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Surgical treatment of salivary malignant tumors

Davide Lombardi ^{a,*}, Marc McGurk ^b, Vincent Vander Poorten ^{c,d}, Marco Guzzo ^e, Remo Accorona ^a, Vittorio Rampinelli ^a, Piero Nicolai ^a

- ^a Department of Otorhinolaryngology Head and Neck Surgery, University of Brescia, Italy
- ^b Guys and St. Thomas NHS Trust, London, United Kingdom
- Cotorhinolaryngology Head and Neck Surgery and Department of Oncology, Section Head and Neck Oncology, University Hospitals Leuven, KU Leuven, Leuven, Belgium
- ^d European Salivary Gland Society, Geneva, Switzerland
- ^e Department of Head and Neck Surgery, Istituto Nazionale dei Tumori, Milan, Italy

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ABSTRACT

Salivary gland malignant tumors (SGMT) are of key interest for head and neck surgeons since surgery with adjuvant radiotherapy is considered the treatment of choice in most of the cases. Some factors, namely rarity, high histologic heterogeneity, and possible occurrence in all the head and neck subsites, contribute to make this topic very controversial; some unclear aspects pertain surgical treatment. When dealing with major salivary gland malignant tumors (MaSGMT), the most debated issues remain the extent of surgery and management of facial nerve. In minor salivary gland malignant tumors (MiSGMT), conversely, surgical planning is influenced by the specific pattern of growth of the different neoplasms as well as the site of origin of the lesion. Finally, two additional issues, the treatment of the neck (therapeutic or elective) and reconstructive strategy after ablative surgery, are of pivotal importance in management of both MaSGMT and MiSGMT. In this review, we discuss the most relevant and controversial issues concerning surgery of SGMT.

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Surgery of major salivary gland malignant tumors

Introduction

Although they are of key interest for surgeons, major salivary gland malignant tumors (MaSGMT) are uncommon, with an annual incidence of 6-11 in the parotid and 2-3 cases in the submandibular per 10^6 population [1-5].

A study extending over two decades showed the risk of malignancy in the parotid and submandibular glands was 10% and 30%, respectively [6]. MaSGMT have been categorized into 24 histologies, but the most common four are adenoid cystic carcinoma (AdCC: \sim 26%), mucoepidermoid carcinoma (MEC: \sim 17%), acinic cell carcinoma (AcCC: \sim 14%), and adenocarcinoma not otherwise specified (ACNOS \sim 11%) [3,4,6].

Two main factors contribute to the success of treatment: rigorous pre-surgical work-up and appropriate planning of surgery and radiotherapy (which is required in the majority of patients). More limited is the role of chemotherapy (CHT) and biotherapy, which

E-mail address: davinter@libero.it (D. Lombardi).

may find an application in specific histologies. The anatomic complexity of the region in relation to the facial nerve for the parotid gland, and lingual and hypoglossal nerves for the submandibular and adjoining vascular and musculoskeletal structures, requires accurate preoperative planning and intraoperative assessment [7]. Moreover, specific problems related to histology, tumor grade, and size have to be considered in management choices. AdCC, which is one of the most frequent histologies, is characterized by a specific tendency to spread along nerves and subperiosteal/perichondral planes and poses critical issues in relation to the need for sacrifice of nerves with frozen section examination, or in planning the resection when the tumor spreads along musculoskeletal structures such as the mandible; consequently, the possibility to obtain free surgical margins in AdCC is highly unlikely.

Another important issue concerns locally advanced and/or inoperable disease, with the opportunity to select, as primary treatment, radiotherapy with state-of-the-art technology, when it can be anticipated that any surgical resection would be incomplete, at least macroscopically.

A feature of MaSGMT is that treatment has to be tailored to each patient. A wide range of factors have been linked to outcomes, the most important of which are tumor size, clinical grade (soft tissue and nerve invasion, pain, fixity), nodal status, gender, and age.

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^{*} Corresponding author at: Department of Otorhinolaryngology – Head and Neck Surgery, University of Brescia, Piazza Spedali Civili 1, 25100 Brescia, Italy.

E-mail address: davinter@libero.it (D. Lombardi).

These factors have been incorporated into a useful predictive model that provides prognostic information for individual patients with parotid cancer [8]. Despite differences in terms of histology, local extension, and patient profile, the most important goal in surgery for MaSGMT remains obtaining a complete resection with adequate free surgical margins [7].

Parotid gland surgery and intraoperative facial nerve management

The surgical technique of parotidectomy, entailing facial nerve identification and parotid tissue resection, has been thoroughly described but the extent of resection performed in each case may differ according to local extension and specific growth pattern of the tumor. The different types of parotidectomy are listed below [9]:

- Partial parotidectomy: excision of the tumor with where possible a surrounding cuff of uninvolved parenchyma.
- Superficial parotidectomy: removal of all the parenchyma superficial to the facial nerve.
- Total parotidectomy, removal of all parotid parenchyma (superficial and deep to the facial nerve).
- Radical parotidectomy, total parotidectomy with sacrifice of the facial nerve.
- Extended radical parotidectomy, radical parotidectomy extended to at least one of the surrounding structures (skin, mastoid, mandible, masticatory muscles, infratemporal fossa).

Several authors have proposed different classification systems [10–12]; most recently, the European Salivary Gland Society, published a new and logical classification to better categorize extracapsular dissection and limited parotidectomies [13]. Two different proposals of amendment to this classification suggesting to add also parapharyngeal space [14] and temporo-mandibular joint [15] to the existing parotid levels have been advanced.

The extent of parotid tissue that must be excised in a malignant parotid tumor is controversial. Paradoxically, it is small malignant tumors (Stage I and II) that pose a treatment dilemma. Several authors recommend total parotidectomy for high-grade tumors, or tumors greater than Stage I. However, as early as 1975, Spiro reported that 58% of malignant parotid tumors treated primarily in their institution had been adequately removed by a subtotal parotidectomy [16].

For T1-T2 superficial parotid tumors, one of the most debated issues is whether or not to remove the deep lobe of the gland. Those who advocate superficial or even less-than-superficial parotidectomy underline that, whenever a conservative procedure is correctly planned and performed, the risk of facial nerve neuropraxia is minimized without compromising oncologic results [17]. Mamelle proposed that, for low-grade T1 tumors in the lower pole of the parotid, a procedure less than superficial parotidectomy may be adequate to maintain optimum outcomes [18]. Similar conclusions were reached by Lim et al. who performed less than superficial parotidectomy in 43 patients with low-grade parotid cancer limited to the superficial lobe [17].

Conversely, one of the strongest arguments for those who support total parotidectomy even in low-stage tumors is the presence of lymph nodes both in the superficial and deep lobe, which was demonstrated by several anatomic studies [9,19–23], with direct lymphatic connections between the lymph nodes and cervical lymphatic network [20,21,23].

Klussmann et al. described a series of 142 patients treated for resectable parotid cancer:[24] in that cohort, 55 (39%) patients had locoregional (intraparotid and/or cervical) lymph node metastases (pN+). The rate of metastasis was significantly higher in highgrade tumors (49% vs. 22%, respectively). Among pN+ patients, 36

(25%) had intraparotid lymph node metastases, while 19 (7.5%) had only cervical nodal involvement. For these reasons, the authors recommended to perform at least total parotidectomy in case of malignancy, in order to reduce the rate of loco-regional relapse and, consequently, to obtain a better outcome [24].

More recently, Olsen and Moore presented the experience of the Mayo Clinic on 27 patients with parotid cancers (primary and metastatic) with deep lobe involvement. The study again underlined the importance of performing total parotidectomy in patients with high-grade primary parotid tumors [23].

The management protocols for Stage III and IV parotid cancers do not pose, in most cases, an intellectual problem. It is almost always necessary to have wide exposure to give adequate access to the tumor and a total parotidectomy is minimally required.

The management of the facial nerve is one of the most challenging issues in surgery for parotid gland malignancies, especially when dealing with high-grade and/or high stage lesions. As a general rule, the facial nerve should be preserved whenever preoperatively functioning and detachable by the tumor, and this is easily obtained in the presence of lesions that are not in direct contact with the facial nerve trunk or peripheral branches. When the tumor is close or adherent to a functioning, normal-appearing nerve, every effort should be made to preserve its anatomic and functional integrity by delicately dissecting the nerve from the neoplasm; in this scenario, it is of pivotal importance to not leave any macroscopic remnant of the tumor since only microscopic residual disease may be effectively managed by adjuvant radiotherapy [7]. Conversely, radical parotidectomy with removal of all parotid tissue as well as sacrifice of the facial nerve should be done in cases in which the facial nerve has been encased or invaded by tumor or whenever facial nerve function is preoperatively impaired [5,9]. Noteworthy, in the balance between nervepreserving surgery and oncologic radicality, some factors favor a conservative approach: the sacrifice of a peripheral branch has less dramatic consequences than the resection of the main trunk of the nerve, and low-grade tumors with no propensity for perineural spread are less likely to recur (even if in close contact with or microscopically involving the nerve) than AdCC or high-grade neoplasms. Moreover, recurrent disease requires much more aggressive treatment than that needed when dealing with a previously untreated tumor.

Finally, extended radical parotidectomy is carried out when the parotid cancer invades adjacent structures, such as the temporal bone, mandible, or skin. The procedure can include mandibulectomy, skin resection, infratemporal fossa dissection, and skull base or temporal bone resection. According to Cracchiolo and Shaha, the aggressive management of the primary site results in loco-regional control in 75% of cases [9]. However, the 5-year survival rate is about 22%, thus reinforcing the concept that wide surgical excision warrants good loco-regional control and palliates local symptoms, while survival remains poor due to distant failure, in patients with a locally advanced cancer requiring an extended parotidectomy.

Submandibular gland

Treatment modalities for submandibular malignant tumors encompass exclusive surgery for early-stage tumors, whereas patients with higher stages, high-grade tumors, or histologic risk factors (i.e. positive microscopic margins, perineural spread) are generally treated with a combination of surgery and RT. Unresectable tumors or patients in poor condition for surgery should be treated with non-surgical protocols, mainly RT alone. A recurring problem is the low threshold for submandibulectomy in combination with a low index of suspicion for malignancy at this site, especially in non-referral centers [25,26]. About one-third of patients with submandibular masses are referred after inadequate

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