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Delirium motor subtypes and prognosis in hospitalized geriatric patients – A prospective observational study

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ABSTRACT

Objective: Delirium is common and associated with poor outcomes. Hypoactive motor subtype may predict worse outcome than no-subtype, hyperactive and mixed delirium, but uncertainty remains due to heterogeneity of results and subtyping tools. Other prognostic aspects across delirium motor subtypes are understudied. We investigated differences in one-year mortality, length of stay and institutionalization at discharge and after one year, across delirium motor subtypes in geriatric patients.

Methods: We conducted a prospective observational study, included 311 patients ≥75 years acutely admitted to a geriatric ward, diagnosed delirium using *Diagnostic and Statistical Manual of Mental Disorder* (5th ed.) criteria and used the Delirium Motor Subtype Scale for subtyping. Differences in mortality across subtypes were investigated using Cox proportional-hazard regression analyses, unadjusted and adjusted for age, comorbidity and delirium severity. We investigated differences in length of stay and institutionalization using the Kruskal-Wallis test and Pearson's chi-squared test with subsequent Hommel-adjusted pairwise comparisons.

Results: Ninety-three patients (30%) had delirium; 12 (13%) had no-subtype, 27 (29%) hyperactive, 30 (32%) hypoactive and 24 (26%) mixed delirium. There were no group differences regarding mortality ($p = .61$) or length of stay ($p = .32$). Analyses indicated group differences regarding discharge to an institution ($p = .028$), but pairwise comparisons showed no differences (smallest $p = .071$, no-subtype 45% vs hypoactive 85%). There were no group differences in institutionalization after one year ($p = .26$).

Conclusion: There were no significant differences in one-year mortality, length of stay or institutionalization across delirium motor subtypes in geriatric patients, although the study may indicate better prognosis in the no-subtype group.

1. Introduction

Delirium is an acute and often fluctuating disturbance in attention, awareness and cognition caused by a medical condition [1]. Delirium affects one-third of medical in-patients older than 70 years and is consistently associated with complications, longer length of stay (LOS) and increased health-care costs, in addition to increased risk of mortality, institutionalization and dementia [2–4]. Four different delirium motor subtypes have been described—hyperactive, hypoactive, mixed delirium with both hyperactive and hypoactive features and no-subtype delirium without motor features [5,6]. A systematic review reports that pre-existing dementia and depression, long duration and high severity of the delirium episode and a hypoactive motor subtype are associated with poor prognosis [7].

In 1992, Liptzin and Levkoff reported lower mortality in patients with hyperactive delirium than in patients with hypoactive, mixed and

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no-subtype delirium [5]. Since then, most articles report higher mortality in hypoactive delirium [8–11], but some studies report no differences in mortality across motor subtypes [12–14] and one study reports higher mortality in hip-fracture patients with hyperactive symptoms [15]. These studies used different subtyping tools, such as the Richmond Agitation and Sedation Scale [8], Memorial Delirium Assessment Scale (MDAS) [9,11,15], Delirium Rating Scale-Revised-98 [14], Liptzin and Levkoff schema [5] and a combination of the Brief Psychiatric Rating Scale and Cohen-Mansfield Agitation Inventory [13]. These tools were not developed for motor subtyping, some contain non-motor symptoms and they have low concordance when compared to each other [16]. In our opinion, the weaknesses of these tools create uncertainties about conclusions in reviews stating that the hypoactive subtype is associated with the worst prognosis [2,3,7].

Based on previous subtyping tools, Meagher et al. developed the Delirium Motor Subtype Scale (DMSS), which is a dedicated tool for delirium motor subtyping that focuses on pure motor features [6] and has been validated against electronic measures of motor activity [17]. Using the DMSS among 100 patients with delirium in a palliative care unit, Meagher et al. found the highest one-month mortality rate in patients with hypoactive delirium [18]. The long-term impact of DMSS-defined delirium motor subtypes on mortality has not been investigated in hospitalized geriatric patients, which is of interest since delirium is highly prevalent in such patients [3], and since the DMSS seems to be the superior subtyping tool. Few previous studies touch upon the impact of motor subtypes on other aspects of prognosis than mortality [14,15].

The primary aim of the present study is thus to investigate one-year mortality rate across DMSS-defined delirium motor subtypes in patients acutely admitted to a geriatric ward. Secondary aims are to explore differences in LOS and institutionalization at discharge and after one year across motor subtypes. We hypothesized that patients with hypoactive delirium had worse outcomes for all aspects of prognosis.

2. Methods

2.1. Design, settings and participants

We carried out a prospective observational study at the geriatric ward at St. Olavs Hospital, Trondheim University Hospital, Norway. The ward is an integrated part of the medical clinic and has 15 single-bed rooms. Patients receive comprehensive geriatric assessment and care [19] by an interdisciplinary team of nurses, physiotherapists, occupational therapists and physicians. The ward was built and organized to enhance physical activity and orientation and has been described in detail previously [20,21]. We included patients from May 6, 2015 to January 31, 2017 and followed the patients for one year. Inclusion criteria were age ≥ 75 years and acute admittance. No patients were excluded due to admission diagnosis, cognitive impairment or sensory deficits. The present article reports analyses of included patients who had delirium during the hospital stay.

2.2. Ethics

We collected written informed consent from the patients, but in cases with signs of severe cognitive impairment or reduced level of consciousness, we sought consent from a proxy. Patients with mild and moderate cognitive impairment could consent for participation. In such cases, we also informed a proxy about the study if possible. We did not include any patients clearly refusing participation. This procedure was considered acceptable since there were no uncomfortable procedures or follow-ups demanding contribution from patients involved in the study. The Regional Committee for Medical and Health Research Ethics of Mid-Norway approved the study (REK Central 2015/474).

2.3. Diagnosing delirium and motor subtypes

Two geriatricians (SE and OS) who had received training by an experienced delirium researcher (TBW) diagnosed delirium according to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*) criteria, basing the diagnostic work-up on a combination of assessment of the patients, interviews with nurses and proxies and careful chart review as described by Inouye [22]. All new patients were screened for delirium through chart review and interviews with nurses, and the first author visited those with suspected delirium, judging arousal and awareness clinically, testing attention using the digit span forwards and backwards and cognition using the 10 orientation items from the MDAS [23]. If symptoms of delirium were present, MDAS was completed and subtyping performed according to the DMSS. The DMSS contains four hyperactive features and seven hypoactive features. Patients with two or more hyperactive features are considered to have hyperactive delirium, and patients with two or more hypoactive features to have hypoactive delirium. Those with both hyperactive and hypoactive features have mixed delirium, and those with one or no motor features have no-subtype delirium [6]. When in doubt, and if signs of changes in mental status, the patient was visited several times, but strict, repeated assessment was not performed. When designing the study, we decided to use all available information about motor features from the entire delirium episode when finally determining motor subtype, and to consider motor subtype as stable throughout the delirium episode [24].

2.4. Baseline characteristics

We registered age and sex from the hospital records and calculated the Cumulative Illness Rating Scale as a measure of comorbidity (CIRS, 0–56, increasing score indicating increasing comorbidity) [25]. We used the MDAS as a measure of delirium severity (0–30, increasing score indicating delirium with more severe symptoms). Based on all available information, we calculated the Barthel Index as a measure of pre-hospital functioning in primary activities of daily living (p-ADL) (BI, 0–20, increasing score indicating higher level of independency) [26] and the Global Deterioration Scale as a measure of pre-hospital cognitive status (GDS, 1–7, increasing score indicating more severe cognitive impairment) [27]. We calculated a modified APACHE II score as a measure of level of acute illness (0–71, increasing score indicating more severe illness) [28]. We calculated Body Mass Index (BMI) as kg/m^2.

2.5. Outcomes

We registered date of death from the hospital record system, which is synchronized with the National Death Registry. We collected information regarding LOS from the hospital records and collected information about discharge to an institution prospectively. We collected status of permanent institutionalization one year after inclusion by calling a proxy or by contacting the District Medical Officer.

2.6. Statistical analyses

We planned to include 420 patients and expected delirium in 140 patients, assuming 60 patients with hypoactive delirium, 40 patients with hyperactive delirium and a small number of patients with mixed and no-subtype delirium [9,18]. We calculated power to detect differences in one-year mortality between the hypoactive and the hyperactive groups, assuming 50% mortality in the hypoactive group and 20% mortality in the hyperactive group, giving a power of 87.9% with $\alpha = 0.05$. No power calculation was done for LOS or institutionalization.

We describe continuous variables as means and standard deviations (SD) and categorical and nominal variables as numbers and

percentages. To investigate differences in mortality between delirium motor subtypes we created Kaplan-Meier plots and performed Cox proportional-hazard regression analyses with motor subtype as a categorical variable, unadjusted, adjusted for age, and additionally adjusted for the CIRS and MDAS, all well-known prognostic factors in delirium [7]. We used a Kruskal-Wallis test to investigate differences in LOS between the groups. To investigate differences in rates of institutionalization between the groups, we used the Pearson's chi-squared test, followed by pairwise comparisons adjusted by use of the Hommel procedure to preserve the familywise error rate [29]. Patients that died in hospital were excluded from analyses of discharge to an institution, but not from analyses of LOS. Patients living in an institution prior to admission were excluded from the analyses of institutionalization. We report 95% confidence intervals (CI) and consider p-values $< .05$ as a sign of statistical significance. We used SPSS Statistics version 24 for statistical analyses, except for the Hommel procedure which was carried out in R version 3.5.2.

We report methods and results following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

3. Results

In total, we included 311 patients and diagnosed delirium in 93 (30%). Of these, 12 (13%) had no-subtype delirium, 27 (29%) had hyperactive, 30 (32%) had hypoactive, and 24 (26%) had mixed delirium subtypes. Table 1 shows baseline characteristics for the 93 patients with delirium sorted by delirium motor subtypes.

3.1. Mortality

Five patients died in hospital. Overall, one-year mortality rate was 43% ($n = 40$), with 33% (n = 4) in the no-subtype group, 37% ($n = 10$) in the hyperactive group, 43% ($n = 13$) in the hypoactive group and 54% (n = 13) in the mixed group. Fig. 1 shows Kaplan-Meier survival curves for the four motor subtype groups. There were no significant differences in mortality between the groups (overall p-value = .61).

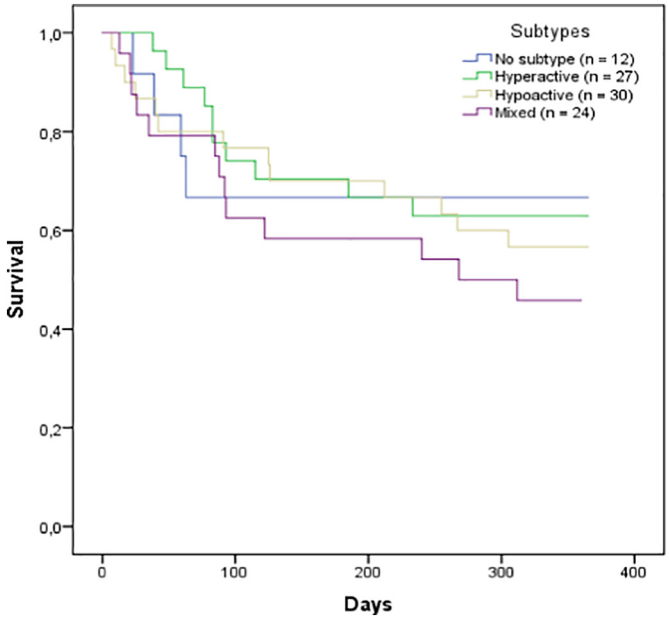

Fig. 1. Kaplan-Meier survival curves for the four delirium motor subtypes.

With the hyperactive group as the reference group, the hazard ratio (HR) was 0.97 (CI 0.30 to 3.09, $p = .96$) for the no-subtype group, 1.23 (CI 0.54 to 2.80, $p = .63$) for the hypoactive group and 1.66 (CI 0.73 to 3.79, $p = .23$) for the mixed group. Adjusting for age, the CIRS and MDAS gave essentially the same results (data not shown).

3.2. Other outcomes

The mean LOS for the entire group was 10.3 days (SD 6.9), 9.4 days (SD 5.9) in the no-subtype group, 9.3 days (SD 7.4) in the hyperactive group, 11.2 days (SD 7.9) in the hypoactive group and 10.8 days (SD 5.5) in the mixed group ($p = .32$). Prior to admission, 84 (90%) were living at home. Four of these died in hospital; after one year, 49 were

Table 1
Baseline characteristics for patients with no-subtype, hyperactive, hypoactive and mixed delirium.

	No-subtype	Hyperactive	Hypoactive	Mixed	p-Value[1]
	($n = 12$)	($n = 27$)	($n = 30$)	($n = 24$)	
	Mean (SD)				
Age (years)	86.3 (5.3)	85.5 (5.7)	86.8 (4.6)	88.3 (4.8)	0.27
Body mass index (kg/m^2)	22.2 (5.1)	24.0 (3.1)	23.9 (3.6)	23.1 (3.8)	0.49
Cognitive function GDS[2] score (1–7)	3.8 (1.0)	4.5 (1.4)	4.1 (1.3)	4.2 (1.4)	0.38
Comorbidity CIRS[3] score (0–56)	13.8 (5.3)	15.2 (4.0)	14.8 (5.4)	14.6 (5.4)	0.88
Morbidity APACHE-II score (0–71)	9.5 (2.1)	8.7 (2.3)	10.1 (10.2)	9.7 (2.4)	0.23
p-ADL[4]-function Barthel Index score (0 − 20)	16.0 (4.2)	15.6 (4.0)	14.1 (4.7)	14.4 (3.7)	0.37
Delirium severity MDAS[5] score (0 − 30)	7.8 (2.5)	9.6 (4.0)	12.9 (4.6)	14.7 (5.3)	< 0.001
	Number (%)				
Female	7 (58)	14 (52)	15 (50)	14 (58)	0.92
Dementia[6]	7 (58)	20 (74)	23 (77)	19 (79)	0.58
Living in nursing home	0 (0)	3 (11)	2 (7)	2 (8)	0.68

[1] P-values are calculated using ANOVA for continuous variables and Pearson's chi-squared test for categorical variables.
[2] Global Deterioration Scale.
[3] Cumulative Illness Rating Scale.
[4] Personal Activities of Daily Living.
[5] Memorial Delirium Assessment Scale.
[6] Dementia: Global Deterioration Scale ≥ 4.

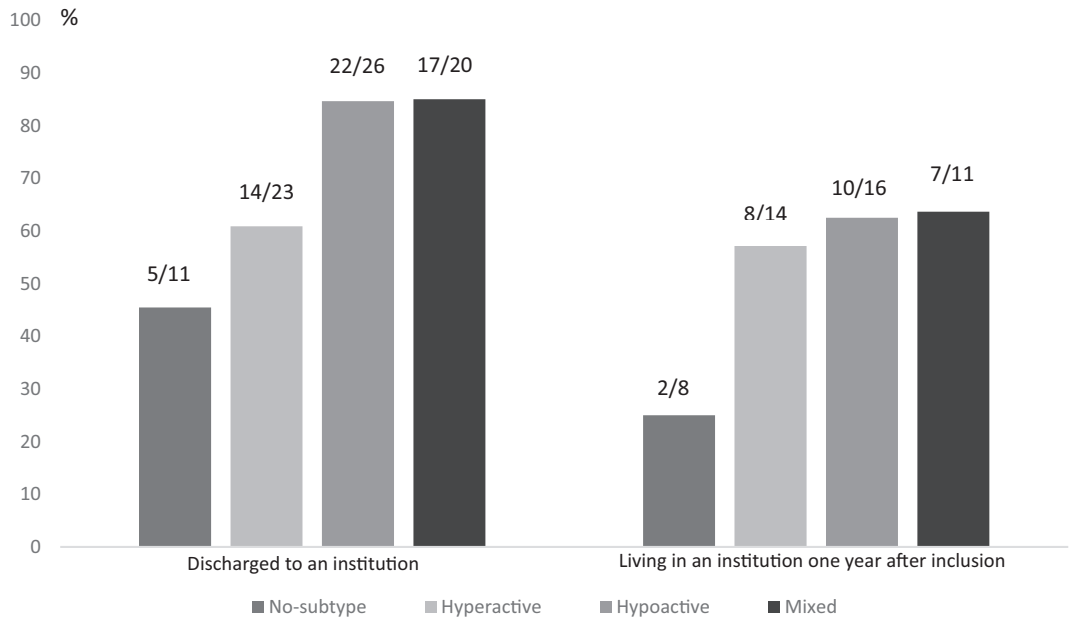

Fig. 2. Bar charts illustrating proportions of patients discharged to an institution and survivors living in an institution one year after discharge, across delirium motor subtypes. Number of patients are listed on the top of the bars. Patients living in an institution prior to admission were excluded from analyses.

alive. Among the survivors, 73% were discharged to an institution—45% in the no-subtype group, 61% in the hyperactive group and 85% in both the hypoactive and mixed groups. The overall *p*-value was 0.028, but subsequent Hommel-adjusted comparisons between all pairs of groups did not identify any significant differences (lowest $p = .071$, hypoactive vs no-subtype). In total, 55% of the survivors were living in an institution one year after inclusion—25% in the no-subtype group, 57% in the hyperactive group, 63% in the hypoactive group and 64% in the mixed group (overall $p = .26$). Fig. 2 illustrates differences in institutionalization at discharge and after one year across the groups and lists the number of patients in each group who were discharged to an institution and lived in an institution after one year, respectively.

4. Discussion

In this study on 93 acutely-admitted geriatric patients with delirium, we confirmed a substantial overall one-year mortality, but we found no differences in mortality across DMSS-defined motor subtypes; neither were there any differences in LOS between the groups. Proportionally, there were large differences between the groups in institutionalization rates, both at discharge and after one year, but these differences did not reach statistical significance.

Few studies have investigated differences in mortality across DMSS-defined delirium motor subtypes. Studying 100 patients in a palliative care unit, Meagher et al. found that patients with hypoactive delirium had the highest one-month mortality [18]. Recently, Gual et al. published findings from a study on 352 older patients in a subacute care unit showing that those with hypoactive delirium had the highest mortality rate at discharge [30]. This study was well conducted and substantially larger than ours. The patients are comparable in terms of age and comorbidities, but likely less acutely ill than our hospitalized patients. The diverging results between Meagher et al., Gual et al. and the present study might be explained by differences in study population, setting, treatment and care. In patients with delirium, a palliative care unit will generally focus on relief of symptoms, whereas geriatric units and subacute care units will try to improve prognosis through identification and treatment of reversible causes and environmental interventions [19]. Our group has previously documented higher levels of physical activity among patients in our ward as compared to other wards [21,31]. A continuous focus on mobilization in our ward could be of special benefit for the hypoactive group in the present study, making these patients less prone to potentially fatal complications of bedrest, such as hypostatic pneumonia, pressure ulcers and thromboembolic events [10,12,18]. Our results raise the question as to whether the poor prognosis of hypoactive delirium is partly iatrogenic and might be improved through mobilization regimes and prevention of complications of bedrest. This would have a large impact on treatment and care for a substantial number of patients and should be an area of future research.

In line with previous reports, we found no differences in LOS between the groups [14,15,30]. Previous studies show diverging results regarding discharge to an institution [14,15,30]. In the present study, 73% of the patients with delirium were discharged to an institution, and 58% of the survivors were living in an institution after one year. Fig. 2 illustrates large proportional differences between the groups regarding both short-term and long-term institutionalization, but these differences did not reach statistical significance. Based on the current literature, firm conclusions about short-term and long-term need of institutionalization across delirium motor subtypes cannot be drawn. There is a need for larger studies investigating whether motor subtypes have an impact on institutionalization. Such studies should also include measures on cognition and ADL function.

Some argue that no-subtype delirium represents a milder delirium than hyperactive, hypoactive and mixed delirium [24]. In our material, the no-subtype group had the lowest mortality rate, lowest risk of being discharged to an institution and lowest risk of permanent institutionalization, although no results reached statistical significance. Further, the patients with the no-subtype variant had a less intense delirium with the lowest MDAS score, which is in line with previous studies [24,32]. We have recently reported that patients with no-subtype delirium have a higher level of physical activity than patients with both hyperactive, hypoactive and mixed delirium [20]. Our knowledge about no-subtype delirium is based on few studies with few patients, but there seem to be differences in both intensity of delirium and prognosis between the minority of delirious patients with no-subtype delirium and the majority with some sort of motor disturbance.

4.1. Strengths and limitations

The main strengths of this study are the use of the DMSS for

delirium motor subtyping and the long-term follow-up. Further, the sample of acutely-admitted geriatric patients makes our results generalizable to older medical in-patients. The study did not reach the predefined number of patients due to slower recruitment than expected, and the small sample size constitutes a limitation as it introduces chances of type-II errors, especially with regards to analyses of institutionalization. Since the study was designed and powered to detect differences in mortality, the results regarding LOS and institutionalization must be considered as exploratory. The lack of strict, repeated assessment of delirium and motor subtypes is a limitation, as well. Another limitation is our consideration of motor subtypes as stable. We based our design on an article from 2011 concluding that 38% of patients with DMSS-defined subtypes changed motor subtype over time [24], but a recent article reported changes over time between DMSS-defined motor subtypes in 62% of the patients [32], although most changes involved changes to and from no-subtype. By including chart review in our diagnostic work-up, this limitation is reduced but not eliminated. The most important consequences of this for our data are that patients with subtype changes involving no-subtype delirium were classified as having a certain motor subtype, and those fluctuating between hyperactive and hypoactive delirium were classified as mixed (and not variable) subtype. Prognostic impact of variation between motor subtypes could be an area for further research.

5. Conclusions

In this study on hospitalized geriatric patients with delirium, we found no significant differences in one-year mortality, LOS, discharge to an institution and institutionalization one year after inclusion, across the motor subtypes. Firm conclusions should not be drawn due to the small sample size and the small subgroups. The only finding in line with our hypothesis that patients with hypoactive delirium have worse prognosis, is the trend that more patients with hypoactive delirium were discharged to an institution when compared to patients with no-subtype delirium. Our results challenge the statement that hypoactive delirium has the worst prognosis and may also indicate better prognosis in the no-subtype group. Future studies should investigate the prognostic impact of delirium motor subtypes in a broad sense and address if mobilizing interventions could improve the prognosis of patients with hypoactive delirium.

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Declaration of interest

None.

Data statement

Data from this study are unavailable as we do not have approval from patients or from the Regional Committee for Medical and Health Research Ethics of Mid-Norway to share data.

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