ORIGINAL ARTICLE

The Influence of Comorbidity and the Simplified Comorbidity Score on Overall Survival in Non-Small Cell Lung Cancer—A Prospective Cohort Study

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ABSTRACT

Introduction: We addressed the uncertainty of comorbidity as a prognosticator by evaluating comorbidity and the Simplified Comorbidity Score (SCS) as predictors of overall survival in non–small cell lung cancer (NSCLC).

Methods: A prospective study included patients in whom NSCLC was diagnosed at an Australian cancer hospital between 2012 and 2014. Patients were assessed for SCS at recruitment and followed up every 3 months until death.

Results: The cohort included 633 patients; their median age was 67 years (range 28–93), 63% were male, and 86% were ever-smokers. The median SCS at enrolment was 8 (range 0–19); 20% had an SCS higher than 9, and 11% had an SCS of 0. An SCS higher than 9 was associated with male sex, age older than 75 years, an Eastern Cooperative Oncology Group performance status of 2 or higher, and fewer cancer treatments. The 1-year overall survival rate was 62% (95% confidence interval: 58–66). In multivariate analysis, the strongest associations with mortality were metastatic disease (hazard ratio [HR] = 2.8, $p < 0.01$), Eastern Cooperative Oncology Group performance status of 2 or higher (HR = 2.0, $p < 0.01$), male sex (HR = 1.6, $p < 0.01$), more than 10% weight loss at diagnosis (HR = 1.5, $p < 0.01$), and age older than 75 years (HR = 1.5, $p = 0.01$). An SCS higher than 9 was not associated with overall survival (HR = 1.0, $p = 0.8$), and the effect of continuous SCS (HR = 1.1, $p < 0.01$) was explained by smoking status.

Conclusions: In this cohort of patients with NSCLC the SCS was not a clinically significant predictor of overall survival over and above basic patient and disease factors.

Keywords: Comorbidity; Simplified comorbidity score; Lung cancer; Survival; Risk score

Background

Lung cancer, a smoking related cancer with a sharply rising incidence in the over-60 population, is associated with a high level of both smoking-related and non–smoking-related comorbidity.[1] The importance of comorbid conditions to the prognosis of patients with lung cancer remains contentious, but they likely negatively

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affect survival directly or through effects on performance status and deliverability and tolerability of treatment.

The prognostic value of comorbidity in lung cancer survival has been widely investigated.[2–24] The two most utilized comorbidity risk scores are the Charlson Comorbidity Index (CCI) and the more recently developed Colinet Simplified Comorbidity Score (SCS).[3,25] The CCI was originally developed in a noncancer population but has since been validated in many cancer populations, including lung cancer populations. The SCS was developed and validated in a cohort of patients with non–small cell lung cancer (NSCLC) with its intended use specifically in this population. Derivation within a lung cancer population and inclusion of fewer parameters than in the CCI make the SCS an appealing tool for prognostication of lung cancer.

The predictive value of the SCS remains unclear, however, with few published studies and divergent findings. Since publication of the SCS in 2005,[3] four studies have evaluated its prognostic value: one in NSCLC,[4] one in SCLC,[6] and two in mixed NSCLC/SCLC cohorts.[2,5] One study each in NSCLC and in SCLC demonstrated an increased risk of mortality with elevated SCS (score >9 versus ≤ 9).[4,6] However, the remaining two studies found no association between the SCS and mortality.[2,5] A recent review of the effect of comorbidity on cancer survival reported minimal impact of comorbid conditions on the 5-year survival of patients with lung cancer relative to patients with other cancer diagnoses.[26] A plausible explanation posed by the authors is that that the poor survival outcome for lung patients with cancer generally means that any effect of comorbid disease on a relative scale is small.

The primary objective of this study was to evaluate the capability of the SCS to predict overall survival in a prospective cohort study of patients with NSCLC who were staged with the seventh edition of the tumor, node, and metastasis system (Union for International Cancer Control).[27] Secondary objectives included evaluation of overall comorbidity burden and the prognostic significance of individual comorbidities.

Methods

Population

The population for analysis was derived from the Peter MacCallum Cancer Centre Thoracic Malignancies Cohort (TMC) study, an ongoing single-center prospective observational study designed to monitor patients with lung cancer from first presentation until death. The TMC began recruiting in 2012 with approval of the institutional ethics committee. The TMC eligibility criteria included presentation to the lung cancer service of an Australian tertiary referral cancer hospital, diagnosis of lung or other respiratory/mediastinal cancer, and provision of informed consent. Further eligibility criteria for the current study included a histological diagnosis of NSCLC between January 1, 2012, and December 31, 2014, and at least one study follow-up after diagnosis. The earliest diagnosis date was restricted to January 1, 2012, to limit inclusion to only newly diagnosed cases from the TMC and thereby prevent survival bias associated with inclusion of long-term survivors enrolled in the TMC for ongoing treatment and/or surveillance.

Data

Data were collected by completion of a case report form at study entry and then periodically (every 3 months) at routine clinical appointments. The case report forms were completed by a dedicated project officer and verified by the treating clinician. Data included patient demographics, comorbid disease, cancer diagnosis, staging, and treatment. Staging was reported according to the seventh edition of the Union for International Cancer Control staging criteria,[27] which are based on the recommendations of the International Association for the Study of Lung Cancer staging project.[28] Comorbidities were documented at first consultation and defined according to the SCS, which includes the following health events (weighting in parentheses): past or current tobacco consumption (7), diabetes mellitus (5), renal insufficiency (4), respiratory comorbidity (1), cardiovascular comorbidity (1), neoplastic comorbidity (1), and alcoholism (1).[3] Performance status was reported according to the Eastern European Cooperative Group performance status (ECOG PS) criteria.[29] Loss of weight (LOW) refers to weight loss within 3 months of diagnosis and was analyzed categorically as 0% to 10%, 11% to 15%, or more than 15%. Smoking history was defined as current, past, or never, and when relevant, pack-years smoked and years since cessation of smoking were recorded.

Statistical Analyses

Data were summarized using descriptive statistics—for continuous variables, median, minimum, and maximum, and for categorical variables, counts and percentages. All statistical tests to compare comorbidity burden with other characteristics were performed using a two-sided significance level of 5% and corresponding 95% confidence intervals (CIs) were calculated. The association of SCS with patient, disease, and treatment factors was assessed using the chi-square statistic. SCS was assessed as a continuous variable, at a predefined threshold of higher than 9 versus 9 or lower,[3] and at various other thresholds. Survival probability was estimated using the Kaplan-Meier method and was calculated from date of tissue diagnosis until date of death, with living patients considered censored at date of last