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ORIGINAL ARTICLE

Marital status is an independent prognostic factor for pancreatic neuroendocrine tumors patients: An analysis of the Surveillance, Epidemiology, and End Results (SEER) database

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KEYWORDS

Pancreatic neuroendocrine tumors;
Marital status;
Survival analysis;
Prognosis;
SEER

Summary

Background and objectives: Marital status's prognostic impact on pancreatic neuroendocrine tumors (PNET) has not been rigorously studied. We aimed to explore the relationship between marital status and outcomes of PNET.

Methods: We retrospectively investigated 2060 PNET cases between 2004 and 2010 from Surveillance, Epidemiology, and End Results (SEER) database. Variables were compared by Chi² test, *t*-test as appropriate. Kaplan–Meier methods and COX proportional hazard models were used to ascertain independent prognostic factors.

Results: Married patients had better 5-year overall survival (OS) (53.37% vs. 42.27%, $P < 0.001$) and 5-year pancreatic neuroendocrine tumor specific survival (PNSS) (67.76% vs. 59.82%, $P = 0.001$) comparing with unmarried patients. Multivariate analysis revealed marital status is an independent prognostic factor, with married patients showing better OS (HR = 0.74; 95% CI: 0.65–0.84; $P < 0.001$) and PNSS (HR = 0.78; 95% CI: 0.66–0.92; $P = 0.004$). Subgroup analysis suggested marital status plays a more important role in the PNET patients with distant stage rather than regional or localized disease.

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Conclusions: Marital status is an independent prognostic factor for survival in PNET patients. Poor prognosis in unmarried patients may be associated with a delayed diagnosis with advanced tumor stage, psychosocial and socioeconomic factors. Further studies are needed.
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Introduction

Pancreatic neuroendocrine tumors (PNET) are relatively rare pancreatic neoplasms in the world [1]. The incidence of PNET has obviously increased over the past few decades [2,3]. Although their biologic behavior is relatively indolent, PNET can be aggressive. Many studies have reported the prognostic factors of PNET, which mainly focused on clinicopathological characteristics, such as treatment strategy, tumor size, TNM stage and histologic grade [4,5]. More emphasis is now being placed on the role of social determinants in the development of disease [6]. Researchers have elucidated that marital status is an independent prognostic factor of survival in some cancers, and married patients have better survival in colorectal cancer, lung cancer, prostate cancer, and pancreatic cancer [7–9]. Marital status was an independent predictor of increased risk of an additional malignancy after diagnosis of PNET [10]. Yet, the impact of marital status on PNET survival has not been rigorously studied, only with limited knowledge.

The SEER program of the National Cancer Institute provides authoritative information on cancer statistics, which covers about 30% of population in the United States (<https://seer.cancer.gov/>). SEER Data have been widely used to explore the relationship between marital status and survival outcome in patients with cancer [8]. In the study, we aimed to explore the relationship between marital status and PNET survival outcomes by using the Surveillance, Epidemiology, and End Results (SEER) database.

Materials and methods

Data sources and study population

We extracted data about patients with histopathologic diagnosis of PNET between January 2004 and December 2010 eligible data from the SEER database (1973–2013) released in April 2016, by using SEER*Stat software version 8.3.2 (Accession number: 13693-Nov2015) [11,12]. International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) morphology codes 8150, 8151, 8152, 8153, 8155, 8156, 8157, 8240, 8241, 8242, 8243, 8246 and 8249 were used to identify PNET [13]. All pancreatic anatomical sites (C25.0–C25.9) were included in the study, including C25.0 – Head of pancreas, C25.1 – Body of pancreas, C25.2 – Tail of pancreas, C25.3 – Pancreatic duct, C25.4 – Endocrine pancreas, C25.8 – Overlapping lesion of pancreas, C25.7 – other parts of pancreas and C25.9 – unspecific location [13]. The year 2004 was selected as the first year of the study given that several employed covariates were introduced in SEER in 2004

[American Joint Committee on Cancer: AJCC Staging Manual (6th edition). <http://www.cancerstaging.org>] [8]. As of the beginning of our study, the available SEER Data were limited to 2013, so we set 2010 as the follow-up cutoff date to ensure that all included cases were followed up for at least 3 years [14].

The exclusion criteria were as follows:

- who had more than one primary cancer and the PNET was not the first;
- age at diagnosis < 18 years;
- unknown marital status;
- incomplete follow-up information or unknown survival length;
- and who had an unknown cause of death.

Study variables

We extracted the demographic and clinicopathological data from SEER database, including sex, age, race, tumor location, tumor size, histologic type, pathology grade, extent of disease, TNM stage, radiotherapy and marital status. Patients were divided into two groups according to age at diagnosis (≤ 60 years vs. > 60 years). Race was divided into white, black and others.

We set 2 and 4 cm as the cutoff points of tumor size according to The European Neuroendocrine Tumor Society Staging Classification (ENETS) [15]. Histologic type was further classified as Functional PNET and nonfunctional PNET. According to the SEER staging system, disease extension was categorized using the Collaborative Stage classification criteria, including localized, regional and distant. The TNM stage was established according to the criteria described in the American Joint Committee on Cancer (AJCC) Cancer Staging Manual (6th edition). Within the SEER database, Marital status was coded as married, divorced, widowed, separated, never married and unmarried or domestic partner. We classified patients as married or unmarried (including never married single, divorced, separated, and widowed).

Outcomes

The primary outcomes of this study were OS and PNSS. OS was defined as the time from diagnosis to date of any death. PNSS was derived from the time of diagnosis to date of PNET cancer-specific death. Death attributed to PNET was regarded as an event. Patients who died from other causes or were still alive at the follow-up cutoff date were treated as censored observations. The follow-up cutoff date was December 31, 2010.

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