Adjuvant Chemotherapy Benefits Older and Younger Non–Small Cell Lung Cancer Patients Alike

A recent study suggests that elderly patients with early stage non–small cell lung cancer (NSCLC) tolerate adjuvant chemotherapy similarly to younger patients and also derive a survival benefit (J Clin Oncol. 2012; doi: 10.1200/JCO.2011.39.3330). According to lead author Sinead Cuffe, MD, clinical research fellow in medical oncology at the Princess Margaret Hospital in Toronto, Canada, these findings will hopefully keep fit older patients from being denied adjuvant chemotherapy based on age alone.

Comparable Tolerability and Benefits
Dr. Cuffe and colleagues conducted a retrospective cohort study to evaluate by age the use and efficacy of adjuvant chemotherapy for patients with early stage NSCLC who have had tumor resection. Researchers identified 6304 patients in the Ontario Cancer Registry with resected NSCLC from 2001 to 2006 and linked them to electronic treatment records. Of these patients, 43.8% (2763) were elderly, defined as those aged 70 years or older. Patients who were treated with preoperative chemotherapy or radiation therapy were excluded.

There was a significant increase in the administration of adjuvant chemotherapy among the elderly when comparing the 2001 to 2003 cohort and the 2004 to 2006 cohort (3.3% vs 16.2%, respectively). The increase in uptake of adjuvant therapy in the later cohort corresponds to the reporting of pivotal trials of adjuvant chemotherapy for early NSCLC, showing that oncologists were incorporating trial results into practice (N Engl J Med. 2004;350:351-360; N Engl J Med. 2005;352:2589-2597; Lancet Oncol. 2006;7: 719-727). The older the patients, the less likely they were to receive adjuvant chemotherapy. In the 2004 to 2006 cohort, 43% of patients under age 70 years received chemotherapy, 23% of those aged 70 to 74 years received the treatment, and 13% of those 75 to 79 years and 5% of those 80 years or older received it.

Patients with stage II or III cancer were significantly more likely to receive adjuvant chemotherapy over those with stage I cancer, which is consistent with current guidelines from the American Society of Clinical Oncology and Cancer Care Ontario (J Clin Oncol. 2007;25: 5506-5518). There was no significant association between comorbidity score and receipt of chemotherapy; however, there was a trend that did not reach statistical significance for patients with 3 or more comorbidities to not receive chemotherapy. Two-thirds of the patients across all age groups received the regimen of cisplatin and vinorelbine. However, the likelihood of receiving carboplatin-based regimens, particularly carboplatin and paclitaxel increased with age: 7% in those under 70 years of age, 18% in those aged 70 to 79 years, and 29% in the cohort of those 80 years and older. This is likely because carboplatin is, in general, better tolerated than cisplatin.

Chemotherapy appeared to be equally tolerated across age groups. Rates of substitution of carboplatin for cisplatin or other drug changes during the treatment period was not different between age groups, nor was the frequency of dose reductions or omissions.

The 4-year survival for all patients treated between 2004 to 2006 was significantly better than those treated from 2001 to 2003 (56.1% vs 52.5%, P = .001). This remained true for the elderly patients overall (49.9% vs 47.1%, P = .01), suggesting a benefit from adjuvant therapy. The hazard ratio of mortality was favorable in the later
versus earlier cohorts for all age groups except the cohort of those aged 80 years and older (and significantly so, except for the 75 to 79 year cohort); 0.85 for those under 70 years of age, 0.83 for those aged 70 to 74 years, 0.84 for those aged 75 to 79 years, and 1.00 for those 80 years or older. Hospitalization rates at 6 to 24 weeks after surgery, the time that chemotherapy is most likely to be given, did not vary significantly between age groups, suggesting serious complication rates did not differ between groups.

According to Dr. Cuffe, the study’s strengths include its large population size, robust data collection, and province-wide evaluation of the entire population of interest, which helps avoid the selection/referral biases that often hamper traditional institution-based observational studies. “Of course it carries the limitations of being retrospective and unfortunately not all patients had pathological staging available,” she says.

“The study results are in line with other population-based [studies] in colon and breast cancer showing a benefit of adjuvant chemotherapy in the elderly, but that a smaller percent of patients get treated,” says Arti Hurria, MD, director of the Cancer and Aging Research Program at the City of Hope Cancer Center in Duarte, California. Dr. Hurria says the challenge lies in finding out why this happens. For example, is it lack of referral to oncologists, oncologists not treating, patient choice, or social factors? “I suspect it is multifactorial,” she says.

Data Lacking in the Elderly
NSCLC is a disease dominated by elderly patients with a median age at diagnosis of 70 years. Adjuvant chemotherapy has become the standard of care for patients with resected stage II to IIIA NSCLC. Although no elderly-specific trials for adjuvant chemotherapy in this setting have been reported, a retrospective analysis of the National Cancer Institute of Canada Clinical Trial Group JBR.10 trial and the Lung Adjuvant Cisplatin Evaluation (LACE) meta-analysis suggest that older patients do benefit from adjuvant chemotherapy (J Clin Oncol. 2007;25:1553-1561; J Clin Oncol. 2008;26:3573-3581). However, the elderly were underrepresented in these trials. In fact, according to the American Society of Clinical Oncology and Cancer Care Ontario guidelines, there is insufficient data to make recommendations for patients 75 years of age or older.

This study was done to address this information gap. “Elderly patients appear to derive significant benefit from adjuvant treatment in our study and there is a possibility that adjuvant chemotherapy may be underused in this population. We believe that there is a real opportunity for an educational campaign to help promote appropriate selection and referral of elderly NSCLC patients to medical oncology, especially as previous studies suggest that advanced age can significantly influence a surgeon’s decision to refer,” Dr. Cuffe says.

To avoid underrepresentation in clinical trials, Dr. Hurria says protocols should be written that either dedicate trials to the elderly or specify a proportion of elderly patients to be enrolled to represent the real population. “An evidence-based approach to assess the risks and benefits of chemotherapy toxicity in the elderly is needed,” she says.

Researchers have developed a geriatric assessment for oncologists that aims to quantify the patient’s functional age in comparison to chronological age by evaluating the patient’s functional status, comorbid medical conditions, psychological state, social support, nutritional status, and cognitive function. This geriatric assessment tool has been used to develop a predictive model for chemotherapy toxicity that includes patient age, tumor and treatment characteristics, laboratory test values, and 5 key geriatric assessment questions (J Clin Oncol. 2011;29:1290-1296; J Clin Oncol. 2011;29:3457-3465). “This tool can be used to better quantify a patient’s risk of toxicity and if incorporated into clinical trials can help better define the population. This will help the clinician when trying to apply data in practice,” Dr. Hurria says.

Dr. Cuffe adds that she hopes the current study and an increased inclusion of the elderly in future studies will help to end decisions to treat patients based on age alone and lead to more evidence-based treatment decisions.

doi:10.3322/caac.21151