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Depression and survival in head and neck cancer patients

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ABSTRACT

Objective: Though depression often afflicts head and neck cancer (HNC) patients, few studies have examined the association between depression and survival in this particular cancer population. The objective of this study is to investigate the five-year survival of HNC patients by depression status.
Materials and methods: This study used SEER-Medicare data from 2002–2010 and identified depression diagnosis two years before and one year after cancer diagnosis. HNC patients were identified using ICD-O3 codes and depression was identified using ICD-9-CM codes from Medicare claims.
Results: Of the 3466 patients included in the study, 642 (18.5%) were diagnosed with depression during the study period. Compared to those who received no depression diagnosis, those diagnosed with depression prior to cancer or after cancer diagnosis were more likely to die of cancer (HR = 1.49; 95% CI = 1.27, 1.76 and HR = 1.38; 95% CI = 1.16, 1.65, respectively). Similarly, when looking at death from any cause, those diagnosed with depression prior to cancer diagnosis and those who received a diagnosis of depression after cancer were more likely to die from any death compared to those without depression (HR = 1.55; 95% CI = 1.36, 1.76 and HR = 1.40; 95% CI = 1.21, 1.62, respectively).
Conclusions: The results emphasize the need for early identification and treatment of depression in HNC patients, as well as the establishment of policies to routinely screen these patients throughout the cancer treatment process.

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Introduction

Lower survival and poorer outcomes have been demonstrated in cancer patients with depression [1–3]. Previous studies examining depression in cancer populations have found higher cancer recurrence and lower quality of life in cancer patients with clinical depression or depressive symptomology [1,4]. Depression has also been associated with increased mortality in patients with cancer, with mortality rates up to 25% higher in cancer patients who experience depression [5,6]. Though previous studies have examined the effect that depression may have on cancer mortality rates, there are few large-scale studies that have examined the association between depression and survival in patients with head and neck cancers (HNC).[1]

HNC patients face unique psychological challenges compared to many other cancer sites. HNCs and their treatments can cause severe physical and functional impairments, which have been associated with depression development in HNC patients [7–10]. Further, radiation therapy has been shown to be significantly associated with depression [11]. Moreover, patients with HNC may experience permanent facial disfigurement from treatments [10], and unlike other cancer sites, patients may be left with visible scars or deformities that cannot be concealed, which may cause issues with personal shame and self-consciousness, and ultimately lead to depression [12–14].

Because of the associations between HNC and depression, as well as the psychological impact that these cancers and their treatments may have on patients, we previously examined depression rates in HNC patients both before and after cancer diagnosis utilizing two linked national datasets [15]. The results of this study showed not only that depression diagnosis in HNC patients was moderately higher than estimates from other cancer sites, but also that depression was associated with advanced stage at diagnosis.

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[1] HNC: Head and neck cancer.

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However the question still remains as to the effect that depression has on the survival of HNC patients. Therefore, the objective of the present study is to investigate the five-year survival of HNC patients by depression status.

Materials and methods

We utilized the Surveillance Epidemiology and End Results (SEER)-Medicare[2] linked data from 2002–2010. We identified all individuals diagnosed with HNC from 2004–2005 based on International Classification of Disease for Oncology, Version 3 (ICD-O3)[3] codes who were linked to Medicare data. Individuals had to have HNC as their only cancer diagnosis and be 67 years of age or older at the time of diagnosis in order to ensure a minimum of two years of Medicare enrolment prior to cancer diagnosis. Individuals had to be continuously enrolled in Medicare Parts A and B for 24 months prior to their HNC diagnosis until December of 2010 or their death, and could not be enrolled in a health maintenance organization (HMO)[4] during this same time period due to the possibility of incomplete claims records [2,15].

From this group, diagnosis of depression two years prior to cancer diagnosis was identified using ICD-9-CM codes from Medicare claims data. To be included in the preexisting depression group, subjects had to have at least one claim diagnosis of depression within the 24 months prior to HNC diagnosis. To be considered part of the post-HNC depression group, participants could not have been diagnosed with depression before cancer diagnosis and had to have at least one inpatient, outpatient, or carrier claim diagnosis of depression within one year after diagnosis of HNC. Individuals whose reporting source indicated they were diagnosed with HNC at the time of death or autopsy were excluded from all analyses for the present study [15].

Five-year survival of all patients was examined, with censoring time being December 2010 (the end of the study period). The survival of patients was identified using the number of years and months of survival provided in SEER data. For this variable, survival time was calculated using the date of diagnosis and either the date of death, date last known to be alive, or December of 2010 for the study data. Survival outcomes of interest included all-cause and cancer-specific death based on SEER data reporting. For all-cause mortality, vital status at the end of the study period (December 2010) was used. For cancer specific survival, deaths attributed to HNC were treated as events and deaths from other causes were treated as censored observation [16].

Statistical analysis

Kaplan-Meier curves were used to examine basic survival estimates by depression status of patients. Cox regression models were used to control for potential confounding variables. Covariates included in the models were determined using forward selection and clinical importance. Candidate covariates included sociodemographic information taken from SEER data, with education and income based on census tract. Because survival outcomes may differ by treatment received, radiation as part of the initial course of treatment (dichotomous variable) was included as a potential covariate. Additionally, because survival may differ by time of onset of depression, depression based on time of diagnosis was examined as a potential covariate in the model. Medical comorbidity was measured using an adaptation of the Charlson Comorbidity Index (CCI)[5] developed for Medicare data [17–19]. All analyses were performed using SAS 9.4, with the default method used to handle ties within the data (Breslow method). For the multivariable models, interaction terms were entered into the models to test the proportional hazard assumption of each variable, with those violating this assumption left in the model to control this violation [20].

[2] SEER: Surveillance, Epidemiology, and End Results.
[3] ICD-O3: International Classification of Disease for Oncology.
[4] HMO: Health maintenance organization.
[5] Charlson Comorbidity Index.

Results

Bivariate analysis

Based on the inclusion and exclusion criteria listed above, there were 3533 individuals eligible for inclusion in the analyses. From these, an additional 67 individuals were excluded for being diagnosed with cancer at the time of death or autopsy, leaving a total of 3466 individuals in the study sample. Table 1 shows the demographic and clinical characteristics of the study sample by depression status over the course of cancer. Of the study sample, 361 individuals (10.4%) had a diagnosis of depression prior to HNC diagnosis, an additional 281 individuals (8.1%) developed depression after cancer diagnosis, and 2824 individuals (81.5%) were not diagnosed with depression at any point during the study period. As can be seen from Table 1, there were significant differences between the groups in terms of survival for both cancer–specific and all-cause mortality. For cancer-specific deaths, there were over 35% more deaths from cancer in those who were diagnosed with depression prior to cancer compared to those who were never diagnosed with depression (48.8% vs. 36.0%, respectively). Similarly, there were over 41% more deaths from cancer in those who were diagnosed with depression after their cancer diagnosis compared to those where never diagnosed with depression (50.9% vs. 36.0%, respectively). Other significant differences between groups included age, gender, ethnicity, marital status, stage, medical comorbidity, and receipt of radiation. When looking at all-cause mortality, there were over 35% more deaths in the group diagnosed with depression prior to cancer diagnosis compared to those who were never diagnosed with depression (77.6% vs. 57.4%, respectively). Similarly, when looking at those who developed depression after cancer diagnosis compared to those who were never diagnosed with depression, there were nearly 30% more deaths in the group that developed depression after cancer (74.4% compared to 57.4%, respectively).

Based on the Kaplan-Meier survival curves for cancer-specific mortality, those without a diagnosis of depression during the specific time period had better survival compared to those who received a depression diagnosis, either before or after cancer (Log Rank chi square = 63.03, p = <0.0001). Those who received a diagnosis of depression prior to cancer had a median survival time of 37 months, compared to 29 months for those who received a diagnosis of depression after cancer diagnosis. The median survival time could not be computed for those who received no diagnosis of depression as median survival exceeded the 60 month follow-up period.

Similarly, for all-cause mortality, individuals without a depression diagnosis had better survival outcomes compared to those who received a depression diagnosis, either before or after cancer diagnosis (Log Rank chi square = 99.56, p = <0.0001). Those who received a diagnosis of depression prior to cancer had a median survival time of 17 months, compared to 18 months for those who received a diagnosis of depression after cancer diagnosis, and 46 months for those who received no diagnosis of depression.

Multivariable analysis

Table 2 shows the multivariable analysis results for the outcome of cancer-specific death. For this model, the interaction term

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