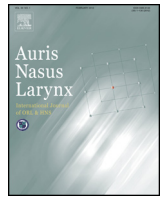




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A population-based comparison of European and North American sinonasal cancer survival

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ABSTRACT

Objective: Sinonasal cancers (SNC) are rare, thus limiting previous prognostic studies on a multinational level. The aim of this study is to utilize two population-based datasets to compare prognoses for SNC between the United States (US) and Europe.

Methods: The European Cancer Registry (EUROCCARE) database and the United States National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database were searched to identify survival of patients diagnosed with SNC between 1990 and 2007. Relative survival (RS) data were stratified by age group, gender, geographic location, and diagnostic time period.

Results: 12,541 SNC cases were identified in EUROCCARE, while SEER identified 4,312. Males comprised the majority in Europe (62.3%) and the US (58.3%). Most patients were over 55 years in Europe (77.0%) and the US (69.5%). Age over 75 was a statistically significant poor prognostic indicator for 5-year RS in the US (48.2%; 95% CI = [43.9, 52.4]) and Europe (38.5%; [34.7, 42.7]). Female gender imparted a favorable 5-year RS in all regions except in Central Europe. By region, the US had the highest 5-year RS (58.8%; [56.4, 61.1]) and Eastern Europe had the lowest 5-year RS (37.1%; [34.0, 40.6]). The aggregate European 5-year RS was 48.1% [46.4, 49.8].

Conclusion: SNC in Europe and the US most commonly affects males and individuals over the age of 55 years. Male gender and age over 75 are poor prognostic factors at 5 years. Five-year RS in the US is higher than the 5-year European aggregate RS.

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¹ See Appendix A.

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1. Introduction

Sinonasal cancers (SNC) are uncommon, comprising only about 3–5% of all head and neck cancers, and less than 1% of all diagnosed cancers [1]. As compared to other head and neck locations, the nasal cavity and paranasal sinuses harbor

malignancies that often present at advanced stages, and have poorer prognoses [2]. The nasal cavity has been reported as the most commonly involved sinonasal subsite, followed by the maxillary sinuses [3]. Commonly recognized risk factors associated with SNC include exposure to nickel, wood dust, leather-working, and cigarette smoke [2,4,5].

These malignancies have been historically difficult to study due to their rarity in the general population. Recently, cancer registry databases have remedied this by allowing researchers and clinicians to analyze survival through large sample sizes with data spanning multiple institutions. However, a majority of studies investigating SNC have been limited to the United States population data. To date, there have been few studies examining survival characteristics amongst sinonasal malignancies across global regions, which may identify geographic variations in epidemiology and survival.

The present study utilizes data from the European Cancer Registry (EUROCARE) in conjunction with data from the Surveillance, Epidemiology, and End Results (SEER) database in order to investigate global trends and survival across multiple countries. Our analysis includes a comparison of demographic distributions and relative survival rates for sinonasal malignancies by age, gender, country, and geographic region. Additionally, the authors seek to assess any changes to survival across these regions over the span of two decades.

2. Materials and methods

2.1. EUROCARE

Frequency and survival information for Europe was obtained from the EUROCARE database website (www.eurocare.it). EUROCARE is a population-based cancer database that contains information from 116 registries across 30 countries in Europe [6]. The main results from the 3rd, 4th, and 5th iterations of the EUROCARE studies are available on the database website [7]. EUROCARE-5 (2000–2007) covers approximately 50% of the entire European population, and 100% of the Northern European (Denmark, Finland, Iceland, Norway, Sweden) and British Isles (United Kingdom, Ireland) population [6]. Half of the Eastern European (Bulgaria, Czech Republic, Estonia, Latvia, Lithuania, Poland, and Slovakia) population is covered. Approximately 35% of the Central European (Austria, Belgium, France, Germany, Switzerland, and The Netherlands), and 36% of the Southern European (Croatia, Italy, Malta, Portugal, Slovenia, Spain) population are covered. The database only includes malignant tumors, and excludes patients under 15 years of age. The relative survival rates provided by EUROCARE-5 were estimated by the EUROCARE team with the Ederer II method in SEER*Stat (version 8.3.2) [6]. Age-standardized relative survival rates were estimated based on the International Cancer Survival Standard (ICSS) 1 weightings.

For this study, “Nasal cavities and sinuses” was selected as the primary cancer entity. The EUROCARE team defined this cancer entity as the “nasal cavities, accessory sinuses, middle and inner ear”, ICD-O-3 (International Statistical Classification of Diseases for Oncology, 3rd Edition) primary site codes

C30–C31 [8]. Additionally, ICD-O-3 morphology codes 9590–9989 (all leukemias and lymphomas) are excluded [8]. In our analysis of the available data, number of cases that were “alive at start,” and 1-to-5-year relative survival (RS) rates, with their 95% confidence intervals, were obtained for all countries and geographic regions included in the database. RS describes the survival of a particular patient population compared to the expected age-adjusted survival rate of a similar segment of the general population. Results were then broken down by age classes (15–44, 45–54, 55–64, 65–74, 75+ years), and sex.

To analyze trends in survival, data were also obtained from the EUROCARE-4 (1995–1999), and EUROCARE-3 (1990–1994) databases. A notable difference of these previous iterations is that EUROCARE team used the Hakulinen method to estimate RS rates, as opposed to the Ederer II method used in EUROCARE-5 [9,10].

2.2. SEER

Frequency and relative survival information for the United States was obtained from the SEER (Surveillance, Epidemiology, and End Results) 18 database using SEER*Stat (version 8.3.2). SEER is a cancer database maintained by the National Cancer Institute. It contains information from 18 states and metropolitan areas in the U.S., covering approximately 28% of the nation’s population.

To allow for comparison of the data with EUROCARE results, malignant tumors with the same ICD-O-3 primary site codes used in EUROCARE (C30–C31) were selected in SEER*Stat. Additionally, the “age ≥ 15 years old” filter was applied. The “year of diagnosis” filter was applied to match that used in EUROCARE. When estimating RS, the Ederer II method was used for cases diagnosed between 2000 and 2007, and the Hakulinen method was used for cases diagnosed between 1990 and 1999. Results were separated by gender, and the same age groups used in the EUROCARE analysis.

Because no P-values are provided with the EUROCARE dataset, all comparisons between data values were made with 95% confidence intervals. As per recent epidemiologic studies, any non-overlapping confidence intervals will always calculate to $P < 0.05$ and thus this has been used to determine statistical significance throughout the study [11].

According to the policies of the institutional review board (IRB) at Rutgers New Jersey Medical School, since neither database has any patient-identifier information, IRB approval was not needed.

3. Results

In the EUROCARE-5 database, 12,541 cases of sinonasal cancer were identified. In SEER, 4312 cases were identified. The number of cases by age and gender, for each geographical region (i.e., U.S., Eastern Europe) is listed in Table 1. A male predominance was observed in each geographic region. Furthermore, SNC most commonly affected older individuals (over 55 years), regardless of geographic location.

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