The Cause of Delirium in Patients With Hip Fracture

Christopher Brauer, MD; R. Sean Morrison, MD; Stacey B. Silberzweig, MS, RD; Albert L. Siu, MD, MSPH

Objectives: To ascertain the most common causes of delirium, to establish the initiation and timing of delirium, and to determine the duration of delirium in patients with hip fracture.

Methods: Five hundred seventy-one (88%) of 650 patients with hip fracture admitted to 4 New York City hospitals were prospectively interviewed on a daily basis, 5 days a week, with the Confusion Assessment Method for the presence of delirium. The patients were enrolled within 48 hours of admission. Their medical charts and the data collected by the study staff were reviewed and summarized. Two of us (R.S.M. and A.L.S.) reviewed the case summaries independently and assigned a cause based on a previously developed classification system, estimated the onset of the delirious episode, and determined whether the delirium had cleared, improved, or persisted at discharge. Subsequently, discrepancies in cause, timing of initiation, and mental status on discharge between the 2 physicians reviewers were discussed until consensus was reached.

Results: The prevalence of delirium was 9.5% (54/571; 95% confidence interval, 7.0-11.9). Seven percent of episodes were assigned a definite cause, 20% a probable cause, 11% a possible cause, and 61% were attributable to 1 or more comorbid conditions. Twenty-eight (53%) of 54 subjects developed delirium after surgery. The delirium had cleared or improved in 40 (74%) of 54 subjects at the time of discharge.

Conclusions: Delirium in patients with hip fracture appears to be a different syndrome from that observed in patients who are otherwise medically ill; it also appears to follow a different clinical course. These results have important implications for the management of delirium in patients with hip fracture.

Arch Intern Med. 2000;160:1856-1860

Delirium occurs in 11% to 42% of the hospitalized elderly and is associated with increased mortality, delayed rehabilitation efforts, prolonged length of hospital stay, poorer functional outcomes, and increased risk of nursing home placement.

Several studies have identified specific patient characteristics, medical conditions, and iatrogenic interventions that place patients at increased risk for the development of delirium, and it is now possible to identify high-risk patients and to correct or avoid modifiable risk factors. Once delirium develops, the cornerstone for its management is the treatment of the underlying cause. Surprisingly, there have been few studies that have systematically described the frequency of different causes of the delirium syndrome, and the current recommended diagnostic approach is thus largely empirical and based on expert opinion. The data that are available are drawn from 3 relatively small studies. Moses and Kaden reported a case series involving 105 patients with delirium. In their study, no single cause was found in 47% of cases, a medication was implicated in 17%, a fluid or electrolyte abnormality in 12%, and hypoxia or hypotension in 10%. Another series of 56 patients with delirium reported that the “discharge diagnoses” were related to toxic diagnoses in 39% of cases, fluid and electrolyte problems in 11%, alcohol withdrawal in 11%, and other diagnoses less commonly. The most systematic classification of cause was in a study of 229 elderly patients, 50 of whom developed delirium during hospitalization. Fluid and electrolyte abnormalities had a possible role in 40% of cases, infection in 40%, drug toxicity in 30%, metabolic disorders in 26%, sensory and environmental problems in 24%, and low perfusion in 14%. In sum-
PATIENTS AND METHODS

PATIENTS

We reviewed daily admissions to 4 New York City metropolitan area hospitals for patients admitted with hip fracture during a 12-month period starting in August 1997. We included patients with fractures of the proximal femur and excluded patients younger than 50 years; patients with fractures that occurred during their hospital stay; patients transferred from the inpatient service of another hospital after surgical repair; and patients with bilateral fractures, isolated pelvic or acetabular fractures, fractures accompanied by internal injury, pathologic fractures, and fractures in a previously fractured or surgically treated hip. Six hundred fifty of 802 subjects screened met these eligibility criteria, and 571 (88%) gave informed consent to participate.

METHODS

Within 48 hours of hospital admission, all patients were interviewed by a research nurse who used the confusion assessment method (CAM) developed by Inouye et al,13 to assess for delirium. We selected the CAM because it is a standardized algorithm that is feasible for a research nurse to administer on a daily basis in the hospital in less than 5 minutes (unlike standardized questions of memory and orientation).14 The CAM was used to detect delirium based on the presence of acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness. Its feasibility, reliability (interobserver k, 0.81-1.0), sensitivity (94%-100%), and specificity (90%-95%) have been characterized.15 Subjects were assessed with the CAM on a daily basis, 5 days a week. All patients who were found to be delirious by the CAM were included in this study. In addition to administering the CAM, the study staff reviewed the medical records daily and spoke to hospital staff. The results of these observations were recorded concurrently for all patients who developed delirium according to the CAM. The mental status of patients without delirium was assessed by interviewing patients and surrogates as to the presence of Alzheimer disease, another dementing illness, or a history of memory loss and by reviewing chart notes for a history of dementia or memory loss.

DELIRIUM CLASSIFICATION

All patients' medical charts and the data collected by the study staff were reviewed and summarized by one of us (C.B.). Specifically, all references to confusion, agitation, or altered mental status were recorded verbatim from the chart along with the date and time of the entry. Any relevant medical investigations and/or abnormal test results were recorded. All pain and psychotropic medications given were documented.

We modified an instrument, based on the work of Francis et al,10 for classifying the causes of delirium. Francis and colleagues classified possible causes into 8 categories (ie, drug-induced delirium, infection, fluid-electrolyte disturbance, metabolic disturbance, intracranial process, low perfusion state, alcohol and drug withdrawal, and sensory/environmental delirium). We expanded the metabolic disturbance category to include metabolic and endocrine disturbances that could cause delirium. The low-perfusion state category was renamed cardiopulmonary compromise and/or hypoxia and was expanded to include not only low cardiac output, but also pulmonary compromise and cerebrovascular insufficiency. The full instrument that was used for classifying the causes of delirium may be found in Table 1.

The causes were then classified as definite, probable, possible, or comorbid based on the number of criteria that were present in the case. For a cause to be considered definite, all clinical criteria had to have been met and no criteria for another cause were present. A cause was considered probable if all 3 clinical criteria were met but criteria for another cause were also present. A cause was considered possible if 2 criteria were met and no other criteria for another cause were found. Finally, we attributed the delirious episode to a comorbid condition if only 1 or 2 criteria for a given cause were present (ie, no single definite, probable, or possible cause could be identified).

Two of us (R.S.M. and A.L.S.) reviewed the case summaries independently and assigned a cause to the delirious episode based on the classification system described in Table 1. The physician reviewers were permitted to override any classification derived from Table 1 if the physician believed that another characterization of the cause was more appropriate. Also, the reviewers estimated whether the delirium was present on admission or developed either preoperatively or postoperatively and whether the delirium had cleared, improved, or persisted at discharge. After independently reviewing each case and recording their observations, the 2 reviewers discussed discrepancies in cause, classification of cause, time of initiation of delirium, and the mental status of each patient on discharge.

The physician reviewers had a 61.5% agreement on the independent classification of the causes of delirium on initial review. After subsequent discussion, the reviewers reached consensus on all cases. Similarly, the reviewers had a 67.3% agreement on the independent estimation of the initiation of delirium and reached consensus after discussion in all cases. Finally, the reviewers had a 70.4% agreement on the total independent estimation of the patients' mental status on discharge (cleared or improved vs persistent) and 100% agreement on the final classification after discussion.
Table 1. Classification of the Causes of Delirium

<table>
<thead>
<tr>
<th>Drug-induced delirium</th>
<th>Definite</th>
<th>Probable</th>
<th>Possible</th>
<th>Comorbid Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbid</td>
<td>11 (20)</td>
<td>0 (0)</td>
<td>2 (4)</td>
<td>16 (30)</td>
</tr>
<tr>
<td>Infection-induced</td>
<td>2 (4)</td>
<td>4 (7)</td>
<td>2 (4)</td>
<td>17 (31)</td>
</tr>
<tr>
<td>Fluid-electrolyte</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>11 (20)</td>
</tr>
<tr>
<td>Metabolic/endocrine</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Intracranial</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Cardiopulmonary</td>
<td>0 (0)</td>
<td>4 (7)</td>
<td>1 (2)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Drug withdrawal</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Sensory/environmental</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>24 (44)</td>
</tr>
</tbody>
</table>

*Total comorbid cases, 33; total comorbid causes will exceed total cases owing to multiple causation.

Table 2. Consensus Causes of Delirium Among 54 Patients With Hip Fracture

| Table 3. Classification of Cause vs Consensus Mental Status on Discharge |
|--------------------------|----------|----------|----------|------------|
|                         | Total    | Probable | Possible | Comorbid   |
| Cleared                 | 5         | 1 (2)    | 1 (2)    | 1 (2)      |
| Improved                | 21        | 2 (4)    | 5 (10)   | 3 (6)      |
| Persistent/Unknown      | 13        | 0 (0)    | 2 (4)    | 11 (20)    |
| Total                   | 39        | 7 (14)   | 13 (26)  | 19 (38)    |

Table 3. Classification of Cause vs Consensus Mental Status on Discharge

The prevalence of delirium in patients with hip fracture in this study was 9.5% (54/571; 95% confidence interval, 7.0-11.9). The median age of the 54 patients was 85 years (age range, 69-101 years); 81% were women; and the median length of hospital stay was 9 days (range, 3-34 days). The consensus timing of delirium was as follows: 4 patients (7%) were delirious on admission; 16 patients (30%) became delirious before surgery; 5 patients (9%) became delirious on the day of surgery; and 29 patients (54%) became delirious after surgery. The consensus causes of delirium are shown in Table 2. Of the 54 episodes of delirium, 4 (7%) were assigned a definite cause, 11 (20%) were classified as possible, 6 (11%) were classified as probable, and the remaining 33 (61%) were determined to be related to a comorbid condition. Of note, there were 74 identifiable causes attributable to the 33 comorbid cases. The most frequent comorbid causes were sensory/environmental, infection, drug use, and fluid-electrolyte disturbances.

Although there was disagreement between the two reviewing physicians concerning mental status on discharge, disagreements were frequently about whether the delirium had cleared or merely improved, and this variance was often attributable to sparse chart documentation. After consensus, 40 (74%) of the 54 subjects were determined to have a cleared or improved mental status on discharge. By the time of discharge, the delirium had cleared in 4 patients (7%), improved in 36 patients (67%), and was persistent in 13 patients (24%). One patient’s mental status could not be determined at the time of discharge.

The results of this study suggest that delirium in patients with hip fracture may be a different syndrome from

RESULT

The prevalence of delirium in patients with hip fracture in this study was 9.5% (54/571; 95% confidence interval, 7.0-11.9). The median age of the 54 patients was 85 years (age range, 69-101 years); 81% were women; and the median length of hospital stay was 9 days (range, 3-34 days). The consensus timing of delirium was as follows: 4 patients (7%) were delirious on admission; 16 patients (30%) became delirious before surgery; 5 patients (9%) became delirious on the day of surgery; and 29 patients (54%) became delirious after surgery. The consensus causes of delirium are shown in Table 2. Of the 54 episodes of delirium, 4 (7%) were assigned a definite cause, 11 (20%) were classified as possible, 6 (11%) were classified as probable, and the remaining 33 (61%) were determined to be related to a comorbid condition. Of note, there were 74 identifiable causes attributable to the 33 comorbid cases. The most frequent comorbid causes were sensory/environmental, infection, drug use, and fluid-electrolyte disturbances.

Although there was disagreement between the two reviewing physicians concerning mental status on discharge, disagreements were frequently about whether the delirium had cleared or merely improved, and this variance was often attributable to sparse chart documentation. After consensus, 40 (74%) of the 54 subjects were determined to have a cleared or improved mental status on discharge. By the time of discharge, the delirium had cleared in 4 patients (7%), improved in 36 patients (67%), and was persistent in 13 patients (24%). One patient’s mental status could not be determined at the time of discharge.

Table 3 lists the classification of cause vs mental status on discharge. The mental status of 19 (90%) of 21 patients with a definite, probable, or possible cause for their delirium cleared or improved by discharge as compared with 23 (67%) of 33 patients classified as having a comorbid cause for their delirium ($\chi^2 = 6.7; P = .04$).

COMMENT

The results of this study suggest that delirium in patients with hip fracture may be a different syndrome from
that observed in patients who are medically ill. Delirium in hip fracture appears to result from different causes and appears to follow a different clinical course. These findings have important implications for the management of delirium in the patient with hip fracture.

In our study, we found a prevalence of delirium that was much lower than that found in previous studies: 3-10: 9.3% vs 11% to 42%, respectively. There are several possible explanations for these differences. Some of the other studies described “acute confusional states” and did not use standardized instruments to assess for delirium. Thus, some of these studies may have been measuring other conditions (eg, dementia) that inflated the rates of delirium. In this study, we used the CAM that was developed by Inouye et al13 to identify delirious patients. The CAM has been demonstrated to be a reliable and valid measure of delirium. Alternatively, our study did have limitations that could have underestimated the case rate. We observed patients only for 5 days of every week of hospitalization, and the patients were also observed only once per day; therefore, we might have missed some episodes of delirium. Nevertheless, given the believed extended duration of delirium,16 it is unlikely that we would have missed a significant number of cases.

We identified a definite cause of delirium in only 3 (6%) of 54 cases, and only 14 (26%) of 54 cases were rated as definitive or probable. The majority of patients (62%) in this study were classified with comorbid causes of delirium, meaning that several etiologic factors together caused delirium, yet no one cause could be identified as being more important than any other. In contrast, in the only other large study that systematically classified the pathogenesis of delirium in a sample largely composed of medically ill subjects, a definitive cause was identified in 36% of cases, and a definitive or probable cause was identified in 56% of cases. Differences in the study samples and methodological differences between our study and that of Francis et al10 might account for some of the observed disparities. Francis and colleagues’ study was a prospective study of patients with delirium, whereas our study consisted of data collected retrospectively from medical records along with written observations of research nurses who interviewed subjects with the CAM on a daily basis. Also, our definition of probable cause differed slightly from that used in Francis and coworkers’ study. Nevertheless, we believe that it is unlikely that these different definitions could account for the differences observed and that the observed variance in assignment of cause was mainly the result of differences in the patient populations. For example, although patients with hip fracture frequently have many chronic medical problems, they are typically not admitted with the complex cardiopulmonary, renal, infectious, and metabolic problems that are frequently observed in hospitalized medically ill geriatric patients. Furthermore, because of the nature of the surgery and the procedures involved, patients who are surgically treated may be more at risk for complications and iatrogenic conditions (eg, bleeding, thromboembolic pain, and immobility) than medically ill patients who do not undergo surgery, and these factors can further result in or contribute to delirium. Finally, the patients in our study were 6 years older on average than those in Francis and colleagues’ study, and this may have contributed to the observed differences.

The time course and resolution of delirium observed in this study also differed from those previously reported. In contrast to other studies of delirium in medically ill patients, in which approximately 33% to 50% of the patients who were diagnosed with delirium were delirious on presentation to the hospital,1-10,16 only 7% of the patients in our study were delirious on admission. Ninety-three percent of the patients in our study developed delirium after admission, and more than 50% developed delirium after surgery. Furthermore, although a cause for the delirious episode was identified in only a minority of cases, 74% of subjects had an improved mental status or had returned to their baseline mental status on discharge. These findings are in contrast to the data reported by Levkoff et al,16 who observed that 58% of medically ill patients still met Diagnostic and Statistical Manual of Mental Disorders, Third Edition,17 criteria for delirium on hospital discharge. In the vast majority of cases of delirium in our study, improvement also occurred without any specific intervention directed toward the underlying cause (which could not be identified in the majority of cases). This spontaneous resolution of delirium appears not to occur in medically ill patients. That is, delirium in the medically ill tends not to resolve spontaneously and tends to improve only after therapeutic intervention.1

Our study had several limitations that should be noted. It was a retrospective chart review, and chart documentation was sometimes sparse. However, chart data were supplemented with prospective observations by the study staff, concurrent record review, and interviews with hospital staff, and we used all this information to determine the cause and timing of delirium. Also, while there were some disagreements in the initial independent reviews, many of the disagreements were settled when the cases were discussed and information to support conclusions was aired. Furthermore, the disagreements were typically not major but were centered around issues such as whether the delirium had improved or cleared completely.

The findings from our study suggest that delirium in patients with hip fracture may be a different syndrome from that observed in the medically ill. Our data also suggest that the current recommended strategy for managing delirium (ie, a search for the underlying cause) may need to be modified in the hip fracture population. Therefore, because an underlying cause could not be identified in the majority of our patients, and because the patients improved or got better without a cause being identified, we suggest that a focused search directed at the most likely cause should be undertaken and that, in concert, efforts should be directed toward the symptomatic management of the delirious episode using environmental, behavioral, and pharmacologic interventions (eg, major tranquilizers) rather than on an exhaustive (and perhaps futile) search for all common causes. Finally, as delirium in patients with hip fracture appears to result from causes that are different from those seen in the medically ill, further studies are needed to explore whether previously identified risk factors for the development of
delirium in the medically ill are applicable to patients with hip fracture and whether there are other conditions unique to hip fracture (eg, pain and anesthesia) that predispose these patients to the development of delirium.

Accepted for publication December 20, 1999.

Dr Morrison is an Open Society Institute Project on Death in America Faculty Scholar and the recipient of a Mentored Clinical Scientist Development Award (K08AG00833-01) from the National Institute on Aging, Bethesda, Md. Dr Siu is the recipient of a Midcareer Investigator Award in Patient-Oriented Research (K24AG00918-01) from the National Institute on Aging. This project was partly supported by grant U18HS09459-0 from the Agency for Health Care Policy and Research, Rockville, Md.

Corresponding author: R. Sean Morrison, MD, Hertzberg Palliative Care Institute of the Department of Geriatrics and Adult Development, Box 1070, The Mount Sinai School of Medicine, New York, NY 10029.

REFERENCES