

Time to First Neutropenia Hospitalization During First-Course Chemotherapy Among Newly Diagnosed Non-Hodgkin's Lymphoma Patients: National SEER-Medicare Study

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Origin of Study	USA
Type of Study	RETROSPECTIVE ANALYSIS OF SEER-MEDICARE DATA
Objectives	Estimate incidence of and time to first neutropenia hospitalization and identify associated risk factors among patients with non-Hodgkin's lymphoma (NHL) receiving their first course of chemotherapy
Study Design	<p>The National Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database (including 11 SEER registries) identified patients newly diagnosed with NHL between 1991 and 1999.</p> <p>Patients with first primary NHL, aged 66 or older at diagnosis, and having continuous non-HMO Medicare Part A and Part B benefits, a reliable death date, and chemotherapy within 5 months of diagnosis were included. Patients unlikely to have had systemic chemotherapy or those hospitalized for neutropenia prior to a Medicare chemotherapy claim were excluded.</p> <p>SEER data provided stage, histology, and diagnosis date. Medicare claims identified chemotherapy agents, prediagnosis comorbidities, neutropenia hospitalization (ICD-9 code, 288.0) dates, and first course starting and stopping dates.</p> <p>Time to neutropenia hospitalization was defined as the number of days from chemotherapy start to first neutropenia hospitalization admission, censoring at death, first-course final chemotherapy administration date (+ 21 days), bone marrow transplantation, or 365 days.</p> <p>Relative risks were calculated using cohort study methods. Time to first neutropenia hospitalization (survival) and instantaneous risk (hazard rate) plots were generated using Kaplan-Meier methods. Univariate and multivariate analyses employed Cox proportional hazards regression models.</p>
Patients	Of 35,063 individuals with NHL diagnosed between 1991 and 1999, 7,238 met the inclusion/exclusion criteria. Median patient age was 75 years (range, 66–100 years).
Observations	<p>Of the 1,619 patients hospitalized for neutropenia (22.4% [95% CI: 21.4%–23.4%]) of all patients who met the eligibility criteria, 370 patients (22.9%) were hospitalized more than once.</p> <p>Of all first neutropenia hospitalizations, 56% occurred within the first 42 days of treatment and 39% by day 21. Mean number of days to neutropenia hospitalization was 55.7 ± 1.43 (SE), and the median was 34 days (10th–90th percentile: 9–130). The neutropenia hospitalization hazard rate peaked by the 11th day of the first cycle (hazard ratio, 0.012; SE: 0.001), more than twice that of any period after cycle 1.</p> <p>The factors univariately associated with incidence of neutropenia hospitalization were gender, age, SEER site, chemotherapy type, histology, and disease stage ($P \leq 0.05$). The highest relative risks were for cyclophosphamide plus either doxorubicin or mitoxantrone (relative risk, 1.6; 95% CI: 1.4–1.8) and diffuse histology (relative risk, 1.6; 95% CI: 1.4–1.9).</p> <p>Risk of neutropenia hospitalization increased until 80 years of age, diminishing thereafter. Stratified by histology and chemotherapy type, age, stage, SEER registry site, and anemia were multivariately associated with time to neutropenia hospitalization ($P \leq 0.05$).</p>

First-Time Neutropenia Hospitalization of Newly Diagnosed Patients With Non-Hodgkin's Lymphoma Receiving Chemotherapy

Among 4,549 patients receiving cyclophosphamide plus doxorubicin or mitoxantrone, advanced stage (hazard ratio, 1.2; 95% CI: 1.1–1.4), anemia (hazard ratio, 1.5; 95% CI: 1.1–2), diffuse histology (hazard ratio, 1.2; 95% CI: 1–1.3), SEER registry site, and age were independently associated with shorter time to neutropenia hospitalization.

Conclusions

Hospitalization for neutropenia occurred mostly in the first two chemotherapy cycles.

Independent predictors of neutropenia hospitalization included clinical (chemotherapy type, disease stage, histology, anemia) and demographic (age, gender, SEER site) factors.

Assessment of neutropenia hospitalization risk factors before commencing chemotherapy is suggested to target preventive interventions to subgroups of older adults most likely to benefit.

Discussion

Combination chemotherapy for NHL can cause severe neutropenia that can be dose-limiting, require hospitalization, and result in discontinuation of chemotherapy. The incidence of chemotherapy-related febrile neutropenia is highest in patients > 65 years old. Being able to predict which older patients would most likely be affected by severe neutropenia would enable clinicians to target preventive interventions to subgroups of persons most likely to benefit. This study identified several predictors of neutropenia hospitalization, including disease stage, histology, anemia, age, and SEER site registry.

Voelker and colleagues examined first-time neutropenia hospitalization among a large cohort of elderly NHL patients who had received chemotherapy within 5 months of diagnosis. The median age of the patients was 75, with a range of 66 to 100. Among the 7,238 patients included in the study, 1,619 (22.4%) had been hospitalized for neutropenia, 370 of them (22.9%) more than once.

For patients experiencing neutropenia hospitalization for the first time, 39% of hospitalizations occurred within 21 days of the first chemotherapy treatment date, and a total of 56% of hospitalizations occurred within the first 42 days. The mean number of days to neutropenia hospitalization for the entire group was 55.7, and the median was 34 days. The hazard ratio for neutropenia hospitalization in the first cycle of chemotherapy was more than double that of any other cycle and peaked by day 11.

Factors univariately associated with the incidence of neutropenia hospitalization were gender, age, SEER registry site, chemotherapy type, histology, and disease stage ($P < 0.05$). The risk of neutropenia hospitalization increased until age 80 and then began to diminish.

The highest relative risks were for patients known to have received cyclophosphamide plus doxorubicin or mitoxantrone (Novantrone) and for those with diffuse histology. Stratified by histology and chemotherapy type, the following factors were significantly ($P < 0.05$) associated with neutropenia: age, advanced stage, SEER tumor registry site, and anemia. Among patients treated with cyclophosphamide plus doxorubicin or mitoxantrone ($n = 4,549$), factors independently associated with a shorter time to neutropenia hospitalization were advanced stage, anemia, diffuse histology, SEER registry site, and age.

Key Points

- Both clinical (chemotherapy type, disease stage, histology, anemia) and socioeconomic factors (age, gender, SEER site) are independent predictors of neutropenia hospitalization of NHL patients receiving their first course of chemotherapy.
- First-time neutropenia hospitalization is most prevalent in the first two chemotherapy cycles.
- Pretreatment risk assessment of risk factors for neutropenia hospitalization may help to target preventive interventions to older adults most likely to benefit from them.

References

Voelker MD, Rubenstein LM, Chrischilles EA, et al. Time to first neutropenia hospitalization during first course chemotherapy among newly diagnosed non-Hodgkin's lymphoma patients: national SEER-Medicare study. Poster presented at the 45th Annual Meeting of the American Society of Hematology; December 6–9, 2003; San Diego, Calif. Abstract 888.