The Association Between Major Depressive Disorder and Outcomes in Older Veterans Hospitalized With Pneumonia

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ABSTRACT

Background: Major depressive disorder ("depression") has been identified as an independent risk factor for mortality for many comorbid conditions, including heart failure, cancer and stroke. Major depressive disorder has also been linked to immune suppression by generating a chronic inflammatory state. However, the association between major depression and pneumonia has not been examined. The aim of this study was to examine the association between depression and outcomes, including mortality and intensive care unit admission, in Veterans hospitalized with pneumonia.

Materials and Methods: We conducted a retrospective national study using administrative data of patients hospitalized at any Veterans Administration acute care hospital. We included patients ≥65 years old hospitalized with pneumonia from 2002-2012. Depressed patients were further analyzed based on whether they were receiving medications to treat depression. We used generalized linear mixed effect models to examine the association of depression with the outcomes of interest after controlling for potential confounders.

Results: Patients with depression had a significantly higher 90-day mortality (odds ratio 1.12, 95% confidence interval 1.07-1.17) compared to patients without depression. Patients with untreated depression had a significantly higher 30-day (1.11, 1.04-1.20) and 90-day (1.20, 1.13-1.28) mortality, as well as significantly higher intensive care unit admission rates (1.12, 1.03-1.21), compared to patients with treated depression.

Conclusion: For older veterans hospitalized with pneumonia, a concurrent diagnosis of major depressive disorder, and especially untreated depression, was associated with higher mortality. This highlights that untreated major depressive disorder is an independent risk factor for mortality for patients with pneumonia.

Key Indexing Terms: Mortality; Major depressive disorder; Pneumonia. **[Am J Med Sci 2018;355(1):21–26.]**

INTRODUCTION

Approximately 35 million people in the United States will be diagnosed with major depressive disorder in their lifetime,[1] making it one of the most prevalent mental health diseases. The Centers for Disease Control and Prevention state that major depressive disorder is responsible for 8 million ambulatory care visits a year.[2] This significant health and economic burden of depression has necessitated a better understanding of the disease and its role as a significant risk factor in many other common medical conditions. Depression has already been shown to be an independent risk factor for mortality in heart failure, stroke and cancer.[3-5] In addition, depression has been shown to cause immune dysregulation and suppression, which is believed to be one possible mechanism of depression's associated risk.[6] However, despite those facts, there is limited data on the relationship between depression and acute infections, such as pneumonia.

Pneumonia and influenza are the leading infectious causes of death in the United States.[7] Pneumonia is responsible for approximately 1.2 million hospital discharges a year.[8] A recent study found that there was an increased independent association between depression and the odds of hospitalization for pneumonia.[9] However, to our knowledge, there are no previous studies on whether depression may worsen clinical outcomes in patients hospitalized with pneumonia.

The aim of this study is to determine the association between major depressive disorder and outcomes, namely 30- and 90-day mortality and intensive care unit (ICU) admission, in patients ≥65 years of age who are hospitalized with pneumonia after adjusting for potential confounders. Given that depression has been linked to immune dysregulation, our *a priori* hypothesis was that a diagnosis of depression would be associated with increased mortality for older patients hospitalized with pneumonia.

MATERIALS AND METHODS

We conducted a retrospective cohort study using clinical and administrative databases of the Department of Veterans Affairs (VA) Health Care System.

These databases are the repositories of clinical data from all VA hospitals and outpatient clinics.[10] The Institutional Review Board of the VA North Texas Health Care System approved this study. A more detailed discussion of the methods of this study has been previously published.[10]

Inclusion Criteria

Inclusion criteria included

(1) Hospitalization between October 1, 2001 and September 30, 2012.
(2) Aged 65 years or older on the date of admission.
(3) Discharged with a diagnosis of pneumonia defined as either a primary diagnosis of pneumonia (International Classification of Diseases, Ninth Revision [ICD-9] codes 480.0-483.99 or 485.0-487.0) or a secondary diagnosis of pneumonia with a primary diagnosis of respiratory failure (ICD-9 code 518.81) or sepsis (ICD-9 code 0.38xx).
(4) Had at least 1 dose of antimicrobial therapy within the first 48 hours of admission.
(5) Present at 3 or more VA outpatient clinic visits in the year preceding admission.

For patients who were admitted more than once during the study period, only their first hospitalization was included.

Data Sources and Definitions

The inpatient and outpatient demographic, utilization, pharmacy and comorbidity data from the VA Corporate Data Warehouse were used.

Major depressive disorder was identified using ICD-9 codes 296.2, 296.3 or 311 listed in the 12 months before admission. Treated depression was defined as having an outpatient prescription filled for a selective serotonin reuptake inhibitor, serotonin-norepinephrine reuptake inhibitor or tricyclic antidepressant in the 90 days before admission. The specific medications included in the definition were Bupropion, Citalopram, Fluoxetine, Mirtazapine, Paroxetine, Sertraline, Trazodone, Venlafaxine, Amitripytline, Clomipramine, Desipramine, Doxepin, Imipramine and Nortriptyline. Anxiolytics and antipsychotic medications were excluded from the definition of treated depression due to their frequent use in treating conditions other than depression.

The date of death identified by the VA Vital Status file was used to determine mortality, which has approximately a 98% accuracy in reporting mortality.[11]

Race and ethnicity categories included white, black, Hispanic and other or unknown. Tobacco use and smoking cessation efforts were identified using ICD-9 codes for tobacco use (305.1, V15.82), smoking cessation clinic use and use of medications for the treatment of nicotine dependence (bupropion, nicotine replacement, or varenicline). Alcohol abuse was defined using ICD-9 codes 291, 303, 305.0 and illicit drug use by ICD-9 codes 292, 304, 305 (excluding 305.0-.1). Mental health conditions, including bipolar disorder, schizophrenia and posttraumatic stress disorder, were defined using the Selim method, which includes a patient-reported mental health survey validated in the elderly VA patient population.[12,13] We used the Charlson-Deyo comorbidity methodology to classify other preexisting comorbid conditions.[14] Priority status was used as a proxy for socioeconomic status.[15]

To further control for potential confounding by medications, a count of unique drugs in each of the following classes was calculated for outpatient prescriptions filled within 90 days before presentation: statins, β-blockers, calcium channel blockers, anxiolytics, antipsychotics, oral antidiabetic agents, insulin, other antihypertensive agents, inhaled beta agonists, other bronchodilators, theophylline and oral corticosteroids. In addition, dichotomous variables were created to identify those with corticosteroid use or outpatient use of any antibiotics within 90 days before admission.

Outcomes

Primary outcomes were 30-day and 90-day mortality. While 30-day mortality has largely been shown to be associated with pneumonia-related mortality, 90-day mortality has been shown to be comorbidity related.[16] Therefore, both were used as primary outcomes. A secondary outcome was ICU admission rate, which was chosen as a proxy for severity of illness while hospitalized.

Statistical Analysis

Bivariate statistics were used to test the association of sociodemographic and clinical characteristics with all-cause 30-day and 90-day mortality as well as our secondary outcome. Categorical variables were analyzed using the chi-square test and continuous variables were analyzed using Student's *t*-test or Wilcoxon rank-sum test where appropriate.

We used generalized linear mixed effect models to examine the association of major depressive disorder with the outcomes of interest after controlling for potential confounders, including sociodemographics (age, race, sex, marital status and priority status), comorbid conditions based on a Charlson comorbidity score (such as heart failure and cirrhosis), mental health conditions (such as bipolar disorder and alcohol abuse) identified using the Selim method, prior outpatient health care utilization in the 12 months before admission, severity of illness and the admitting hospital. The model was then adjusted to examine the association between treated depression, as defined earlier, with the outcomes of interest, as opposed to the association between untreated depression with the outcomes of interest.