myocardial infarction, pyelonephritis and patients undergoing emergency open or laparoscopic abdominal surgery (not including diseases of the appendix, diseases of the gallbladder, liver, spleen, kidney, pancreas and emergency hernia surgery without bowel resection). The surgical diagnoses were based on the criteria for patients included in the OMEGA protocol which describes a multidisciplinary treatment bundle for patients with major emergency abdominal surgery.[5] This group of patients are known to have a high disease severity and a poor outcome.[6]

Exclusion criteria were: severe dementia or inability to communicate in Danish (including aphasia, deafness or severe brain damage), patients discharged to terminal care, patients admitted under coercive measures or actively psychotic, patients living outside the Region of Zealand or transferred to a hospital outside the Region of Zealand, patients admitted to ICU and patients who were either blind or severely physically impaired.

Study Design

During the study period, we performed daily rounds at the medical and abdominal surgery departments evaluating all patients for eligibility. Patients were included while still admitted to hospital. The eligible diagnoses were chosen as they were thought to represent similar disease severities and are usually admitted for more than three days, which was hypothesised to be enough to cause a functional impact.

Visits took place three and twelve months after discharge from the ward and were performed by the first or second author. During the visit, the following assessments were performed: Repeatable Battery for the Assessment of Neuropsychological Status (RBANS),[7] Chelsea Critical Care Physical Assessment tool (CPAx),[8] Short Form Health Survey (SF-36),[9] Hospital Anxiety and Depression Scale (HADS),[10] Trail Making Test Part A and B,[11] Pittsburgh Sleep Quality Index,[12] Insomnia Severity Index,[13] and Epworth Sleepiness Scale.[14] Results from the sleep questionnaires are reported in a separate article. Patients were questioned about use of medication, work status, mobilisation aids and use of healthcare services.

The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) is a validated tool to evaluate neurocognitive function.[7] It consists of twelve subtests and gives five domain scores describing immediate memory, visuospatial function, language, attention and delayed memory and completion takes approximately 30 minutes. The RBANS evaluation is compared with a validated Scandinavian reference population with an age-adjusted standardized score for global cognition and for each of the separate domain scores, with mean (SD): 100 (15).[7] It has limitations in evaluating executive function, therefore we also used Trail Making Test.

Outcomes

Primary outcome was cognitive function measured by RBANS at three months after discharge from the medical or surgical ward. Secondary outcomes were: Health-related quality of life (SF-36), risk of anxiety and depression (HADS), physical function (CPAx) and information processing and executive function (Trail Making Test Part A and B) at three and twelve months after hospital discharge and RBANS at twelve months. Furthermore, we measured use of opioids, anti-depressants, statins and sleep medication at hospital admission and at the three- and twelve-month follow-up.

Data collection

From the electronic patient charts (OPUS (CSC Healthcare, Copenhagen, Denmark) or EPIC (Epic Systems Corporation, Verona, Wisconsin, United States)), we collected the following data: Age, sex, admission type (medical/surgical), length of stay (LOS), medical treatment: opioid, statins, sleep medication and antidepressants at hospital admission.

Statistics

Statistical analyses were performed with the SAS 9.4 package (SAS Institute, Cary, NC, USA). To show a difference in global cognition score of 10 compared with the reference population with a power of 80% and an α of 0.05, we would need 18 patients. To show the same size difference compared with our own data from ICU patients[15] we would need 35 patients. As we recognize that such studies traditionally experience high dropout rates, we chose to include 100 patients. Data were described and analysed using non-parametric or parametric statistics depending on the distribution of data. Associations of risk factors for cognitive impairment were analysed by multiple linear regression. All covariates were chosen in advance and were measured before outcomes. Interaction between variables was tested by inserting a combined variable in the model. Model fit was tested with evaluation of residual spread, Cook's distance and tests for linearity. A p-value <0.05 was considered significant.

Results

From 6 November 2017 to 7 April 2018 we screened 201 and included 101 patients, of whom 60 patients were visited at three-month follow-up and 36 were visited at one year (Figure 1).

Description of the cohort

Visited patients at three months were 66 (IQR 52-73) years of age, 53% were male, and 57% admitted to a surgical ward. Characteristics were similar for patients receiving the one-year visit (Table 1). We found an increase in domiciliary support from 5% at baseline to 14% at one-year follow-up. At admission, 38% were working compared to 32% at three- and 42% at twelve-month follow-up. Patients with a medical admission had a mean Early Warning Score (EWS) of 3, while patients with a surgical admission had a mean score of 2 (Table 2).

Cognitive function

The RBANS value at three months was 84 (IQR 69-96) (Scandinavian reference population normal value: 100 (SD 15)) (Table 3). At one-year visit, RBANS increased to 88 (IQR 69-101). We found 30% (29% at one year) to have moderate cognitive impairments comparable to that of patients with traumatic brain injury and 16% (9% at one year) to be severely impaired comparable to patients with Alzheimer's disease.[16,17]

To investigate for covariates associated with a difference in cognitive outcome we performed multiple linear regression. The results are shown in Table 4. Model 1 investigated the effect of age (per 10-year increase) and sex. These covariates were also part of all other models. Both covariates showed no significant correlation to cognitive outcome. Model 1 also investigated the effect of admission type (medical/surgical) and employment before admission; no covariates showed significant correlation to cognitive outcome. Model 2 investigated the effect of treatment with opioids, anti-depressants and statins and all covariates showed insignificant results. Model 3 investigated the effects of use of mobilisation aids, physiotherapy and domiciliary support, all at inclusion. In this model we found that patients using a mobilisation aid had a 30.73 point (95% CI -55.67;-5.79) lower global cognition score (p=0.017) (Table 4).

Secondary outcomes

The physical function tested with CPAx showed a median score of 48 (SD 4) at three months rising to 50 (SD 1) at one year. Grip strength did not change from three months to one year.

For health-related quality of life (SF-36) mental component score (MCS) was 53 (IQR 48-62) at three months and 54 (46-59) at one year. The physical component score (PCS) was 47 (IQR 37-54) at three months and 46 (38-51) at one year. Bodily pain, mental health, general health and vitality showed a marked reduction with no improvement from three to twelve months (Table 3).

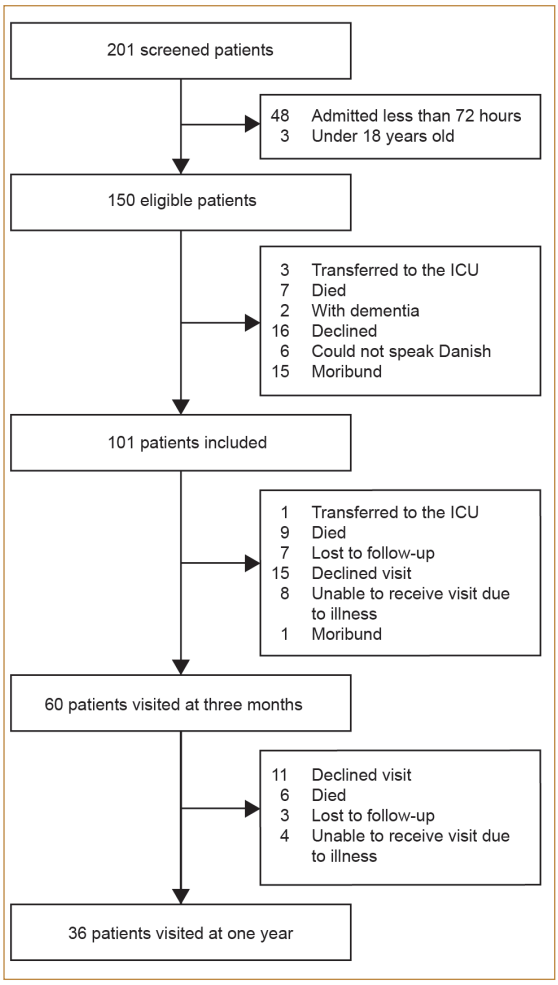

Figure 1. Patient flow

The total HADS score was 3 (IQR 1-6) at three months and 6 (IQR 3-8,5) at one year. For anxiety, the score increased from 2 (IQR 1-4) to 4 (IQR 1,5-6) and for depression 1 (IQR 0-3) to 2 (IQR 2-2,5). We found 10% at three and 17% at twelve months to have risk of anxiety and 5% and 8% to have risk of depression.

For Trail Making Test Part A the median completion time was 39 s (IQR 29-49) decreasing to 28 s (IQR 22-41) and for Trail Making Part B it was 74 s (IQR 56-114) decreasing to 62 s (IQR 53-136).

Discussion

In this prospective cohort study, we examined acutely admitted medical and abdominal surgical Danish patients at three and twelve months after discharge and found moderately reduced global cognition

Table 1. Demographics

Variable	Before admission (n=60)	Visited at three months (n=60)	Visited at one year (n=36)
Age, median (IQR)	-	66 (52-73)	63 (51-72)
Sex, male, n (%)	-	32 (53)	19 (54)
Surgical admission, n (%)	-	34 (57)	21 (60)
LOS, days, median (IQR)	-	5 (4-10)	5 (4-8)
Admission during follow-up, n (%)	-	8 (13)	12 (33)
Contacts to GP, median (IQR)	-	2 (1.5-3.0)	4 (1.5-9.5)
Home (independent living), n (%)	58 (97)	59 (98)	34 (94)
Opioids, n (%)	4 (7)	9 (15)	4 (11)
Anti-depressants, n (%)	5 (8)	4 (7)	3 (8)
Statins, n (%)	10 (17)	9 (15)	6 (17)
Working status, n (%)	23 (38)	19 (32)	15 (42)
Domiciliary support, n (%)	3 (5)	5 (8)	5 (14)
Physiotherapy, n (%)	9 (15)	9 (15)	7 (19)
Mobilization aids, n (%)	8 (13)	8 (13)	6 (17)
Contact to the psychiatric care system, n (%)	2 (3)	1 (2)	3 (8)

LOS: Length of stay, IQR= Interquartile range, GP=General Practitioner

Table 2. Baseline data for patients according to admission type

Variable	Medical	N (%)	Surgical	N (%)
Diagnoses	Pneumonia Pyelonephritis	22 4		
			Adhesiolysis Bowel resection/ repair Intraperitoneal abscess Anastomosis leak Fascial dishiscence	13 13 4 3 1
ASA physical status classification			1-2 3 4	15 15 4
		Mean (IQR)		Mean (IQR)
EWS at admission		3 (1.25-6)		2 (0.25-3)

ASA: American Society of Anaesthesiologists. EWS: Early Warning Score. IQR: Interquartile range

score, low risk of developing anxiety or depression, no reduction in physical function or health-related quality of life and normal executive function.

We found reduced cognitive function with an RBANS-score of 84 (IQR 69-96), which is below the age–adjusted population mean of 100. There was no change from three to twelve months. A recent study by Girard *et al*[3] examined the cognitive function in patients two months after hospitalization for community-acquired pneumonia at a medical ward. Their findings were similar to this study with a median of 86 (IQR 77-95). Deficits were most often noted in visuospatial function, attention, and memory. These findings are consistent with our results. These deficits can affect the patients' ability to understand the often extensive information given during an acute hospitalisation. An effort should be made to assure retention of information, either by presence of a next of kin or by meticulous discharge summaries to the primary physician.

Table 3. Test scores at three month and 1 year follow up.

Variable	Three months (n=60)	One year (n=36)
RBANS, median (IQR)		
Global cognition	84 (69-96)	88 (69-101)
Immediate memory	81 (60- 94)	81 (68-97)
Visuospatial function	103 (95-110)	93 (75-103)
Verbal function	84 (76-100)	94 (83-107)
Attention	85 (74-94)	92 (82-101)
Delayed memory	95 (80-107)	87 (77-104)
CPAx, mean (SD)		
Total score	48 (4)	50 (1)
Left hand	31 (12)	31 (13)
Right hand	35 (13)	33 (13)
SF-36, median (IQR)		
Mental component score (MCS)	55 (48-61)	54 (46-59)
Physical component score (PCS)	47 (37-54)	46 (38-51)
Bodily pain	74 (61-90)	72 (51-84)
Mental health	84 (68-92)	84 (60-92)
General health	67 (45-87)	67 (42-77)
Social functioning	100 (69-100)	100 (75-100)
Vitality	65 (50-85)	65 (45-75)
Role emotional	100 (67-100)	100 (33-100)
Role physical	100 (25-100)	75 (25-100)
Physical functioning	90 (70-100)	80 (65-95)
HADS, median (IQR)		
Total score	3 (1-6)	6 (3-8,5)
Anxiety	2 (1-4)	4 (1,5-6)
Depression	1 (0-3)	2 (2-2,5)
Trail making test, median (IQR)		
Trail A	39 (29-49)	28 (22-41)
Trail B	74 (56-113)	62 (53-136)

RBANS= Repeatable Battery for the Assessment of Neuropsychological Status; IQR = Interquartile range; CPAx=Chelsea critical care Physical Assessment tool; SD=Standard Deviation; HADS=Hospital Anxiety and Depression Scale; SF-36=Short Form health survey.

In exploratory analyses, we examined covariates associated with a difference in cognitive outcome and found that patients using a mobilization aid before admission had a lower global cognition score (Table 4). Using a mobilization aid can be considered as a marker for frailty, something which has been linked to poorer outcomes, especially in the older population [18]. We did not find other covarites affecting the cognitive outcome. Thus, we could not confirm our previous findings[15] that patients working before admission or being admitted for a surgical condition had a better outcome. Patients with surgical admissions had a slightly lower EWS at admission whereof half of them had an ASA score of 1 or 2. In spite of these differences, the trend was toward patients with a medical admission having a better cognitive score.

Health-related quality of life was measured with SF-36 and we found both the MCS and the PCS to be within normal ranges and with no change from three to twelve months. Previous studies have suggested that acute treatment for life-threatening surgical conditions may impede quality of life.[19,20] The physical component was also found to be impaired in patients recovering from acute respiratory distress syndrome, treated in the ICU.[21] These findings were not confirmed by the current study, but we did find reduced scores for bodily pain, mental health, general health and vitality indicating that there still may be areas with significant problems for the patients.

We also examined the risk of developing anxiety and depression and found a risk that increased from three to twelve months. Risk of both anxiety and depression is well known after acute illness such as

Table 4. Multiple linear regression models for cognition measured by RBANS at three months

Covariate	Model 1		Model 2		Model 3	
	Estimate and 95% CI	P-value	Estimate and 95% CI	P-value	Estimate and 95% CI	P-value
Age, pr. 10 years	-1.40 (-5.96; 3.16)	0.54	-2.82 (-6.82; 1.18)	0.16	-0.73 (-4.63; -3.16)	0.71
Sex	7.40 (-4.72; 19.51)	0.23	6.60 (-5.50; 18.70)	0.28	9.35 (-2.22; 20.91)	0.11
Admission type	1.40 (-10.83; 13.64)	0.82				
Working preadmission	7.99 (-6.44; 22.42)	0.27				
Opioids			-1.93 (-26.30; 22.43)	0.87		
Anti-depressants			-15.15 (-36.97; 6.67)	0.17		
Statins			-1.60 (-18.16; 14.96)	0.85		
Mobilization aids					-30.73 (-55.67; -5.79)	0.017
Physiotherapy					2.15 (-15.27; 19.57)	0.81
Domiciliary support					-0.13 (-34.19; 33.92)	0.99

CI=Confidence interval. For sex the reference is male. For admission type the reference is surgical patients. For work the reference is unemployment or not working. For medication the reference is patients not receiving medication.

acute myocardial infarction[22] and our data suggest that this risk might increase during the first year.

Executive function and information processing speed was within the normal range and completion time decreased from three to twelve months.[23] This could be indicative of overall better integration of cognitive functions.

The reduced cognitive function can affect the ability to understand and remember the given information. This can reduce the compliance and adherence to rehabilitation plans.

This highlights the need for individually tailored information.

Study limitations

The most important limitation is the unknown baseline function for the patients. Therefore, we do not know if the premorbid cognitive, physical and mental function of our patients differed from the reference population. Our patients were acutely ill with an emergent admission and therefore we have very limited possibilities in assessing this. For surgical admissions, we added the ASA score, showing that a large proportion had only few comorbidities. To further assess the severity of illness, we reported EWS which was low at admission for patients with both medical and surgical admissions.

Another limitation is the relatively large number of patients lost to follow-up. This number was, however, similar to other studies.[3,15] In spite of the large number of patients lost, we still maintained statistical power according to our power calculation. Nevertheless, results should be interpreted with caution as the different samples at three and twelve months can introduce selection bias.

We planned to include five different medical diagnoses, but because of short lengths of stay for most of them and referral to another hospital for the acute myocardial infarctions, we ended up only visiting patients with pneumonia and pyelonephritis. This makes the cohort more homogenous, but can certainly decrease generalisability.

Test were used twice, which can introduce bias and lead to better scores on second testing. RBANS has two different test sets and we used version A on first test and B on second or vice versa. Practice effects are small and retest abilities are generally acceptable.[24,25]

A strength of the study is visiting the patients twice and including patients from both the medical and surgical ward.

Conclusion

In this prospective cohort study of unselected, consecutive acutely admitted Danish medical and surgical patients, we found moderately reduced cognitive function with no improvement from three to twelve months after discharge from the ward. Executive function and information processing were not affected. We found low risk of developing anxiety and depression, although this risk increased during the first year. The health-related quality of life and the physical function was not impaired.

Conflicts of Interests

No conflicts of interest declared.

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