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Original Article

History of Depression in Lung Cancer Patients: Impact of Delay

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Abstract

Aims: To examine the influence of a history of depression in the process of diagnostic evaluation and the choice of treatment in lung cancer.**Materials and methods:** The analysis was based on all patients with non-small cell lung cancer who were registered in 2008–2014; in total, 27 234 patients. To estimate the effect of depression on the diagnostic process and the choice of treatment in lung cancer we fitted a logistic regression model and a Cox regression model adjusting for age, gender, resection and stage.**Results:** Depression in a patient's anamnesis had no significant effect on the delay in diagnostic evaluation (hazard ratio = 0.99 with 95% confidence interval 0.90; 1.09). Patients with a history of periodic depression had a 33% lower treatment rate (odds ratio = 0.66 with 95% confidence interval 0.51; 0.85) than patients without a history of depression.**Conclusions:** Our study shows that patients with a history of periodic depression need special attention when diagnosed with lung cancer.

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Key words: Depression; diagnostic evaluation; lung cancer; socio-economic status; treatment

Introduction

With an annual incidence of 4500 patients, primary lung cancer is one of the most common cancers in Denmark. In general, the lung cancer prognosis is poor, with a 5 year survival of about 10–12%. Comorbidity is common in patients with lung cancer (26–81%) [1] and an increased comorbidity increases mortality significantly [2]. Depression has been associated with increased mortality in patients with lung cancer [3,4], but not much is known as to the reason. Spiegel and Giese-Davis [5] identified several reasons why depression may have an effect on the mortality of cancer patients in general. First, depression may have a pathophysiological effect via a neuroendocrine and

immunological function that influences mortality. Second, many of the symptoms of cancer and the side-effects of its treatment are similar to those of depression, e.g. sleep disturbance, anorexia, fatigue and concentration difficulties. Therefore, referral to an examination for cancer can be delayed for depressed patients. Third, patients with depression may be less likely to adhere to preventive screening procedures, cancer treatments or recommendations for maintaining good health. Depression and smoking are associated [6] and lung cancer-specific symptoms, such as cough and shortness of breath, are common in heavy smokers, thus hiding the lung cancer symptoms and adding further delay to the diagnosis. Depressed patients may miss screening appointments and are thus more likely to delay the treatment and less likely to receive treatment or to implement treatment [7].

Diagnostic procedures in suspected lung cancer are carried out to establish a diagnosis and the stage of lung cancer. The choice of treatment is furthermore based on the patient

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performance and comorbidity. Patients may be treated with surgical resection or chemo- and/or radiotherapy. Recently targeted and immunotherapy are added to treatment options. Surgical resection of the tumour is associated with the best survival, but only about 20% of the patients are eligible for resection. The clinical stage and performance are the most important factors when deciding on the treatment. A range of other prognostic factors are also taken into account before the final decision about treatment is made, including age, smoking, alcohol or drug abuse, patient preferences and comorbidity.

The aim of this study was to examine the influence of the history of depression in the process of diagnostic evaluation and the choice of treatment in lung cancer. A similar study has previously been carried out in the USA by Sullivan *et al.* [4], but without taking into account the differences in the patient's socio-economic status. They found no association of depression diagnosis with receiving treatment. It is well known that there is a strong association between socio-economic position and the experience of depression [8] and that a low socio-economic status is associated with late-stage cancer diagnoses and the type of treatment received [9,10]. Here we investigated the effect of a history of depression when adjusting for the patient's socio-economic status.

Materials and Methods

We used data from the four national registries:

The Danish Lung Cancer Registry

We used the Danish Lung Cancer Registry (DLCR) to identify patients in Denmark with lung cancer. Since 2000 the DLCR has monitored and evaluated the quality of treatment effort concerning lung cancer [11]. All Danish lung cancer patients are included in the DLCR and to this date the database contains data on more than 55 000 cases of lung cancer. Between 2000 and 2002 clinicians identified and reported new patients to the DLCR, but since 2003 lung cancer patients have been identified in the Danish National Patient Registry (DNPR), where the first occurrence of the diagnostic codes DC34 and DC33, according to the International Classification of Diseases 10 (ICD-10), are identified. Information about these patients and their activities (procedures and treatments) registered with the DNPR, together with information from the Danish Pathology Registry, provides the basis of establishing patient trajectories and associated diagnostic procedures and treatments in the DLCR. Only about 75% of the information required for the DLCR is available in the Danish central registries and the participating clinicians are requested to supplement with the remaining about 25% of information from their medical records. As participation in this supplementation is mandatory by law, data completeness is very high (more than 95%). Data on comorbidity were obtained from the DNPR [12]. The history and status on depression is not

requested routinely by the DLCR and was obtained specifically for this project.

The Danish Depression Database

We retrieved data from the Danish Depression Database [13] to identify patients with a history of depression. The database includes all patients who are 18 years or older with a diagnosis of depression, have permanent residence in Denmark and are hospitalised or affiliated with a psychiatric hospital in Denmark. The disease is diagnosed according to ICD-10 criteria and includes all sub-codes: DF32.X - depressive episode (DF32.0; DF32.1; DF32.2; DF32.3; DF32.8; DF32.9); DF33.X - recurrent depressive disorder (DF33.0; DF33.1; DF33.2; DF33.3; DF33.4; DF32.8; DF32.9); DF34.1X - dysthymia; DF06.32 - organic affective disorder, depressive.

We included both in-patients and out-patients who had at least one hospital contact with depression (DF32.X depressive episode and DF33.X recurrent depressive disorder) within 10 years before the start of the lung cancer diagnostics process. We excluded from our analysis patients with dysthymia and organic depression as the definition and diagnostic delineation of these two groups is more uncertain. Here we will examine the effect of the following three groups of patients: one includes patients with the diagnosis 'depressive episode' (ICD-10 DF32.X), another includes patients with the diagnosis 'recurrent depressive disorder' (ICD-10 DF33.X) and the last one includes patients from both groups.

The National Patient Register

We included information on comorbidity for each patient up to 10 years before the lung cancer diagnosis, using the DNPR, which was established in 1977. This register contains data on all interventions related to diagnostic evaluation and treatment for somatic patient admissions in Denmark [14]. We used a modification of the Charlson comorbidity index (CCI) for the classification of somatic comorbidity [15]. All hospital contacts represented with a cancer diagnosis, registered within 150 days before the date of lung cancer diagnosis, were excluded from contribution to the cancer comorbidity group in order to avoid the influence of misclassification of cases with lung cancer before the final diagnosis.

The Income Statistics Register

We included information on the socio-economic status of each patient at the time of the lung cancer diagnosis, using information available with The Income Statistics Register [16]. The socio-economic class was defined as household income in the year the patient was diagnosed with lung cancer, adjusted for the number of people in the household. The socio-economic class was divided by the median into two groups, low and high.

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