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Original Article

Treatment Receipt and Outcomes among Lung Cancer Patients with Depression

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Abstract

Aims: Among lung cancer patients, depression has been associated with increased mortality, although the mechanisms are unknown. We evaluated the association of depression with mortality and receipt of cancer therapies among depressed veterans with lung cancer.
Materials and methods: A retrospective, cohort study of lung cancer patients in the Veterans Affairs-Northwest Health Network from 1995 to 2010. Depression was defined by ICD-9 coding within 24 months before lung cancer diagnosis. Multivariable Cox proportional analysis and logistic regression were used.
Results: In total, 3869 lung cancer patients were evaluated; 14% had a diagnosis of depression. A diagnosis of depression was associated with increased mortality among all stage lung cancer patients (hazard ratio = 1.14, 95% confidence interval: 1.03–1.27, $P = 0.01$). Among early-stage (I and II) non-small cell lung cancer (NSCLC) patients, the hazard ratio was 1.37 (95% confidence interval: 1.12–1.68, $P = 0.003$). There was no association of depression diagnosis with surgery (odds ratio = 0.83, 95% confidence interval: 0.56–1.22, $P = 0.34$) among early-stage NSCLC patients. A depression diagnosis was not associated with mortality (hazard ratio = 1.02, 95% confidence interval: 0.89–1.16, $P = 0.78$) or chemotherapy (odds ratio = 1.07, 95% confidence interval: 0.83–1.39, $P = 0.59$) or radiation (odds ratio = 1.04, 95% confidence interval: 0.81–1.34, $P = 0.75$) receipt among advanced-stage (III and IV) NSCLC patients. Increased utilisation of health services for depression was associated with increased mortality among depressed patients.
Conclusions: Depression is associated with increased mortality in lung cancer patients and this association is higher among those with increased measures of depression care utilisation. Differences in lung cancer treatment receipt are probably not responsible for the observed mortality differences between depressed and non-depressed patients. Clinicians should recognise the significant effect of depression on lung cancer survival.

Key words: Depression; epidemiology; lung cancer; lung cancer treatment; patient outcomes

Introduction

Lung cancer is the leading cause of cancer-related death in the USA [1] and is associated with significant psychological distress [2]. Depression or depressive symptoms have been associated with worse mortality among lung cancer patients [3,4], although this relationship has been inconsistent [4–10]. Previous research examining lung cancer mortality has been limited by small sample sizes [3,6–11], and discordant definitions of depression and methods of adjustment for other psychiatric comorbidities [3–9].

Studies examining the association of depression with mortality among lung cancer patients have only begun to explore the potential mechanisms of reduced survival.

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There is some suggestion that quality of life may be a key intermediary [12,13]. It is possible that depressed patients choose not to initiate or continue treatments [14], although therapy adherence and its effect on mortality have not been systematically studied among lung cancer patients.

In order to examine this association and to ascertain mechanisms, we examined mortality among lung cancer patients with comorbid depression, adjusting for patient, tumour and treatment characteristics. We explored possible mechanisms responsible for worse outcomes among depressed patients by evaluating the effect of lung cancer treatment receipt. We hypothesised that patients with depression would be less likely to receive treatment and may be more likely to delay treatment.

Materials and Methods

We identified patients with lung cancer in the Veterans Integrated Service Network 20 (VISN20) oncology registry, 1 January 1995 to 31 December 2010. VISN20 includes patients receiving care in the Veterans Affairs health network from Alaska, Idaho, Oregon and Washington. Veterans Affairs registrars carry out identification, abstraction and follow-up activities with adherence to the standards of the Commission on Cancer [15].

We combined relevant demographic, medical and cancer treatment history utilising information from the registry and the patients' electronic medical record from the VISN20 data warehouse. Of the 3914 patients initially identified, we excluded 19 whose vital status was unknown, 13 with stage 0 lung cancer, eight with non-primary lung cancer histologies (e.g. metastatic renal cell carcinoma), one with mesothelioma histology and four with a lung cancer diagnosis recorded only on the death certificate or at autopsy. We excluded 491 patients who did not have an outpatient clinical encounter in the 2 years before their lung cancer diagnosis, as information on a possible diagnosis of concomitant depression was unavailable.

This study was approved by the Institutional Review Board at the Portland Veterans Affairs Health Care System (IRB#2588).

We identified patients with a diagnosis of depression as recorded in the VISN20 data warehouse (ICD-9: 296.2x/296.3x/311.xx/309.1x/300.4x/309.0x/298.0x) [16–18]. We used the following criteria to define concomitant depression within 2 years before the lung cancer diagnosis date: (i) one or more primary diagnosis as an inpatient or outpatient; (ii) one or more secondary diagnosis during any inpatient stay or (iii) at least two secondary diagnoses as an outpatient on different days, which were no more than 12 months apart [16,19].

Active antidepressant medications were defined as a prescription listed in the VISN20 data warehouse, received by the patient within 90 days before the lung cancer diagnosis date. We included the following medications: amitriptyline, isocarboxazid, citalopram, desvenlafaxine, bupropion, mirtazapine, clomipramine, phenelzine, escitalopram, duloxetine, desipramine, seleginine, fluoxetine, venlafaxine, doxepin, tranylcypromine, paroxetine, milnacipran, imipramine, sertraline, nortriptyline, fluvoxamine, protriptyline, amoxapine, maprotiline, and trimipramine [16,20]. Depression-related hospitalisations and mental health clinic visits [19] within 24 months of cancer diagnosis were collected from the VISN20 data warehouse utilising ICD-9 codes and primary stop codes of outpatient encounters, respectively [21,22].

The primary outcome was all-cause mortality. Veterans Affairs cancer registrars obtain vital status information from the Social Security Administration Death Master File (SSADMF). In addition, registrars identify deceased veterans through death certificates internal to the Veterans Health Administration, as well as other Veterans Affairs programmes, including pension and burial services. The Veterans Affairs exchanges mortality information with the Center for Medicare/Medicaid Services and the SSADMF. Vital status in Veterans Affairs cancer registries is updated at least annually. Therefore, we censored vital status for all living patients to the last date they were known to be living at data extraction.

We identified three secondary outcomes of primary cancer treatment administered within 180 days of the cancer diagnosis date [23]; all categorised dichotomously (yes/no): radiation receipt, surgical resection and chemotherapy receipt. Receipt of radiation and/or surgery was recorded in the cancer registry. Receipt of chemotherapy was defined as receipt of any of the following medications as recorded in the VISN20 data warehouse: carboplatin, cisplatin, paclitaxel, docetaxel, gemcitabine, vinorelbine, etoposide, teniposide, irinotecan, topotecan, ifosfamide, cyclophosphamide, doxorubicin, epirubicin, amrubicin or vincristine [24].

Patients' demographic characteristics were collected at the diagnosis date from the VISN20 data warehouse or Veterans Affairs cancer registries and included, but were not limited to, patients' zone improvement plan at the place of primary residence, which was used to calculate distance in miles from the primary residence to the nearest tertiary Veterans Affairs medical centre and comorbidities during the year before lung cancer diagnosis were collected using the Deyo adaptation of the Charlson Comorbidity Index (CCI) score [25,26].

Analysis

Descriptive statistics were used to categorise race/ethnicity, age at diagnosis, gender, tobacco use at diagnosis, tumour stage, histological subtype and CCI.

Survival for lung cancer patients with and without a depression diagnosis was compared between patients using Cox proportional hazard models with robust standard errors. Survival models were *a priori* adjusted for age, year of diagnosis, CCI, race/ethnicity, tobacco use at diagnosis, lung cancer stage and histology. Survival was evaluated separately by stage at diagnosis.

We used a robust logistic regression model to calculate odds ratios to evaluate the association of depression diagnosis with treatment receipt. Separate models were created