Further Considerations About NHL in the Elderly

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As noted in part 1 of this two-part article, non-Hodgkin's lymphoma is one of a few malignancies that have been increasing in incidence over the past several decades. Likewise, these disorders are more common in elderly patients, with a median age of occurrence of 65 years. Therapy in elderly patients may be affected by multiple factors, especially attendant comorbidities. The approaches to management of these patients, with either indolent or aggressive disease processes, have been based on prospective clinical trial results, many of which have included a younger patient population. Fortunately over the past decade, results of treatment trials that have targeted an older patient population have emerged. The disease incidence and treatment approaches for both follicular (part 1) and diffuse aggressive (part 2) histologies in elderly patients are reviewed, as well as the impact of aging on the care of these patients.

The topic "non-Hodgkin's lymphoma (NHL) in the elderly" comprises a heterogeneous set of malignancies in a very heterogeneous population. As the incidence of NHL is increasing by approximately 1% to 2% per year, with the greatest change in incidence occurring in patients aged 75 to 84, a comprehensive review of the prognosis and treatment of NHL specifically in elderly populations is greatly needed. Age is recognized as an adverse prognostic risk factor in NHL, with potential causes including a possible difference in the biology of disease by age group, an increased number of coexisting illnesses, altered pharmacokinetics, changes in hematologic reserve, and an increased number of treatment-related complications in the frail elderly.

Morrison presents a wide overview of important issues related to caring for elderly patients with lymphoma, such as ageism, stereotyping, polypharmacy and toxicity, competing risks for mortality, and historical lack of enrollment of elderly patients in clinical trials. In addition, the author describes in detail the efficacy and outcomes of several phase II and III clinical trials of chemotherapy and targeted therapies, as well as the use of growth factor support, in broad subgroups of lymphoma types (follicular vs diffuse aggressive) in healthy patients aged 60 years and older. Important issues that should be highlighted include: (1) information gained from a comprehensive assessment of the health status of the patient, including comorbidity, performance status and functional status, and quality of life that can be used to evaluate and guide management decisions, and (2) unanswered questions that need to be explored in future research.

Comprehensive Assessment

A significant ongoing effort is aimed at determining the feasibility of a cancer-specific geriatric assessment and whether such an assessment affects treatment toxicity and outcome.[1] Clearly, the most challenging goal is to segregate frail older lymphoma patients from a healthier cohort. Universally accepted criteria for frailty have yet to be defined. One definition, utilized by the National Cancer Institute, Aviano, Italy, in their lymphoma trials, is dependency in one or more activities of daily living (ADLs, such as bathing, dressing, toileting, transferring, and feeding), three or more comorbidities, or one or more geriatric syndromes (such as dementia, gait or hearing imbalance, depression, cachexia, or functional decline). Based on this definition of frailty, older NHL patients at Aviano were segregated into the nonfrail, who were treated with curative intent with standard dosing, and the frail, who were dose-reduced or not given a modified regimen.[2]

Frailty in older patients is often a marker for life expectancy, and studies have shown that a combination of ADLs and performance measures in addition to age predict 2-year mortality.[3] Moreover, an 80-year-old in the upper quartile of health based on a geriatric assessment has a similar life expectancy to that of a 70-year-old in a middle quartile.[4] Few studies have looked at additional prognostic measures in older lymphoma patients beyond the International Prognostic Index (IPI) risk, a gold standard prognostic marker. However, in older NHL patients, comorbidities have been shown to affect prognosis independent of IPI risk,[5] and it is conceivable that elderly-specific or frailty-specific measures could be added to the IPI. In addition to survival, it is important to consider the health-related quality of life of the older NHL patient and survivor. A small
study of older NHL patients demonstrated that physical functioning and quality of life deteriorated during treatment in patients with lower age-adjusted IPI scores, with a rebound in quality of life to baseline after treatment.[6] Data suggest that NHL survivors report worse general health and decreased vitality levels.[7] It is unclear to what extent the treatment of NHL in older patients reduces performance status and independence, or the extent to which aggressive rehabilitation can mitigate these treatment effects.

Unanswered Questions

Unanswered questions remain in the quest for curative therapy for the elderly patient with aggressive NHL. While the German High-Grade Non-Hodgkin's Lymphoma Study Group data have suggested the superiority of R-CHOP-14 (rituximab [Rituxan] plus cyclophosphamide, doxorubicin HCl, vincristine [Oncovin], prednisone) for six cycles in patients aged 61 to 80,[8,9] we await confirmatory data from the Groupe d'Etudes des Lymphomes de l'Adulte (GELA). A recent presentation of the Dutch-Belgian Hemato-Oncology Cooperative Group (HOVON) study of dose-dense R-CHOP[10] suggests that in patients over the age of 75, that toxicity may impair successful delivery of this regimen.

Fruitful areas for further study would include the prospective use of a comprehensive geriatric assessment in the determination of the regimen and dose used in the elderly[especially the ultra and frail elderly]as in the study undertaken by the Gruppo Oncoematologico Linfoma.[11] For geriatric patients with high-risk histologies (such as mantle cell lymphoma or peripheral T-cell lymphoma), or relapsed diffuse large B-cell lymphoma, information on feasibility, toxicity, and long-term outcome of high-dose therapy with peripheral stem cell infusion is lacking. An alternative approach under investigation for patients with high-risk diffuse large B-cell lymphoma is the use of consolidative radioimmunotherapy.[12]

Non-Hodgkin's lymphoma in the elderly is an exciting area of research that may serve as a model for assessment, treatment, supportive care, and outcomes research in dealing with the challenges of older cancer patients in general.

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References:


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