Purpose/Objective(s): Dysphagia is a crippling comorbidity of head and neck cancer (HNC) treatment. The underlying structural insults of dysphagia associated with HNC treatment paradigms are poorly understood. In this study, morphological analysis of coordinates that map swallowing structures collected from Modified Barium Swallow Studies (MBSS) is used to indicate structural changes associated with treatment paradigms.

Materials/Methods: A cohort of oropharyngeal cancer patients from the Medical University of South Carolina was identified from patient records (n=55). Using MBSS videos of 5ml thin liquid and 5ml pudding swallows morphometric analysis of swallowing function and indicators of swallowing safety and efficiency were compared by treatment group: surgical only (SX), chemo-radiation (CXRT), and mixed therapy. Coordinates mapping swallowing structures were collected at maximum and minimum swallow excursion points for the hyoid, larynx, and pharynx. Canonical variate analysis was performed to determine shape changes associated with HNC treatment paradigms. Indicators of swallowing safety and efficiency were compared by group using the penetration aspiration score (PAS) and normalized residue ratio scale (NRRS).

Results: A canonical variate analysis of coordinates by swallowing excursion and treatment group resulted in eigenvalues that accounted for 71.7% of the variance by swallow function and 22.5% by treatment group. A significant difference in shape change was noted by discriminate analysis between SX (n=17) and CXRT (n=12) treatment groups (D= 2.51, p< .0001). Eigenvectors associated with swallowing indicated increased extension of the head and neck in the SX group and reduced pharyngeal shortening in CXRT group. No significant differences were noted in airway invasion and pharyngeal clearance (PAS, NRRSp, NRRSv) between SX and CXRT groups.

Conclusions: Morphological changes in the swallowing structure varied by treatment paradigm with SX and CXRT comprising two ends of the shape change spectrum. Changes indicate compensatory movement of the head and neck in the SX cohort and reduced function of the long pharyngeal muscles in CXRT cohort. While changes in the functional anatomy of swallowing between treatment groups are significant, indicators of swallowing safety and efficiency, penetration-aspiration and residue, are not indicating adaptation to structural insults. Morphometric analysis of swallowing function is a novel approach to evaluating what structural insults are associated with treatment paradigms. These methods coupled with swallowing outcome measurements may provide better insight into dysphagias associated with head and neck cancer treatment.
Background: Lesions involving the hypoglossal canal and inferolateral clivus are rare, but often include schwannomas, clival chordomas, petroclival meningiomas, and jugulotympanic paragangliomas. Improvements in endoscopic technology and reconstructive techniques have made the endoscopic endonasal approach (EEA) a viable option to approach ventromedial lesions in the region of the hypoglossal canal. A thorough understanding of the anatomical relationships is essential to safely approach this region of the posterior skull base through an EEA.

Objective: To describe the surgical technique and anatomic landmarks of the EEA to the hypoglossal canal through referencing nasopharyngeal and posterior skull base anatomy

Methods: An EEA to the hypoglossal canal was carried out bilaterally in five embalmed, latex-injected cadaver heads. Intracadaveric measurements of anatomic landmarks and relationships in the approach were obtained using a standard 10-centimeter surgical ruler and were reported as mean distances.

Results: The distance between the superolateral boundary, the lacerum segment of the internal carotid artery, and the inferolateral boundary, the anterolateral edge of the occipital condyle, was 32mm and 19mm, respectively. The supracondylar groove was identified in the same plane as the nasopharyngeal orifice of the Eustachian tube on the anteroposterior axis and the anterior edge of the occipital condyle was 13mm from the posterosuperior edge of the salpingopharyngeal fold. Additionally, the transtubercular corridor was in the same plane as the superior edge of the Torus Tubarius in the anteroposterior axis. The distance to the hypoglossal canal from midline was 10mm, which was found after completing drilling in the transcondylar and transtubercular corridors. Lastly, after opening dura, the hypoglossal nerve rootlets were identified entering the canal 6mm inferiorly and 8mm laterally from the vertebrobasilar junction (VBJ).

Conclusion: The Eustachian tube and other elements of nasopharyngeal anatomy are fixed landmarks that provide an important point of reference when approaching the posterior skull base and hypoglossal canal through an EEA. With its ability to achieve superior visualization and minimize displacement of normal tissue, the EEA offers a direct surgical window in approaching ventromedial lesions in the posterior skull base.
INTESTINAL-TYPE SINONASAL ADENOCARCINOMA: A RETROSPECTIVE ANALYSIS ON A SERIES OF 169 PATIENTS TREATED OVER 16 YEARS

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Background: Intestinal-type sinonasal adenocarcinoma (ITAC) is a neoplasm almost invariably occurring in wood and leather workers. Surgery (+/- adjuvant radiotherapy) is the mainstay of treatment.

Patients and methods: All patients affected by ITAC who underwent surgery with curative intent by different approaches (endoscopic resection without [ER] or with transnasal craniectomy [ERTC], cranio-endoscopic resection [CER]) at the Universities of Brescia and Varese from October 1997 to September 2013 were retrospectively reviewed. Overall survival (OS) was defined as time from surgery to death for any cause. Event-free survival (EFS) was defined as time from surgical treatment until relapse (any site) or death from neoplastic disease (DOD). Both survivals were estimated using the Kaplan-Meier method and compared with the log-rank test. Statistically significant variables at univariate analysis were entered in a multivariate Cox regression model.

Results: One hundred sixty-nine patients were included. The male/female ratio was 8.4. Mean age was 66.1 years (range: 29-84). In all patients the tumor originated within the naso-ethmoidal complex. Wood or leather exposure was demonstrated in 128 (82%) patients. Forty-two (24.8%) patients were referred to our Departments for recurrent/persistent disease. ER, ERTC, CER were performed in 38 (22.5%), 103 (61%), 28 (16.5%) cases, respectively. Major complications occurred in 9.5% (8 [4.7%] CSF-leak, 6 [3.6%] neurological complications, 1 [0.6%] frontal osteomyelitis, 1 [0.6%] pulmonary embolism). No perioperative death was observed. Pathologic T staging was distributed as follows: 34 (20.1%) pT1, 48 (28.4%) pT2, 33 (19.5%) pT3, 11 (6.5%) pT4a, 43 (25.5%) pT4b. Histologic examination revealed well, moderately-, and poorly- differentiated tumor in 21 (12.6%), 109 (65.7%), and 36 (21.7%) patients, respectively. Surgical margins were positive in 18 (10.6%) cases. Dural involvement was demonstrated in 31 (18.5%) patients, 10 (5.9%) of which with brain invasion. Adjuvant treatment was performed in 100 (59.2%) patients (97 radiotherapy, 2 chemo-radiotherapy, 1 chemotherapy). After a mean follow-up of 47.2 months (range, 1-170 months), 36 (21.3%) patients developed recurrence (26 [15.4%] local, 3 [1.8%] regional, 15 [8.9%] distant). Leptomeningeal spread was observed in 9 (5.3%) cases. Patient status was the following: 114 (67.5%) alive without disease, 30 (17.7%) dead of the disease, 21 (12.4%) dead of other cause, 4 (2.4%) alive with disease. Five-year OS and EFS were 68.9% (±4.3) and 63.6% (±4.2), respectively. On univariate analysis, both OS and EFS were affected by advance age (p=0.023 and p=0.002), high pT category (p<0.001), high grading (p<0.001), a more extensive surgical approach (p<0.001 and p=0.003), brain/dural involvement (p<0.001), and positive margins (p<0.001). Male (p=0.036) and professional exposure (p=0.038) impacted only EFS. On multivariate analysis, OS and EFS were independently correlated with grading (G3 vs G1, p=0.036 and p=0.008, respectively) and surgical margins (p=0.001). pT category (T4b vs T1-T2, p=0.008) affected only OS. Surgical approach and dural involvement did not impact survival.

Conclusions: ITAC is characterized by a locally aggressive behavior with low risk of regional and distant metastasis. Endoscopic surgery can be considered a valid treatment in most cases. pT category, grading and surgical margins are independent prognostic factors.
RELATIONSHIP OF HYDRATION DURING RAI EXPOSURE TO POSTTREATMENT SALIVARY GLAND DYSFUNCTION
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Approximately 44,000 new cases of thyroid cancer are expected each year in the US. During the care for these cancers, surgery is frequently followed by radioactive iodine (RAI) administration. One of the side effects of RAI use is sialadenitis, an inflammation of salivary tissue secondary to uptake of RAI. Recent studies have debated the role of hydration during RAI administration as an mitigating factor in dry eyes and/or dry mouth (DEDM).

3908 responses were collected from THYCA, an online thyroid cancer survivor group, regarding RAI usage following surgery for well differentiated thyroid cancer. Responses were excluded if the patients did not receive RAI, had pretreatment dry eyes/mouth, if they did not have well differentiated thyroid cancer or their data were grossly incomplete. This resulted in 2940 survey responses. There were 316 men, 2592 women and 31 no responses (NR). 1729 were quarantined at home, 869 in the hospital, 96 in hotel/motels, 77 in summer homes and 47 NR. 1558 had DEDM as a result of RAI. 1296 had no DEDM. 1643 (57%) were warned about DEDM, 723 (25%) were not warned pretreatment. 18% could not remember if they were told. 1960 were told to hydrate immediately upon receiving RAI. 104 started hydrating the next day, 798 could not recall and 78 NR. 1071/1935 (55%) had dry mouth, 864/1935 (45%) did not. Similarly, patients who hydrated a day later had DEDM 65/104 (62%) and did not have DEDM 39/104 (38%). Patients who could not recall when they hydrated had DEDM 408/783 (52%) and 375/783 (48%).

These data suggest that DEDM is underestimated after RAI administration. At least half of the patients had DEDM. There was no significant difference between hydrating immediately or a day later. A quarter of the patients were not told that DEDM could happen. Most patients were isolated at home or hospital.
Background: Despite the prevalence of thyroidectomy, there is no standardized surgical armamentarium, technique or anesthetic procedure. Clinical effectiveness takes precedence in decision-making; however, physician preference plays a major role in cases of equivalent safety and efficacy. In this study, we analyze the effect of physician preference regarding instrumentation and medications on total operating room (OR) cost for thyroidectomy.

Methods: Observational data included technique, decision points and instrument/disposable use for 17 total thyroidectomies performed by 5 full-time surgeons at the University of Chicago. Disposable acquisition costs, case lengths, anesthetic costs and total OR costs in fiscal year 2013 were analyzed.

Results: Dynamic operative mapping (DOM) of thyroidectomy identifies four main decision points that reflect variation in disposable instrument selection among surgeons: nerve monitoring, thyroid dissection, hemostasis and skin closure. Theoretical modeling yields 54 distinct combinations of selections in these four decision points ranging in cost from $298 to $1633. In practice, the costs range from $298 to $1632 for the lowest- and highest-cost surgeon, respectively. For the highest-cost surgeon, the four preferences account for 86% of the total disposable cost. Average total OR cost, including anesthetic costs, for total thyroidectomy is $8046, 23% of which is total disposable cost for the highest cost surgeon. There was no difference in OR case time between the highest- and lowest-cost surgeon. Variations in anesthetic technique had little effect on total OR costs (<1%).

Conclusions: Surgeon preference has a direct influence on operating costs in thyroidectomy. Cost-minimizing selections in disposable use reflect potential savings of 70% of total disposable cost and 16% of total OR cost. These results demonstrate that decisions influenced by physician preference present significant opportunities to manage procedural costs.
Background  Thyroid cancer stood out with the highest family risk ratio of cancers. Five single nucleotide polymorphisms (SNPs) were previously reported to be associated with thyroid cancer in European populations in two genome-wide association studies (GWAS) by Nature Genetics: rs965513 (9q22.33), rs944289 (14q13.3), rs116909374 (14q13.3), rs966423 (2q35) and rs2439302 (8p12). Only the first two SNPs have been validated in independent populations and none were replicated in Chinese populations. The chromosomal region 8q24(rs6983267) has been associated with PTC risk in a European population, we also genotyped the rs6983267 polymorphism in the same Chinese population to determine its status. Finally, we examine if the variants with highly significant associations will make large contributions to PTC risk prediction for prevention and early detection.

Methods  The above SNPs were genotyped in 845 papillary thyroid carcinoma (PTC) and 503 benign thyroid tumour (BN) patients and 1,005 controls in a Chinese population using the SNaPshot multiplex single nucleotide extension system. The thyroid cancer risk predictions were performed with nine machine learning methods (K-nearest neighbors, logistic regression, naïve Bayes, random forest, support vector machine, Bayesian additive regression trees, recursive partitioning, fuzzy rule-based system, boosting).

Results  Significant associations were detected between PTC and rs944289 (P = 8.007e-11), rs965513 (P = 1.013e-4), rs966423 (P = 1.688e-3) and rs2439302 (P = 1.096e-4) in a dominant model, while the rs116909374 SNP was not detected in the Chinese population. The PTC risk increased with rise in accumulative numbers of risk alleles carried by individuals (P = 5.929e-13). The PTC odds ratio of carriers of six risk alleles (1.4% of the control population) was 23.587 compared with non-risk homozygotes (1.0% of the control population, with zero risk alleles). No individuals were homozygous for all the four SNPs (carriers of eight risk alleles) and only three PTC cases were carriers of seven risk alleles. A significant association between 14q13.3 SNP rs944289T and BN was also found (P = 0.0076). Although the four SNPs were significantly associated with thyroid cancer in Han Chinese population, but with small familial relative risks (1.02-1.05) and limited power to predict thyroid cancer (AUCs: 0.54-0.60). Functional prediction by bioinformatic analysis showed that rs966423 (2q35) and rs2439302 (8p12) are located within CTCF binding regions, which may change the transcriptional regulation of DIRC3 and NRG1, respectively. However, the association between rs6983267 at 8q24 and thyroid tumour risk was not replicated.

Conclusions  Four candidate loci, rs965513 (9q22.33), rs944289 (14q13.3), rs966423 (2q35) and rs2439302 (8p12), identified by GWAS for PTC risk were confirmed in a Chinese population. The PTC risk of accumulative risk allele carriers increased with the number of risk alleles. While current significant SNPs have limited prediction ability for thyroid cancer in the populations. Our current work focused on the fine mapping and functional analysis of thyroid cancer predisposition gene in these four chromosome regions, and conducted a new GWAS in a multi-institution based cooperative study of Chinese population.
SURGICAL TREATMENT OF NON-MALIGNANT TRISMUS OF ORAL SUBMUCUS FIBROSIS (OSMF): RESULTS FROM 308 CASES

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Context: Oral submucus fibrosis (OSMF) is a chronic peculiar condition seen commonly in South East Asia and India, and is related to the habit of arecanut and betel quid chewing. Trismus resulting from OSMF is progressive, and can often be debilitating. While several medical and surgical lines of management have been used for this non-malignant trismus, there is no consensus regarding treatment, especially surgical.

Objectives: To study different methods of surgical intervention in OSMF associated trismus, and ascertain factors predicting surgical outcome.

Design: Prospective single-institutional cohort study, carried out from 1999-2012.

Setting: Private Hospital

Patients: Data of 308 patients undergoing surgery for non-malignant OSMF associated trismus.

Outcome Measures: The degree of trismus was graded (according to inter-incisor distance) and recorded before, immediately after, and at least 3 months after surgery. The extent of trismus improvement was found out for different surgery types. Logistic regression was used to find predictors of success after surgery: factors considered being age, gender, duration of habit, habit cessation, tobacco or tobacco-arecanut preparations, coronoidectomy, post-operative jaw stretching exercises.

Results: There were 308 patients, comprising 89.9% males and 10.1% females, with median age of 31 years. Island cuts were done in 47 patients, ‘Y’ shaped mucosal cuts with mandibular mucoperiosteal flap (MMPF) was done in 91 patients, Coronoidectomy with MMPF was done in 95 patients, while coronoidectomy with platysma flap was done in 75 patients. The median follow-up was 5 months with a range of 3 to 62 months. The improvement in trismus was graded as increase in inter-incisor distance. Maximum improvement was seen in patients receiving coronoidectomy + platysma flap. On logistic regression, the factors that independently predicted improvement in trismus post-operatively were coronoidectomy (p=0.034), and jaw stretching exercises (p=0.025).

Conclusions: This is the largest study of its kind examining the various forms of surgical intervention in OSMF associated trismus. We postulate that coronoidectomy is an important aspect in surgical treatment of trismus. Further continuation of post-opertaive jaw stretching exercises is crucial to maintaining the benefit obtained.
S375 ACCURACY OF ULTRASOUND GUIDED FNA IN DETECTING PERSISTENT DISEASE IN LYMPH NODES OF PATIENTS WITH HNSCC AFTER DEFINITIVE CHEMORADIOThERAPY.
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Background:

Planned post-treatment neck dissection in patients with advanced nodal disease has been shown to reduce regional recurrence rates when performed within 4 to 12 weeks after chemoradiation. However, pathologic positivity rates of the dissected post-treatment lymph nodes are in the range of 30-40%, indicating that 60-70% of patients have unnecessary surgery. The clinical challenge, thus, is to accurately detect residual cancer in post-radiation neck nodes, so that unnecessary neck dissections for fully resolved disease may be avoided. The objective of our study, therefore, is to evaluate the diagnostic accuracy of ultrasound-guided fine needle aspiration (UgFNA) for detecting persistent malignancy in lymph nodes of patients with head and neck squamous cell carcinoma (HNSCC) after definitive treatment with chemoradiotherapy (CRT).

Methods: 14 adult HNSCC patients with squamous cell carcinoma of the nasopharynx, oropharynx, larynx, oral cavity or hypopharynx treated with CRT with curative intent, who had persistent adenopathy on contrasted-CT scan of the neck after completion of definitive CRT, were prospectively recruited. A planned post-treatment neck dissection was performed within 8 weeks of CRT-completion on each patient, as is the standard practice at our institution. UgFNA was performed within a 2 week window prior to the neck dissection. Each node deemed suspicious on the post treatment CT underwent UgFNA, and all nodes that underwent UgFNA were removed at neck dissection. Touch prep slides, formalin fixed slides, and cell aspirates were collected and independently reviewed by blinded pathologists. Results of UgFNA were reported prior to pathology of the neck dissection. Accuracy, Sensitivity, Specificity, Positive (PPV) and Negative (NPV) predictive values of UgFNA was assessed by correlating the cytology results from the needle biopsy to those of permanent pathology from the neck dissection.

Results: 17 suspicious metastatic lymph nodes were identified among 14 patients. No malignant cells were found in 12 of the 17 nodes. SCC was indentified on permanent pathology in 5 lymph node specimens. UgFNA was able to detect presence of SCC in 4 of these 5 SCC-positive nodes, but was unable to detect a minute 1-mm focus of viable squamous cell in one of the nodes. Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value were 80%, 100%, 100%, and 92.3%, respectively. Diagnostic accuracy of UgFNA at detecting residual persistent malignancy was 88%.

Conclusions:

UgFNA is a highly accurate, safe, and inexpensive method of assessing lymph node metastasis in patients with persistent adenopathy on contrasted-CT scan of the neck after completion of definitive CRT. UgFNA can help predict which patients will benefit from salvage neck dissection after definitive chemoradiation, avoiding unnecessary surgery in many patients with persistent post-treatment lymphadenopathy.