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Incidence of Delirium and Associated Mortality in Hematopoietic Stem Cell Transplantation Patients

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ABSTRACT

Delirium has been associated with a high risk of mortality in medical patients. Despite the high incidence of delirium in patients who undergo hemapoietic stem cell transplantation (HSCT), delirium as a risk factor for death has not been examined in this population. Thirty adult patients undergoing HSCT who were admitted to the University of Iowa Blood and Marrow Transplantation Program inpatient unit were assessed prospectively from 1 to 2 weeks before transplantation, throughout their inpatient stay, and at 100 days after transplantation. The Delirium Rating Scale and Memorial Delirium Assessment Scale were used twice weekly during the inpatient period to assess delirium severity and occurence. Patients' self-reports of medical history, computerized medical records, and neuropsychological and psychiatric assessments were used to identify pretransplantation risk factors. The incidence of delirium (Delirium Rating Scale score >12 or Memorial Delirium Assessment Scale score ≥8) was 43% and occurred with highest frequency in the first 2 weeks after transplantion. The presence of delirium at any point during hospitalization after transplantation and transplant type (allogeneic) were highly predictive of mortality ($p < .0005$; odds ratios, 14.0 and 14.4). In conclusion, this study highlights the importance of monitoring for delirium during the acute recovery period after transplantation and suggests that early or even prophylactic treatment for delirium should be studied. Studies to determine the factors that connect delerium soon after transplantation to mortality are highly warranted.

KEY WORDS

Delirium • Mortality • Bone marrow transplant • Cognition

INTRODUCTION

Delirium is a common medical morbidity in cancer patients, with up to 40% experiencing this alteration in consciousness [1]. The incidence is as high as 85% in patients with additional medical burden, such as late-stage and terminal cancers [2]. Unfortunately, delirium is poorly recognized in cancer patients, with as many as 66% undiagnosed [2,3]. Poor detection is probably exacerbated by the common presentation of *hypoactive* delirium in cancer patients, which is less likely to draw attention from the treatment team and family [4]. Early detection and proper treatment of delirium is critical because delirium has been associated with a significantly increased risk of mortality [3,5] and a host of other negative outcomes (eg, longer hospital stay, poorer long-term outcome) [6,7].

Previous research has identified risk factors associated with delirium in medical patients, including advanced age, cognitive impairment, illness, opioid use, and undergoing medical procedures [1,4,7-9]. In a series of the only published studies examining delirium in patients undergoing hemapoietic stem cell transplantation (HSCT), Fann and colleagues [6,10] reported very high rates of delirium (73%) in patients during the 4 weeks after HSCT. In those studies, delirium was predicted by poorer cognitive performance and metabolic abnormalities (serum urea nitrogen [BUN]) at baseline before transplantation.

Predictors of major complications and mortality in patients undergoing HSCT have been examined in several studies and multiple risk factors have been identified. Although the exact mechanisms of treat-

ment-related mortality and interrelations among risk factors are not fully understood, there is agreement that mortality is multifactorial [11]. Older age of the patient, HLA mismatch, intensive treatment regimens, total body irradiation, graft-versus-host disease prophylaxis, and allogeneic transplant type have been associated with poor outcome [11-13]. Metabolic laboratory variables, such as BUN and bilirubin levels before [13] or soon after [14] transplantation, have predicted mortality months to years after transplantation. In addition, unrelated donor status predicted mortality, but at a much weaker level. Robin et al [15] found pretransplantation and late bacterial infections, ABO blood group incompatibility, and chronic graft-versus-host disease to predict mortality. Recently, Hahn and colleagues [11] found high-intensity myeloablative therapy to predict mortality in allogeneic patients. Despite the high incidence of delirium in patients who undergo HSCT and the serious complications associated with delirium in medical patients, there are no reports of delirium associated mortality in this population. We sought to replicate and extend the work of Fann and colleagues [6] by prospectively assessing the incidence of delirium after HSCT and examining a set of a priori defined predictors of delirium from the literature and the associated risk for mortality in 30 adult patients at the University of Iowa Holden Comprehensive Cancer Center (Iowa City, Iowa).

METHODS

Patients

Patients were from the University of Iowa Blood and Marrow Transplantation Program (BMTP) and were approached for participation in the study upon their admission to the BMTP inpatient unit for an allogeneic or autologous bone marrow or peripheral blood HSCT from 2004 to 2005.

Procedures

The protocol and all study procedures were approved by the University of Iowa institutional review board. All patients provided written informed consent and were financially compensated for their participation in the study. Patients were assessed prospectively from before transplantation through 100 days after transplantation. In addition, patients are currently being followed for 1-year follow-up data. During a pretransplantation appointment, when patients were ambulatory and before beginning their pretransplantation preparative conditioning (eg, chemotherapy), they were approached by a BMTP nurse research coordinator and invited to participate in the study. Participants were contacted to set up the pretransplantation (baseline) assessment. During the baseline assessment, a comprehensive battery assessing demographic and medical information, cognitive and psychiatric functioning, and delirium was administered to the patients. Additional demographic and medical information was obtained from computerized records (eg, laboratory values including BUN, creatinine, and white blood cell count). At 5 days after transplantation, patients began a twice-per-week assessment regimen consisting of a brief cognitive functioning and delirium assessment battery. This twice-per-week assessment schedule continued for the duration of the inpatient stay until 28 days after transplantation or when the patient was discharged, whichever occurred first. Patients were assessed at 100 days after transplantation with the same cognitive and affective functioning and delirium assessment battery used at the baseline assessment. All but 3 patients had been discharged and were tested as outpatients at the 100-day follow-up. BMTP staff were notified if patients' psychiatric functioning levels at the baseline assessment were elevated. In addition, if staff noticed symptoms of delirium during a nonassessment day, the research team was notified and a visit was scheduled as soon as possible. This resulted identifying 6 additional episodes of delirium.

Measurements

Medical history and status. Patients' general and medical backgrounds were assessed by using a structured clinical interview. The clinical interview gathered the following information: demographics (age, date of birth, education, handedness, weight, current and previous employment, and marital status); history of diagnosis (including specific diagnosis and date of diagnosis); previous treatment (including date and medications/procedures); other significant medical history (eg, heart attack); family history (eg, cancer, heart disease); cognitive history (current cognitive complaints and time of onset); psychiatric history (current complaints and time of onset); and history of alcohol, drug, and/or tobacco use or abuse.

Cognitive functioning. The following neuropsychological tests were administered to assess the areas of cognition most prone to dysfunction in patients who underwent HSCT. (1) The Modified Mini-Mental State Examination is an expanded version of the Mini-Mental State Examination, with 100 points to assess global cognitive functioning [16]. (2) Trailmaking Test Parts A and B [17] are widely used standardized tests of psychomotor speed, attention, and set shifting that have been shown to be predictive of delirium in patients undergoing HSCT [6] and have strong reliability and validity [18]. (3) The Repeatable Battery for the Assessment of Neuropsychological Status [19] is a brief, individually administered battery of tests measuring attention, language, visuospatial/construc-

tional abilities, and immediate and delayed memories. (4) The Wechsler Abbreviated Scale of Intelligence [20] provides an estimate of full-scale IQ based on 2 subtests (Vocabulary and Matrix Reasoning). (5) A visual analog scale of thinking clarity consists of a 100-mm straight line with verbal descriptors and images at each end. The verbal descriptors are short phrases describing the variable being measured (eg, "clear thinking"/"trouble with thinking"). The patient draws a line to represent cognition at the time of assessment.

Psychiatric assessment. The Symptom Checklist-90-Revised [21] is a 90-item self-report symptom inventory designed to reflect patterns of current psychological symptoms. Each item is rated on a 5-point scale, from "not at all" to "extremely." The measure yields 3 global indices of distress (Global Severity Index, Positive Symptom Total, and Positive Symptom Distress Index) and 9 primary symptom dimensions (Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism). Normative data are available for gender and patient status (inpatient, outpatient, nonpatient) that results in T scores, which have a mean of 50 (SD, 10). Visual analog scales of pain and mood were also administered.

Delirium assessment. The Delirium Rating Scale (DRS) [22] is a 10-item clinician rating scale of delirium severity based on all available information from patient interview, family, and nurses' reports, cognitive tests, and medical reports measured over a 24-hour period. The maximum possible score is 32, with higher scores being more indicative of delirium. A DRS score >12 was used as a cutoff for delirium.

The Memorial Delirium Assessment Scale (MDAS) [23] is a 10-item clinician rating scale of delirium presence and severity and can be administered multiple times in 1 day. The MDAS has been validated against many commonly used delirium assessment measurements [24] and in patient populations with malignant disease [25]. Items on the MDAS range from 0 to 3, depending on severity and frequency. A MDAS score ≥8 was used as a cutoff for delirium, with higher scores being more indicative of delirium.

Statistical Analyses

Patients were coded as having delirium if they exceeded the cutoff value on the DRS or MDAS at any point after transplantation. Univariate logistic regression was used to predict which patients experienced delirium from cognitive, psychiatric, and medical laboratory variables at baseline. Due to a small absolute number of deaths, exact logistic regression [26] was conducted to examine predictors of mortality.

RESULTS

Patient Characteristics

Thirty-two patients who were admitted to the University of Iowa BMTP for HSCT consented to participate in the study. Two patients who completed the baseline assessment did not proceed to a HSCT and therefore did not complete testing after transplantation. These patients were excluded from the analyses. The remaining 30 patients completed 2 to 8 acute-phase assessments after transplantation (mean, 4.8; SD, 1.7). At the time of assessment 100 days after transplantation, 6 patients were deceased and 1 declined to participate. One additional patient died at day 369 after transplantation and was included in the analysis.

An equal number of patients received autologous (n = 15) and allogeneic (n = 15) transplants. Most patients had lymphomas or leukemias (67%). Patients who underwent an autologous HSCT received high-dose, multiagent chemotherapy for myeloablative therapy. Allogeneic HSCT patients received mostly total body irradiation and high-dose chemotherapy or Busulfan-based high-dose chemotherapy. One patient previously underwent allogeneic HSCT and 1 patient previously underwent autologous HSCT. Patient characteristics are listed in Table 1.

Descriptive Delirium Results

The number of patients who exceeded the cutoff for delirium on either scale at any point during the acute phase after transplantation was 13, or a cumulative incidence of 43%. The highest prevalence of delirium was at visit 3 (28%), or approximately 12 days after transplantation. As shown in Figure 1, delirium occurred most frequently in the first and second weeks after HSCT. The average duration of delirium was 2.8 days (SD, 2.9; range, 1-9). All patients had only 1 period of delirium while in the hospital followed by a normal sensorium, and once delirium resolved, they did not experience another discrete delirium. However, 1 patient had a second delirium episode immediately before his death 2 months later. The mean scores on the DRS and MDAS in patients who did and did not have delirium are reported in Table 2.

Baseline risk factors for delirium were examined with univariate logistic regression. The following pretransplantation variables were significant predictors: white blood cell count, hematocrit, and platelet count (all $P < .05$). No demographic, neuropsychological, psychiatric, or delirium measurements at baseline significantly predicted delirium acutely after transplantation.

Mortality Risk Factors

The total rate of mortality during the study period was 23% (7 patients deceased by 1-year follow-up).

Table 1. *Demographic Characteristics of Patients Undergoing Hematopoietic Stem Cell Transplantation (n = 30 Patients) and Univariate Regression for Delirium Risk*

Demographics	n	Range	Delirium* (n = 13)	No Delirium* (n = 17)	Odds Ratio	P
Age (y)	30	21-64	45.7 ± 10.3	49.1 ± 11.7	0.75	NS
Education (y)	30	11-24	15.5 ± 4.2	14.6 ± 2.7	1.08	NS
Sex						
Male	20		7	13	—	NS
Female	10		6	4	2.79	NS
Diagnosis (vs other)						<.05†
Leukemia	7		4	3	0.35	
Lymphoma	13		4	9	0.11	
Myeloma	6		1	5	0.09	
Other	4		4	0	8.93	
Donor type						NS
Autologous	15		5	10		
Allogeneic	15		8	7	2.29	
Stem cell type						NS
Bone marrow	14		7	7	1.67	
Peripheral blood	16		6	10		
Myeloablative						NS
Yes	26		12	14	2.57	
No	4		1	3		

NS indicates not significant.

*Mean ± SD or number of patients.

†For diagnosis type, the test for significant differences across all types was significant at $P = .03$ by exact logistic regression. (The concomitant odds ratio estimates differ slightly from what would be obtained from the usual observed data calculation.) Follow-up pairwise analyses showed significant differences only between the "other" group and lymphoma and myeloma. In light of 100% delirium in the other group, median unbiased estimated odds ratios are presented. For parsimony, the (nonsignificant) estimated odds ratios of other pairwise comparisons are deleted.

The average number of days between onset of delirium and death was 114.8 ± 130 (range, 1-369); delirium occurred ≥55 days before death in all but 1 patient. Regression analyses described below were completed with and without this participant and results were very similar, except that odds ratios and *P* values were slightly lower, but the interpretation remained the same. Our primary analysis examined the following variables in exact logistic regression as predictors of mortality: delirium (present or absent), transplant type (autologous versus allogeneic), myeloablative therapy (present or absent), and age. As a secondary, exploratory analysis, the following variables were also examined as possible predictors of mortality: creatinine, BUN, baseline cognition (Repeatable Battery for the Assessment of Neuropsychological Status total score), IQ, age, Trail Making Test Part B, and mental status (Modified Mini-Mental State Examination). Only delirium ($P = .03$) and transplant type ($P = .01$) were significant predictors of mortality. The odds ratios were 14.0 for delirium and 14.4 for transplant type. The classification table is shown in Table 3 and yielded on overall accuracy of 90.0%. When controlling for age and myeloablative therapy, delirium and transplant type remained significant as listed above, but the odds ratios were lowered to 4.2 (delirium) and 8.6 (transplant type). The regression was also run to control for each of the 3 laboratory values that predicted delirium (Table 2). Although controlling for hematocrit did not appreciably lower the delirium odds ratio (12.5), controlling for platelets or white blood cells did decrease the delirium odds ratios to 3.0 and 5.6, respectively. Delirium was no longer statistically significant in either of these models. The loss of statistical significance can be explained by the predictive influence of these hematologic variables on the development of delirium (see above.) At the same time, the continued elevation of the estimated odds ratio suggests a unique contribution from delirium to mortality. The deaths in the

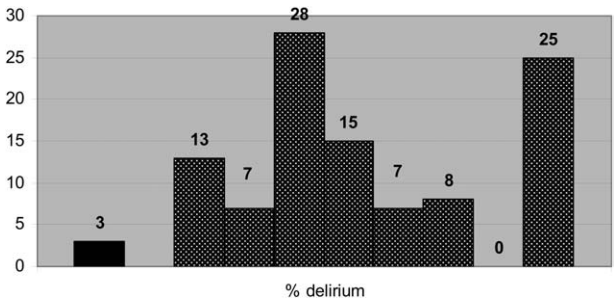

Figure 1. Percentage of patients exceeding the threshold for delirium (DRS score >12 or MDAS score ≥8) at baseline (solid bar) and during the 4 weeks after HSCT (gray bars represent visits occurring twice weekly after HSCT beginning on day 5 after transplantation).

Table 2. *Clinical, Neuropsychological, and Psychiatric Pretransplantation Risk Factors for Delirium*

Variable	Range	Patients With Delirium*	Patients Without Delirium*	Odds Ratio†	P
Metabolic					
BUN	8-36	17.8 ± 9.0	15.2 ± 4.5	3.93	NS
Creatinine	0.6-1.1	0.82 ± 0.14	0.88 ± 0.15	0.2	NS
Alkaline phosphatase	35-356	66.6 ± 19.9	165.8 ± 101.3	0.02	NS
Bilirubin	0.2-4.8	0.95 ± 1.24	0.47 ± 0.22	>99.9	NS
Hematologic					
White blood cells	0.1-56.4	3.3 ± 3.7	14.7 ± 18.3	0.13	.04
Hematocrit	21-44	28.5 ± 5.3	34.1 ± 5.7	0.36	.03
Platelets	6-294	81.6 ± 63.0	145.0 ± 82.0	0.34	.02
Electrolytes					
Sodium	133-144	138.1 ± 2.5	139.6 ± 3.0	0.54	NS
Potassium	3.3-5.1	4.0 ± 0.5	3.9 ± 0.2	1.68	NS
Magnesium	1.5-2.2	1.9 ± 0.2	1.9 ± 0.2	1.34	NS
Calcium	7.2-9.6	8.2 ± 0.8	8.9 ± 0.9	0.16	NS
Phosphorous	2.0-4.4	3.5 ± 0.8	3.5 ± 0.6	0.9	NS
Neuropsychological					
3MS total	81-100	94.1 ± 5.3	93.7 ± 4.7	1.02	NS
RBANS total	57-121	90.9 ± 12.8	93.7 ± 20.6	0.99	NS
Trails A Z score	−4.8 to 1.42	−0.5 ± 1.2	−1.2 ± 1.6	1.42	NS
Trails B Z score	−9.3 to 1.3	−1.9 ± 2.7	−1.6 ± 2.2	0.95	NS
WASI FSIQ	67-128	103.6 ± 16.1	106.8 ± 13.6	0.99	NS
Psychiatric					
SCL-90-R					
Global severity	35-80	60.2 ± 13.2	57.4 ± 9.9	1.02	NS
Depression	38-80	63.2 ± 12.7	60.8 ± 9.6	1.02	NS
Anxiety	37-80	59.1 ± 11.1	56.9 ± 10.8	1.02	NS
Pain rating	0-84	20.0 ± 27.7	13.8 ± 20.6	1.01	NS
Delirium scales					
DRS	1-7	4.2 ± 1.8	3.5 ± 1.9	1.24	NS
MDAS	0-8	3.1 ± 2.4	2.3 ± 1.9	1.19	NS

BUN indicates serum urea nitrogen; 3MS, Modified Mini-Mental State Examination; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; Trails A Z, Trailmaking Test Part A; Trails B Z, Trailmaking Test Part B; NS, not significant; WASI FSIQ, Wechsler Abbreviated Scale of Intelligence Full-Scale IQ; SCL-90-R, Symptom Checklist-90-Revised; DRS, Delirium Rating Scale; MDAS, Memorial Delirium Assessment Scale.

*Mean ± SD.

†Odds ratios are reported per SD change in predictor variable unless otherwise indicated (based on the SD of our pooled total sample).

sample were too few to disentangle the relative influence of delirium and these delirium predictors with any statistical power.

DISCUSSION

In the present sample of adult patients undergoing HSCT, the incidence of delirium was 43% and occurred most frequently in the first and second weeks after transplantation. This study addresses an important and previously unanswered question in this population by examining whether delirium predicts mortality. The presence of delirium and allogeneic transplantation strongly predicted mortality, with odds ratios of 14 and 14.4, respectively. These are large odds ratios, thus underscoring the importance of recognizing delirium immediately after transplantation. Further, although white blood cell and platelet counts were clearly associated with delirium, there is no strong evidence that these laboratory values before transplantation fully explain the relation between delirium and death. These are important open questions that can not be answered with this small dataset.

Transplantation-related mortality has been associated with several factors in previous research, including poor performance status before transplantation, active tumor at transplantation, high-dose myeloablative therapy, mismatched donor, allogeneic transplantation, and graft-versus-host disease. The present study adds to the literature by providing evidence of a strong association between delirium and mortality in patients who undergo HSCT. This link is

Table 3. *Logistic Regression Classification Table of Risk Factors for Mortality**

	Predicted Death	
Actual Death	**No**	**Yes**
No	21	2
Yes	1	6

*Model accuracy is 90.0%. Overall model was significant at $P < .0005$ (delirium, $P = .03$; transplant type, $P < .01$).

well established in other patient populations and is likely multifactorial [5]. The present study has several strengths, including the several risk factors examined based on the previous literature and the prospective study design. There were similarities and differences regarding predictors of transplantation-related mortality. Similar to other studies, we found allogeneic type transplantation to be a risk factor for mortality, but other risk factors such as age and cognitive status did not predict death. Our results did not support the findings by Hahn and coworkers [11] that myeloablative therapy is related to mortality. However, our sample is smaller and most of our patients received myeloablative conditioning.

Although delirium is clearly associated with mortality, it does not explain the underlying mechanism and is better conceptualized as an overall marker of dysfunction (ie, a "sick" brain). In cancer patients, delirium has been described as an "indirect effect" resulting from infection, metabolic abnormalities (organ failure, electrolyte imbalance), hematologic complications, medication and treatment effects (opioids, chemotherapy, radiation), and general factors such as reduced nutrition, dehydration, and poor oxygenation [1,4,27]. In medical patients, delirium is associated with cholinergic dysfunction and often treated with antipsychotics that indirectly increase acetylcholine [4]. (For a review of possible mechanisms of delirium related to cholinergic deficiency, see Kalisvaart et al [28].) The central mechanism is an alteration in acetylcholine modulation, which could result from abnormal oxygenation or nutrition. An imbalance of dopamine or norepinephrine compared with acetylcholine is also postulated to cause multisystem dysfunction.

The observations that delirium onset in our patients preceded death by ≥55 days in all but 1 patient (in that patient delirium was 1 day before death) and that markers of organ dysfunction measured at *baseline* were significant predictors of delirium support the potential for early identification of the underlying problem and possible treatment. Alternatively, the intensity of therapy that is required to control the patient's malignancy before transplantation might adversely affect not only bilirubin and albumin levels but also other critical organ system functions. This would place a subset of patients at increased risk for delirium and at disadvantage for surviving transplantation. Thus, delirium may be in some way an early surrogate marker of intolerance of the organism to the ultimate cumulative stress of transplantation. In future research with larger samples, an assessment of the causes of death may reveal what specific monitoring should be done or what interventions might be important. The finding that delirium occurred within the first or second week of transplantation and preceded death by a number of weeks certainly provides time to identify and correct medical factors that might be implicated.

Our finding of 43% delirium incidence is lower than the 73% described by Fann et al [6] in 2002. Although the exact explanation for this discrepancy is unknown, changes in conditioning regimens and treatment improvements in the 5 years since their data were collected may be responsible for our lower rates of delirium. Nevertheless, these rates of delirium are notable when compared with those in other vulnerable populations, such as the elderly (10%) [29], medical patients (20%-30%) [9,28], and cancer patients (40%) [1]. With regard to the timing of delirium, results between our study and theirs are remarkably consistent, with the 2 studies finding the highest prevalence at week 2 after transplantation. The converging results of these 2 studies underscore the importance of monitoring for delirium immediately after transplantation because nearly 50% of patients are likely to develop at least mild symptoms. The emerging evidence of the reliability of the timing of delirium may also inform preventative treatment efforts similar to those in elderly surgical patients before they undergo the procedure [28].

The timing of delirium in patients after HSCT may shed light on the underlying mechanism. For example, 2 weeks after transplantation is a common time during which patients are neutropenic and may experience fever and sepsis, which can cause delirium. In addition, other clinical variables associated with HSCT are likely to be etiologically related to delirium, such as use of opioid pain medications, medications for nausea, medications for infusion and antibiotics, disease refractoriness, and pretransplantation factors such as type and amount of chemotherapy and cranial irradiation. Delirium-associated risk of death may be context specific. For example, delirium secondary to infection is quite plausibly a greater risk factor than delirium secondary to anticholinergic medication. Alternatively, delirium, regardless of exacerbating circumstance, may represent the expression of an underlying central nervous system fragility, which is a risk factor for mortality regardless of context. Unfortunately, our sample of 13 patients with delirium is too small to address this question in a meaningful way. In either case, the present research underscores the importance of recognizing delirium as an empirical risk factor for poor outcome. Future research with larger samples is urgently needed to clarify the contextual issues outlined above.

From a monitoring perspective, it is important to note that there are subtypes of delirium. Levkoff and colleagues [30] described the traditional hyperactive delirium in addition to a hypoactive and mixed delirium. Interestingly, the highest rate of mortality in hospitalized patients was found in the hypoactive group. Fann and Sullivan [4] described the importance

of monitoring for hypoactive delirium, which is more common in cancer patients. Recently, Fann et al. [10] described the presentation of delirium from their initial sample collected between 1997 and 1999. In addition to the traditional symptoms necessary for diagnosis, the most common symptoms were sleep-wake cycle disturbance, psychomotor disturbance, and cognitive impairment. Nearly all patients with delirium had psychomotor alteration and 86% were hypoactive. They also found that fatigue, depression, and anxiety were strongly related to delirium and argued that these symptoms may also alert staff to delirium in patients with fewer typical overt symptoms. Further, because any form of delirium, but particularly hypoactive delirium, has been associated with cognitive impairments in the areas of attention and memory, staff and families need to be aware of the reduced capacity of patients to fully understand and consider treatment and research options. Decreased decisional capacity may not be obvious in a patient with hypoactive delirium. Further research is needed to evaluate patients' ability to provide appropriate consent in the first few weeks after transplantation.

Some limitations of the present study should be noted. The participants in the present sample had heterogeneous diagnoses and conditioning regimens. It will be important in future studies to examine the incidence of delirium and mortality in specific diagnostic subgroups. Our sample was also relatively small, and these results should be considered preliminary and need to be replicated. Several intriguing trends may become significant with a larger sample. For example, female gender, myeloablative therapy, and allogeneic transplantation had odds ratios >2.5 as predictors of delirium, but none were statistically significant due to limited power. Similarly, many of the clinical variables mentioned above (eg, fever, sepsis) are likely related in a causal way to delirium and, as noted earlier, the interplay between these obvious risk factors and delirium needs to be studied. Moreover, the generalizability of these findings may be limited to high functioning groups because our average patient was highly educated (2-3 years of college) and may have had greater cognitive reserve.

In conclusion, these results highlight the importance of monitoring for delirium in patients after HSCT, particularly in the first and second weeks after transplantation. Nursing staff and others with frequent patient contact are particularly well suited to detect delirium early in its course and should be aware of the high incidence immediately after transplantation and the atypical presentation of delirium symptoms (ie, fatigue, sleep cycle disturbance, reduced cognition and affect). Future research examining the clinical factors underlying delirium and whether medical intervention for delirium may decrease mortality are of critical importance.

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