Wassily Kandinsky (1866-1944). *Oriental*, 1909.

Early CSF use may be warranted in a preventive clinical intervention in older patients receiving CHOP chemotherapy for non-Hodgkin's lymphoma.

Impact of Age and Colony-Stimulating Factor Use on Hospital Length of Stay for Febrile Neutropenia in CHOP-Treated Non-Hodgkin's Lymphoma

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Background: *In intermediate-grade non-Hodgkin's lymphoma (NHL) patients, full-dose CHOP improves survival but increases myelosuppression, causing febrile neutropenia hospitalization (FNH) in 28% of patients 65 years of age or greater. Several risk factors for FNH are known, but their relationship to length of stay (LOS), an indicator of the total burden of FNH, is unclear.*

Methods: *We conducted a study to identify factors associated with the incidence, recurrence, and duration of hospitalizations for FN and to describe the frequency of administration of colony-stimulating factor (CSF) as primary and secondary prophylaxis and its association with repeated hospitalization episodes.*

Results: *Compared with patients who did not experience hospitalizations for FN, those who did were significantly older, had more comorbid conditions, were planned for standard dose intensity, and received CSF less often during the first 5 days of cycle 1 (early CSF). Overall, 73% of these hospitalizations occurred within the first 2 cycles of chemotherapy, with 56% occurring within the first cycle. Patients age ≥65 years accounted for 66% of cycle 1 FNH. Patients receiving early CSF were less likely to experience repeated hospitalizations (0% vs 12%; P<.05). Multiple regression analysis of those hospitalized found a 3.9-day longer LOS for patients age ≥65 years and a 5.13-day longer LOS for those not receiving early CSF.*

Conclusions: *Older NHL patients have a higher risk of hospitalization for FN and longer LOS. The majority of hospitalization days occur in the first 2 cycles of chemotherapy. Early CSF use is associated with decreased risk of repeated hospitalizations and shorter total LOS. Secondary CSF use is also associated with reduced risk of repeated FNH.*

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Introduction and Rationale

Despite decreases in the incidence and mortality of most cancers in the United States, non-Hodgkin's lymphoma (NHL) remains the exception.[1] An estimated 53,900 new cases and 24,400 deaths will be attributed to NHL in 2002.[2] Utilization of combination chemotherapy has increased from 23% in 1985-1988 to 51% in 1990-1993, based on the National Cancer Database series of 91,306 NHL patients.[3] In spite of the increased utilization of combination chemotherapy, which has led to lower mortality in other tumor groups, NHL remains a deadly malignancy, primarily affecting the elderly (61% were age >60 years).[3] CHOP therapy, consisting of cyclophosphamide 750 mg/m^2, doxorubicin 50 mg/m^2, and vincristine 1.4 mg/m^2 (maximum dose, 2.0 mg), all given intravenously on day 1, together with prednisone 60-100 mg/m^2 PO on days 1-5, administered every 21 days for 6-8 cycles, remains the standard curative treatment for patients with advanced-stage intermediate-grade NHL.[4-7]

Several retrospective studies have suggested that delivery of standard therapy may improve the outcome of patients with NHL; dose reductions of 20% to 30% have been associated with lower complete response rates and/or reduced survival.[8-12] Chemotherapy-induced neutropenia is an important reason for not maintaining desired dose intensity of CHOP therapy. Studies have described a large percentage of neutropenia-related deaths occurring within the first 2 cycles of therapy, serving to underscore the rapidity and severity of these events.[13,14] Patients surviving initial events may experience repeated events during their course of treatment.[15] These repeated neutropenic complications may impact the total length of stay (LOS) of febrile neutropenia hospitalization (FNH). Granulocyte colony-stimulating factor (G-CSF) administration reduces the incidence and duration of neutropenia in patients treated with chemotherapy for various malignancies.[16-19] Myelotoxicity associated with standard-dose CHOP, or regimens of similar dose-intensity, can be reduced in older adults who are supported with G-CSF.[20-23]

A description of the incidence, cycle of occurrence, recurrence, and duration of FNH, as well as the utilization of CSFs, remains unclear in community practice. In a recent retrospective study of practice patterns for intermediate- and high-grade NHL, Morrison et al[24] reported that the incidence of FN in older patients was 34%, compared with 21% in those age <65 years (P<.05). In nonclinical trial settings, therefore, the incidence of FNH for elderly NHL patients treated with CHOP chemotherapy merits consideration of primary CSF therapy.

This study examined the relationship of age and early CSF use with the incidence, recurrence, and duration of FNH, as well as described the frequency of secondary prophylaxis CSF use. This study was completed in a series of patients with intermediate-grade NHL who received initial CHOP chemotherapy. We report on the relationship of age and early CSF use with increased total LOS for FNH.

Materials and Methods

Patient Selection and Study Design

This historical case series study was conducted in 12 diverse practice settings in the United States among patients treated from 1991-1999. The goal was to collect approximately 100 patient records per site for medical review. At nine of the sites, records were identified for consecutive patients; at three of the sites, a random sample of patients was drawn from all eligible patients treated between 1993 and 1996 (identified from the statewide Surveillance, Epidemiology, and End Results program [SEER] database). Patients were eligible if they had intermediate-grade NHL, received only 1 chemotherapy regimen within 3 years of study initiation, and were at least 18 years of age. Patients were excluded if they were on a clinical trial treatment protocol or had human immunodeficiency virus (HIV) infection.

A total of 930 medical records met these criteria. The number of available cases ranged from 25 to 111 (median = 48) per site. Fifty-eight patients (6%) were excluded because of concurrent radiation therapy and/or missing clinical or chemotherapy dosing information. An additional 45 patients (5%) were excluded because CHOP therapy was discontinued and replaced with another regimen. A total of 577 patients (62%) received initial chemotherapy with CHOP, 94 (10%) received cyclophosphamide, mitoxantrone, vincristine, and prednisone (CNOP), 33 (4%) received cyclophosphamide, vincristine, and prednisone (COP/CVP), and 123 (13%) received other regimens. The analyses focused on the 577 patients who received CHOP therapy, with a subset of 126 who were hospitalized for FN, defined as having a temperature of ≥100.6ºF and an absolute neutrophil count (ANC) ≤1,000/mm^3. Data collected included patient demographics, planned and delivered chemotherapy doses, complete blood counts, use of CSF and antibiotics, radiation therapy, short-term treatment complications, and any medical record notation regarding modifications of chemotherapy or early termination of therapy.

We examined the associations between risk factors and the incidence of FNH and report the chemothera-

py cycle of the first episode of hospitalization. The associations between age, CSF administration, and the incidence of repeated hospitalizations for FN are examined, and the risk factors associated with total duration of these hospitalizations are reported.

Study Independent Variables and Operational Definitions

Pretreatment patient characteristics that were abstracted from medical records included age, gender, treatment period, comorbid conditions (including the presence of heart and renal disease), disease stage, number of extranodal sites, B symptoms, histology, and serum lactate dehydrogenase (LDH) level. Age was classified as 18 to 64 years or ≥65 years. Treatment period was defined as 1991-1994 or 1995-1999. Comorbid conditions varied from 0 to 12 and were classified according to a modified Charlson Comorbidity Index (CCI).[25-27] The CCI was divided into two ordinal categories: 0 and ≥1. In addition to the overall CCI, we separately analyzed the comorbid conditions of heart disease and renal disease to evaluate and control for the known toxicities of the chemotherapy agents. Heart disease was classified as either present (ICD9-CM codes 410, 411, 412, 414, 427, and 428) or absent. Renal disease was classified as either present (ICD9-CM codes 403, 404, 580-586, and 588) or absent. Disease stage was categorized as limited (Ann Arbor stages I or II) or advanced (Ann Arbor stages III or IV).[28] The number of extranodal sites was classified as 0-1 or ≥2. B symptoms (eg, recurrent fever, night sweats, or the loss of more than 10% of body weight) were defined as present or absent. Lymphoma histology was according to the Working Formulation.[29] Serum lactate dehydrogenase level was classified as either elevated or normal.

Treatment Characteristics and Outcomes

Early CSF Use This was defined as any administration of colony-stimulating factor during the first 5 days of the first cycle of chemotherapy. Of the 83 patients receiving early CSF, 74 (89.2%) received G-CSF.

Secondary CSF Use This was defined as any administration of CSF in patients with a prior episode of FNH. Of the 47 patients receiving secondary CSF, 43 (91.5%) received G-CSF.

Planned Average Relative Dose Intensity The average relative dose intensity (ARDI)[30] for each patient was obtained by averaging the planned relative dose intensities (RDIs) for cyclophosphamide and doxorubicin. Each RDI was calculated as the ratio of the planned first-cycle dose intensity of the drug, in mg/m^2 per week, divided by the corresponding dose intensity of the drug in a standard CHOP regimen. For example, the standard dose intensity of cyclophosphamide is 750 mg/m^2 per week. A patient planned for 500 mg/m^2 per week would have an RDI of 0.667 (500 divided by 750). If the corresponding RDI for doxorubicin for this patient were 0.833 (similarly calculated), the ARDI would be 0.75: (0.667 + 0.833) divided by 2.

Total LOS for FNH These hospitalizations were identified from medical record documentation and laboratory results. Total LOS was the sum of all days a patient was hospitalized for FN across all hospitalizations. Each hospitalization was also analyzed in order to account for repeated hospitalizations experienced by many of the patients.

Statistical Methods

Continuity-adjusted χ^2, *t* test, and Wilcoxon rank sum tests were used for bivariate comparisons. Multivariate analyses of predictors of total LOS for FNH employed ordinary least-squares regression. Additional nonparametric tests of differences in medians examined the effect of skewed LOS distribution.

Results

Description of Incidence of FNH

A total of 577 intermediate-grade NHL patients who were not on a clinical trial protocol and who had received initial CHOP chemotherapy between 1991 and 1999 were included in the initial study sample. The median patient age for the 577 patients who received CHOP chemotherapy was 65.1 years (mean = 65, range = 19-89). A total of 126 patients (21.8%) were hospitalized for FN. Of the 17 reported deaths in this group, the cause of death was attributed to chemotherapy in 1 patient, tumor in 7 patients, nonrelated to tumor or therapy in 4 patients, and unknown in 5 patients.

Patient characteristics by incidence of FNH are summarized in Table 1. Compared with the 451 patients who were not hospitalized for FN, the 126 FN patients who were hospitalized were significantly more likely to be age ≥65 years (63.5% vs 46.6%, $P<.001$) and have a CCI ≥1 (44.4% vs 29.1%, $P<.001$), renal disease (11.9% vs 3.1%, $P<.001$), heart disease (21.4% vs 12.2%, ($P=.009$), and elevated LDH (57.6% vs 42.3%, ($P=.013$). In treatment planning, patients who were hospitalized for FN were less likely to receive early CSF (8.7% vs 16.0%, ($P=.041$) and more likely to be planned to receive at least 80% ARDI (92.9% vs 85.1%, ($P=.024$).

Prophylactic CSF was administered to 83 (14.5%) of the study patients in whom the subsequent rate of FNH was only 13.3% compared with 23.3% in those did not receive prophylactic CSF ($P<.001$).

The overall incidence of FNH among older patients was 27.6% (80 of 290) compared with 16.0% (46 of 287) for younger patients ($P<.001$). Among elderly patients planned to receive standard-dose (>80% ARDI) CHOP, 75 (30.9%) of 243 patients experienced hospitalization for FN. Moreover, of the elderly patients planned to receive standard-dose CHOP (and who did not receive early CSF), 66 patients (33.3%) of 198 experienced an FNH.

Table 1. — Characteristics of 577 Patients With Intermediate-Grade NHL Receiving CHOP Chemotherapy by Hospitalization for Febrile Neutropenia

Patient Characteristics	No. of Patients With FN Hospitalizations (%)	No. of Patients Without FN Hospitalizations (%)	*P* Value
Treatment years:			
1991-1994	49 (38.9)	147 (32.6)	.187
1995-1999	77 (61.1)	304 (67.4)	
Age:			
<65	46 (36.5)	241 (53.4)	<.001
≥65	80 (63.5)	210 (46.6)	
Gender:			
Men	59 (46.8)	239 (53.0)	.221
Women	67 (53.2)	212 (47.0)	
Charlson Comorbidity Index:			
0	70 (55.6)	320 (70.9)	<.001
≥1	56 (44.4)	131 (29.1)	
Renal disease:			
Present	15 (11.9)	14 (3.1)	<.001
Absent	111 (88.1)	437 (96.9)	
Heart disease:			
Present	27 (21.4)	55 (12.2)	.009
Absent	99 (78.6)	396 (87.8)	
Ann Arbor stage:[a]			
Limited (I-II)	51 (43.6)	213 (51.8)	.116
Advanced (III-IV)	66 (56.4)	198 (48.2)	
Extranodal sites:[a]			
0-1	72 (74.2)	284 (78.9)	.326
≥2	25 (25.8)	76 (21.1)	
B symptoms:			
Present	24 (19.0)	92 (20.4)	.738
Absent	102 (81.0)	359 (79.6)	
Histology A:[a] Follicular, large cell, immunoblastic, and intermediate-grade NOS	36 (30.8)	108 (24.9)	.258
Histology B:[a] Diffuse small cleaved cell, diffuse mixed small cleaved, and large cell	17 (14.5)	87 (20.1)	
Histology C:[a] Large, cleaved, or noncleaved cell/diffuse	64 (54.7)	239 (55.1)	
LDH:[a]			
Normal	36 (42.4)	165 (57.7)	.013
Elevated	49 (57.6)	121 (42.3)	
Planned ARDI:			
≤80%	9 (7.1)	67 (14.9)	.024
>80%	117 (92.9)	384 (85.1)	
Early CSF use:[b]			
Yes	11 (8.7)	72 (16.0)	.041
No	115 (91.3)	379 (84.0)	

[a] Sample size was smaller due to missing values.
[b] Defined as CSF use within the first 5 days of cycle 1.

Early Occurrence of First FNH

We next examined the cycle in which the first FNH occurred to describe the timing of these hospitalizations. The distribution of first hospitalization for FN by cycle of chemotherapy is displayed in Fig 1. Overall, 56% of first hospitalization occurred during cycle 1 and 73% occurred during cycles 1 and 2, underscoring that the majority of hospitalizations occurred early during the delivery of the CHOP chemotherapy regimen. The elderly accounted for 66% of first-cycle FNH.

Age, CSF Administration, and Incidence of Repeated FNH

Hospitalizations for FN patients occurred as single (75%) or multiple (25%) incidents. Ninety-four of the 126 patients with FN were hospitalized only once. Among patients requiring multiple hospitalizations, 24 patients were hospitalized twice, 5 patients were hospitalized 3 times, and 3 patients were hospitalized 4 times. Information on LOS for these hospitalizations was available for 117 (92.9%) of the 126 patients.

Although age was not associated with repeat hospitalizations, early CSF use exhibited a protective effect on repeated neutropenic complications. In our series, patients hospitalized for FN who received early CSF were less likely to experience repeated hospitalizations (0% vs 12%, $P<.05$). Secondary CSF use was also associated with reduced repeated hospitalizations. We compared the rate of repeated hospitalizations with and without secondary CSF support in a subset of patients who did not receive early CSF and who did not experience their first hospitalization in the last cycle of chemotherapy (n = 90). Overall, 32 (35.5%) of these patients experienced a repeated hospitalization. Of these 32 patients, 12 (37.5%) were supported with secondary CSF. Of the 58 patients who did not experience repeat hospitalizations, 35 (60.3%) were supported with secondary CSF ($P<.05$). Finally, of these 90 patients, 43 (47.8%) did not receive secondary CSF support following their first FNH.

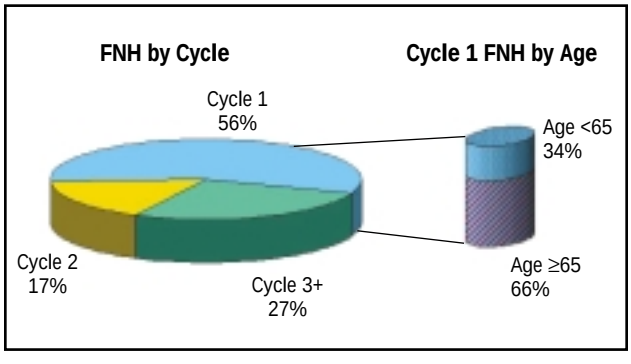

Fig 1. — Distribution of first hospitalization for FN by cycle and age.

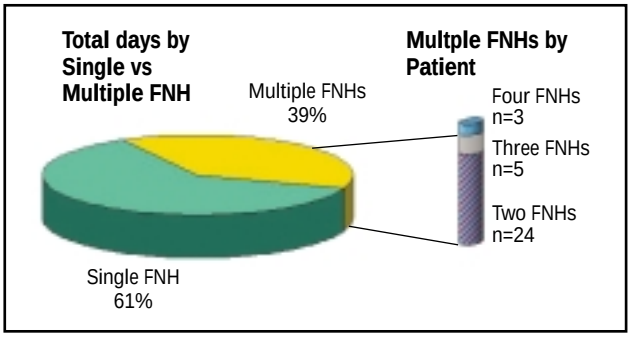

Fig 2. — Distribution of total days of hospitalization for FN by single vs multiple events. Thirty-nine percent of total days of hospitalization occurred among 32 patients (25%) of study population.

Risk Factors Associated With Total LOS for FNH

A total of 117 patients (with LOS data available) experienced 153 hospitalizations for FN, totaling 1,195 days. A total of 733 days (61.3%) of hospitalization occurred in 88 patients who had a single hospitalization event. The remaining 462 days (38.7%) occurred in 29 patients who experienced multiple hospitalization events (Fig 2). The average total LOS in FN patients with a single hospitalization was 8.3 days (95% confidence interval [CI], 7.16 to 9.50) vs 15.9 days (95% CI, 13.1 to 18.8) for patients with multiple hospitalizations ($P<.0001$).

Table 2 presents the bivariate results comparing the means of total FNH LOS across all predictors. Testing the difference between mean total LOS among variables revealed that treatment year, age, and early CSF use were significantly related to mean total LOS for FNH. Older patients had an average total LOS of 11.5 days, as compared to younger patients with an average total LOS of 8.1 days. Among patients receiving early CSF, the average total LOS was 6.6 days compared with 10.6 days for those not receiving CSF. In addition, patients diagnosed in the 1991-1994 period had a 3.4-day longer average total LOS. As for heart disease, a 3.0-day longer average total LOS was the case for patients who presented with heart disease.

The significant variables identified by bivariate analysis (treatment year, age, heart disease, and early CSF use) were further tested in a multiple stepwise regression (Table 2). The two factors found to be significantly associated with total FNH LOS were patient age ≥65 years and lack of early CSF administration. This multivariate regression analysis revealed that the total LOS for FNH was an average of 3.9 days longer for patients ≥65 years of age (95% CI, 1.39 to 6.44) and 5.1 days longer for patients not receiving early CSF (95% CI, 0.75 to 9.51). The model-derived predicted average total LOS for FNH (along with 95% CI) was plotted for all the com-

Table 2. — Impact of Patient Characteristics on the Total Hospitalization Length of Stay for Febrile Neutropenia During CHOP Chemotherapy

Patient Characteristics	No. of Patients[a] (n = 117)	Total FN Hospitalization LOS (Bivariate)		Total FN Hospitalization LOS (Multivariate)	
		Mean (days)	*P* Value[b]	Parameter Estimate (days)	*P* Value[c]
Treatment years:					
1991-1994	45	12.3	.010		
1995-1999	72	8.9			
Age:					
<65	44	8.1	.009	3.92	.003
≥65	73	11.5			
Gender:					
Men	54	10.8	.387		
Women	63	9.7			
Charlson Comorbidity Index:					
0	64	9.3	.139		
≥1	53	11.3			
Renal disease:					
Present	14	11.9	.322		
Absent	103	10.0			
Heart disease:					
Present	24	12.6	.054		
Absent	93	9.6			
Ann Arbor stage:					
Limited (I-II)	46	9.4	.241		
Advanced (III-IV)	63	10.9			
Extranodal sites:					
0-1	66	10.0	.714		
≥2	22	10.6			
B symptoms:					
Present	22	9.1	.417		
Absent	95	10.5			
Histology A: Follicular, large cell, immunoblastic, and intermediate-grade NOS	34	9.5	.405[d]		
Histology B: Diffuse small cleaved cell, diffuse mixed small cleaved, and large cell	15	12.4			
Histology C: Large cleaved or noncleaved cell/diffuse	59	10.2			
Lactate dehydrogenase level (LDH):					
Normal	33	10.3	.883		
Elevated	46	10.1			
Planned ARDI:					
≤80%	8	8.8	.535		
>80%	109	10.3			
Early CSF use:[e]					
Yes	10	6.6	.005	5.13	.022
No	107	10.6			

[a] Total (n = 117) is less than the total FNH (n = 126, Table 1) because total hospitalization LOS was not available for 9 hospitalizations.
[b] *P* value based on Student's *t* test.
[c] *P* value based on multiple regression *t* tests.
[d] *P* value based on ANOVA *f* test.
[e] Defined as CSF use within the first 5 days of cycle 1.

binations of the model predictors (Fig 3). The predicted total LOS ranged from an average of 3.1 days for younger patients receiving early CSF to an average of 12.1 days for older patients not receiving early CSF.

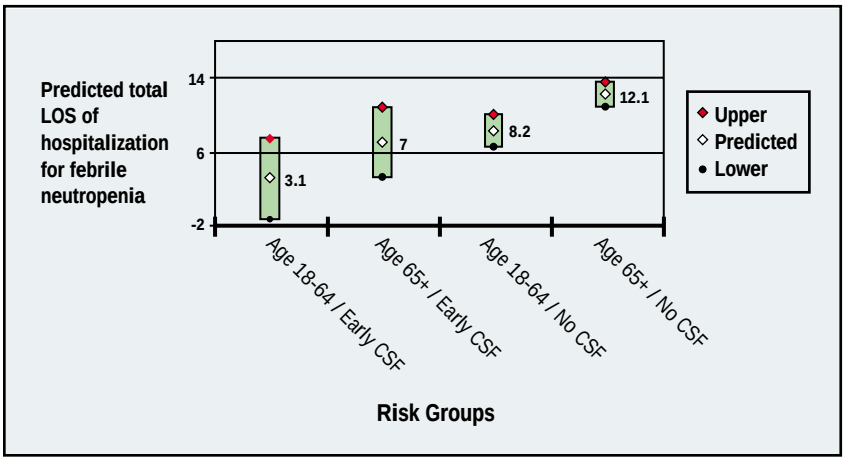

Fig 3. — Impact of age and CSF use on LOS of hospitalizations for FN in NHL patients receiving CHOP chemotherapy. CSF = early CSF use.

Discussion

This historical case series study examined variations in the incidence, recurrence, and duration of FNHs and described the frequency of CSF use in patients with intermediate-grade NHL. Patients included in this series received initial CHOP chemotherapy primarily in community oncology practices, as well as in various academic sites.

We observed that among patients age ≥65 years who were planned to receive standard CHOP therapy (and had no administration of prophylactic CSF), 33% experienced a hospitalization for FN. In a recent report about this same database of NHL patients treated primarily in community settings, Morrison et al[24] reported that the incidence of FNH increased with age, from 14% (ages 18 to 60 years) to 35% (ages ≥75 years) (P<.001), not controlling for other factors. These findings underscore how susceptibility to myelosuppression may increase with age. Age itself is not a contraindication to full-dose chemotherapy; comorbidity and poor functional status are the main limiting factors.[31] Patients ≥65 years of age often experience changes in liver and kidney functions, a reduced bone marrow reserve, and metabolic and cardiovascular diseases.[32] Furthermore, because toxicity may be enhanced, many physicians believe that elderly patients are unable to withstand intensive chemotherapy or radiotherapy.[32] In addition, it is difficult to determine drug dosage in the elderly because typical blood concentrations are altered by reduced absorption from the intestinal tract, decreased serum albumin concentration, and reduced hepatic and renal function.[33] Among patients ≥65 years of age in our series who were treated with the intent to cure, not providing supportive care resulted in a higher proportion of hospitalizations that may have been avoided with appropriate preventive care. Until a better method is developed to identify patients at risk for hospitalization due to FN, the elderly will require special consideration for primary prophylaxis with CSFs.

In our series, 56% of FNH occurred within the first cycle of CHOP chemotherapy, 66% of which occurred in patients ≥65 years of age. This finding of early hospitalizations is supported by two studies that report a high percentage of toxic deaths occurring in the first 2 cycles of CHOP chemotherapy.[13,14] Armitage et al[13] reported in their single-arm series that 25% of patients 70 years of age or greater died within the first 2 treatment cycles of CHOP.[13] In a retrospective study of patients 60 years of age or greater with intermediate-grade NHL (and treated with CHOP), 29 (82%) of 35 toxic deaths were due to infection and 22 (63%) occurred in the first cycle of chemotherapy.[14]

We observed that early CSF and secondary prophylactic CSF use were significantly associated with a lower incidence of repeated hospitalizations. In addition, patients with FN having repeated vs single hospitalizations had a 7.6-day longer average total LOS. Balducci[31] defines secondary prophylaxis as the use of CSFs in subsequent chemotherapy cycles after the occurrence of neutropenia in at least the previous cycle.[31] In our series we were more conservative: we selected the more severe subset of patients who were hospitalized for FN. In doing so, we found that 47.8% of the subset of patients with FN who experienced hospitalizations did not receive secondary prophylaxis with CSF (in disagreement with the American Society of Clinical Oncology [ASCO] guidelines for 2000 for the secondary use of CSFs).

The magnitude of this apparent protective effect of secondary prophylaxis for recurrent FNH may even be underestimated in this retrospective study, if secondary prophylaxis is most likely to be prescribed for those at greatest risk of recurrence. Our findings suggest underutilization of secondary intervention.

We found that the total LOS for FNH was an average of 3.9 days longer for patients who were ≥65 years. This extended total LOS in the elderly is compatible with a body of literature documenting that, when the elderly are hospitalized, their functional status declines

and that this decline is associated with longer stays that can be managed via geriatric evaluation and monitoring (GEM) units.[34] We also found that the total LOS for FNH was an average of 5.1 days longer for those not receiving early CSF. This is in part due to the observed protective effect of early CSF use on recurrent hospitalizations for FN. Past studies support our finding that the use of CSF is significantly associated with a lower incidence and duration of hospitalization for FN. In a study of intermediate-grade NHL patients, the incidence of neutropenia (ANC <1,000/mm^3) was 33% (2 to 6 cycles of CHOP plus G-CSF) vs 75% (for 2 to 6 cycles of CHOP alone) for NHL patients treated with standard dose CHOP.[35] Zinzani and colleagues[21] suggested that the role of age as a significant risk factor for complete response and relapse-free survival may be ameliorated by using less myelosuppressive regimens as well as using G-CSF. In a randomized study with aggressive histology NHL in patients 60 years or greater, Zinzani et al[22] reported that G-CSF significantly lowered the incidence of neutropenia, the number of infections, the requirements for antibiotics, and days of hospitalization. Prophylactic utilization of CSF may be an effective measure in reducing the costs associated with longer hospitalizations experienced by elderly patients treated with CHOP-like regimens.

The 2000 update of the ASCO clinical practice guidelines for the use of hematopoietic CSF recommends primary use of CSF (ie, in the first cycle before the onset of neutropenia) to reduce the likelihood of hospitalization when the expected incidence of FN is at least 40%.[36-38] In our community-based study, 71 (12.3%) of 577 patients experienced an FNH in the first cycle. This group constituted 56% of the 126 patients who were hospitalized for FN. To prevent the majority of hospitalizations due to FN will thus require prophylaxis at the start of chemotherapy. Prophylactic CSF was administered to 83 (14.5%) of the study patients, in whom the subsequent rate of FNH was only 13.3% compared with a 23.3% FNH rate among those who did not receive prophylactic CSF. In our study, first-cycle hospitalizations were disproportionately concentrated among the elderly, underscoring that primary prevention offers the greatest potential to reduce the health and economic burden of hospitalization for FN in the elderly. Our findings also support guidelines recently proposed by the National Cancer Center Network (NCCN) for managing older cancer patients.[39,40] These NCCN guidelines recommend primary CSF for patients older than 70 years of age receiving CHOP. The authors also advocate the use of the Comprehensive Geriatric Assessment to guide the management of cancer in elderly patients,[39] especially those who may be at greater risk from aggressive chemotherapy due to functional dependence and comorbidity.

Conclusions

Our study, which was conducted in 12 diverse practice settings, found that FNH often occurred in the early cycles of chemotherapy and resulted in prolonged hospitalization in patients who were 65 years of age and older. Lack of primary and secondary support with CSFs was associated with an increased risk of recurrent hospitalizations. These findings suggest that treatment of NHL patients age ≥65 receiving CHOP-like regimens (and treated with curative intent) should be considered special circumstances for utilizing primary CSF. This recommendation is appropriate under both 2000 ASCO and proposed NCCN guidelines. In the community, secondary prophylaxis with CSF is effective, underused, and too late to prevent the 56% of FNH occurring in the first cycle of CHOP chemotherapy.

The data used in this article were provided by the Non-Hodgkin's Lymphoma Oncology Practice Pattern Study Working Group.

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