The natural history of delirium in older hospitalized patients: a syndrome of heterogeneity

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Abstract

Objectives: to determine the presentation, course and duration of delirium in hospitalized older people.
Design: observational cohort study.
Setting: inpatient surgical and medical wards at a university hospital.
Participants: 432 people over the age of 65.
Measurements: all participants were screened daily for confusion and, in those who were confused, delirium was ascertained using the Diagnostic and Statistical Manual of Mental Disorders (DSM) III-R criteria. Those who were found to be delirious were followed daily while in hospital for evidence of delirium. The Delirium Rating Scale (DRS) was used to describe the clinical characteristics of delirium.
Results: about 15% of subjects had delirium. Sixty-nine percent of delirious subjects had delirium on a single day. The DRS total was higher on the first day of delirium for those with delirium on multiple days than those with delirium on a single day ($P = 0.03$). Among those with delirium on multiple days, there were no patterns of change over time in specific DRS items.
Conclusions: delirium in hospitalized older people is common and has a varied presentation and time course. Clinicians and researchers need to consider this great heterogeneity when caring for patients and when studying delirium.

Keywords: *ageing, confusion, delirium, elderly people, hospital, natural history*

Introduction

Delirium, as defined in Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised (DSM-III-R) [1], is common in hospitalized older people. Most studies have shown that delirium is related to many important outcomes such as death, longer hospitalization and institutionalization, as well as increased patient care costs and increased intensity of nursing care [2–5]. Other studies have identified predictors of delirium, such as age, cognitive function and co-morbidity [2, 3, 6–10].

Less is known about the attributes of delirium and how these change during the course of delirium. In other words, what are the differences among those with delirium in terms of presentation, as well as kinds,

severity and duration of symptoms? It may be hypothesized that because delirium is a syndrome and not a disease, variation should be expected, especially in older populations which contain much heterogeneity [11]. In support of this hypothesis, Rockwood [12] has shown that the mean duration of delirium in hospitalized older people varies greatly with a mean of 7 days and a range of 9 days, and Wada and Yamaguchi [13] have shown that symptom intensity as measured by the Delirium Rating Scale (DRS) [14] correlates with duration.

The purpose of this study was to determine the natural history of delirium in hospitalized older people. In particular, for those older people who develop delirium in hospital, what are the clinical characteristics of delirium in terms of presentation, course and duration?

Methods

Study sample

This was a prospective cohort study of delirium in hospitalized older performed in the University of Chicago Hospitals between November 1989 and June 1991. Patients who were 65 years of age or older and who were admitted to one of four 24-bed wards were eligible for enrolment. Two of the wards were for general medical patients and two were for surgical patients (primarily patients with orthopaedic, urological or general surgical problems).

Patients were excluded if they were unable to provide consent because of cognitive impairment, coma, aphasia or inability to speak English. Patients also were excluded if they were considered too ill for a 40 min interview, if they were in protective isolation, if they were discharged within 48 h of admission or if they were unavailable for interview within 48 h of admission. Informed consent was obtained for all enrolled study subjects.

For a sample of those who were not enrolled into the study, a chart review was performed to find evidence for delirium in order to determine whether the prevalence of delirium was similar in those enrolled and not enrolled.

Delirium ascertainment

Delirium was ascertained in the following manner as described previously [15]. Briefly, research assistants interviewed subjects daily using each of the following four standardized screening instruments to detect changes in attention, cognition or level of consciousness: Digit Span [16], Vigilance A Test [16], Clinical Assessment of Confusion [17] and the Confusion Assessment Method [18]. In addition to administering screening tests, the research assistants sought other evidence for transient mental status changes in the study subjects by consulting with nurses and reviewing the medical records. Subjects who met the predetermined criteria for possible delirium based on the results of the screening instruments [19], or in whom there was a suspicion of delirium based on review of the medical record or conversations with the research assistants, were evaluated within 24 h by one of the clinical investigators. The diagnosis of delirium, either on admission or at any time during hospitalization, was based on the independent assessment of the clinical investigator according to DSM-III-R criteria [1].

Delirium characteristic measures

Participants diagnosed with delirium were then followed daily throughout their hospital stay to determine both the daily occurrence and the specific clinical characteristics of delirium. To characterize the attributes of delirium, we used the (DRS) [14], which was developed to differentiate delirium from other common neuropsychiatric disorders. It is based on the measurement of 10 items: (i) temporal onset of symptoms; (ii) perceptual disturbances; (iii) hallucination type; (iv) delusions; (v) psychomotor behaviour; (vi) cognitive status during formal testing; (vii) physical disorder; (viii) sleep-wake cycle disturbance; (ix) lability of mood; and (x) variability of symptoms. Each item is scored from 0 (characteristic not evident) to 3 or 4 (characteristic highly evident). Total scores can range from 0 to 32.

We defined prevalent cases of delirium as any case in which delirium occurred within 3 days of hospital admission. We chose this definition as used before [15] because it may have taken a maximum of 3 days for a clinical investigator to evaluate a patient. All other cases were considered incident cases. It is hypothesized that this dichotomy may be related to different causes, time courses and outcomes. Another characterization was whether the delirium occurred on one or multiple days. This dichotomy was chosen since it may be that delirium occurring on multiple days has different presentations, partly due to the severity of delirium. Furthermore, it may be that over time the characteristics of delirium in a person may change.

The suspected cause(s) of delirium were ascertained. Suspected causes were determined by clinician researchers by chart review. If more than one cause was probable, all causes were collected and ranked by order of likely cause.

Secondary measures

On admission to the hospital, demographic information was collected, including age, race, gender and education. As two measures of co-morbidity, the number of medications was recorded on the first day of delirium and the number of diagnoses was ascertained following discharge as documented on the billing discharge form.

Statistical methods

Due to the small sample, simple statistics were used throughout this analysis. χ^2 statistics were used for categorical variables and t-tests for continuous variables.

Results

Of the 432 people enrolled in the study, 64 patients (14.8%) were found to have delirium. About 15% of people in the excluded group also had evidence of delirium by chart review. The average age of the subjects with delirium was 75.2 years with a range of 65–95 years. Thirteen percent of the population was over the age of 85 years. Sixty-one percent were African-Americans and 56% were female. Forty-four percent had education up to or below ninth grade.

The pertinent medical and health care characteristics of those determined to be delirious are as follows. Sixty-seven percent were in medical wards. Most of the subjects had high levels of co-morbidity as measured by the number of medical diagnoses (average 6.3, SD 2.3, range 2–10) and the number of medications prescribed (average 6.9 SD 2.6, range 1–13).

Figure 1 shows the occurrence of delirium by hospitalization day for each subject who was found to be delirious. What is obvious is that there is no single pattern of delirium. First, 44 of the 64 subjects experienced a single day of delirium, while 20 of the 64 had delirium on multiple days. For those with delirium on multiple days, no single daily pattern or grouping is apparent. Second, 22 of the 64 people had delirium within 3 days of admission (prevalent cases); the others (incident cases) had the onset of delirium while in the hospital. Even within the
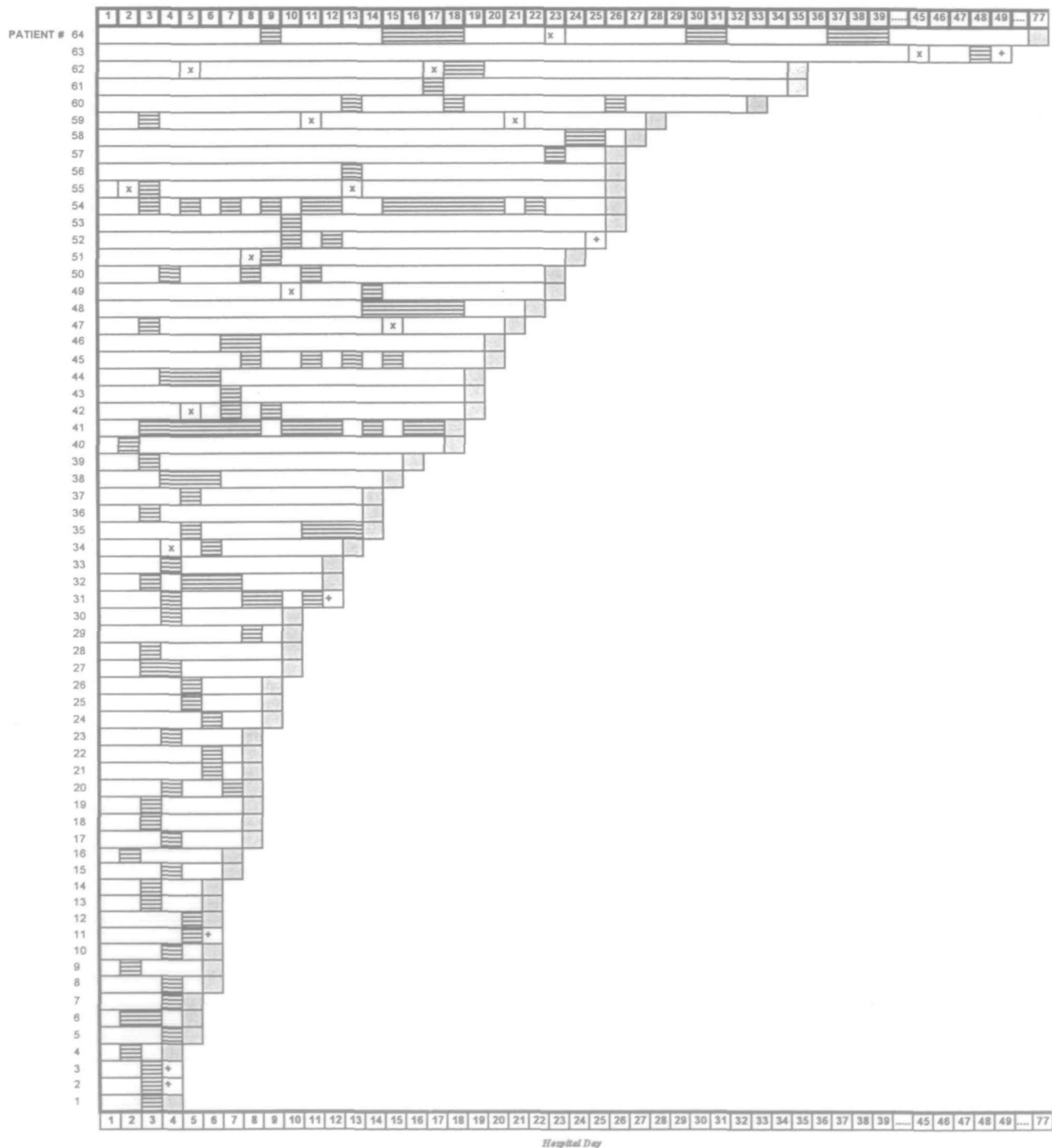

Figure 1. Hospital day(s) of delirium by subject: ■, day of discharge; ▤, delirious; +, day of death; ×, surgery noted.

Table I. Delirium Rating Scale item scores

	Score [mean ± SD (and range)]			
	Day(s) of delirium			
			Multiple	
Specific attribute	All patients[a] (n = 63)	Single (n = 43)	First day (n = 20)	Last day (n = 20)
Temporal symptoms	3.7 ± 0.58 (1-4)	3.7 ± 0.6 (1-4)	3.8 ± 0.4 (3-4)	3.7 ± 0.8 (1-4)
Perceptual disturbances	2.1 ± 1.2 (1-4)	1.9 ± 1.1 (1-4)	2.6 ± 1.4 (1-4)	2.9 ± 1.2 (1-4)
Hallucination type	1.3 ± 0.7 (1-3)	1.2 ± 0.6 (1-3)	1.6 ± 1.0 (1-3)	1.1 ± 0.5 (1-4)
Delusions	1.4 ± 1.0 (1-4)	1.2 ± 0.7 (1-4)	1.8 ± 1.3 (1-4)	1.5 ± 1.1 (1-4)
Psychomotor behaviour	2.5 ± 1.1 (1-4)	2.4 ± 1.0 (1-4)	2.6 ± 1.1 (1-4)	2.7 ± 1.1 (1-4)
Cognitive status	3.0 ± 0.9 (1-4)	2.9 ± 0.8 (1-4)	3.2 ± 0.9 (2-4)	3.1 ± 1.0 (1-4)
Physical disorder	2.8 ± 0.4 (2-3)	2.8 ± 0.4 (2-3)	2.8 ± 0.4 (2-3)	2.5 ± 0.6 (1-3)
Sleep disturbance	2.9 ± 1.3 (1-5)	2.8 ± 1.4 (1-5)	3.0 ± 1.3 (1-5)	3.0 ± 1.6 (1-5)
Lability of mood	1.6 ± 0.8 (1-4)	1.5 ± 0.8 (1-4)	1.7 ± 0.9 (1-4)	1.6 ± 0.9 (1-4)
Variability of symptoms	2.7 ± 0.7 (1-3)	2.6 ± 0.8 (1-3)	2.8 ± 0.4 (1-3)	2.8 ± 0.6 (1-3)
Total rating	23.5 ± 4.4 (14-32)	22.6 ± 4.4 (14-31)	25.4 ± 3.6 (18-32)	24.9 ± 4.9 (16-32)

[a]First day.

surgical patients, 40% of cases did not occur within 3 days of the surgery.

As seen in Table 1, the average DRS total score for those with delirium on a single day was 22.6 ± 4.4 while the average was 25.4 ± 3.6 for those with multiple day delirium on the first day. The difference between the averages was statistically significant at $P = 0.03$. In addition, these groups differed in that the group with delirium on multiple days had a higher average number of diagnoses (7.7 ± 2.0 versus 5.8 ± 2.3, $P = 0.002$) and a higher average number of prescribed medications (7.8 ± 1.9 versus 6.5 ± 2.7, $P = 0.07$). Second, for those people with multiple days of delirium, there is no trend of decreasing DRS total scores between the first and the last day of delirium. In fact, there is much variety and heterogeneity in the DRS total patterns. Third, there were

no significant differences in the average DRS total score between the groups with incident and prevalent cases of delirium.

The DRS item scores were variable in different patients (Table 1). Moreover, there were no differences in the average item scores between those with delirium on a single or a multiple day. Among those with delirium on multiple days, there were no differences between the item scores on the first and the last day of delirium.

As the patterns of delirium are different, so too are the causes of delirium (Table 2). The most likely primary cause of delirium is medication use. The second is metabolic abnormalities, and infections were the third most common primary cause. Over 44 people had delirium that was associated with multiple causes. Ten people had delirium of unknown cause.

Table 2. Distribution of suspected first and second causes of delirium

| | Frequency of suspicion | |
Cause	First	Second
Medication	27	11
Metabolic abnormality	14	11
Infection	5	5
Cardiovascular[a]	2	7
Neurological	5	6
Depression/psychosis	0	1
Gastro-intestinal/genito-urinary obstruction	0	0
No suspected cause	10	-
Total	63	41

[a]Congestive heart failure, altered intravascular volume, dysrhythmia, myocardial infarction.

Discussion

In older people who are hospitalized for acute medical illness at a university hospital, delirium is a common syndrome. In this study, 14.8% of those enrolled had delirium. The screening procedure was very sensitive as we used multiple screening instruments and clinical information. An abnormality in any of these could trigger a clinician-investigator to further evaluate the subject. The diagnosis was specific, being based exclusively on DSM-III-R criteria. Although inter-observer variation was not specifically studied, it should be minimal since DSM-III-R criteria were used to make the diagnosis. Nevertheless, because of the transient nature of delirium, we may have missed some episodes of delirium on the daily evaluations. We attempted to minimize this by having the research assistants screen subjects at a time other than when the clinical researchers did their evaluations.

This rate of delirium appears to be not biased by those people not enrolled into the study. Several patients were excluded from the study sample because they were either too ill or did not consent to be enrolled. These people, however, did not have a very different likelihood of delirium as determined by chart review.

There is much heterogeneity in people with delirium, as shown in Figure 1. The changes over time and the variability among subjects may, in fact, be a cause of some of the variation in previous studies of the rates of delirium as well as the duration of delirium. This is probably related to baseline physiology, the inciting events and compensatory mechanisms, associated investigations and medications, as well as environmental factors such as sensory input. To sort out this heterogeneity further work with larger subject samples is necessary. In addition, the diagnosis of delirium in some cases may be problematic, especially with changing definitions [20], since the time course can be quite long and because of the variability of symptoms. Studies that measure delirium must take this heterogeneity into account.

As seen in work by Wada and Yamaguchi [13] and Trzepacz and Dew [21], the severity of delirium as measured by the DRS total score may be important for predicting who will have delirium on multiple days. A possible explanation for this is that the brain insult(s) and associated compensatory mechanisms, such as inflammation and altered physiology that might contribute to the symptoms, may be more severe or numerous in people with delirium occurring on several days. This is suggested by the fact that those with multiple episodes of delirium had more diagnoses and a trend to take more medications than those with delirium on a single day. Understanding the relationships of specific exposures to certain patterns of delirium may shed light upon this complex and varied syndrome.

That the individual items of the DRS were not associated with different subgroups may be related to the fact that the DRS item scales were not originally intended to measure severity [22]. In addition, important characteristics of delirium, such as attentiveness or level of consciousness, are not measured in the DRS. Finally, the temporal onset and physical disorder subscales will not change from one assessment to the next.

In general, many of the causes of delirium were potentially treatable. On the other hand, the causes in 10 people could not be determined by clinical course or by chart review. The actual cause(s) may have been asceertainable only by further diagnostic procedures not performed by the team in charge of the subject's care.

It is clear that patients hospitalized for medical illnesses and surgical procedures are at risk of delirium. Delirium may occur at any time during a hospital stay, so clinicians should maintain vigilance for it throughout the course of the patient's illness. Indeed, with earlier hospital discharges, it is likely that post-discharge delirium (at home or in the nursing home) may be more common than is generally realised. Nevertheless, delirium as determined by DSM-III-R is a common and varied syndrome that must be considered by both clinicians who diagnose and treat patients and researchers who study the aetiology, process and outcome of delirium.

Acknowledgements

Key points
- Fifteen percent of patients over 65 developed delirium during their stay on medical or surgical wards.
- Over two-thirds had delirium on a single day, but delirium may occur at any time during a hospital stay.
- There was considerable variation in the presentation and time-course of delirium.
- The most common causes of delirium were medications, metabolic abnormality and infection.
- No underlying cause could be found for delirium in 10% of patients.

References

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 3rd ed, revised. Washington, DC: American Psychiatric Association, 1994.

2. Williams-Russo P, Urquhart BL, Sharrock NE, Charlson ME. Post-operative delirium: predictors and prognosis in elderly orthopedic patients. J Am Geriatr Soc 1992; 40: 759-67.

3. Francis J, Martin D, Kapoor WN. A prospective study of delirium in hospitalized elderly. JAMA 1990; 263: 1097-101.

4. Thomas RI, Cameron DJ, Fahs MC. A prospective study of delirium and prolonged hospital stay. Arch Gen Psychiatry 1988; 45: 937-40.

5. Weddington WW Jr. The mortality of delirium: an under-appreciated problem. Psychosomatics 1982; 23: 1232-5.

6. Schorr JD, Levkoff SE, Lipsitz LA, Reilly CH, Cleary PD, Rowe JW, et al. Risk factors for delirium in hospitalized elderly. JAMA 1992; 267: 827-31.

7. Rogers MR, Liang MH, Daltroy LH et al. Delirium after elective orthopedic surgery: risk factors and natural history. Int J Psychiatr Med 1989; 19: 109-21.

8. Berggren D, Gustafson Y, Eriksson B et al. Postoperative confusion after anesthesia in elderly patients with femoral neck fractures. Anesth Analg 1987; 66: 497-504.

9. Seymour DG, Henschke PJ, Cape RDT, Campbell AJ. Acute confusional states and dementia in the elderly: the role of dehydration/volume depletion, physical illness and age. Age Ageing 1980; 9: 137-46.

10. Inouye SK, Viscoli CM, Horwitz RI et al. A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. Ann Intern Med 1993; 119: 474-81.

11. Lazaridis EN, Rudberg, MA, Furner SE, Cassel CK. Do activities of daily living have a hierarchical structure? An analysis of using the longitudinal study of aging. J Gerontol Med Sci 1994; 49: M47-51.

12. Rockwood K. The occurrence and duration of symptoms in elderly patients with delirium J Gerontol Med Sci 1993; 48: M162-6.

13. Wada Y, Yamaguchi N. Delirium in the elderly: relationship of clinical symptoms to outcome. Dementia 1993; 4: 113-6.

14. Trzepacz PT, Baker RW, Greenhouse J. A symptom rating scale for delirium. Psychiatry Res 1988; 23: 89-97.

15. Pompei P, Foreman M, Rudberg MA, Inouye SK, Braund V, Cassel CK. Delirium in hospitalized older people: outcomes and predictors. J Am Geriatr Soc 1994; 42: 809-15.

16. Strub RL, Black FW. The Mental Status Evaluation in Neurology, 2nd ed. Philadelphia, PA: FA Davis 1985, pp. 42-3.

17. Vermeersch PEH. The clinical assessment of confusion. App Nursing Res 1990; 113: 941-948.

18. Inouye SK, van Dyke CH, Alessi CA, Balkin S, Siegal AP, Horowitz RI. Clarifying confusion: the confusion assessment method. Ann Intern Med 1990: 113; 941-8.

19. Pompei P, Foreman M, Cassel CK, Alessi C, Cox D. Detecting delirium in hospitalized older people. Arch Intern Med 1994; 155: 301-7.

20. Levkoff S, Cleary P, Liptzin B, Evans DA. Epidemiology of delirium: an overview of research issues and findings. Int Psychogeriatrics 1991; 3: 149-67.

21. Trzepacz PT, Dew MA. Further analyses of the delirium rating scale. Gen Hosp Psychiatry 1995; 17: 75-9.

22. Smith MJ, Breitbart WS, Platt MM. A critique of instruments and methods to detect, diagnose and rate delirium. J Pain Symptom Management 1995; 10: 35-77.