

ARTICLES

Delirium in Hospitalized Older Patients With Cancer

Stewart M. Bond, RN, MSN, AOCN®, Virginia J. Neelon, RN, PhD, and Michael J. Belyea, PhD

Purpose/Objectives: To examine key aspects of delirium in a sample of hospitalized older patients with cancer.

Design: Secondary analysis of data from studies on acute confusion in hospitalized older adults.

Setting: Tertiary teaching hospital in the southeastern United States.

Sample: 76 hospitalized older patients with cancer (\bar{X} age = 74.4 years) evenly divided by gender and ethnicity and with multiple cancer diagnoses.

Methods: Data were collected during three studies of acute confusion in hospitalized older patients. Delirium was measured with the NEECHAM Confusion Scale on admission, daily during hospitalization, and at discharge. Patient characteristics and clinical risk markers were determined at admission.

Main Research Variables: Prevalent and incident delirium, etiologic risk patterns, and patient characteristics.

Findings: Delirium was noted in 43 (57%) patients; 29 (38%) were delirious on admission. Fourteen of 47 (30%) who were not delirious at admission became delirious during hospitalization. Delirium was present in 30 patients (39%) at discharge. Most delirious patients had evidence of multiple (\bar{X} = 2.3) etiologic patterns for delirium.

Conclusions: Delirium was common in this sample of hospitalized older patients with cancer. Patients with delirium were more severely ill, were more functionally impaired, and exhibited more etiologic patterns than nondelirious patients.

Implications for Nursing: Nurses caring for older patients with cancer should perform systematic and ongoing assessments of cognitive behavioral performance to detect delirium early. The prevention and management of delirium hinge on the identification and treatment of the multiple risk factors and etiologic mechanisms that underlie delirium. The large number of patients discharged while still delirious has significant implications for posthospital care and recovery.

Key Points . . .

- Delirium is a common and troubling symptom in hospitalized patients with cancer.
- Older patients with cancer may be at increased risk.
- Little is known about delirium in this population.
- The early identification of patients at risk, ongoing assessment of cognitive function and behavior, and treatment of underlying etiologic mechanisms are keys to the prevention and management of delirium.

Eden, Foreman, & Sisk, 1998; Schor et al., 1992), advanced illness (Francis, Martin, & Kapoor, 1990; Inouye, Viscoli, Horwitz, Hurst, & Tinetti, 1993; Rockwood, 1989), comorbidity (Andersson et al.; Eden et al.; Pompei et al., 1994; Rahkonen et al., 2001), and preexisting cognitive impairment (Duppils & Wikblad, 2000; Eden et al.; Fisher & Flowerdew, 1995; Francis et al.; Pompei et al.; Rahkonen et al.; Rockwood, 1989) increase the risk of delirium. Still, little is known about delirium in the population, but the projected aging of the overall population (with increases in cancer and in delirium) underscores the need to better understand the clinical problem.

Pathophysiologic Basis and Etiologies of Delirium in Older Patients With Cancer

Delirium in older patients with cancer is complex and has multiple etiologies, including age-related physiologic changes in the brain and other organs and associated declines in functional organ reserves (Lipowski, 1990). Engel and Romano

Delirium (also called acute confusion) is a syndrome of disordered cognition, attention, and behavior resulting from pathophysiologic disturbances of central nervous system (CNS) function. It is a common and serious problem in hospitalized older adults and has been detected in 14%–55% of hospitalized patients with cancer (Folstein, Fetting, Lobo, Niaz, & Capozzoli, 1984; Levine, Silberfarb, & Lipowski, 1978; Tuma & DeAngelis, 2000). Delirium is the second most common psychiatric diagnosis in patients with cancer (Massie & Holland, 1987); as many as 90% of patients with advanced cancer exhibit delirium in the final weeks of life (Bruera et al., 1992; Lawlor et al., 2000; Massie, Holland, & Glass, 1983; Minagawa, Uchitomi, Yamawaki, & Ishitani, 1996; Morita, Tei, Tsunoda, Inoue, & Chihara, 2001).

Sixty percent of all cancers and 70% of cancer deaths occur in older adults (Yancik & Ries, 2000). Older patients with cancer are particularly susceptible to delirium because age (Andersson, Gustafson, & Hallberg, 2001; Duppils & Wikblad, 2000;

Stewart M. Bond, RN, MSN, AOCN®, is a doctoral candidate and a John A. Hartford Foundation Building Academic Geriatric Nursing Capacity Scholar and Virginia J. Neelon, RN, PhD, is an associate professor and the director of the Biobehavioral Laboratory, both in the School of Nursing at the University of North Carolina at Chapel Hill; and Michael J. Belyea, PhD, is a research professor in the College of Nursing and Health Care Innovation at Arizona State University in Phoenix. This work was supported, in part, by a grant from the National Institute for Nursing Research T32 NR07091: Interventions to Prevent and Manage Chronic Illness, the John A. Hartford Foundation Building Academic Geriatric Nursing Capacity Scholarship Program, and a doctoral scholarship in cancer nursing (#DSCN-01-203-03-SCN) from the American Cancer Society. (Submitted January 2006. Accepted for publication March 9, 2006.)

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(1959) characterized delirium as a “syndrome of cerebral insufficiency” representing a global failure of brain metabolism, but several more recent reviews (Flacker & Lipsitz, 1999; Trzepacz, 1999; van der Mast, 1998) have suggested that delirium arises from dysfunction of specific cortical and subcortical brain regions and from alterations in interacting neurotransmitter systems, rather than from global metabolic failure. Electrophysiologic, neuroimaging, and neurotransmitter studies (Gaudreau & Gagnon, 2005; Jacobson & Jerrier, 2000; Koponen, 1999; Reischies et al., 2005) have supported this new understanding of delirium. Reischies et al. found that patients who became delirious after electroconvulsive therapy had excess theta activity in the anterior cingulate gyrus and the right frontotemporal brain, areas associated with attention and awareness. Medications that alter cholinergic, dopaminergic, serotonergic, glutamatergic, and gamma-aminobutyric acid (GABA) pathways can cause delirium (Gaudreau & Gagnon; Karlsson, 1999). Gaudreau and Gagnon proposed that disturbed cholinergic, dopaminergic, glutamatergic, and GABA-ergic neurotransmitter systems induce a transitory psychosis (delirium). Abnormal cortisol (Flacker & Lipsitz; van der Mast) and cytokine levels (Broadhurst & Wilson, 2001; Dunlop & Campbell, 2000; Flacker & Lipsitz; van der Mast) also may be involved in the pathogenesis of delirium.

Delirium in patients with cancer is related to the direct and indirect effects of cancer (and cancer treatment) on the CNS (Fann & Sullivan, 2003; Meyers, 2000). Delirium also may be caused by factors unrelated to cancer such as prior stroke, preexisting dementia, or other comorbid processes common in older adults. Primary and metastatic brain tumors can compress the brain and its blood vessels, obstructing the flow of blood and cerebral spinal fluid, thus causing delirium and other neurologic symptoms. Encephalopathy following therapeutic radiation of the brain can occur within hours of the first treatment or be delayed by weeks, months, or years after treatment (Keime-Guibert, Napolitano, & Delattre, 1998; Moretti, Torre, Antonello, & Cazzato, 2001). Biotherapies such as interleukin-2 and interferon- α can produce acute confusion or other disorders such as depression and mania (Forman, 1994; Raison, Demetrashvili, Capuron, & Miller, 2005).

Metabolic encephalopathies are common in patients with cancer, particularly those with primary or metastatic liver involvement and those with underlying liver or renal dysfunction. Wernicke encephalopathy (thiamine deficiency) is a reversible cause of delirium in malnourished patients with cancer (Onishi et al., 2004; Turner, Alley, & Sharpless, 2004). Hypoxia, ischemia, infection, and electrolyte abnormalities (Morita et al., 2001; Tuma & DeAngelis, 2000), as well as paraneoplastic syndromes, resulting from tumor elaboration of proinflammatory cytokines or antineuronal autoantibodies or other substances, also can induce delirium in patients with cancer (Kung, Mueller, Geda, & Krahn, 2002; Munshi et al., 2005; Young, 1998; Zeimer, 2000).

Medications used to treat cancer or ameliorate symptoms can cause delirium. They include anticholinergics such as diphenhydramine (Tune & Egeli, 1999), chemotherapeutic and biologic agents (Lerner, Stoudemire, & Rosenstein, 1999; Young, 1998), opioids (Lawlor, 2002), corticosteroids (Jenkins & Bruera, 2000; Stiefel, Breitbart, & Holland, 1989), and nonopioid psychoactive medications, including benzodiazepines, hypnotics, and antiemetics (Lawlor et al., 2000).

Reversibility of Delirium

Delirium is potentially reversible if underlying pathophysiologic disturbances and etiologic factors are addressed. Patient factors (e.g., age, overall physical condition, baseline cognitive function), recognition and treatment of delirium in an appropriate and timely fashion, and the underlying cause determine the reversibility of delirium (Lipowski, 1990). Interventions such as risk-factor identification and treatment and routine monitoring of cognitive function can prevent delirium or promote its early treatment in hospitalized medical and surgical patients (Inouye et al., 1999; Milisen, Lemiengre, Braes, & Foreman, 2005; Neelon, Champagne, Moore, et al., 1992). Although difficult, the successful prevention and management of delirium in older patients with cancer are possible and can significantly enhance the quality of their care and improve their quality of life.

Impact of Delirium on Older Patients With Cancer

Delirium is distressing for patients, their families, and professional caregivers (Brajtman, 2003; Breitbart, Gibson, & Tremblay, 2002; Hallberg, 1999; Hull, 1990; Morita, Hirai, Sakaguchi, Tsuneto, & Shima, 2004; Schofield, 1997). Delirium negatively affects quality of life and care by impairing patient-family communication and hindering treatment decision making (Breitbart, Bruera, Chochinov, & Lynch, 1995). It impedes the recognition and management of other symptoms (Feldt, Ryden, & Miles, 1998; Miller, Moore, Schofield, & Ng'andu, 1996) and forecasts shortened survival (Caraceni et al., 2000; Lawlor et al., 2000; Morita, Tsunoda, Inoue, & Chihara, 1999). Delirium may abrogate patients' desire to remain at home during their final days (Fainsinger, Demoissac, Cole, Mead-Wood, & Lee, 2000), instead leading to hospitalization or institutional placement (Berkman, Stolberg, Calhoun, Parker, & Stearns, 1983).

In 1988, Welch-McCaffrey and Dodge identified delirium as a problem for older patients with cancer. Since then, four additional review papers (Boyle, 2006; Milisen, Steeman, & Foreman, 2004; Roth & Modi, 2003; Weinrich & Sarna, 1994) have highlighted the problem. The reviews mostly extrapolated from clinical observations, general studies of delirium in hospitalized older adults, studies of hospitalized patients with cancer, and studies of advanced cancer. Delirium, per se, has not been studied systematically in older adults with cancer. Indeed, as Boyle stated, “Research on delirium in older patients with cancer is nonexistent” (p. 71).

The Current Study

The present study addresses the empirical gap in knowledge about delirium in older adults with cancer by examining key aspects in a sample of hospitalized older patients with cancer. Specific aims of the study were to (a) determine the prevalence and incidence of delirium in such a population, (b) examine the nature and course of delirium in the cohort, (c) identify patterns of etiologic risk, and (d) compare characteristics and risk factors in patients with and without delirium.

Methods

This report is a secondary analysis of data collected in three studies looking at acute confusion in hospitalized older adults (Neelon & Champagne, n.d.). The first study identified factors

associated with delirium and patterns of delirium development in a sample of 158 hospitalized older patients with medical problems. Written informed consent was obtained from patients or family surrogates. The second study determined the incidence of delirium in a sample of 168 hospitalized older patients with medical problems. The third study tested pattern-specific interventions in 301 older adults with medical problems admitted to an intervention unit or a control unit. The second and third studies were conducted in conjunction with a program to incorporate regular cognitive and functional assessments into usual nursing care. All studies were approved by the institutional review board.

Sample

The analysis sample consisted of 76 hospitalized older subjects in whom cancer was a primary or secondary admitting diagnosis; they comprised a subset of the 627 patients enrolled in the three parent studies. All subjects were admitted to general medical units in a tertiary teaching hospital in the southeastern United States, were older than 65 years, and were able to speak English. Patients with a primary psychiatric diagnosis and those admitted solely for terminal care were excluded from the parent studies.

Main Research Variables and Measures

Delirium: The **NEECHAM Confusion Scale** (Neelon, Champagne, Carlson, & Funk, 1996) was used to assess delirium in all subjects at admission, daily during hospitalization, and at discharge. The NEECHAM scale provides rapid, unobtrusive bedside assessment of cognitive function and behavioral performance, permitting early detection of delirium and monitoring response to treatment; nurses can obtain the necessary data while performing routine patient assessments. The NEECHAM scale consists of nine items organized into three subscales related to processing, behavior, and physiologic control. Item-specific scores are summed to determine a score for each subscale and an overall score that ranges from 0–30. Higher scores indicate better cognitive and behavioral function.

The NEECHAM scale has been used to assess delirium in hospitalized older adults and nursing home residents. In older hospitalized patients with acute illnesses, the alpha coefficient was 0.90, and interrater reliability was 0.91. Concurrent validity was established (Neelon, Champagne, et al., 1996) by correlating NEECHAM scores to other measurements of cognitive function and delirium, including the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) ($r = 0.87$) and the sum of Diagnostic and Statistical Manual III-Revised (DSM-III-R) criteria positive items (American Psychiatric Association [APA], 1987) ($r = -0.91$). The NEECHAM exhibited excellent sensitivity (0.95) and acceptable specificity (0.78) when compared with the DSM-III criteria for delirium (APA, 1980), the MMSE, and report of mental status problem (Neelon, Champagne, McConnell, Carlson, & Funk, 1992).

NEECHAM scores distinguish four categories of confusion (Neelon, Champagne, et al., 1996): Scores equal to or greater than 27 indicate normal function and low risk for delirium; scores of 25–26 or greater than 26 but with a concurrent risk marker (respiratory rate greater than 23 breaths per minute, use of supplementary oxygen, oxygen saturation less than 91%, serum albumin less than 3.0, or report of mental status change) indicate risk for confusion; scores of 20–24 indicate mild (or early) delirium; scores less than 20 indicate moderate to severe

delirium. Subjects with NEECHAM scores less than 20 usually satisfy DSM-III and DSM-III-R criteria for delirium. Neelon, Champagne, McConnell, et al. (1992) found that 78% of patients with NEECHAM scores less than 20 met at least six of eight DSM-III criteria. In another analysis (Neelon, Champagne, et al., 1996), 96% of patients with NEECHAM scores less than 20 on admission had diagnosable delirium by DSM-III-R criteria.

Clinical markers and etiologic risk patterns: Several clinical variables, including laboratory tests, were used to establish patterns that predict an increased risk of developing delirium. Cluster analysis and likelihood ratios demonstrated five such patterns: metabolic-nutritional, hypoxic, metabolic-toxic, orthostatic-dehydration, and chronic cognitive impairment (Belyea, Champagne, Ng'andu, & Neelon, 1992; Neelon, Champagne, Moore, et al., 1992). Figure 1 lists the clinical markers associated with each pattern. In this study, patients were classified as exhibiting a pattern if any one of the appropriate clinical risk markers was present (except as noted for chronic cognitive impairment).

Patient characteristics: Data regarding patient age, gender, ethnicity, severity of illness, and functional status were collected at the time of admission. Severity of illness was measured with the **Acute Physiology and Chronic Health Evaluation (APACHE II) scale** (Knaus, Draper, Wagner, & Zimmerman, 1985); scores range from 0–71, with higher scores indicating greater severity of illness. Functional status was measured by the Instrumental Activities of Daily Living (IADL) subscale of the **Older Americans Resources Scale** (Fillenbaum, 1978); scores range from 0–14, with lower scores indicating greater functional impairment. The IADL items measured performance for the month prior to hospital-

Metabolic-Nutritional

- Body mass index < 20
- Weight loss > 5 kg or 10%
- Albumin < 3.5 g/dl
- Lymphocyte count < 1,000/cubic mm

Hypoxic

- On oxygen
- O₂ saturation < 91%
- Hemoglobin < 9.0 g/dl

Metabolic-Toxic

- Albumin < 3.0 g/dl
- Creatinine > 2.0 mg/dl
- Diagnosis of liver or renal failure

Orthostatic-Dehydration

- Diagnosis of dehydration
- Presence of orthostatic symptoms
- Blood urea nitrogen/creatinine ratio > 20

Chronic Cognitive Impairment

- Report of mental status problems and inability to take medications without assistance
 - Diagnosis of dementia
-

Figure 1. Clinical Markers and Etiologic Risk Patterns

Note. From "Acute Confusion in Hospitalized Elders: Patterns—Interventions," by V.J. Neelon & M.T. Champagne, n.d. Funded by the National Institutes of Health, National Center for Nursing Research, 1988–1993 (NR01339-05). Adapted with permission.

ization to determine each patient’s baseline of function before the acute episode or hospital admission. Length of stay was measured in days from admission to discharge.

Data Analysis

Descriptive statistics were used to characterize clinical features, the prevalence and incidence of delirium, and etiologic patterns. The NEECHAM score on admission, the lowest NEECHAM score during hospitalization, and the NEECHAM score at discharge were used to examine the overall course of delirium during hospitalization (a score equal to or less than 24 indicated the presence of delirium). Prevalent delirium was defined as that present on admission and incident delirium as that which developed at any time thereafter if not present at admission. Chi-square and t tests were used to compare patient characteristics and etiologic patterns in patients with and without delirium.

Results

Patient Characteristics

Characteristics of the 76 hospitalized older patients with cancer are summarized in Table 1. The mean age was 74.4 years. Patients were divided evenly by gender and ethnicity: 54% were men, and 54% were white (32 of 35 nonwhite patients were African American). The sample had 17 different cancer diagnoses, the most common being multiple myeloma (17%), lung cancer (15%), prostate cancer (15%), breast cancer (11%), and lymphoma (8%). The mean educational level was 9.9 years. The mean APACHE II score of 14.9 indicated moderate illness severity, and the mean IADL score of 8.5 reflected a moderate degree of functional impairment. The average length of hospital stay was 9.8 days.

Table 1. Patient Characteristics

Variable	\bar{X}	SD	Range
Age (years)	74.4	7.29	65–96
Education (years)	9.9	4.69	0–20
APACHE II	14.9	4.88	6–30
IADLs	8.5	4.65	0–14
Length of stay (days)	9.8	8.67	2–43
Variable	n	%	
Gender			
Male	41	54	
Female	35	46	
Ethnicity			
Caucasian	41	54	
African American	32	42	
Other	3	4	
Cancer diagnosis			
Multiple myeloma	13	17	
Lung	11	15	
Prostate	11	15	
Breast	8	11	
Lymphoma	6	8	
Other	27	36	

N = 76
APACHE II—Acute Physiology and Chronic Health Evaluation; IADLs—Instrumental Activities of Daily Living
Note. Because of rounding, percentages may not total 100.

Table 2. Frequency of Delirium at Admission by NEECHAM Category

NEECHAM Category	n	%
Severe delirium	8	11
Mild delirium	21	28
At risk	29	38
Low risk	18	24

N = 76
Note. Because of rounding, percentages may not total 100.

Prevalence and Incidence of Delirium

Table 2 shows that delirium of some degree was present at admission in 29 patients (38%), in 21 (72%) it was mild (NEECHAM score of 20–24), and in 8 (28%) it was severe (NEECHAM score of < 20). Of the remaining 47 patients, 29 (38%) were considered at risk for delirium at admission (NEECHAM score of 25–26 or > 26 but with risk marker), and 18 (24%) were considered not delirious (NEECHAM score of ≥ 27). Fourteen of the 47 patients not delirious at admission developed delirium at some later point, an incidence rate of 30%; in those 14 patients, delirium was mild in 8 and severe in 6. The cumulative rate of delirium (prevalent plus incident cases) during the entire hospitalization period was 57%.

Nature and Course of Delirium

Figure 2 depicts the course of delirium during hospitalization as represented by changes in mean NEECHAM scores for patients in each NEECHAM category on admission. The mean NEECHAM scores for each category worsened during hospitalization but improved at discharge. In other words, in patients with delirium and in those at risk on admission, delirium worsened during hospitalization but improved prior to discharge. Even in patients with no delirium at admission, mean NEECHAM scores dropped slightly during hospitalization. NEECHAM scores were relatively unstable in patients admitted with mild delirium and those at risk for delirium. During hospitalization, 15 of the 21 patients admitted with mild delirium exhibited a clinically significant change of greater than three points in their NEECHAM scores that resulted in a change in delirium category (worsened in 8 and improved in 7). Two additional patients had a one- or two-point change in NEECHAM score that resulted in a change in delirium category (worsened in 1 and improved in 1). Of the 29 at-risk patients, 14 (48%) had a clinically significant change in level of delirium; 11 developed mild (in 5) or severe (in 6) delirium, and 3 moved from the at-risk category to the low-risk category. Delirium was present in 30 of 76 (39%) patients at discharge; in 18, it was mild, and in 12 severe. Twenty-one of 29 patients (72%) who were delirious on admission were still delirious at discharge; in the 8 with severe delirium at admission, delirium improved in 3 but remained severe in 5. In addition, in 6 of the 21 patients with mild delirium and in 1 of the 29 at risk for delirium at admission, delirium was severe at discharge. Delirium resolved prior to discharge in 13 of the 43 patients (30%) who were delirious at some point during hospitalization.

Etiologic Patterns

All patients were classified as having etiologic risk patterns based on clinical markers at admission. Most patients

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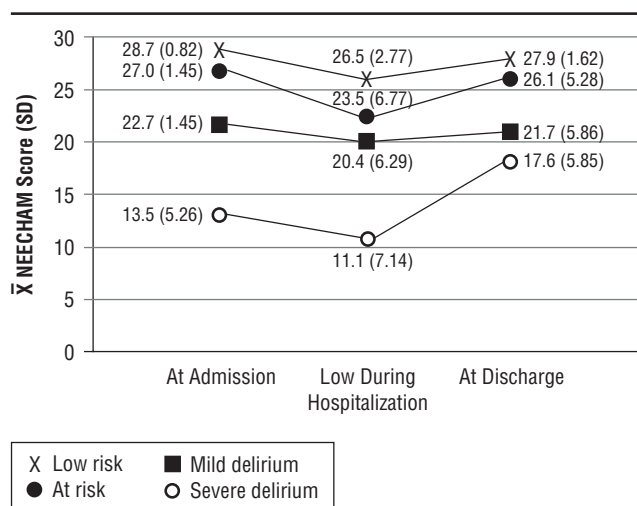


Figure 2. Mean NEECHAM Scores Across Hospitalization by NEECHAM Category

exhibited markers compatible with more than one etiologic risk pattern ($\bar{X} = 2.3$, $SD = 1.07$, range = 0–5). The most common pattern in patients with and without delirium was the metabolic-nutritional (91%), followed by hypoxic (62%), metabolic-toxic (40%), orthostatic-dehydration (36%), and chronic cognitive impairment (7%). However, patients with hypoxic risk-pattern markers were more likely to have or develop delirium ($\chi^2 = 4.410$, $p = 0.036$) (see Table 3).

Only five (7%) of the hospitalized older patients with cancer had chronic cognitive impairment. Of those five, three had severe delirium on admission, one had mild delirium, and the other was at risk. All five had severe delirium at some point during hospitalization, and all were delirious at discharge. Among those patients, severe delirium persisted in two and improved in three.

Characteristics of Patients With and Without Delirium

Table 4 compares the characteristics of patients who had no delirium to those who were delirious at some time during hospitalization. Patients with delirium were more severely ill (\bar{X} APACHE II score = 15.9 versus 13.5, $p = 0.032$) and had a greater level of functional impairment prior to hospitalization (\bar{X} IADL score = 6.8 versus 10.7, $p < 0.001$). Patients with delirium exhibited more risk markers ($\bar{X} = 2.6$ versus 2.1, $p = 0.045$). Although not statistically significant, hospitalization was longer ($\bar{X} = 11.5$ versus 7.7 days, $p = 0.056$) in patients with delirium compared to those without.

Discussion

Delirium was common in the sample of hospitalized older patients with cancer. The prevalence and incidence of delirium, 38% and 30%, respectively, are consistent with other studies of hospitalized patients with cancer (Tuma & DeAngelis, 2000). Ljubicavljec and Kelly (2003) found a lower incidence of delirium (18%), but their patients were younger (\bar{X} age = 53.4 years).

Subsyndromal delirium—symptoms that do not meet psychiatric diagnostic criteria for the full syndrome (APA,

2000)—is common in hospitalized older patients (Cole, McCusker, Dendukuri, & Han, 2003; Levkoff et al., 1996). The authors found that 21 patients had mild delirium (NEECHAM score of 20–24) at admission. Those patients likely had subsyndromal delirium, which may be a precursor to more severe delirium (Duppils & Wikblad, 2004; Lipowski, 1990). Delirium fluctuated in those patients; at discharge, it had resolved in seven, was persistent but mild in eight, and had become persistently severe in six. Such patients may benefit most from early recognition and intervention.

The NEECHAM scores of patients with mild delirium and those at risk for delirium exhibited more instability during hospitalization; 71% of patients with mild delirium and 48% of those at risk on admission had clinically significant changes (≥ 3 points) in their NEECHAM scores during hospitalization. The findings may reflect a measurement phenomenon because patients scoring in the mid-range of the scale can improve or worsen in their scores, but they also may reflect the fact that mild delirium and delirium risk may resolve if recognized and treated early—or worsen if not identified.

The older patients with cancer in the study had a mean APACHE II score of 14.9 ± 4.88 , a level of illness severity typical of older medical inpatients (13.8 ± 3.2 to 15.4 ± 3.5) (Inouye & Charpentier, 1996; Inouye et al., 1993) and of older patients in a medical intensive care unit (13.2 ± 5.2) (Bo et al., 2003). The patients in the current sample were admitted for cancer treatment, complications associated with cancer or its treatment, or other medical conditions. The mean APACHE II score in the sample indicates a clinically significant level of illness severity.

The researchers found that patients with delirium tended to be more severely ill and to have greater functional impairment than those without delirium. Both factors have been associated with delirium in general hospital inpatients (Francis et al., 1990; Inouye et al., 1993; Rockwood, 1989), but neither has been associated with delirium in older patients with cancer. The current findings suggest that both are associated with delirium in older patients with cancer. Ljubicavljec and Kelly (2003) found that markers of illness severity such as low albumin level or bone metastases were associated with delirium in a younger sample of hospitalized patients with cancer.

Consistent with the multifactorial etiology of delirium, the patients in the current study exhibited multiple patterns of clinical risk markers, particularly the metabolic-nutritional, hypoxic, and orthostatic-dehydration patterns. Most patients

Table 3. Etiologic Patterns in Patients With and Without Delirium

Etiologic Pattern	Patients With Delirium (N = 43)		Patients Without Delirium (N = 33)		p
	n	%	n	%	
Metabolic-nutritional	41	95	28	85	0.117
Hypoxic	31	72	16	49	0.036
Metabolic-toxic	18	42	12	36	0.627
Orthostatic-dehydration	15	35	12	36	0.894
Chronic cognitive impairment	5	12	—	—	—

Table 4. Characteristics of Patients With and Without Delirium

Variable	Patients With Delirium (N = 43)		Patients Without Delirium (N = 33)		p
	\bar{X}	SD	\bar{X}	SD	
Age	74.6	7.71	74.1	6.82	0.790
Education	9.9	5.02	10.1	4.35	0.864
APACHE II	15.9	5.24	13.5	4.02	0.032
IADLs	6.8	4.75	10.7	3.47	0.000
Length of stay	11.5	9.66	7.7	6.70	0.056
Etiologic patterns	2.6	1.05	2.1	1.06	0.045

Variable	Patients With Delirium		Patients Without Delirium		p
	n	%	n	%	
Gender					0.927
Male	23	54	18	55	
Female	20	47	15	45	
Ethnicity					0.138
White	20	47	21	64	
Nonwhite	23	54	12	36	

APACHE II—Acute Physiology and Chronic Health Evaluation; IADLs—Instrumental Activities of Daily Living
Note. Because of rounding, percentages may not total 100.

demonstrated metabolic-nutritional markers, as might be expected in older patients with cancer; almost two-thirds also had hypoxic markers that significantly increased the risk of developing delirium compared to those without hypoxic markers. Other studies of delirium in hospitalized patients with cancer (Tuma & DeAngelis, 2000) and in patients with advanced cancer (de Stoutz, Tapper, & Fainsinger, 1995; Lawlor et al., 2000; Morita et al., 2001) have identified hypoxia as a cause of delirium, which is important because hypoxia is potentially treatable. Neelon, Ng'andu, et al. (1996) found that delirium resolved within 24 hours in a significant number of hypoxic patients treated to improve oxygenation. Aakerlund and Rosenberg (1994) found that hypoxemia was the sole cause of postoperative delirium in five patients undergoing thoracic surgery and that delirium resolved in all after treatment with supplemental oxygen. De Stoutz et al. reported that delirium resolved in four terminally ill patients with cancer in whom hypoxia was treated.

On the other hand, Lawlor et al. (2000) and Morita et al. (2001) found hypoxia to be the primary cause of delirium in patients with advanced cancer, but both studies found that hypoxia was associated with nonreversibility of delirium. The underlying cause of hypoxia and whether it can be alleviated may determine whether delirium resolves. In the study by Lawlor et al., for example, hypoxia was ascribed primarily to pulmonary cancer and respiratory infection.

Preexisting cognitive impairment significantly increases the risk of developing delirium (Duppils & Wikblad, 2000; Eden et al., 1998; Fisher & Flowerdew, 1995; Francis et al., 1990; Galanakis, Bickel, Grading, von Gumpfenberg, & Forstl, 2001; Inouye et al., 1993; Pompei et al., 1994; Rahkonen et al., 2001; Rockwood, 1989; Schor et al., 1992). The prevalence of delirium in hospitalized and community-dwelling

older people with dementia ranges from 22%–89% (Fick, Agostini, & Inouye, 2002). Ljubicavljovic and Kelly (2003) found that impaired cognitive function was a risk factor for delirium in hospitalized patients with cancer. In the current cohort, only five (7%) patients had chronic cognitive impairment, and all of them experienced severe delirium at some point during hospitalization. However, delirium improved in three of the five patients by discharge, suggesting that delirium is potentially reversible even in patients with dementia.

In the current study, patients with delirium exhibited a greater number of etiologic patterns than those without delirium. Inouye et al. (1993) found that delirium risk increased progressively as risk factors multiplied: Cumulative rate of delirium in patients with no risk factors was 9%; with one or two risk factors, 23%; and with three or four factors, 83%. The contribution of specific combinations or clusters of patterns was not evaluated in the current study but may play a key role in determining delirium risk.

Delirium was present in 30 of 76 patients at discharge; in 18 of the 30 (60%), it was mild; and in 12 (40%), severe. A large majority (72%) of those who were delirious on admission had persistent delirium at discharge. Two possible explanations exist. First, delirium often is underrecognized and undertreated (Breitbart et al., 1995; Stiefel, Kornblith, & Holland, 1990). Second, delirium may be less transient than previously believed. Studies of hospitalized older medical-surgical patients have found that delirium symptoms often were present at discharge and could persist for six months or longer (Levkoff et al., 1992; Rockwood, 1993; Rockwood et al., 1999).

Patients with delirium during hospitalization are more likely to be discharged to institutional settings (Inouye, Rushing, Foreman, Palmer, & Pompei, 1998), are more likely to experience impaired functional recovery (Andrew, Freter, & Rockwood, 2005; Marcantonio, Flacker, Michaels, & Resnick, 2000), and are at risk for future loss of physical and cognitive function (Francis & Kapoor, 1992; Murray et al., 1993; Rockwood et al., 1999), as well as increased posthospital mortality (Curyto et al., 2001; Francis & Kapoor; Rockwood et al.). Persistent delirium also may be a risk factor for rehospitalization. Marcantonio et al. (2005) found that patients with delirium on entry to a postacute care facility were more than twice as likely to be rehospitalized within 30 days. Similar outcomes can be anticipated in hospitalized older patients with cancer who are delirious.

The high prevalence of delirium at discharge places added burden on family caregivers. Naylor, Stephens, Bowles, and Bixby (2005) found that cognitive impairment (delirium, dementia, or both) meant that patients and their family caregivers had multiple unmet needs in the weeks following hospital discharge. Delirium distresses family caregivers (Brajtman, 2003; Breitbart et al., 2002; Morita et al., 2004), in part because patients with delirium need more assistance with self-care and require close monitoring to prevent injury.

Although it did not quite reach statistical significance in the current study, length of hospital stay was longer for patients with delirium. Other researchers have noted this as well. Ljubicavljovic and Kelly (2003) found that hospitalization was longer for delirious patients with cancer (8.8 days compared to 4.5 days for patients without delirium), and Gagnon, Gaudreau, Harel, and Tremblay (2004) found that delirious patients with cancer stayed twice as long as nondelirious patients (26 days versus 13 days).

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Limitations

This study is one of the first to focus on delirium in a sample of hospitalized older patients with cancer. However, the findings should be interpreted in light of several methodologic and analytical limitations. In the analysis, the researchers used the NEECHAM score at admission, the lowest NEECHAM score during hospitalization, and the NEECHAM score at discharge to describe the course of delirium. The use of only three time points does not provide a full picture of the day-to-day course of delirium during hospitalization, nor does it capture the occurrence of multiple episodes of delirium in individual patients.

The small sample of older patients with cancer was very heterogeneous. The patients had a wide range of cancer diagnoses and cancer stages. Patients were at different points along their disease trajectories and were receiving a variety of treatments. Some were hospitalized for cancer treatment, others for complications associated with cancer or its treatment, and others for acute complications associated with comorbid medical conditions. The researchers did not examine the effects of other diseases or various treatments.

The older patients with cancer in the study exhibited multiple etiologic patterns of delirium risk. However, the researchers did not examine the effects of combinations of patterns or pattern clusters on the development of delirium. Nor did they examine other factors commonly associated with delirium in patients with cancer (for example, medication use or stage of disease). In addition, specific strategies used to treat and manage delirium during hospitalization were not recorded.

Conclusions

The findings from this study highlight the magnitude of delirium in hospitalized older patients with cancer and underscore the need for a better understanding that would enhance the prevention and management of delirium in that population. The findings provide directions for improvements in nursing care of older patients with cancer and for future research.

Early identification and intervention can shorten the course and decrease the severity of delirium (Milisen et al., 2005;

Olofsson, Weitzner, Valentine, Baile, & Meyers, 1996). Nurses play a key role in the early identification of delirium, but they often do not recognize it, particularly mild delirium or hypoactive presentations (Inouye, Foreman, Mion, Katz, & Cooney, 2001; Neelon, Champagne, McConnell, et al., 1992). Recognition of delirium by oncology nurses may be enhanced by education about delirium and its presentations and about delirium risk factors in older patients with cancer. Screening for delirium risk factors and etiologic patterns can facilitate targeted use of intervention strategies. Ongoing assessment of cognitive function and behavioral performance using bedside screening instruments such as the NEECHAM scale can enhance the recognition and identification of mild or subsyndromal delirium and promote early intervention that potentially can prevent the development of more severe delirium.

Future research is needed to clarify the risk factors for and etiologic mechanisms of delirium in older patients with cancer and to describe the clinical presentation and characteristics in specific subpopulations. In addition, research should focus on outcomes of delirium and delirium treatment in such patients. Today, most patients with cancer receive care in outpatient settings, and family caregivers are expected to monitor and manage complex symptoms at home. This study found that many hospitalized older patients with cancer were delirious at discharge, but no studies have examined the effects of delirium on care in the home setting. Researchers should examine how to help family caregivers monitor for early signs of delirium. Also needed are interventions to help family caregivers better understand delirium and to prevent and manage it at home. The successful prevention and management of delirium will improve quality of life and care and minimize distress for older patients with cancer and their families and may enhance life expectancy.

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Author Contact: Stewart M. Bond, RN, MSN, AOCN®, can be reached at bond@email.unc.edu, with copy to editor at ONFEditor@ons.org.

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