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Stability of Post-Operative Delirium Psychomotor Subtypes Among Hip Fracture Patients

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Abstract

Objectives—To determine the stability of psychomotor subtypes of delirium over time and identify characteristics associated with delirium psychomotor subtypes in patients undergoing surgical repair of hip fracture.

Design—Prospective cohort study.

Setting—The Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair Cognitive Ancillary Study was conducted at 13 participating sites from 2008-2009.

Participants—139 patients who had undergone surgical repair of hip fracture

Measurements—Delirium was assessed up to four times post-operatively using the Confusion Assessment Method (CAM) and the Memorial Delirium Assessment Scale. Psychomotor subtypes of delirium were categorized as hypoactive, hyperactive, mixed, and normal psychomotor activity.

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The authors declare no other potential conflicts of interest.

Results—Incidence of post-operative delirium was 41% (n=57). Among CAM+ observations (n=90), 56% were hypoactive, 10% hyperactive, 21% mixed, and 14% had normal psychomotor symptoms. Among patients with more than one CAM+ assessment (n=26), 50% maintained subtype stability over time. Patients with hypoactive or normal psychomotor symptoms (n=31) were less likely to have chart documentation of delirium compared to patients with any hyperactive symptoms (n=19) (22% vs. 58%, $p=0.009$).

Conclusion—Psychomotor subtypes of delirium often fluctuate from assessment to assessment, rather than representing fixed categories of delirium. Hypoactive delirium is the most common presentation of delirium, but is the least likely to be documented by healthcare providers.

Keywords

delirium; psychomotor subtypes; hip fracture; Memorial Delirium Assessment Scale; Confusion Assessment Method

INTRODUCTION

Delirium after hip fracture occurs in 23%-56% of patients and is associated with poor functional outcome, higher cost, nursing home placement, and increased mortality.¹⁻⁶ Historically, there has been interest in investigating psychomotor subtypes of delirium.^{4,7-9} Four psychomotor subtypes of delirium have been described: hyperactive, hypoactive, mixed, and delirium with normal psychomotor features. The hypoactive subtype is characterized by decreased levels of activity, speech, and alertness as well as apathy, withdrawal and hypersomnolence.⁸⁻¹⁰ The hyperactive subtype is characterized by restlessness, wandering, hyperactivity, loudness, fear, and irritability, and the mixed subtype is characterized by elements of both hypo- and hyperactivity within a short time frame.⁸⁻¹⁰ Patients can also fulfill delirium diagnostic criteria with normal psychomotor features, yielding the fourth subtype. Classification remains inconsistent, however, and there is no 'gold-standard' for defining psychomotor subtypes.^{7,10}

The hypoactive subtype has been most often observed (31%-71% of cases), but is least likely to be recognized by healthcare professionals.^{4,11-14} Research relating psychomotor subtypes to outcomes has not provided consistent results. Several studies reported that patients experiencing hypoactive delirium had worse outcomes compared to those with hyperactive or mixed delirium.¹³⁻¹⁵ Other studies reported better outcomes among patients with hypoactive delirium or no difference in outcomes between psychomotor subtypes.^{4,15,16} Notably, most of these studies assessed outcomes of psychomotor subtypes based upon a single delirium assessment.^{12,14} The inconsistencies reported by prior studies may be due to subtype instability, which must be assessed longitudinally. A better understanding about the differing presentations and stability of delirium will aid healthcare professionals in identifying postoperative patients with delirium so that they may receive treatment.

The primary aim of the present study is to assess the stability of psychomotor subtypes of delirium over time among hip fracture patients. A secondary aim is to analyze patient characteristics associated with post-operative delirium psychomotor subtypes.

METHODS

Study Population

The Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS) was a randomized multicenter trial that investigated whether a liberal blood transfusion strategy in patients with cardiovascular disease or cardiovascular disease risk factors resulted in better functional outcomes following hip fracture surgery than a restrictive blood transfusion strategy.¹⁷ Methods for FOCUS have been previously reported.¹⁷ Briefly, patient recruitment began at multiple sites across North America in January 2005 and ended February 2009. Patients were eligible if they were 50 years of age or older, were undergoing surgical repair of hip fracture, and had clinical evidence for cardiovascular disease or cardiovascular disease risk factors. Patients for whom consent was obtained were randomized if they had hemoglobin concentrations less than 10 g/dL within three days following surgery. FOCUS enrolled 2,016 patients across 47 clinical sites.

The primary goal of the FOCUS Cognitive Ancillary Study (CAS) was to determine if a liberal blood transfusion strategy would prevent new or worsening in-hospital delirium symptoms after hip fracture surgery.¹⁸ Recruitment for the CAS began April 2008 and ended February 2009. In all, 13 of the 47 clinical sites participating in FOCUS participated in the CAS. Eligibility criteria for the CAS were identical to FOCUS, except one additional exclusion criteria was an inability to speak English because there are no translations of many of the cognitive function measures. Consent for the CAS was obtained for a total of 174 patients. Of the 174 patients, 139 (80%) were randomized. Of these, one patient was missing all in-hospital delirium assessment data, leaving 138 patients for this data analysis.

Protocols for the FOCUS and CAS studies were approved by the Institutional Review Boards/Ethics Committees at all participating institutions. An independent Data and Safety Monitoring Board approved the protocol and continually monitored data and safety. Written informed consent was obtained from all study patients or proxies for both studies.

Delirium Assessment

Baseline delirium was assessed post-operatively, but pre-randomization. Assessments were performed at least 12 hours after cessation of anesthesia. Delirium was assessed up to three times over five days post-randomization; therefore, each subject could have had up to four in-hospital post-operative assessments.

Delirium presence and severity was determined with a battery of assessments including the Mini-Mental State Examination (MMSE), Digit Span, and the Albert Delirium Symptom Interview (DSI).^{4,16-22} These assessments were used to score the following:

1. Confusion Assessment Method Diagnostic Algorithm (CAM): The 4-feature CAM algorithm operationalizes the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R) criteria of delirium including acute onset/fluctuating course and inattention, with either disorganized thinking or altered consciousness.²³

2. Memorial Delirium Assessment Scale (MDAS): The MDAS is a 10-item rating scale that captures the severity of delirium. Each item is rated from 0 (not present) to 3 (severe) to generate a 0-30 scale.²⁴

This combination of measures, when administered by trained, non-clinician research staff, has high validity and inter-rater agreement (Kappa>0.95 for delirium diagnosis, Kappa=0.94 for delirium severity).²⁵ Research staff conducting delirium assessments at the 13 participating sites were not blinded to patient treatment status, but were trained and tested in performance of the assessments. Medical chart documentation of delirium was not used to determine delirium status in this study.

Descriptive Measures

Demographics, chart abstractions, and proxy reports of diagnostic history were obtained as part of FOCUS.¹⁷ For the CAS patients, additional information was collected on the following: number of years of formal education, marital status, and chart notations of dementia at admission (abstracted from the medical chart after baseline). Proxy report of pre-fracture cognition was obtained at baseline using the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE).²⁶ Histories of degenerative dementia and vascular dementia were also obtained from interviews with the same proxy who provided answers to the IQCODE.

Variable Definition and Statistical Analysis—Delirium was defined according to symptoms meeting the CAM criteria (CAM+) at any point after surgery up to five days post-randomization. A patient who was deemed as not meeting the CAM criteria (CAM-) at one assessment but was CAM+ at the next assessment would be considered CAM+ for this analysis. Similarly, the maximum MDAS score was the highest score (i.e., most severe delirium symptoms) occurring after surgery and up to five days post-randomization. Previous analyses found no impact of randomization group on delirium presence or severity; hence, the analyses reported in this study combine the two treatment arms.¹⁸

Psychomotor subtypes of delirium were assessed among CAM+ patients. They were categorized as hypoactive, hyperactive, mixed, and normal psychomotor activity using items from the DSI and MDAS. Patients categorized as hypoactive exhibited only hypoactive symptoms (e.g., lethargy, slowness of motor response, staring into space) during the 30-45 minute assessment(s). Hyperactive patients exhibited only symptoms of hyperactivity (e.g., restlessness, sudden movements, wandering) during the assessment(s). Patients who exhibited symptoms of both hypo- and hyperactivity during the same assessment were considered to have the mixed subtype. Those who were CAM+ but did not exhibit psychomotor abnormalities from either hypo- or hyper-active classifications were defined as having delirium with normal psychomotor activity. Patients could fluctuate between being CAM+ and CAM- over the postoperative period (up to four assessments through the fifth post-operative day). Psychomotor subtypes of delirium among those who were CAM+ could fluctuate as well. Over the course of the assessment period, patients who were CAM+ over multiple time points and exhibited more than one psychomotor subtype were considered to be “varying over time”.

For subsequent bivariate analyses, patients defined as CAM+ for the study who exhibited only symptoms of hypoactive delirium or normal psychomotor activity during each CAM+ post operative in-hospital assessment were grouped into a category of “hypoactive/ normal psychomotor subtypes”.^{4,13} Other subtype combinations (e.g., hyperactive, mixed, etc.) at CAM+ assessments were grouped as “any hyperactivity” subtype.

To determine the stability of psychomotor subtypes over time, we tracked the number of CAM– and CAM+ observations per patient as well as the delirium subtype among those who were CAM+. Then, we calculated the mean number of CAM+ observations per patient by dividing the number of CAM+ observations by the total number of patients for each subtype. We used two-way analysis of variance (ANOVA) to determine if there were significant differences in mean CAM+ observations per patient between subtypes. We also compared the mean number of assessments per patient between subtypes.

Associations between baseline covariates and delirium psychomotor subtypes were tested using tests for the homogeneity of proportions and Student's t-tests. Frequencies, percentages, means, and p-values were calculated. Associations of baseline covariates with the maximum MDAS score were assessed using Student's t-tests and ANOVA. Statistical significance was defined as $p \leq 0.05$. Analyses were performed with SAS version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

Among the 138 patients, the average age was 81.5 (standard deviation (s.d.) 9.1) years, 73% were female, and 88% were white and non-Hispanic. (Table 1) The most common comorbidities according to chart history notations were hypertension (84%), coronary artery disease (33%) and atrial fibrillation (32%), and 80% of patients had an American Society of Anesthesiologists (ASA) score of 3 or higher. The ASA score is a measure of patient fitness before surgery and ranges from 1-6, with higher scores indicating more disease. A score of three indicates severe systemic disease. Dementia prevalence identified from any source (chart, proxy, IQCODE) was 31%.

In-hospital post-operative CAM+ delirium was observed in 57 patients (41%). The mean maximum MDAS score among these patients was 11.9 (s.d. 5.1), consistent with moderate delirium severity. Overall, there were 150 observations across the 57 subjects who were ever CAM+, of which 97 (65%) were CAM+ and 53 (35%) were CAM–. (Figure 1 and Table 2) Among the 57 CAM+ patients, 6 (11%) had only one delirium assessment, 20 (35%) had two, 19 (33%) had three, and 12 (21%) had four assessments. Due to limited staffing coverage on weekends at some participating facilities, 26/138 (19%) patients did not receive pre-randomization assessments.

The remainder of the analysis was conducted among patients with more than one delirium assessment. Over the 145 observations across the 51 subjects with two or more assessments who were ever CAM+, the majority exhibited the hypoactive subtype (55%). In terms of the stability of psychomotor subtypes, 21 (41%) CAM+ patients were hypoactive at all CAM+ assessments, 5 (10%) were hyperactive at all CAM+ assessments, 6 (12%) were mixed at all

CAM+ assessments, 6 (12%) displayed normal psychomotor activity at all CAM+ assessments, and 13 (25%) demonstrated varying subtypes in their CAM+ assessments (Figure 1 and Table 2).

Among patients with more than one CAM+ assessment (n=26 of the total 51 CAM+, 51%), 9/26 (35%) were hypoactive at all CAM+ assessments, 4/26 (15%) were mixed at all CAM+ assessments, and 13/26 (50%) were varying across the CAM+ assessments (Figure 1 and Table 2). Among patients with two CAM+ assessments, 6/16 (38%) exhibited varying subtypes, while among patients with three or four CAM+ assessments, 5/7 (71%) and 2/3 (67%) exhibited varying subtypes. No patient displaying uniquely the hyperactive only subtype or normal psychomotor activity had more than one CAM+ assessment. Overall, longitudinal stability among patients with more than one CAM+ assessment was 50%.

Thirty-one patients (63% of CAM+ patients with more than one assessment) displaying either the hypoactive subtype or normal psychomotor activity were combined to create our hypoactive/normal psychomotor activity category. These patients had lower maximum MDAS scores than patients with mixed/hyperactive subtypes (10.4 (s.d. 4.5) vs. 15.1 (s.d. 5.1), $p<0.001$, respectively), and were less likely to have chart documentation of delirium (22% vs. 58%, $p=0.009$). We did not identify any other statistically significant associations between the baseline patient or clinical characteristics listed in Table 1 and delirium subtype categories.

DISCUSSION

During the post-operative period, patients fluctuated between CAM+ and CAM- observations, and between delirium psychomotor subtypes. Longitudinal stability of delirium psychomotor subtypes was 50%. Hypoactive delirium accounted for the majority (55%) of CAM+ observations, and represented the most common delirium presentation.

The assessment of stability of delirium psychomotor subtypes over time has been hindered by inconsistent methods and heterogeneous populations.^{4,11,13,27,28} The longitudinal delirium assessments in this study provide evidence that patients oscillate between CAM- and CAM+ states, and often exhibit different (or no) psychomotor subtypes while in the CAM+ state. In our study, 50% of hip-fracture patients with more than one CAM+ assessment maintained subtype stability over time. Prior studies have reported a wide range of longitudinal stability estimates (13%-62%); however, differences in methodology and populations make direct comparisons difficult.^{11,29} Previous longitudinal studies did not report CAM- assessments, and therefore it is unclear how many CAM- assessments were recorded. In this study, 35% of assessments among patients who were ever CAM+ were also CAM-.

It is possible that with a greater number of assessments, patients with delirium might exhibit more or even all motoric presentations.^{8,9,26} This view is supported by our observation that patients whose subtype "varied over time" had more CAM+ observations compared to patients with any other psychomotor subtype. Nonetheless, our data support hypoactive delirium as a common presentation of delirium, and this is important because these types of

episodes are less likely to be recognized as delirium, putting these patients at higher risk of poor outcomes.^{4,10-13,29,30}

Patients with the hypoactive subtype of delirium or normal psychomotor activity had less severe delirium symptoms (as measured by the MDAS) compared to those with hyperactive/mixed motoric subtypes, but this finding must be interpreted cautiously because the MDAS, along with most other delirium severity measures, gives emphasis to hyperactivity. Our inability to detect any other significant associations between baseline patient characteristics and psychomotor subtypes of delirium could be due to the variable and multifactorial nature of delirium, pharmacological treatment effects, subtype categorization error, small sample size, or restriction of the distribution of patient characteristics in FOCUS. The absence of significant differences between subtypes may also reflect patient oscillation through subtypes during a delirium episode, which could help to explain the inconsistency of previous research on associations between subtypes and outcomes.^{4,12-16} Continual monitoring at regular intervals may be needed to determine stability and patterns of subtype oscillation. Furthermore, consistent methods for measuring and subtyping delirium episodes would facilitate comparisons between studies.

Patients with the hypoactive/normal psychomotor activity subtypes were less likely to have a diagnosis of delirium in the medical chart compared to patients with hyperactive and mixed subtypes. It is possible that hallucinations and agitated behavior - hallmarks of hyperactive delirium - lead to increased staffing care demands and thus to clinical recognition, despite its lower prevalence.¹⁰

This study was conducted among hip fracture patients with cardiovascular disease or risk factors who became anemic following surgery. As such, the results may not be generalizable to all hip fracture patients. Nonetheless, this longitudinal study reports CAM- assessments as well as delirium psychomotor subtypes. Our data suggest that patients with delirium spend a significant proportion of time in the CAM- state, which has important implications for diagnosis and treatment.

In conclusion, delirium psychomotor subtypes may not be distinct, but rather represent a spectrum of delirium symptoms consistent with the fluctuating presentation of delirium. Hypoactive delirium represents the most common but also the most often missed presentation of delirium. Our findings demonstrate the challenges of studying this heterogeneous syndrome, and the need for additional studies to better understand the implications for diagnosis and treatment of delirium.

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Figure 1.
 Longitudinal Sequence of Delirium Assessments over Five Days Post-Surgery among CAM
 + Patients with more than one delirium assessment, by Day and Motoric Subtype, n=51

Table 1Characteristics of Randomized Patients, n=138^a

Characteristic	
Age, mean (s.d.)	81.5 (9.1)
Age categories, n(%)	
50-64	8 (6)
65-74	18 (13)
75-84	58 (42)
85+	54 (39)
Race/Ethnicity, n (%)	
White, non-Hispanic	121 (88)
Other	17 (12)
Sex, n (%)	
Male	37 (27)
Female	101 (73)
Education, n(%)	
<High School	37 (29)
High School Graduate	52 (41)
>High School	39 (30)
Currently Married, n (%)	
Yes	48 (36)
No	86 (64)
Dementia Diagnosis, n (%)	
Yes	43 (31)
No	94 (69)
Anesthesia Type, n (%)	
General	80 (58)
Regional/Spinal only	58 (42)
Fracture Type, n (%)	
Femoral Neck	63 (46)
Other	75 (54)
Surgery Duration in minutes, mean (s.d.)	135.6 (49.9)
Length of Stay in days, mean (s.d.)	7.1 (5.0)
Delirium (from chart), n(%)	
Yes	26 (19)
No	110 (81)
Comorbidities (History from chart), n (%)	
Heart failure	22 (16)
Coronary artery disease	46 (33)
Hypertension	116 (84)
Stroke or TIA ^b	17 (12)
Chronic lung disease	29 (21)

Characteristic	
Cancer	22 (16)
Diabetes	28 (20)
Atrial fibrillation	44 (32)
Parkinson's disease	4 (3)
Hearing problems or Deaf	25 (18)
Visual problems or Blind	16 (12)
Alcohol abuse or Withdrawal	7 (5)
Malnourished or Cachectic	5 (4)
Labs at admission	
Albumin, mean (s.d.)	3.7 (0.5)
White Blood Count, mean (s.d.)	10.4 (4.1)
BUN ^c /creatinine ratio 18, n (%)	85 (63)
ASA ^d Score III, n(%)	111 (80)

^a Column numbers may not add up due to missing data

^b Transient Ischemic Attack

^c Blood Urea Nitrogen

^d American Society of Anesthesiologists

Distribution of delirium motoric subtypes and observations among randomized CAM^a + patients observed over 5 days post hip-fracture surgery with two or more assessments, n=51

Table 2

Psychomotor subtype	Number of Patients	Total Number Observations	CAM- Observations	Hypoactive Observations	Hyperactive Observations	Mixed Observations	No Psychomotor Symptoms Observations	Mean Observations per Patient ^b	Mean CAM+ Observations per Patient
Hypoactive	21	58	24	34	0	0	0	2.8	1.6
Hyperactive	5	14	9	0	5	0	0	2.8	1.0
Mixed	6	18	8	0	0	10	0	3.0	1.6
No Psychomotor Symptoms	6	15	9	0	0	0	6	2.5	1.0
Varying Over Time	13	40	4	16	4	9	7	3.1	2.8

^a Confusion Assessment Method

^b Mean number of assessments among CAM- participants was 2.4 (s.d.1.1)