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Swallowing Structure Related to Acute Dysphagia in Head and Neck Cancer

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Abstract:

Progress in head and neck cancer (HNC) therapies has improved tumor response, loco-regional control, and survival. However, treatment intensification also increases early and late toxicities. Dysphagia is an underestimated symptom in HNC patients. Impairment of swallowing process could cause malnutrition, dehydration, aspiration, and pneumonia. Unidentified dysphagia caused significant morbidity, increased mortality, and decreased the quality of life.

Keywords: Swallowing, acute dysphagia, head and neck cancer.

Head and neck cancers remain a significant global health issue, with over 930,000 new cases and 467,000 deaths annually as of 2023 **(1).** The incidence of HNC continues to rise in Low- and Middle-Income Countries (LMICs) particularly in South Asia and Sub-Saharan Africa, due to high rates of tobacco use, betel quid chewing, and limited access to healthcare (**2).** In Egypt the incidence of HNSCCs is 17–20% of all cancers (**3).**

Oral cavity cancers remain the most common, driven by tobacco chewing, betel quid, and areca nut use. India accounts for one-third of global oral cancer cases in South Asia. **(4).** HPV-related oropharyngeal cancer continues to rise in North America, Europe, and Australia, particularly among younger, non-smoking individuals **(5).**

HPV-16 remains the most common subtype associated with oropharyngeal cancer, accounting for 70–90% of cases in high-income countries **(6).** Traditional HNC cases are more common in individuals over 50, but HPV-related oropharyngeal cancers are increasingly seen in younger populations (40–60 years). **(5).**

Men are 2–4 times more likely to develop HNC than women, though the gap is narrowing due to rising HPV-related cancers in women. **(7).** Cancers of the larynx, lip, oral cavity, salivary glands, nasopharynx, hypopharynx, and oropharynx caused 1061, 544, 150, 160, 136, and 69 deaths in Egypt in 2020. **(8).** Between nations in the same geographic region and between subregions of the same nation, there are noticeable variations in incidence and death rates **(9)**

Etiology and risk factors of HNC:-

The main factor contributing to cancer and cancerrelated deaths worldwide is tobacco usage. It has been demonstrated that it directly causes oral cavity, laryngeal, and pharyngeal cancer in the head and neck **(10).** Smoking with a pipe or a cigar is less frequent than smoking cigarettes, but it might expose you to higher levels of carcinogens. The overall risk (OR) for getting HNSCCs in cigar smokers was 2.54 and in pipe smokers it was 2.08**. (10).** Oral cavity cancers remain the most common, driven by tobacco chewing, betel quid, and areca nut use. India accounts for one-third of global oral cancer cases in South Asia. (**4).**

Although marijuana has been demonstrated to be mutagenic in vitro, some studies have linked it to carcin ogenicity in people, and it is still biologically plausible for marijuana smoke to contribute to the pathophysiolog y of HNC. **(10).**

Drinking alcohol is a wellknown risk factor for the majority of head and neck, esophageal, and gastric ca ncer subtypes. Alcohol has a higher chance of causing cancer in women than in men, and the increased risk of

HNC that comes along with drinking more alcohol is more pronounced in women than in males. **(11).** The risk of HNSCCs is 35 times higher when alcohol and cigarettes are used concurrently than when either substance is used alone (5 times for alcohol and 9 times for tobacco) **(10).**

HPV-related oropharyngeal cancer continues to rise in North America, Europe, and Australia, particularly among younger, non-smoking individuals. (5). HPV-16 remains the most common subtype associated with oropharyngeal cancer, accounting for 70–90% of cases in high-income countries **(6).**

Genetic susceptibility:

There are several genetic variants that have been linked to an increased risk of HNSCCs. Single nucleotide polymorphisms in genes involved in metabolism, cell cycle control, and alcohol metabolism account for the majority of the genetic relationships investigated. **(11).**

Treatment of HNC

All members of the multidisciplinary oncology group should be involved in choosing an individually tailored treatment plan including surgeons, radiation oncologists, medical oncologists, dentists, nurses, social workers, and rehabilitation personnel **(12).** All goals of treatment should be considered which are; cure, organ preservation, palliation, and a desire to minimize toxicity, reduce symptoms, and maintain quality of life **(13).** Single- modality treatment with surgery or RT is generally recommended for the approximately 30% to 40% of patients who present with early-stage disease (stage I or II) **(14).**

Surgical treatment:

Resectable Versus Unresectable Disease:

Surgery is one of the main modalities of treatment in patients with HNC. Treatment of the primary tumor requires removal of the tumor and its locoregional extensions. **(12).** En bloc resection of the primary tumor should be attempted whenever feasible **(14).** It's important to have free margins after surgery as positive margins will increase the risk for local relapse **(14).**

Neck dissection:

Neck dissection, with or without post-operative RT or chemoradiotherapy, is one of the main options in the treatment of neck metastasis **(15).** In general, patients undergoing surgery for resection of the primary tumor will undergo dissection of the ipsilateral side of the neck **(14).** The radical neck dissection represented the traditional surgical management of the clinically positive neck for many years, until the modified radical neck dissection, was developed **(15).**

Selective neck dissections have been developed based on the common pathways for spread of HNC to regional nodes. Depending on the site, selective neck dissection is often recommended for N0 disease. A comprehensive neck dissection is one that removes all lymph node groups that would be included in a classic radical neck dissection, and is often recommended for N3 disease. SLN biopsy is an alternative to elective neck dissection for identifying occult cervical metastasis in patients with early (T1 or T2) oral cavity carcinoma **(14).**

Postoperative management of high risk disease:

Most patients with extranodal extension with or without positive surgical margins receive adjuvant chemoradiotherapy after surgery **(14).**

Head and Neck radiation therapy:

Indications for postoperative RT include (12):

a- Close or inadequate resection margins

b- Poorly differentiated cancers

c- Involvement of lymphatics, including cervical nodes

d- Perineural invasion

Role of chemotherapy in HNC:

Chemotherapy does not have a role in most early stage (I and II) HMSCC. The greatest benefit derived from chemotherapy is in patients with locally advanced disease when chemotherapy is used either sequentially or concurrently with RT, with or without surgery. Many drugs have shown activity (10% to 20%) as single agents in the recurrent and metastatic setting including cisplatin, bleomycin, 5- fluorouracil, capecitabine, paclitaxel, docetaxel, carboplatin, gemcitabine, and ifosfamide **(12).**

Induction chemotherapy:

It is considered with bulky N3 disease or if there is a significant delay with initiation of RT such as cisplatin and 5-FU in combination with a benefit of adding a taxane **(12).**

Concurrent chemoradiotherapy (CCRT):

It is an established standard for definitive treatment of locally advanced HNSCCs. In patients with locally advanced HNSCCs, CCRT has shown statistically significant improvement in OS (absolute improvement 8%) compared to RT alone. **(12).**

Adjuvant chemotherapy:

It is not recommended as standard of care after RT, with the single exception of nasopharyngeal carcinoma. Concurrent cisplatin and RT followed by three cycles of adjuvant cisplatin and 5-FU is considered the standard of care in stage III/IV nasopharyngeal carcinoma **(12).**

Target therapy and immunotherapy in HNC:

1)Therapies Targeting Epidermal Growth Factor Receptor:

Targeting EGFR can be achieved either by blocking the ligand- binding domain using monoclonal antibodies (mAbs), or by inhibiting the activity of the tyrosine kinase domain using small-molecule tyrosine kinase inhibitors (TKIs) **(16).** Cetuximab, a chimeric monoclonal antibody with high specificity and affinity to EGFR, remains the only approved targeted therapy for HNSCCs in combination with RT/chemotherapy **(17).** Other anti-EGFR antibodies (panitumumab, zalutumumab, nimotuzumab) have shown promising results in preclinical studies **(18).**

Anatomy of Pharynx:

The pharynx is a conductive structure located in the midline of the neck. It is the main structure in addition to the oral cavity, shared by two organ systems, i.e., the gastrointestinal tract (GIT) and the respiratory system (**19**).

It is funnel-shaped with its upper end being wider and located just below the lower surface of the skull. And its lower end is narrower and located at the level of the sixth cervical vertebra (C6) where the commencement of the esophagus posteriorly and the larynx anteriorly takes place. Its muscular-membranous integrity allows it to mediate several vital functions related to either organ system, e.g., food swallowing, air conduction, and voice production.

Structure and Function :

The pharyngeal tube is highly muscular. Pharyngeal muscles are arranged in layers, as described below**.** The pharyngeal constrictor muscles form the outer circular layer of the pharynx and are pivotal in swallowing. (**20).** This layer consists of 3 constrictor muscles—superior, middle, and inferior. **(21).**

Superior constrictor:

This muscle originates from the pterygoid process, the posterior end of the mandible's mylohyoid line, and the pterygomandibular raphe. The superior constrictor inserts onto the pharyngeal tubercle of the skull base and the pharyngeal raphe, a midline tendinous seam where the constrictor muscles converge.(**20).** Contraction of this muscle narrows the upper pharyngeal segment and closes the nasopharynx during swallowing. **(21).**

Middle constrictor:

This muscle arises from the greater and lesser horns of the hyoid bone and the stylohyoid ligament he middle constrictor also inserts onto the median pharyngeal raphe, blending with superior and inferior constrictor fibers. (**20).** This muscle constricts the middle pharyngeal portion during swallowing. **(21).**

Inferior constrictor:

The inferior constrictor is subdivided into the thyropharyngeus superiorly and the cricopharyngeus inferior **(21).** The thyropharyngeus originates from the thyroid cartilage, whereas the cricopharyngeus arises from the cricoid cartilage and merges with the esophageal muscle. **(21).**

Inner Longitudinal Pharyngeal Layer

The inner longitudinal layer consists of muscles that primarily act to elevate the pharynx and larynx. This layer consists of the palatopharyngeus, salpingopharyngeus, and stylopharyngeus

Palatopharyngeus:

This muscle begins at the posterior hard palate and the palatine aponeurosis, inserting onto the thyroid cartilageThe palatopharyngeus elevates the pharynx superiorly during swallowing. (**22).**

Salpingopharyngeus:

This muscle originates from the auditory tube's inferior aspect and inserts onto the palatopharyngeus muscle**.** Contraction of this muscle raises the pharynx and opens the auditory tube, equalizing ear pressure during swallowing **(23)**

Stylopharyngeus:

This muscle is the only pharyngeal muscle innervated by cranial nerve IX. The stylopharyngeus originates from the styloid process of the temporal bone and inserts onto the thyroid cartilage, blending with the fibers of the palatopharyngeus muscle **(24)**

Dysphagia :

Dysphagia is the difficulty of swallowing foods or liquids. The condition may be due to pharyngeal muscle dysmotility. Stroke may present with dysphagia if the cranial nerves supplying the pharyngeal muscles are involved.**(25).**

Outline of swallowing structures:

The SWOARs comprise of the following five muscles: the superior constrictor muscle (SCM), middle constrictor muscle (MCM) and inferior constrictor muscle (ICM) which are part of the pharyngeal constrictor muscle (PCM), the cricopharyngeus muscle (CPM), and the esophagus inlet muscle (EIM). **(26).**

The SCM, MCM and ICM form the posterior and lateral pharyngeal walls. The SCM extends from the caudal tip of the pterygoid plate to the lower edge of second cervical vertebra, MCM extends from the upper edge of third cervical vertebra to the lower edge of the hyoid bone, and ICM extends from below the lower edge of the hyoid bone to the lower edge of the arytenoid cartilage. **(26).** CPM extended from below the lower edge of the arytenoid cartilage to the lower edge of the cricoid cartilage, and EIM consisted of the 1 cm of the muscular compartment of the esophagus inlet. Anatomical borders of each SWOAR are indicated in Table **(27).**

Table 1. Anatomic borders of the SWOARs **(28).**

SWOARs	Cranial	Caudal	Anterior	Posterior	Lateral
SCM	Caudal tip of the pterygoid plate	Lower edge of second cervical vertebra	Pterygoid plate or the base of tongue	Prevertebral muscle	Medial pterygoid muscle
MCM	Upper edge of third cervical vertebra	Lower edge of hyoid bone	Base of tongue or the hyoid bone	Prevertebral muscle	Greater horn of the hyoid bone
ICM	Below the lower edge of hyoid bone	Lower edge of arytenoid cartilage	Soft tissue of larynx	Prevertebral muscle	Superior horn of thyroid cartilage
CPM	Below the lower edge of arytenoid cartilage	Lower edge of cricoid cartilage	Posterior margin of the cricoid cartilage	Prevertebral muscle	Thyroid cartilage, soft tissue or thyroid gland

EIM	Below the lower edge of cricoid cartilage	1 cm caudal to esophagus inlet	Posterior margin of the trachea	Prevertebral muscle	Soft tissue or the thyroid gland

Abbreviations: SCM: the superior constrictor muscle, MCM: the middle constrictor muscle, ICM: the inferior constrictor muscle, CPM: cricopharyngeus muscle, EIM: esophagus inlet muscle, cm = centimeter.

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