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Original Article

Receipt of Care Discordant with Practice Guidelines is Associated with Compromised Overall Survival in Nasopharyngeal Carcinoma

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Abstract

Aims: It is unknown whether receiving treatment that is discordant with practice guidelines is associated with improved survival in patients with nasopharyngeal carcinoma. The objectives of this study were to characterise national treatment patterns, analyse whether treatment outside of practice guidelines is associated with overall survival, and identify variables associated with receiving guidelines-discordant care in the USA.

Materials and methods: This was a retrospective cohort study of 1741 nasopharyngeal carcinoma patients in the National Cancer Data Base (2003–2006). Treatment regimens were compared with the 2004–2006 National Comprehensive Cancer Network guidelines. Statistical analyses included chi-square, Kaplan–Meier, multivariable logistic, and Cox regression.

Results: Nearly 26% of our cohort received care discordant with practice guidelines. In multivariable analysis, patients with stage IVC disease (odds ratio 2.59, 95% confidence interval 1.66–4.04) were more likely to receive guidelines-discordant care when compared with those with stage II–IVB disease. The most common treatment deviation for those with stage I disease was overtreatment with chemoradiation therapy. Receiving guidelines-discordant care was associated with an increased risk of death (hazard ratio 1.46, 95% confidence interval 1.25–1.69).

Conclusions: Many patients with stages I and IVC nasopharyngeal carcinoma do not receive care in accordance with practice guidelines. Receiving guidelines-discordant care is associated with compromised overall survival in the USA.

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Key words: Head and neck cancer; nasopharyngeal carcinoma; National Cancer Data Base; practice guideline

Introduction

Nasopharyngeal carcinoma is relatively uncommon in the USA, with an annual incidence of <1 case per 100 000 people [1,2]. This is in contrast to southern China, where it is endemic, with an annual incidence 25–50-fold higher [2]. Nasopharyngeal carcinoma has been associated with Epstein–Barr virus (EBV) [3], genetic susceptibility, and consumption of salted, preserved foods [4]. It is typically found in the pharyngeal recess posterior and medial to the Eustachian tube [5,6].

The National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) make treatment suggestions based on the best available evidence using a consensus process for 97% of cancers [7]. It has been reported that up to 43% of head and neck cancer patients receive NCCN-discordant care [8]. The NCCN Guidelines[®] for nasopharyngeal carcinoma between 2004 and 2006 state that patients with stage I and select patients with stage II disease should receive definitive radiation to the primary lesion and elective radiation to the neck [9–11]. Patients with distant metastases should receive chemotherapy, and if there is a complete response, radiation. All other patients should receive combination chemoradiation followed by chemotherapy, with a neck dissection for residual nodal disease. There is no therapeutic role for resection of the primary lesion. The 2015

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NCCN Guidelines[®] differ in that patients with stage II–IVB disease may receive concurrent chemoradiation alone, or with adjuvant or neoadjuvant chemotherapy [12]. Those with distant metastases may receive concurrent chemoradiation or chemotherapy followed by adjuvant radiation or chemoradiation.

There is a paucity of data with respect to national treatment patterns for nasopharyngeal carcinoma in the USA and whether they are associated with survival in the context of other factors. We sought to characterise national treatment patterns benchmarked against the NCCN Guidelines[®], examine the association of receipt of NCCN Guidelines[®] with overall survival, and characterise risk factors associated with receiving care discordant with the NCCN Guidelines[®] for nasopharyngeal carcinoma.

Materials and Methods

Description of Data Source

We conducted a retrospective cohort study of the National Cancer Data Base (NCDB) between 2003 and 2006. The NCDB is a joint project of the Commission on Cancer and the American Cancer Society. It accounts for more than 1440 Commission on Cancer-approved cancer programme registries [13,14] and about 75% of cancers diagnosed in the USA [13]. The NCDB uses the same definitions and standards as federal cancer registry systems [15], with coding guidelines found in the Facility Oncology Registry Data Standards manual [16].

Selection Criteria

Data were extracted using the following International Classification of Diseases for Oncology, third edition (ICD-O-3) primary site topography codes: C11.0–11.3, 11.8, and 11.9 [17]. ICD-O-3 morphologic codes 8071 (keratinising squamous cell carcinoma [SCC]), 8072, 8073 (non-keratinising SCC), 8020 (undifferentiated carcinoma), 8082 (lymphoepithelioma) and 8070 (SCC, not otherwise specified [NOS]) were included [17]. Tumour histology was characterised according to the original World Health Organization (WHO) scheme: type I (keratinising SCC), II (non-keratinising SCC) and III (undifferentiated/lymphoepithelioma) [5], as well as SCC NOS. Clinical TNM classifications and overall clinical stage reflect the American Joint Committee on Cancer staging system, sixth edition [18]. We initially identified 17 509 patients diagnosed between 1998 and 2011 in the database. Patients with classifications outside of T1-4, N0-3 and M0-1 parameters, such as T0, TX, Tis, NX or overall stage 0 disease were excluded. Also excluded were cases with prior malignancies, multiple primaries or missing data for patient age, gender, race, Hispanic origin, insurance status, income, education, Charlson–Deyo comorbidity index [19] (recorded after 2003), facility type, facility location, last known contact/death, vital status (recorded until 2006), clinical TNM classifications and overall clinical stage, and treatment-

related data such as receipt of chemotherapy, radiation, time-course to start of treatment and scope of regional lymph node surgery.

Definition of Patient Demographic Variables

Variable definitions reflect those found in the NCDB Data Dictionary [20], with a few exceptions. Race and Hispanic origin were combined, and Asian patients were separated into Chinese and other Asian. Categories for insurance status were private, uninsured/Medicaid and Medicare/other government. Income data were obtained from the 2000 US Census and were stratified into zip codes with median yearly household income of \geq \$46 000/year (highest quartile) and $<$ \$46 000/year. Education reflects the percentage of residents in a patient's zip code having earned a high school diploma. Outcomes included $>$ 86% (highest quartile) and \leq 86% with a high school diploma. Facility type reflects the category classification assigned by the Commission on Cancer accreditation programme [20,21] and was dichotomised into academic/research and non-academic centres [22]. Facility volume as it pertained to nasopharyngeal carcinoma was calculated and divided into high-volume centres (\geq 90th percentile or \geq 7 cases during the study period) and low-volume ($<$ 7 cases) centres. Facility locations were relabelled to reflect the four census regions of northeast, midwest, south and west [23].

Definition of Treatment Variables

Patients coded as receiving chemotherapy included those receiving single-agent, multi-agent or unspecified regimens. Radiation consisted of external beam radiation alone or in combination with implants or isotopes. If the patient received multimodal therapy (both chemotherapy and radiation), they were characterised as receiving one of two therapeutic regimens: those receiving radiation and adjuvant chemotherapy (RAC) began chemotherapy at least 8 weeks (\geq 56 days) after starting radiation and all others receiving multimodal therapy were coded as receiving combination chemotherapy and radiation (CRT). This includes concurrent chemoradiation as well as chemotherapy followed by adjuvant radiation. It is not possible to tell whether patients received adjuvant chemotherapy after CRT. Patients were coded as receiving a neck dissection if they underwent regional lymph node surgery [22].

Treatment data were then compared with the NCCN Guidelines[®] [9–11] from the corresponding year on a stage-wise basis (there are no head and neck cancer guidelines from 2003; patients diagnosed in 2003 were treated as if diagnosed in 2004). As neck dissection is warranted for residual nodal disease for patients with stage II–IVB disease and data on residual nodal disease are not available, patients with stage II–IVB disease receiving neck dissections were not coded as having received care discordant with the NCCN Guidelines[®].

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