

# SCCHN

Subjects: Oncology

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Squamous cell carcinoma of the head and neck (SCCHN) is a complex group of malignancies, posing several challenges to treating physicians.

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## 1. Introduction

Squamous cell carcinoma of the head and neck (SCCHN) represents the sixth most common malignancy worldwide and its mean incidence rate is about 20 per 100,000 people in the regions of Europe, China, the Indian subcontinent, South America, and among African Americans in the United States. The incidence of SCCHN widely varies according to the areas of the globe, with these neoplasms being much more frequent in the Eastern countries rather than in the Western ones <sup>[1]</sup>.

The well acknowledged risk factors are smoking, alcohol consumption, different forms of chewing tobacco, and chronic oral trauma. Lately, the infection sustained by Human Papilloma Virus (HPV) has been recognized as responsible for a fair percentage of SCCHNs, in particular those arising from oropharynx, whose incidence is steadily increasing in the last 10 years <sup>[2]</sup>.

In the clinical practice, most patients with diagnosis of SCCHN have a locoregionally limited disease (from T1-2N0M0 to T4N3M0), and only 10% of them suffer from distant metastases. Upfront surgery followed by adjuvant radiotherapy or chemoradiotherapy, or in alternative exclusive chemoradiation (concomitant or sequential) are the current treatment options for locoregional disease. Even with recent advances in surgery and radiation, however, a subset of patients will eventually experience disease progression <sup>[3]</sup>.

Mounting evidence highlight that, in patients diagnosed with locoregionally advanced SCCHN who have been treated with upfront surgery or upfront chemoradiation, the percent of locoregional failure is about 40–50%, while distant failure is 20–30% <sup>[4][5]</sup>.

Thus, as a consequence, about a half of the patients with SCCHN have a recurrent/metastatic disease in common clinical practice. Recurrent/metastatic SCCHN is a difficult disease to treat, with poor prognosis and a median survival of about 12 months <sup>[6]</sup>. Several therapeutic strategies have been developed over the years, the monochemotherapy, the polychemotherapy, the association of chemotherapy plus cetuximab and, lately, the “new generation immunotherapy”, which exploits check-point inhibitors.

All the aforementioned strategies have a common feature, namely the idea that the recurrent/metastatic disease could be considered as a systemic disease, characterized by both macro and/or micrometastases disseminated in the blood and in the organs supplied by it. This is the reason for which the categories “recurrent” and “metastatic” SCCHN are grouped in the same prognostic category (recurrent/metastatic disease) and they share the same poor prognosis. Nevertheless, in some rare cases, particularly as regards patients with single locoregional relapse (recurrent SCCHN), surgery and/or radiotherapy are able to “cure” the patient, offering him an excellent chance of survival. Surgery and irradiation/re-irradiation are limited to few and selected cases, namely in patients with a single recurrence suitable for a locoregional treatment <sup>[3]</sup>, and they should be evaluated as first option in these cases, being a strategy associated with longer overall survival.

## 2. Salvage Surgery in Patients with Recurrent/Metastatic Disease

Surgery and/or radiotherapy with or without concurrent chemotherapy has been established as a primary treatment for all newly diagnosed SCCHN. Nevertheless, loco(regional) failure occurs in up to 50% of patients, and for these lasts, salvage surgery is considered the best treatment option [3]. Even after aggressive multimodal therapy, many patients have persistent or recurrent disease due to their multiple risk factors and induced field cancerization. Salvage surgery represents the optimal approach in this category of patients, but it is not always easy to identify the ideal candidate for surgical approach, and moreover, salvage surgery may not be performed in all patients. With persistence/recurrence rates as high as 40% to 50%, and only 20% to 30% of these patients eligible for curative salvage therapy [7][8], it is clearly important to determine which factors predict successful salvage.

Matoscevic et al., performed a descriptive analysis of 176 patients with SCCHN, who relapsed after the primary curative treatment. Patients with a previous diagnosis of primaries arising from the oral cavity, larynx, oropharynx, and hypopharynx and who were treated with upfront surgery or in alternative radiation therapy were enrolled. Salvage surgery was the most frequently chosen modality of salvage treatment, being performed in 67.2% of patients affected by laryngeal cancer, 45.3% of those with oropharyngeal cancer, 56.5% of patients with hypopharyngeal carcinoma, and 37.8% of those affected by oral cavity cancer. The salvage rate was significantly better in patients affected by larynx and oral cavity recurrent tumors, while those suffering for oropharynx and hypopharynx recurrences had worse outcome. The authors also highlighted that lower initial T and N stage, developing local relapse in larynx and oral cavity have the best chances for salvage [9].

Elbers et al., used salvage surgery in 189 patients with a diagnosis of recurrent SCCHN carcinoma, previously treated with radiotherapy alone or chemoradiotherapy as an upfront approach. Oral cavity primaries were excluded from the analysis, upfront surgery being in this case the best option in site of radiation therapy. The authors found that larynx carcinomas were associated with more favorable local and locoregional control than pharyngeal (both oropharynx and hypopharynx) carcinomas. Overall, surgery reached a five-year overall survival (OS) of 33%, and a median OS of 18 months. Moreover, a sharp distinction was made between the “local” disease (recurrence on T) and “locoregional” disease (recurrence upon T and/or N), and interestingly, survival following salvage surgery for locoregional disease was significantly worse if compared with those obtained in local disease. In patients with locoregional recurrence, due to the higher tumor burden, prognosis was significantly worse. In this category of patients, the authors also found that rpT stage and ASA (American Society of Anesthetists) score were independent predictors for worse DFS [10].

Most data from the literature have highlighted that salvage surgery for laryngeal and oral cavity tumor recurrences does result in better survival, if compared to other subsites (hypopharynx and oropharynx), and this may be due to the major difficulty in resecting pharyngeal recurrences due to nearby anatomical structures (e.g., carotid artery and skull base) [9][10]. Nevertheless, salvage surgery may be taken into account, especially in high expertise centers, as modality of choice also in recurrent pharyngeal cancers. When choosing surgery as salvage strategy is important to acknowledge some important features, mainly the site of recurrence and then the extent of recurrent disease (pT), the ASA score, the disease-free interval, the feasibility of postoperative radiation, and the previous radiotherapy received, the performance status of the patient and the family and social environment.

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