

Early palliative care in patients with metastatic non-small cell lung cancer

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Metastatic or stage IV non-small cell lung cancer (NSCLC) is among the most serious diagnoses that oncologists have to communicate to their patients. In some cases, distant metastases might be found already at initial cancer diagnosis. In others, locoregionally advanced stage III or even earlier disease might evolve into the terminal, disseminated stage. Better treatment options including drugs inhibiting the epidermal growth factor receptor (EGFR) and activated lymphoma kinase (ALK) pathways have been developed, allowing for individually tailored approaches in patients whose tumor cells carry mutations that will render them sensitive to such drugs. Even if there is marked heterogeneity in disease presentation, pathology features, and outcomes, and occasional patients might present with minimal systemic disease such as a single resectable brain metastasis, typical patients have multiple metastases, are elderly, have seriously compromised organ function as a result of comorbidity, and are offered palliative systemic therapy with limited probability of response, possibly supplemented by local measures such as radiation treatment or tracheobronchial stent insertion.

For 2005-2007, 1-year survival of patients with lung cancer was reported around 30% in the UK, 35% in Denmark, and 39-44% in Australia, Canada, Norway, and Sweden (1). Five-year survival was between 9-11% in the UK and Denmark versus

15-20% in the other four countries. The number of estimated deaths from lung cancer in the US in 2010 was 157,300, with NSCLC being the largest contributor (2). Many patients might experience a considerable symptom burden when their disease becomes refractory to a given line of treatment and in the terminal phase. Ideally, it would be desirable to obtain symptom control without aggressive end-of-life care, thus avoiding overuse of costly, potentially toxic and distressing treatments (3). Reality still looks different, but increasing awareness of these challenges and well-designed research will eventually lead to better clinical care.

In a recent study from Nordland Hospital, Bodø, Norway, our group reported that during the last 3 months of life, systemic treatment was given to 28% and thoracic radiotherapy to 23% of patients who died from NSCLC, respectively (4). During the last 4 weeks of life, 27% of the patients received some type of active oncologic therapy, *i.e.* radiotherapy and/or chemotherapy including tyrosine kinase inhibitors. Only 15% of our patients were not hospitalized at least once during their last 3 months of life and 53% eventually deceased in a hospital. A minority of 23% were referred to the hospital's multidisciplinary palliative team, and few referrals were made before the last 3 months of life. Other studies suggest that standard oncologic care often follows comparable traits (5-7) and leave us with several important questions, all revolving around one main issue: how to improve these often frustrating and health economically unsustainable patterns of care.

Recently, a randomized trial of early palliative care for patients with newly diagnosed metastatic NSCLC, which recruited patients in the time period between 2006 and 2009, was published (8). This single institution trial included 151 patients with defined performance status (ECOG 0-2) who were younger than the general NSCLC population (mean 65 years). Early palliative care integrated with standard oncology care was compared to standard oncology care alone. Patients assigned to the experimental arm consulted with a member of the palliative

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care team within 3 weeks of enrollment and at least monthly thereafter. Those assigned to the standard care arm only met with the palliative care team on request from the patient, family, or oncologist. Early palliative care integrated with standard oncologic care led to significant improvements in quality of life (QoL) and mood from baseline to 12 weeks. Moreover, more patients assigned to early palliative care had their resuscitation preferences documented. Fewer patients received aggressive end-of-life care, yet median survival was longer among patients receiving early palliative care (11.6 versus 8.9 months). No significant differences were observed with regard to number of lines of chemotherapy participants received (9). The groups were similar with respect to time between first- and second-line chemotherapy as well as between second- and third-line chemotherapy. Adjusted for age, sex, and performance status, patients in the early palliative care group had half the odds of receiving chemotherapy in the final 2 months of life ($P=0.05$). Within 30 days of death, chemotherapy was received by 43% (standard care) and 30% (experimental arm), respectively ($P=0.14$). Whereas 54% of the patients in the standard oncologic care arm were admitted to a hospital within 30 days of death, the rate was reduced to 37% in the early palliative care arm. Hospice utilization was improved in the experimental arm, and home death was common in both arms (55% versus 66%, not significant).

As with many randomized studies, this one included selected patients with metastatic NSCLC and therefore confirmation from unselected, more representative patient populations is needed. It is also important to notice that the focus of the recent publication is on chemotherapy (9). Imbalances in other treatments such as radiotherapy still might have existed. Of all eligible patients 53% enrolled onto the study. The reasons for not to participate might have varied, but if some patients should have been concerned about negative impact of early palliative care on treatment intensity, duration, and eventually survival, the study results do not confirm that such a strategy compromises oncologic outcome, for example by directing patients away from available oncologic approaches. In line with previously shown improvements resulting from multidisciplinary cancer therapy (chemoradiation, surgery plus adjuvant radio- and/or chemotherapy), it rather suggests that additional expertise and intervention might be beneficial in several ways, possibly even in terms of longer survival. The aim and primary endpoint of the study was not to detect improved survival, and there could be other explanations why a rather small randomized trial shows an apparent survival advantage for one of the study arms. Possible reasons include imbalances in unreported prognostic factors such as pre-treatment weight loss, serum lactate dehydrogenase

level and others. However, other data suggest that patients with metastatic NSCLC and impaired QoL had shorter survival than those with better QoL (10,11). So if early palliative care enhances QoL, for example by providing psychosocial support (actually not all patients have sufficient network of family and friends), better symptom control and fewer treatment complications, survival might increase.

Should this trial lead to implementation of early palliative care in all patients with metastatic NSCLC? At least in Norway, practical reasons would preclude this strategy. The existing palliative teams would not have sufficient capacity to handle the large number of additional patients with NSCLC who would consult them in a regular fashion during the whole course of disease. Allocation of resources and education of additional specialists would be necessary. Comparable to the process of adopting other therapeutic advances, the question arises of whether the new strategy meets commonly accepted cut-off limits for cost-effectiveness figures. There are reasons to believe that the answer could be yes because costly hospital admissions were reduced to some degree. However, health economy studies are still needed to confirm this hypothesis. Obviously, standard oncology care did not satisfy all aspects of the disease trajectory and patient needs. Wouldn't it sound tempting to develop programs that increase the skills of today's oncology care professionals to deal with these unmet needs? Aggressive end-of-life care and delayed focus on symptom palliation are highly important issues in a world of limited health care budgets. The heightened focus on palliative interventions and terminal care as well as improved communication and shared decision-making is an important and timely development. Time spent on active therapy at the end of life may be better allocated to communication with patients and their relatives, as well as preparation for the final steps of life.

References

1. Coleman MP, Forman D, Bryant H, et al. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995-2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. *Lancet* 2011;377:127-38.
2. Kris MG, Benowitz SI, Adams S, et al. Clinical cancer advances 2010: annual report on progress against cancer from the American Society of Clinical Oncology. *J Clin Oncol* 2010;28:5327-47.
3. Earle CC, Landrum MB, Souza JM, et al. Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? *J Clin Oncol* 2008;26:3860-6.
4. Nieder C, Tollåli T, Norum J, et al. A population-based study of the pattern of terminal care and hospital death in patients with non-small cell lung cancer. *Anticancer Res* 2012;32:189-94.



5. Sharma G, Freeman J, Zhang D, et al. Trends in end-of-life ICU use among older adults with advanced lung cancer. *Chest* 2008;133:72-8.
6. Barbera L, Paszat L, Qiu F. End-of-life care in lung cancer patients in Ontario: aggressiveness of care in the population and a description of hospital admissions. *J Pain Symptom Manage* 2008;35:267-74.
7. Temel JS, McCannon J, Greer JA, et al. Aggressiveness of care in a prospective cohort of patients with advanced NSCLC. *Cancer* 2008;113:826-33.
8. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 2010;363:733-42.
9. Greer JA, Pirl WF, Jackson VA, et al. Effect of early palliative care on chemotherapy use and end-of-life care in patients with metastatic non-small-cell lung cancer. *J Clin Oncol* 2012;30:394-400.
10. Movsas B, Moughan J, Sarna L, et al. Quality of life supersedes the classic prognosticators for long-term survival in locally advanced non-small-cell lung cancer: an analysis of RTOG 9801. *J Clin Oncol* 2009;27:5816-22.
11. Reville B, Miller MN, Toner RW, et al. End-of-life care for hospitalized patients with lung cancer: utilization of a palliative care service. *J Palliat Med* 2010;13:1261-6.

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