HHS Public Access

Author manuscript

J Geriatr Oncol. Author manuscript; available in PMC 2016 September 01.

Published in final edited form as:

J Geriatr Oncol. 2015 September ; 6(5): 344–345. doi:10.1016/j.jgo.2015.07.001.

High dose therapy and autologous hematopoietic stem cell transplantation in septuagenarians with non-Hodgkin lymphoma: Feasible, but for which patients?

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Abstract

Editorial will accompany Hermet et al. “Autologous hematopoietic stem cell transplantation in elderly patients (≥ 70 years) with non-Hodgkin’s lymphoma: a French Society of Bone Marrow Transplantation and Cellular Therapy retrospective study.”

High-dose therapy and autologous stem cell transplantation (ASCT) offers a potential curative therapeutic option for patients with relapsed non-Hodgkin lymphoma or as part of initial therapy for some subtypes. Early reports of the use of ASCT were concerning for excessive treatment-related mortality with increasing age.[1] However, advances in treatment, including the use of peripheral blood stem cells and improved supportive care, have improved the safety and tolerability of the procedure and allowed its application in an increasingly aged population.

In this edition of the *Journal of Geriatric Oncology*, Hermet and colleagues present a multicenter retrospective study of older adults with non-Hodgkin lymphoma (NHL) who underwent high-dose therapy and ASCT.[2] In this analysis, 81 patients over age 70 who underwent ASCT from 1995–2009 were identified, representing the largest cohort reported to date in this population. They found a low 100-day non-relapse mortality rate of 5.4% and a one-year non-relapse mortality rate of 8.5%. Hematopoietic reconstitution and duration of hospitalization were similar in this cohort as in other cohorts of patients age 60 and older. The median progression-free survival was 21 months, and median overall survival was 43 months. The authors conclude that ASCT is acceptable in NHL lymphoma patients aged 70 years and older.

However, it is clear from several of the characteristics of the cohort that the cohort represents highly selected patients. This cohort represented only 1% of all ASCT performed in the 20 participating centers, whereas 48% of all patients diagnosed with NHL in 2009–2011 in the United Kingdom were over age 70 (cancerresearchuk.org). The low rate of comorbidities demonstrate that these patients were highly selected: 73% had a score of 0 on the Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI), while only 17% and

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Disclosures and Conflict of Interest Statement

The authors declare that they have no conflict of interest.

10% had HCT-CI scores of 1–2 or ≥3, respectively. In contrast, in a recent study of over 11,000 patients of all ages who underwent ASCT, only 50% of patients had an HCT-CI score of 0, while 27% had a score of 1–2 and 23% had a score of ≥3.[3] The low rate of non-relapse mortality suggests that the clinicians' assessments were relatively accurate in identifying a population of individuals over age 70 who would be able to tolerate ASCT.

What we do not know from this study, however, is what made, in the clinician's assessment, each individual eligible for transplant. Information on their performance status and geriatric assessment, including dependence, cognitive impairment, depression, polypharmacy, and falls, are not available. It is unknown how many patients were felt to be clinically fit for ASCT, but were unable to mobilize sufficient CD34+ cells to proceed to transplant. Some studies have suggested that older age is associated with poorer stem cell mobilization[4] whereas others have found no influence of age on mobilization success.[5]

In this study, comorbidities were not prognostic. Other studies, however, have found the presence of comorbidities to be prognostic in older adults undergoing ASCT.[6,7] Comorbidities may impact prognosis in several ways. They may increase the risk of treatment toxicity of therapy. Comorbidities may interact with the disease, worsening the behavior of the cancer. Comorbidities may present competing risk for mortality. Indeed, in the present study, several of the patients' causes of death were unrelated to their NHL or toxicity. The competing risk from comorbidities is particularly salient in considering ASCT when it is not expected to be curative and where other, less toxic, treatment alternatives are emerging, as in follicular lymphoma.

One final consideration regarding ASCT in older adults is its impact on function, cognition and quality of life. While engraftment and NRM are similar to that seen in other studies of patients age 60 and older, little is known about nonfatal, nonhematologic toxicity of ASCT. Particularly, we know little about how a 3-week peri-transplant hospitalization impacts functional status, and what the trajectory of functional recovery is. Quality of life studies suggest that, on average, physical and functional quality of life return to baseline by 3–6 months following ASCT[8], but whether there are subgroups who do not return to baseline, and if older adults are more vulnerable to persistent decline, is unknown. Cognitive decline may also be a concern in older adults undergoing ASCT. In a prospective cohort study of 53 patients undergoing ASCT for multiple myeloma, half of patients demonstrated clinically significant declines in one or more measures of cognitive function, which persisted at 3-months post-ASCT.[9] ASCT for lymphoma may also have a long-term impact on quality of life in older adults. In one prospective cohort study of 837 lymphoma survivors, those who had undergone ASCT had poorer quality of life compared with those who had not undergone transplant and with noncancer controls; age was associated with poorer physical, role and cognitive function.[10] In another study of lymphoma survivors, comorbidities and older age were associated with poorer quality of life.[11] Thus, older adults undergoing ASCT may be more vulnerable to physical and cognitive decline, with negative impact on their quality of life.

In summary, Hermet et al. demonstrate the feasibility and acceptability of ASCT in highly selected patients aged 70–80. While this is encouraging data for that select group, questions

remain about how to individualize decision-making about ASCT. Future studies must consider whether the intent of the ASCT is curative or palliative, weighed against competing causes of mortality and risk of toxicities. Studies of ASCT in older adults must look beyond treatment-related mortality and conventional hematologic toxicities and examine outcomes of particular importance in older adults, including functional and cognitive decline.

Acknowledgments

Dr. Wildes' research is supported by Grant Number 1K12CA167540 through the National Cancer Institute (NCI) at the National Institutes of Health (NIH) and Grant Number UL1 TR000448 through the Clinical and Translational Science Award (CTSA) program of the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCI, NCATS or NIH.

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