The influence of psychiatric disorders on the course of lung cancer, chronic obstructive pulmonary disease and tuberculosis

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ARTICLE INFO

Keywords:
COPD
Tuberculosis
Lung cancer
Psychiatric comorbidity

ABSTRACT

Background: This Danish study evaluated the association between psychiatric comorbidity and the course of chronic obstructive pulmonary disease (COPD), lung cancer and tuberculosis (TB) of an entire nation.

Methods: Data from the Danish National Patient Registry (1998–2009), material status, gender, educational level, comorbidities, age at diagnosis and death, medication, and causes of death were extracted from national databases. We identified 71,874 patients with COPD and found 32,282 with a pre-index psychiatric comorbidity, 20,787 patients with lung cancer and found 8406 with a pre-index psychiatric comorbidity, and 3495 patients with TB and found 797 with a pre-index psychiatric morbidity. Within the three groups we compared the patients with/without a pre-index psychiatric comorbidity.

Results: We found a reduced survival in patients with COPD or TB and a pre-existing psychiatric comorbidity. For all three pulmonary diseases, we found significantly higher age (p < .001) at time of diagnosis, higher Deyo-Charlson Comorbidity Index (p < .001), and an overrepresentation of singles (p < .001) in patients with a psychiatric comorbidity. COPD and lung cancer patients with a psychiatric comorbidity were significantly overrepresented by women (p < .001). Patients with COPD and a psychiatric comorbidity died most frequently of lung cancer (24%). Advancing age and Deyo-Charlson index were associated with a higher mortality rate whereas being a woman and married/co-habiting yielded a lower mortality rate for patients with a psychiatric comorbidity.

Conclusion: To our knowledge, this is the first epidemiological study investigating the influence of a psychiatric comorbidity on the course of COPD, lung cancer and TB at a national level. Our results emphasize the importance of detecting these major respiratory diseases in patients with psychiatric comorbidities and intensifying the treatment and follow up of these patients.

1. Background

Little is known about the influence of psychiatric disorders on physical diseases. Pulmonary diseases are amongst the most prevalent diseases and patients with a psychiatric disorder have a higher risk of developing chronic obstructive pulmonary disease (COPD), lung cancer and tuberculosis (TB) compared with the general population.

An increased risk of cancer in patients with bipolar disease and an increased risk of lung cancer/smoking associated cancers in patients with depression has been described [1–4]. Hung et al. [2] found that the younger a patient was when first treated for an affective disorder, the higher the risk of cancer. However, literature on the association between affective disorders and lung cancer is sparse.

The literature on the risk of developing cancer amongst schizophrenics is contradictory and earlier studies found that cancer, especially respiratory cancers, is less common in schizophrenics compared with the general population [5,6]. Reduced exposure to tobacco (due to restrictions on smoking at psychiatric wards in the 50s and 60s), a suggested protective effect of neuroleptica as well as genetic factors have been suggested as possible explanations [7]. Several recent studies have, however, found an increased risk of lung cancer among schizophrenics [4,7–9]. Affective disorder and schizophrenia are also more common in patients with COPD than in the general population [10–13].

TB is a chronic infectious disease caused by Mycobacterium Tuberculosis. Although the worldwide incidence of TB is decreasing, it is still one of the leading causes of morbidity and mortality in the world [14]. The incidence of TB in Denmark is low (2015: 6 per 100,000 per year) [15] but the TB incidence is increasing, particularly in high risk
subpopulations, due to active disease transmission [16].

The literature on the association between TB and psychiatric disorders is sparse and widely based on data from third-world countries due to the high prevalence of TB in these countries. Studies suggest that depression and anxiety is more common in patients with TB infection than in the general population and the incidence of depression increases with age, male gender, and low income [17–19].

Previous studies have suggested that patients with a psychiatric comorbidity may have a poorer course of the respiratory disease. Thus, we studied the influence of a psychiatric comorbidity on the course of lung cancer, COPD, and TB during a period of 12 years in a Danish population of 5.5 million citizens.

2. Methodology

In Denmark, all hospital contacts, primary and secondary diagnoses are registered in the National Patient Registry (NPR) [20]. The NPR includes administrative information, diagnoses, and diagnostic and treatment procedures using several international classification systems, including the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10 Version: 2010).

The NPR is a time-based national database that includes data from all inpatient and outpatient contacts. The data we extracted is representative of all patients in Denmark who has received a first time primary and secondary diagnosis of lung cancer, COPD, and TB, irrespective of other diagnoses. As data are available for the entire 12-year observation period, we can trace patients retrospectively and prospectively relative to the time of diagnosis. Furthermore, all contacts in the primary sector (general practice and specialist care) and use of medication are recorded in the databases of the National Health Security and the Danish Health Authority and the Cause of Death Registry, respectively.

We extracted the following first primary or secondary diagnoses from the NPR in the time period 1998–2009: Malignant neoplasm of bronchus and lung (C34), COPD (J44), and Tuberculosis (A15-A19). The following psychiatric diagnoses were included: Alcohol (F10.1 + F10.2), other substance addiction (F11, F12, F13, F16, F19), schizophrenia (F20), bipolar affective disorder (F31), depressive episode (F32), Recurrent depressive disorder (F33), other (F30), other anxiety episode (F41), other (F4), behavioral syndromes associated with physiological disturbances and physical factors (F5) and disorders of personality and behavior in adult persons (F6). Data on disease severity was not available.

A large number of patients with a psychiatric disorder are solely treated by their general practitioner. In Denmark, ICD-10 classification is, however, only used in the secondary health sector (hospitals). To include these patients, we defined a patient with a psychiatric disorder as a patient who in the three-year pre-index period had at least one registered psychiatric diagnosis and/or received medication for a psychiatric disorder and picked up the same medication on prescription (same ATC main group) at least three times in one year in the three-year period before the index date.

The following types of medications were included (ATC): Antiepileptica (N03A), antipsychotica (N05A), anxiolytica (N05B), hypnotics and sedatives (N05C), antidepresive (N06A), and psycholeptica and psychoanalptica in combination (N06C). Patients are entering the population at index date (year = 0) any time in period 2001–2006, when diagnosed with the somatic diagnosis.

Patients with a first time psychiatric diagnosis and/or who received psychiatric medication for the first time more than three years after the somatic diagnosis index date were included in the population as patients with no psychiatric disorder.

Patients receiving their first time psychiatric diagnosis and/or who received psychiatric medication for the first time in the three-year post-index period after the index date were excluded from the population.

Using data from the Danish Civil Registration System, such as marital status, social factors, educational level, etc. [21], we compared patients with psychiatric comorbidity to patients without psychiatric comorbidities. The Deyo-Charlson Comorbidity Index was used to express pre-comorbidity, and comorbidity was defined as pre-comorbidity in the tree-year period before the somatic diagnosis. Neither the NPR nor any of the other national databases contains information about smoking status.

Patients with psychiatric comorbidity and controls matched on age, gender, geography, and educational level were followed through the entire study period or until death. If a patient or control was not present in the registry on January 1 each year due to death, imprisonment or immigration, the corresponding control or patient control was not included in the dataset for that year.

If a diagnosis of lung cancer, COPD, or TB in any given individual was established in the first year (1998) we would be able to follow that individual 12 years forward in time. If the diagnosis of one of the three diseases in any individual was made in the last year (2009) we would be able to follow that individual 12 years backwards in time.

The study was approved by the Danish Data Protection Agency. Ethics approval was not obtained, as all data was anonymous.

3. Statistical analysis

Statistical analysis was performed using SAS V.9.1.3 (SAS Inc, Cary, North Carolina, USA). A Cox’s regression was used to model the hazard of death after diagnosis index date. Survival was estimated using the Kaplan-Meier method.

4. Results

From the NPR, we identified and extracted patients diagnosed with COPD, lung cancer, and TB in the period between 2001 and 2006 (and looked three years before and after for further data), and patients with a psychiatric comorbidity. We identified 71,874 patients with COPD and 32,282 with a pre-index psychiatric comorbidity, 20,787 patients with lung cancer and 8406 with a pre-index psychiatric comorbidity and 3495 patients with TB and 797 with a pre-index psychiatric comorbidity (Table 1). Characteristics of age at diagnosis, gender, Deyo-Charlson Comorbidity Index, and marital status in patients with COPD, TB, or lung cancer with or without a psychiatric comorbidity are shown in Table 1. For all three pulmonary diseases, we found significantly higher age (p < .001) at time of diagnosis, higher Deyo-Charlson Comorbidity Index (p < .001) and an overrepresentation of singles (p < .001) among patients with a psychiatric comorbidity. In patients diagnosed with COPD and lung cancer with no psychiatric comorbidity, men constituted the majority whereas patients with COPD and lung cancer with a psychiatric comorbidity were significantly over-represented by women (p < .001). Men with TB were overrepresented in both groups (p = .972).

Table 2 shows causes of death in patients with COPD, TB, and lung cancer with or without a psychiatric comorbidity. In patients with COPD and no psychiatric comorbidity, 22% died of COPD whereas in the group of patients with COPD and a psychiatric comorbidity, COPD merely constituted 3.1%. In the latter group the majority died of lung cancer (24%) and other types of cancer, whereas lung cancer constituted 10% in the group without psychiatric comorbidity.

In patients with TB and a psychiatric comorbidity, alcoholic cirrhosis (3.8%) and chronic alcoholism (2.7%) were frequent causes of death, which differed from patients with TB and no psychiatric comorbidity.

The majority of patients diagnosed with lung cancer died from the disease regardless of having a psychiatric comorbidity (83%/80%). Overall, the causes of death in these two groups were comparable.

Fig. 1 shows decreased survival if psychiatric comorbidity was present in patients with TB and COPD, but not in lung cancer.

Mortality hazard ratios for each group with a psychiatric...
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