Original Study

The Impact of Baseline Edmonton Symptom Assessment Scale Scores on Treatment and Survival in Patients With Advanced Non–small-cell Lung Cancer

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Abstract

The rate of receipt of systemic therapy in advanced lung cancer is low. Here, we used the Edmonton Symptom Assessment Scale to identify patient-reported factors that may contribute to this. Results found that patients with a higher symptom burden were less likely to receive chemotherapy and had a reduced overall survival. Targeted intervention of these symptoms could help improve both quality of life and performance status.

Background: Palliative systemic therapy is frequently underutilized in patients with advanced non–small-cell lung cancer (NSCLC), for many reasons. The aim of this study was to identify patient-reported factors that may predict for treatment decisions and survival in advanced NSCLC, using the Edmonton Symptom Assessment Scale (ESAS), which is a self-reported questionnaire that quantifies symptom burden by asking patients to rate the severity of 9 common symptoms. **Patients and Methods:** With ethics approval, we analyzed ESAS scores at initial oncology consultation for 461 patients with advanced NSCLC seen at The Ottawa Hospital Cancer Centre from 2009 to 2012. Subgroup analysis was performed to determine if treatment strategies or overall survival (OS) were related to the total symptom burden, as defined by the sum of the individual ESAS symptom scores. **Results:** The severity of the ESAS total symptom burden score was positively correlated with Eastern Cooperative Oncology Group performance status ($R = 0.48$; $P < .0001$). Furthermore, patients with a higher symptom burden were less likely to receive systemic chemotherapy than those with fewer symptoms (43% vs. 66%; $P < .0001$), and had a significantly reduced OS (5.5 vs. 9.9 months; $P < .0001$). A higher ESAS symptom burden score was also associated with reduced OS by univariate analysis (hazard ratio, 1.78; 95% confidence interval, 1.45-2.18; $P < .0001$), although multivariate analysis showed only a trend towards significance (hazard ratio, 1.27; 95% confidence interval, 0.99-1.62; $P = .06$). **Conclusions:** Overall, this demonstrates a novel role for the ESAS as a prognostic tool that could complement existing patient assessment models, such as Eastern Cooperative Oncology Group performance status, in the development of optimal treatment plans and estimation of survival, in patients with advanced lung cancer.

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Introduction

Non–small-cell lung cancer (NSCLC) is one of the most common cancers in Western populations, and the leading cause of cancer death worldwide, with only modest improvements in outcome achieved in recent decades.[1] The primary reason for the low survival rate is the advanced stage of disease that patients typically present with. Indeed, the majority of NSCLC patients will either present with, or relapse to have, incurable disease. This was illustrated in a recent real-world institutional review, where we reported that of 374 consecutive patients with NSCLC evaluated,

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only 160 (43%) were initially treated with curative intent, and of those, 56% relapsed within a short period of time to have incurable, advanced disease.[2]

The main treatment options for patients with advanced NSCLC include best supportive care, participation in clinical trials, and palliative systemic or radiation therapy. In the case of clinical trials investigating systemic therapy in NSCLC, eligibility criteria typically restrict participation to patients with a good performance status (PS), defined as an Eastern Cooperative Oncology Group (ECOG) score of 0-1, or Karnofsky score of > 70%. However, many patients with advanced lung cancer may also have other smoking-related comorbidities that can impact on their ability to receive systemic therapy (within or outside the context of a clinical trial).[3]

Palliative systemic therapy in advanced NSCLC can improve overall survival (OS) and palliate the symptoms of cancer, thereby improving and/or maintaining quality, and quantity, of life.[4,5] Furthermore, for some NSCLC molecular subtypes, such as epidermal growth factor receptor-mutation positive, or anaplastic-lymphoma kinase-translocation positive, new small molecule drugs that are orally administered can lead to significant improvements in cancer control and outcomes with greater tolerability. Despite these benefits, however, the rate of receipt of palliative systemic therapy in advanced lung cancer is low.[6,7]

Indeed, a population review from the Ontario Cancer Registry and Ontario New Drug Funding Program reported that, among all patients with metastatic lung cancer between 2005 and 2009, less than one-quarter received systemic therapy.[8] Although this review looked at population statistics based on billing codes, a more detailed review at our own institution found that, of 528 cases of advanced NSCLC, only 291 (55%) received systemic chemotherapy. The common stated reasons for not administering palliative systemic therapy were poor PS (67%) and patient choice (23%). Unsurprisingly, median OS was significantly shorter among untreated patients (3.9 vs. 10.7 months; hazard ratio, 1.80; 95% confidence interval, 1.4-2.3; $P < .01$).[9]

Given the significant variation in the treatment of advanced NSCLC, with frequent underutilization of potentially beneficial systemic therapy, we sought to identify additional, possibly reversible, factors that may be related to treatment and survival in these patients. To do this, we focused on patient symptom burden at initial presentation as assessed by the Edmonton Symptom Assessment Scale (ESAS), which was originally developed by Bruera et al as a bedside tool for patient self-reporting of symptom intensity.[10] As such, its primary application is in the palliative care setting, where it is used to monitor symptoms and response to treatment. In recent years, however, it has been applied to various chronic diseases including cancer, where it is used for clinical, administrative, and research purposes.[11]

In its current format, the ESAS consists of 9 common symptoms: pain, fatigue, drowsiness, nausea, anorexia, dyspnea, depression, anxiety, and well-being. Patients are asked to rate each of these on an 11-point scale from 0 (no symptom) to 10 (worst possible symptom).[12] Although the identification of numerical cut-offs defining clinically significant symptoms is challenging, many studies have shown that the intensity of the individual ESAS symptoms can be classified as absent (0), mild (1-3), moderate (4-6), or severe (≥ 7), with clinically significant symptoms defined by a score of ≥ 4.[13,14] Studies have also shown that an overall assessment of symptom severity can be obtained by adding individual symptom scores to yield the ESAS total symptom burden score, reported on a scale from 0 to 90. This too can be subclassified as absent (0), mild (1-30), moderate (31-60), or severe (61-90), with significant symptom burden defined by a score of ≥ 31.[15,16]

In this study, we attempted to determine whether the severity of patient symptoms at initial presentation, as defined by the ESAS total symptom burden score, or its individual symptom scores, were related to treatment decisions and survival in patients with advanced NSCLC.

Patients and Methods

Patient Population

A retrospective chart review was conducted to identify patients with de novo advanced NSCLC that were first seen as an outpatient consult by 1 of 4 thoracic medical oncologists (S.A.L., G.G., G.N., P.W.-P.) at our institution (a regional, academic, tertiary referral cancer center serving a mixed urban and rural population of about 1.4 million). Charts were reviewed between September 2009 and September 2012, with patients selected consecutively from each oncologist, to a maximum of 150 cases each. Inclusion criteria required that patients have histologically confirmed NSCLC, classified as either stage IV or IIIB with palliative treatment intent using the American Joint Commission on Cancer (AJCC) staging system (seventh edition). Patients previously treated with curative intent and referred upon relapse with advanced disease were excluded. Patients first assessed while hospitalized were also excluded.

Following application of inclusion and exclusion criteria, a final database of 528 patients was created. In addition to relevant clinicopathologic, treatment, and survival data, the database also included information related to patient symptomatology at presentation, primarily assessed by the ESAS questionnaire. PS was as rated by the physician, or if not stated, than as estimated from reports. Molecular data, specifically regarding epidermal growth factor receptor and anaplastic-lymphoma kinase status, was not available for the majority of patients (> 96%) as data was collected before the time of routine screening. The overall analyses and other analyses from this database have been presented elsewhere.[17,18] This analysis was confined to the 461 patients within the database with a fully complete ESAS questionnaire at the time of presentation. Approval for the study was obtained from the Ottawa Health Sciences Network Research Ethics Board.

The ESAS

Patient symptom burden was assessed at initial presentation using the ESAS, which as outlined above, consists of 9 common symptoms that patients rate on an 11-point scale, from 0 (no symptom) to 10 (worst possible symptom). All patients attending the cancer center are asked to complete an electronic version of the questionnaire prior to each outpatient consultation. The activity takes less than 15 minutes, and the results of each are used to compile an individual report of symptom development and progression. This data is part of a province-wide initiative to address symptom control.[19,20] For the purpose of this study, only ESAS questionnaires at presentation were analyzed, with an overall assessment of symptom severity obtained by adding individual symptom scores to generate the ESAS total symptom burden score. The total symptom burden