Head and Neck Cancer in Germany

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Analysis of Diagnosis Related Groups (DRG) data of the treatment of head and neck cancer in Germany from 2005 to 2018

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1. Background

Head and neck cancer (HNC) is the seventh most common type of cancer worldwide [1]. HNC represents a diverse group of tumor entities covering several anatomical subsites in the upper aerodigestive region. These entities differ greatly in terms of etiology, risk factors, histology, and therapeutic management. About half of the patients are still diagnosed at advanced stage [2][3]. In most cases, a monotherapeutic approach (surgery alone or radiotherapy alone) is used for early-stage disease, whereas locally-advanced stages are treated by multimodal approaches [1][4][5]. Chemotherapy/immunotherapy regimens are mainly part of concurrent or postoperative radiochemotherapy/immunotherapy. Cetuximab as a first monoclonal antibody was licensed in 2006, first in systematic treatment concepts for recurrent or metastatic disease, and later on as substitute for chemotherapy/immunotherapy in curative radiotherapy concepts [6]. The first checkpoint inhibitor as new treatment option was licensed in 2017, hence did not play a role in the herein examined period from 2005 to 2018 [7].

2. Current Insight Into Head and Neck Cancer

Overall, the burden of cancer incidence including HNC is rapidly growing worldwide. This reflects both aging and growth of the population as well as changes in the prevalence and distribution of the main risk factors for cancer [8]. Increasing numbers of HNC cases will need increasing numbers of treatment. The presented study is based on secondary data analysis from DRG data. Several countries use the DRG system, but to our knowledge the present study is the first to use DRG data to analyze head and neck treatment trends for over time. This data set, incorporating as a major advantage all hospitalized cases in Germany, is based on reimbursement claims. Hence, and this a limitation of the study, it does not include outpatient treatment [9]. Therefore, the absolute number of treatments for HNC will be higher than presented here. The comprehensive picture of inpatient treatment relies on OPS treatment codes that can be linked to ICD codes. The herein presented treatment rates per 100,000 population and year cannot be transferred par for par to incidence rates as some HNC patients, especially when in advanced stage, might receive several treatments.

As no other DRG-based analysis was performed before, the presented results could only be compared to publications based on other population-based data sources, i.e., mainly on cancer registry data. Like in many other countries, it is the task of population-based cancer registries in Germany to estimate and analyze the number of annual incident cancer cases, cancer deaths, survival rates, and additional indicators of cancer epidemiology, particularly prevalence, incidence, and including the investigation of trends over time. Additionally, it is the task of the clinical cancer registries to collect further clinical data, for instance the TNM staging. Therefore, the presented analysis did not allow a linkage of the presented treatment data to TNM staging or any other clinical data. Due to the German Centre for Cancer Registry Data (https://www.krebsdaten.de; accessed on 22 October 2021), for instance, the average incidence of cancer of the oral cavity between 2005 and 2017 (data of 2018 not yet available) was 24.8 for men and 9.6 for women, respectively. The average incidence of laryngeal cancer between 2005 and 2017 was 8.3 for men and 1.3 for women, respectively. In comparison, the DRG data analyses revealed for cancer of the oral cavity a cumulative treatment rate of 46.6 for men and 18.4 for women, respectively. The cumulative treatment rates for laryngeal cancer were 25.6 and 6.8, respectively. This reflects that most patients receive several procedures and not monotherapy. It is known that the hospitalization rates range between 1 and 2 fold of the incidence rates [10].

An older National Cancer Data Base (NCDB) analysis for the years 1990–2004 showed decreasing numbers of surgery, a decrease of radiotherapy as monotherapy, but a massive increase of radiochemotherapy and a slight increase of surgery combined with radiochemotherapy [11]. Cooper et al. relate these changes mainly to the emergence of data from phase III protocols showing that the addition of chemotherapy to radiation therapy enhances the rate of locoregional control in advanced HNC tumors. A Surveillance, Epidemiology, and End Results (SEER) analysis for the years 1997, 2004, and 2009 showed mainly the same results [12]. More appropriate is a population-based analysis using clinical cancer registry data from Thuringia, a federal state in Germany, covering the years 1996–2016 [5]. Here, surgery alone (26.5% of all cases), surgery with adjuvant radiochemotherapy (21.2%), surgery with adjuvant radiotherapy (21.0%), and definitive radiochemotherapy/radioimmunotherapy (11.9%) were in descending order the most predominant strategies. Furthermore, the relative frequency of radiotherapy as a single therapy decreased, instead, radiochemotherapy/radio-immunotherapy increased. In contrast to the mentioned NCDB and SEER data, surgery as a single modality, as a primary treatment in combination with radiochemotherapy/radio-immunotherapy increased in Germany. It seems that surgery plays a larger role even for advanced stage tumors in Germany than compared to the United States. Here, it could separately analyze the surgery of the primary and surgery of the neck. It is striking that the neck dissection rates for all localizations were >50% lower than the surgery rates for the primary tumor. This means that an elective neck dissection was probably not performed in many early cancer cases (stage I) with clinical N0. Whereas this is standard of care or at least matter of debate for most head neck subsites, neck dissection is standard for cancer of the oral cavity even for all N0 necks and independent of the T classification. This suggests that part of the cases with cancer of the oral cavity were undertreated. The neck dissection rate is a quality indicator for the treatment of cancer of the oral cavity for the certified head and neck cancer centers in Germany. In 2020, only 76% of the oral cavity cancer cases treated in certified centers received a neck dissection (https://www.onkozert.de/organ/kopf-hals/; last access: 22 September 2021). Even taking into account that some patients refused a neck dissection or it

was not indicated because of multimorbidity, an undertreatment can be assumed. This shows that more effort has to be made to improve the clinical guideline adherence.

Finally, the use of chemotherapy/biologicals as part of the treatment concept increased. The increase of biologicals in mainly related to cetuximab introduced in 2006 as checkpoint inhibitors were not introduced before 2017 [6][7]. These German cancer registry data correspond better to the presented results, especially as factors, such as the subsite and gender, have to be considered in the presented SEER and NCDB data. Of main interest are inverse trends. For most therapy types, it revealed increasing treatment rates over time, but especially treatment rates for nasopharyngeal cancer and hypopharyngeal cancer, as well as laryngeal cancer in male patients decreased. This seems to be directly associated to a decreasing incidence of these tumor subtypes in Germany [5].

Although it is well known that females have improved survival in comparison with their male counterparts [13], gender disparities were especially neglected so far when analyzing treatment trends. The above-mentioned Thuringian data showed that treatment decisions were different between male and female patients even for the same tumor type and stage [5]. Understanding these gender disparities is essential to providing appropriate care to HNC patients [13]. Therefore, prospective trials are needed to better analyze the decision making for or against a certain treatment strategy.

Although DRG data is collected prospectively through the routine hospital coding process which collects data from virtually all German hospitals, this study has several limitations. First, this study is retrospective, which could lead to misclassification errors and unmeasured variables. Notably, many clinical but important factors with influence on decision making, such as stage, comorbidity, or age, were not included. The calculated treatment rates can only be seen as a proxy for the incidence rates [10]. Furthermore, the DRG data is primarily collected for reimbursement. Although the data underwent plausibility checks for incorrect codes before release of DESTATIS to researchers, it cannot be excluded that in some cases the coding followed the interest of maximizing the profit more than a proper documentation of the actual treatment [14]. As the complete dataset is subject to this uncontrolled bias, the comparisons between subsets, such as the comparisons between men and women or between subsites, are evenly affected by such a bias.

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