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Astrid L Kruse, Klaus W. Grätz

Institutions: University of Zurich

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Abstract

BACKGROUND:: Either excision of the submandibular gland during neck dissection or having the submandibular gland in radiation field can result in xerostomia, leading to reduced quality of life. The purpose of this study was to evaluate the prevalence of metastasis to the submandibular gland and to identify potential risk factors leading to the presence of metastases into the gland. PATIENTS AND METHODS:: Of 376 patients with head and neck malignancy who were treated between 1999 and 2008, 130 patients underwent a neck dissection, and in total, 171 submandibular glands were removed. The average age was 61.1 years. RESULTS:: Twenty-three patients (17.7%) revealed some type of pathology in the submandibular gland such as chronic sialadenitis (15), atrophy (5), tumor infiltration (5), and intraglandular lymph node (1). In the group with sialadenitis, the mean age was 57.7 years. Forty-four percent had a pretreatment (radiation, 9%; local resection, 13%; or combined therapy, 22%) before neck dissection. Of the sialadenitis group, 9 of 12 patients had the primary tumor in the lower jaw, floor of mouth, or tongue. CONCLUSIONS:: One needs to be aware of the possibility of occult metastases in level I in oral cavity carcinomas, whereas oropharynx carcinoma constitutes a lower risk for involvement of lymph node metastases at level I. The excision of the submandibular gland should be performed in cases with positive lymph nodes at level I and in tumor sites with a high risk of occult metastasis at level I.

Evaluation of Metastases in Submandibular Gland in Head and Neck Malignancy

Kruse, Astrid, MD, DMD[1]

Grätz, Klaus W MD, DMD[2]

[1]Resident, Department of Craniomaxillofacial and Oral Surgery, University of Zurich, Switzerland

[2]Professor and Head, Department of Craniomaxillofacial and Oral Surgery, University of Zurich, Switzerland

Address for correspondence:

University Hospital Zurich
Department of Cranio-Maxillofacial Surgery
Astrid Kruse MD, DMD
Frauenklinikstr. 24
CH-8091 Zurich
Switzerland

Phone: +41 44 255 5062
Fax: +41 44 255 4179
E-mail: astrid.kruse@usz.ch

Abstract

Background: Either excision of the submandibular gland during neck dissection or having the submandibular gland in radiation field can result in xerostomia, leading to reduced quality of life. The purpose of this study was to evaluate the prevalence of metastasis to the submandibular gland and to identify potential risk factors leading to the presence of metastases into the gland.

Patients and methods: Of 376 patients with head and neck malignancy who were treated between 1999 and 2008, 130 patients underwent a neck dissection, and in total, 171 submandibular glands were removed. The average age was 61.1 years.

Results: Twenty-three patients (17.7%) revealed some type of pathology in the submandibular gland such as chronic sialadenitis (15), atrophy (5), tumor infiltration (5) and intraglandular lymph node (1). In the group with sialadenitis, the mean age was 57.7 years. Forty-four percent had a pretreatment (radiation 9%, local resection 13% or combined therapy 22%) before neck dissection. Of the sialadentitis group, 9 of 12 patients had the primary tumor in the lower yaw, floor of mouth or tongue.

Conclusion: One needs to be aware of the possibility of occult metastases in level I in oral cavity carcinomas, whereas oropharynx carcinoma constitutes a lower risk for involvement of lymph node metastases in level I. The excision of the submandibular gland should be performed in cases with positive lymph nodes at level I and in tumor sites with a high risk of occult metastasis at level I.

Keywords: Metastasis; submandibular gland; head and neck

Excision of the submandibular gland during neck dissection or having the submandibular gland in radiation field can result in xerostomia, leading to reduced quality of life. The latter was first described by Bergonie [1] in 1911. Radiation with 35 Gy can lead to permanent salivary dysfunction[2]. The histological hallmarks of radiation-induced damage are acinar atrophy and chronic inflammation [3].

Concerning excision of the submandibular gland, the question arises whether there is a need for removing the submandibular gland in neck dissections, because until now, there has been no actual treatment that can completely restore the function of the salivary gland following radiotherapy. Therefore, we intend to examine retrospectively the involvement of submandibular glands in patients who have undergone a neck dissection to explore the possibility of preservation of the submandibular gland.

There are different opinions of the distribution of the lymph nodes in the submandibular gland. Spiegel et al[4] mentioned that there are no intraparenchymal lymph nodes, whereas DiNardo[5] and Lim et al[6] presented 6 different groups of lymph nodes: preglandular, prevascular, retrovascular, retroglandular, deep, and intraglandular.

DiNardo[5] showed in a study of 10 cadavers without evidence of head and neck tumor that 3 lymph nodes, on average, were found in each submandibular space, with 64% of these lymph nodes prevascular and 36% preglandular. In the clinical study with 41 patients with untreated head and neck cancer, submandibular node metastases were found in 39% (2 belonged to the deep submandibular nodal group).

With regard to prevascular lymph nodes, the question arises whether it is useful to preserve the facial artery during excision of the submandibular gland, particularly when the reconstruction follows such as the platysma myocutaneous flap, the lower lip reconstruction using Bernard technique, or the facial artery musculocutaneous flap. Talmi et al[7] examined overall 81 patients (73 patients underwent neck dissection) but recommended preserving the facial artery only in selected cases of malignancy.

Lim et al[6] examining 66 patients with perifacial lymph node dissection, found a 35% incidence rate of metastasis to the perifacial lymph node in oral cavity carcinoma and 8% in oropharynx carcinoma. It was striking that in patients without clinically positive level I lymph nodes, the occult metastases rate of perifacial node was 27% for oral cavity tumors.

On the afferent lymphatic side of the submandibular region, superficial oral lymphatic capillaries from a mucosal network–drain bilaterally to a deep or muscular network ending into a plexus around blood vessels. Collecting trunks then receive lymph from mucosal and submucosal networks and deliver to the submental, submandibular and carotid triangles. On the efferent lymphatic side, lymph can descend from the prevascular and retrovascular nodes, drainage occurs along 1 or 2 vessels that follow the facial artery to the posterior belly of the digastric and stylohyoid muscles, emptying into the subdigastric or internal nodes. Another efferent lymphatic pathway comes from the prevascular and retrovascular nodes descending to the anterior facial vein, ultimately emptying in the anterior internal jugular nodes[5,8] .

Involvement of the gland can be caused by direct invasion of the primary tumor, by extension of locally involved lymph nodes or by the hematogenous spread of a carcinoma originating outside the head and neck. Several cases have been described, for example, breast [9,] lung [10,] and very vascular tumors such as renal cell carcinoma [11].

Spiegel et al[12] showed that the submandibular gland is involved only in cases of ipsilateral oral cavity tumors. Perivascular-submandibular lymph node metastasis in squamous cell carcinoma of the tongue and floor of mouth seems to have a small incidence. Lim et al[6] revealed perivascular level IB lymph-nodes metastasis in 4 out of 72 necks with tongue cancers and 2 out of 27 necks from the floor-of-mouth cancer; 1 deep glandular and 4 pre-glandular lymph nodes were found. In another study concerning larynx[13], only 2% (2/100) of the patients with advanced squamous cell carcinoma (T3-T4) had positive lymph nodes in the submandibular triangle (Level IB). The rare metastases rate at level I laryngeal and hypopharyngeal cancer is supported by Ferlito et al[14]. But it must always be differentiated from floor-of-mouth/tongue cancer and cancer with more posterior origin.

Only very few studies have been published in the literature concerning the involvement of submandibular gland in carcinoma of the head and neck. Seifert et al[10] examined 108 cases of metastatic tumors to the parotid and submandibular gland. Ten cases were found in the parenchyma of submandibular gland, and 23 cases displayed metastases in the lymph nodes of the submandibular gland.

Spiegel et al[12] retrospectively examined in 169 patients with 196 resected submandibular glands whether and how the submandibular gland is involved in metastases of squamous cell carcinoma of the head and neck. Three submandibular glands showed invasion from locally involved lymph nodes, and 6 had direct extension from a primary lesion.

In 2008,[15] 201 patients with neck dissection were examined retrospectively. Forty-four cases (21.9%) revealed ipsilateral level I metastasis. Two cases (1%) had carcinoma involvement in the submandibular gland by direct extension from the primary lesion. There was no isolated metastasis or local extension of metastatic lymph nodes found in submandibular gland.

Patients and Methods

Between January 1999 and December 2008, 376 patients with a diagnosis with malignancy of the head and neck were treated in the Department of Craniomaxillofacial and Oral Surgery of the University Hospital Zurich (Fig.1).

Fig.1: Overview of the treated patients

Retrospectively, all patients who underwent a neck dissection in a standardized fashion were studied. Special attention was paid to TNM status, tumor localization, pathohistology of the submandibular glands that were removed as part of neck dissection in regard to pretreatment, metastases and tumor infiltration. A study of the involved positive lymph node levels was not possible because of not standardized histopathological evaluations being not standardized.

Results

Overview of all Patients that Underwent Neck Dissection

There were 130 patients (53 female, 77 male) who underwent neck dissections where 171 submandibular glands were removed between January 1999 and December 2008 (Fig.1). Of these patients, 38.5% had a pathological status of T2; 45.4% had a pathological N0 status (Fig.2). The average age was 60.8 years.

Fig.1: Overview of the treated patients

Fig.2: Overview of all treated patients that underwent neck dissection

The origin of the tumor was predominantly in the lower jaw (alveolus) (32%), followed by the floor of mouth (22%) and tongue (18%) (Fig. 3).

Fig.3: Overview of locations of all treated patients that underwent neck dissection

Infiltration of Lymph Node Metastasis into the Submandibular Gland (Lymph Node Level)

Twenty-three patients revealed a pathology in the submandibular gland; chronical sialadenitis (12), atrophy (5), tumor infiltration (5) and intraglandular lymph node (1) (Fig. 4).

Fig.4: Determination of patients with submandibular gland pathology in neck dissection

In the group of sialadenitis the mean age was 57.7 years. Of these, 44% had a previous treatment (radiation 9%, local resection 13% or combined therapy 22%) before neck dissection (Fig.5).

Fig.5: Determination of pretreatment in the sialadenitis group

Seventy-five percent (9/12 patients) of the sialadenitis group had the primary tumor in the lower jaw/ floor of mouth or tongue (Fig.6) and all patients of the gland atrophy group had the primary tumor in the floor of mouth.

Fig.6: Determination of cancer location (with salivary gland pathology)

All patients with tumor infiltration into the submandibular gland or with intraglandular lymph node had positive lymph node at level I.

Infiltration of the Tumor into the Submandibular Gland Contralateral Involvement

There was no tumor infiltration or lymph node metastases in the contralateral submandibular gland.

Metastases to the Submandibular Gland

One female patient revealed an intraglandular lymph node metastasis in 2 years after treatment of a pathological T1 tumor of the cheek.

Discussion

Because of poorly developed lymphatics and vasculature of submandibular glands, lymphatic metastases are uncommon unlike in the parotid gland.

Lymph node metastasis surrounding the submandibular gland is relatively common in squamous cell carcinoma of the floor of mouth, and it seems to be extremely unusual to find metastasis of the submandibular gland. Our results reflect these statements; in only 1 case an intraglandular lymph node found. No metastases of head and neck cancer in the contralateral submandibular gland were found in the literature or seen in our study

It is striking that 44% of the sialadenitis patient group had a previous treatment. Scar tissue caused by surgery or radiation can lead to acinar atrophy and fibrosis chronic inflammation, particularly in the periductal and intralobular areas.[3] But tumor also can cause chronic pressure inflammation leading to chronic sialadenitis.

Only a few of the studies performed emphasized salivary flow rates after submandibular gland resection without radiotherapy. Jacob et al [16] compared the salivary flow rates in 29 patients who had undergone unilateral gland resection and 8 patients who underwent bilateral gland resection, with 29 control patients. Unstimulated and stimulated (paraffin) flow rates were significantly lower in both resection groups compared with the control group. Comparing the 2 groups that had a resection,, the difference was significant only for stimulated saliva. The result concerning the comparison between the group who had a unilateral submandibular gland excision (10 patients) and the control group (13 patients) was also supported by Cunning et al. [17]

On the pharmaceutical side, if there is residual salivary function, sialagogues, such as pilocarpine hydrochloride, a cholinergic antagonist, have also been mentioned to maximize the residual gland function by inducing vasodilatation in the salivary glands via stimulating a secretion with similar composition like in normal gland function. [18]

Detection Possibilities of Metastases in Submandibular Gland

All patients in our study with tumor infiltration to the ipsilateral submandibular gland or with intraglandular lymph node had positive lymph nodes in level I. This supports excluding patients with positive lymph nodes in level I from treatment preserving the submandibular gland. Alex and Krag[19] described in 1993 the first use of sentinel node biopsy for staging head and neck cancer. Therefore, the question arises whether it is possible to use this method to estimate the involvement of level I lymph node metastases and therefore estimate the risk for involvement of the submandibular gland. This technique is still controversially discussed in literature[14] and is not a standard method.

Possibilities for Therapy of Postradiation Xerostomia

Concerning the prevention of postradiation xerostomia, multiple methods have been discussed in the literature, for example, shielding the submandibular gland during radiotherapy, but this can lead to incomplete treatment. Bourdin[20], described in 1982 the transfer of the submandibular gland to the submental area in patients with no nodal metastasis of the contralateral side. Jha et al [21] transferred the unilateral submandibular gland to the anterior submental region and prevented radiation-induced xerostomia up to 83% with a minimum follow-up of 2 years. Spiegel et al [12] demonstrated in a rabbit model the possibility of transferring the submandibular gland to the groin region and back to the neck while maintaining its function and integrity. Most of the patients in studies received postsurgical radiation because of positive lymph nodes, therefore long-time results concerning recurrence rate are of high interest, but are still not available in most studies. Al-Qahtani et al[21] presented

8 patients (with N-status from N2a –N3) with a follow-up of 18 months with a recurrence rate and distant metastases rate of 0%.

Other fields of research are salivary gland stem cells and the possibility of cell transplantation and tissue engineering of the salivary gland. The latter has revealed that cells adhere to and grow on biocompatible materials maintaining acinar cell phenotype and showing α-amylase acitivity.[22] It is believed that cells in the duct close to the acini provide all cell types required for the formation of acini and ducts. [23] But this concept still requires further research.

Conclusion

In conclusion, this study demonstrated the following results: the preservation of the submandibular gland during neck dissection can be performed in special cases of necks clinically negative for head and neck carcinoma. One needs to be aware of the possibility of occult metastases at level I in oral cavity carcinomas, whereas oropharynx carcinoma constitutes a lower risk for involvement of lymph node metastases in level I. The excision of the submandibular gland should be performed in cases with positive lymph nodes level I and in tumor sites locations with a high risk of occult metastasis at level I.

Special attention should be paid, on the one hand, to tissue engineering and stem cell research and, on the other hand, to improved techniques for detection of malignancy in submandibular glands and level I lymph nodes, but there is still a need for further investigations.

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Legend

Fig.1: Overview of the treated patients

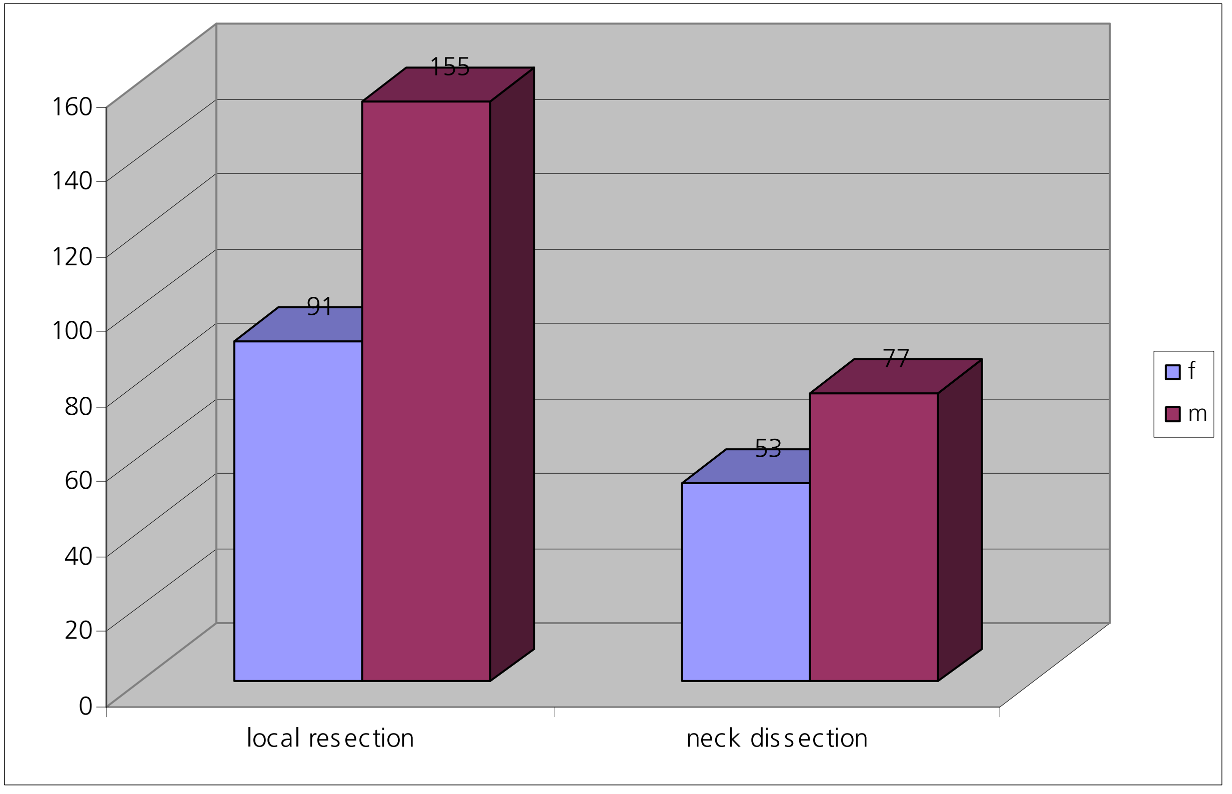
Fig.2: Overview of all treated patients that underwent neck dissection

Fig.3: Overview of locations of all treated patients that underwent neck dissection

Fig.4: Determination of patients with submandibular gland pathology in neck dissection

Fig.5: Determination of pretreatment in the sialadenitis group

Fig. 6: Determination of cancer location (with salivary gland pathology)



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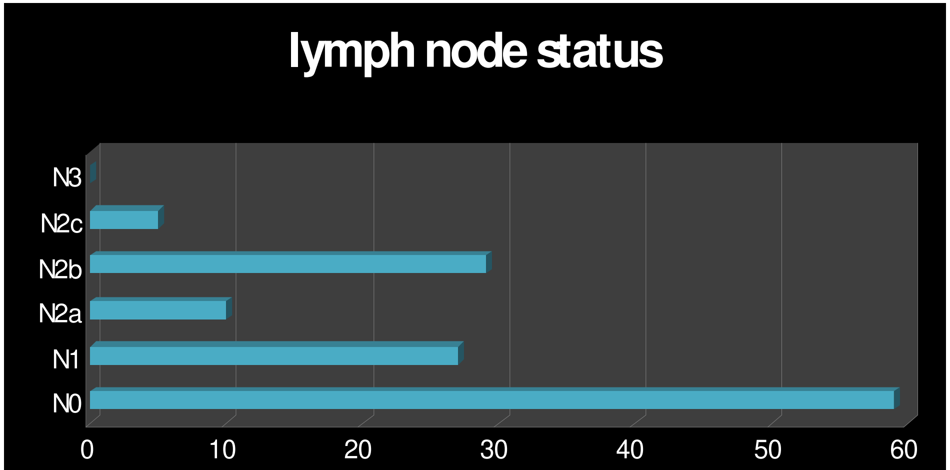


	N0	N1	N2a	N2b	N2c	N3
number	59	27	10	29	5	0

Fig.2: Overview of all treated patients that underwent neck dissection

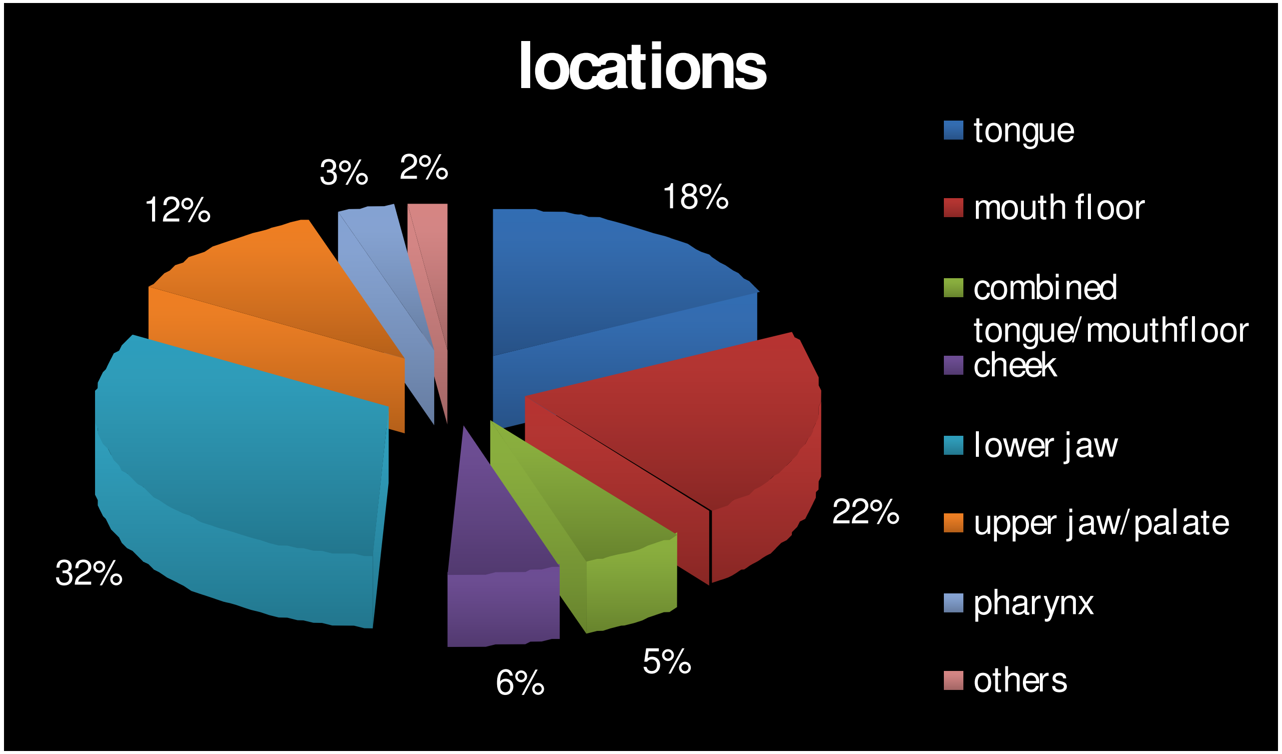


Fig.3: Overview of locations of all treated patients that underwent neck dissection

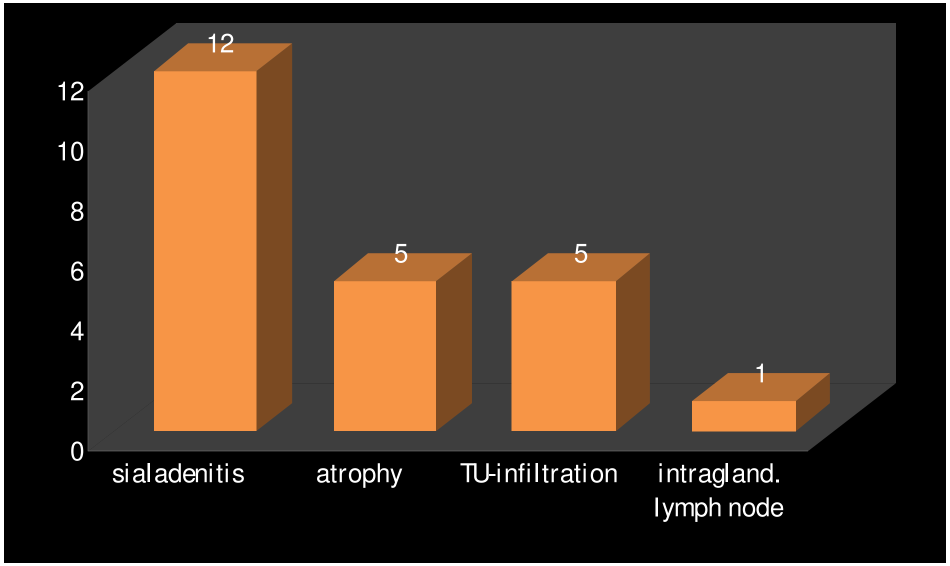
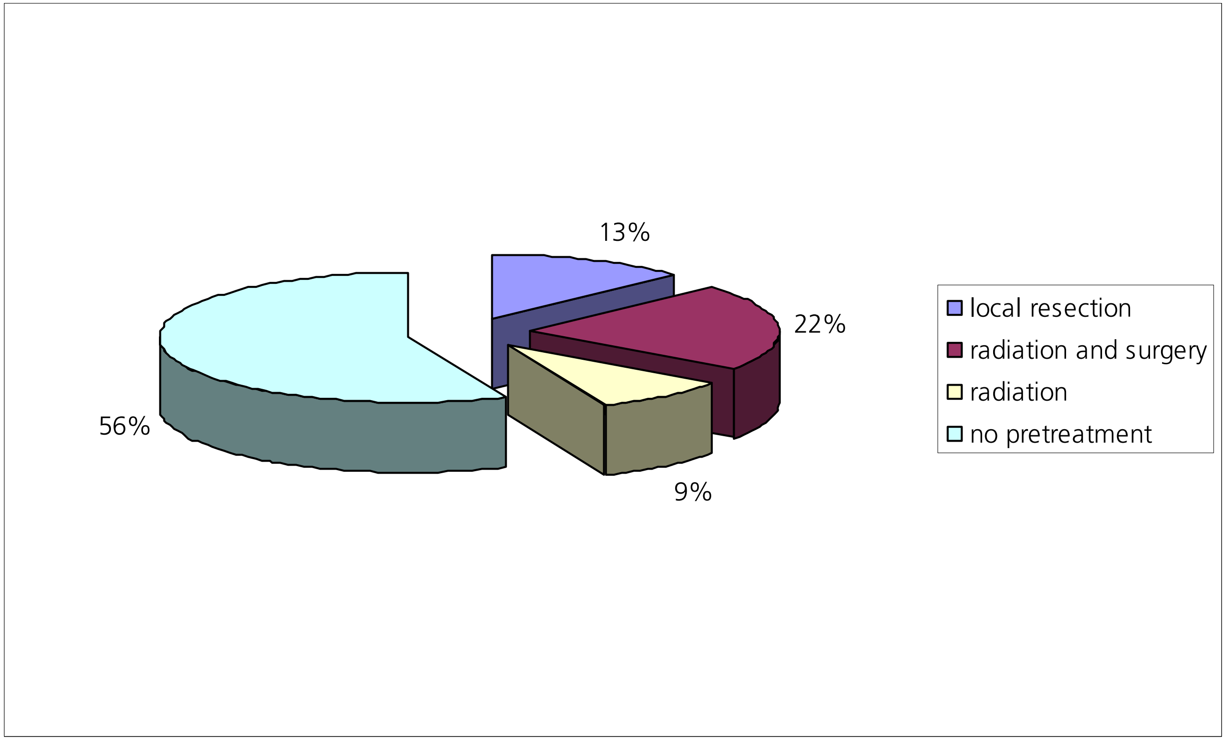


Fig.4: Determination of patients with submandibular gland pathology in neck dissection



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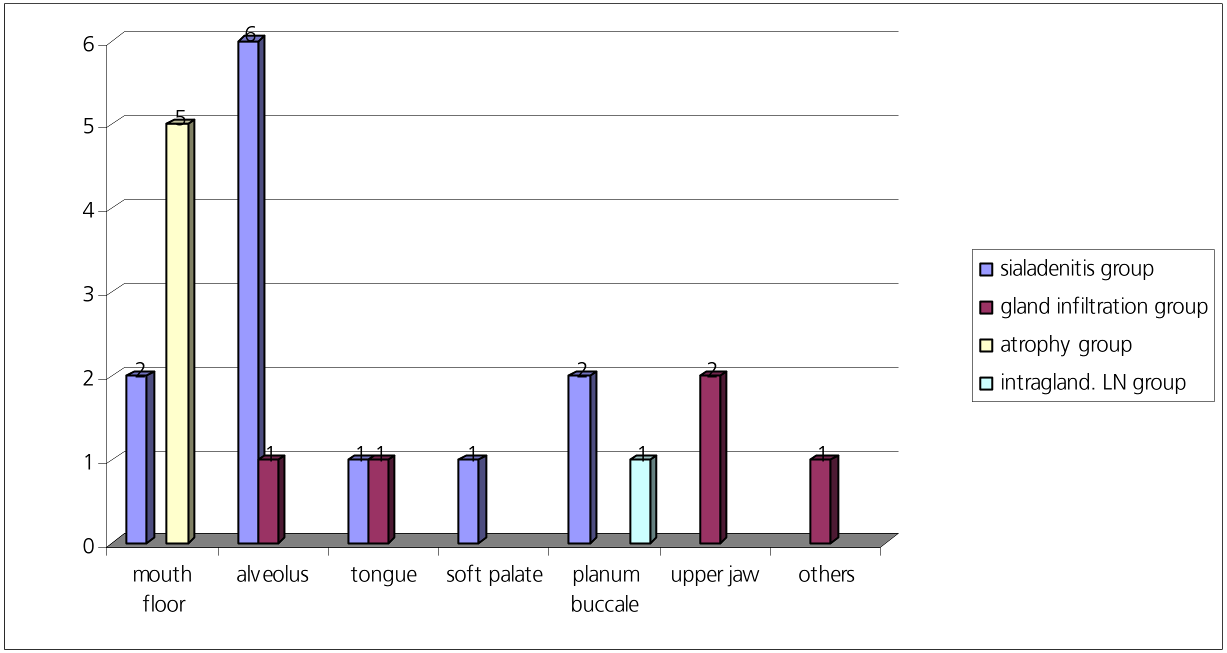

Fig.6: Determination of cancer location (with salivary gland pathology)