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Lung Cancer in the Elderly
So Many Patients, So Little Time!

Lodovico Balducci, MD

Dr. Balducci is Medical Oncologist and Program Leader, Senior Adult Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL.

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Between 1980 and 1998, lung cancer mortality rates decreased for persons younger than 55 years and increased for those older than 65, reflecting generational patterns in smoking prevalence.[1] Consequently, most lung cancer occurs now in patients older than 65 years. Furthermore, this neoplasm is not uncommon among the oldest old, that is, persons older than 85. Several questions of general interest to clinicians emerge from this relatively new epidemic of lung cancer among the elderly:

- Will the patient die of cancer or with cancer?
- Will age affect his or her prognosis?
- Can the patient tolerate usual treatment regimens?
- What is the balance of quality of life and survival in patients with incurable disease (who are the majority of persons with lung cancer)?[2]

In a very elegant and exhaustive review in this issue, Hurria and Kris address these questions and provide important practical answers.[2]

The first question they explore is the assessment of the older person; that is, the determination of physiologic rather than chronologic age. This distinction is necessary because aging represents a progressive loss in functional reserve that varies from person to person and within the same person from function to function.[3] Because aging is multidimensional, a comprehensive assessment accounting for function, comorbidity, and personal and social resources is the appropriate instrument to evaluate the older person. The benefits of this approach include being able to estimate life expectancy and tolerance of treatment and to identify conditions that are reversible but may interfere with cancer treatment if left unattended.[4]

Based on the results of multiple, large patient series, the authors conclude that age alone is not a significant prognostic factor. In fact, according to the European Organization for Research and Treatment of Cancer (EORTC), increased age was a good prognostic factor for response to chemotherapy.[5] These conclusions should be mitigated because the percentage of patients 80 years or older who were enrolled in the studies was probably negligible. As the prevalence of dysfunction and comorbidity increase with age, we may assume that older age would be associated with poorer prognosis. Even so, it is important to identify those unusually healthy older persons who may tolerate aggressive treatments.

Although age is associated with increased risk for surgical and radiation complications, these forms of treatment seem overall to be advantageous to older persons, and age should not impede their use in patients without other contraindications. Of interest, patients older than 70 years were more likely to experience severe complications from pneumonectomy, and this procedure should be avoided whenever possible.

Areas of controversy related to management of non–small cell lung cancer include the use of combined-modality treatment (chemotherapy and radiation) in locally advanced disease and the best regimen of chemotherapy for metastatic disease.

Whereas concomitant chemoradiation improves disease-free survival, overall survival, and quality of life of patients who are 60 years and younger, those 70 and older seem to have a better quality of life with sequential treatment. In the case of metastatic disease, although chemotherapy provides better survival and quality of life than supportive care, controversy lingers over the use of single-agent versus combination treatment.[6] The Multicenter Italian Lung Cancer in the Elderly Study compared the combination of vinorelbine and gemcitabine with either agent alone, failing to show an advantage for the combination.[6] It should be noted, however, that the combination did not contain a platinum congener that current wisdom considers part of any standard chemotherapy regimen for lung cancer. In the Eastern Cooperative Oncology

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Group 5592 study, persons older than 70 benefited from cisplatin-containing combination chemotherapy to the same extent that younger patients did, albeit with an increased risk for myelodepression and neurologic toxicity.[7]

What kind of conclusions may be drawn from this confusing evidence? I am reluctant to make an inflexible recommendation for a chronologic boundary (age 70) beyond which concomitant chemoradiation should not be used or single-agent chemotherapy is preferable to combination. Especially in the case of combined-modality treatment, which may be associated with prolonged survival in a large minority of patients with Stage III disease, it is important to try to identify those older persons who may obtain the most benefit from this therapeutic strategy. Future studies should try to stratify patients according to their functional reserve as estimated using the comprehensive geriatric assessment. Regardless of age, fully functional persons with few comorbid conditions may benefit from aggressive treatment to the same extent as younger persons. In metastatic cancer, for which chemotherapy is mainly palliative, it is more difficult to support aggressive treatment. Furthermore, it is quite possible that sequential treatment with different agents may be as effective and less toxic than the combination of these agents. This is certainly the case with other neoplasms, such as breast cancer.[8]

However, even in metastatic disease, combination chemotherapy should be offered to those elderly persons in whom a rapid response is desirable to improve the patient's quality of life.

The authors also explore the role of new agents, such as gefitinib, in older persons. Clearly, targeted therapy, if effective, may revolutionize the field of oncology and dramatically reduce concerns of age-related toxicity.

Regarding small cell lung cancer, the authors' most important message is that attempts to reduce the doses of treatment to ameliorate toxicity are ill advised, at least in the case of rapidly growing tumors. This was particularly clear in the results of the study that showed oral etoposide to be less effective and more toxic than the combination of cisplatin and etoposide. This is analogous to the case of large-cell lymphoma in the elderly, where attempts to eliminate anthracyclines from the treatment regimen have consistently produced inferior outcomes.

This review is a tremendous service to clinician and scientist alike because:

- It highlights the diversity of aging and the need to account for this diversity in treatment plans and clinical trials involving older persons;
- It provides the practitioner with the instruments to make individualized treatment plans;
- It demonstrates that chronologic age is not a contraindication to effective treatment of older patients with lung cancer, regardless of whether surgery, radiation therapy, cytotoxic chemotherapy, or a combination of these treatments is necessary; and
- It raises two important questions that should be addressed in future studies: how to recognize older persons with non–small cell lung cancer who may benefit from concomitant chemotherapy and radiation therapy in the treatment of locally advanced disease; and the relative merits of combination chemotherapy and sequential single-agent chemotherapy in the management of metastatic cancer.

The management of lung cancer is evolving; the two major novelties are the proposal of postsurgical adjuvant chemotherapy[9] and the introduction of targeted therapy. This review provides a frame of reference for formulating clinical decisions related to older patients for these new treatments and for more traditional therapies.

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Erratum

In the July/August issue, in the article "Agent Orange and Cancer: An Overview for Clinicians" (Frumkin H. *CA Cancer J Clin 2003;53:245–255*), an error appeared in the text on page 252.

The statement which read: "The cancers on the list include Hodgkin disease, multiple myeloma, non-Hodgkin lymphoma, prostate cancer, cancer of the lung, bronchus, larynx, or trachea occurring within 30 years of exposure to Agent Orange, soft tissue sarcoma (other than osteosarcoma, chondrosarcoma, Kaposi sarcoma, or mesothelioma), and chronic lymphocytic leukemia." was incorrect.

The 30-year requirement for respiratory cancers was rescinded effective January 1, 2002, under the Veterans Education and Benefits Expansion Act of 2001 (Public Law 107–103). A veteran who served in Vietnam between 1962 and 1975 who later develops one of these cancers may be eligible for compensation, irrespective of the elapsed time since exposure, and should be advised to contact the Department of Veterans Affairs.

The author apologizes for this error and any confusion it may have caused.

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