Head and Neck oncology (I &II)

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Cancer

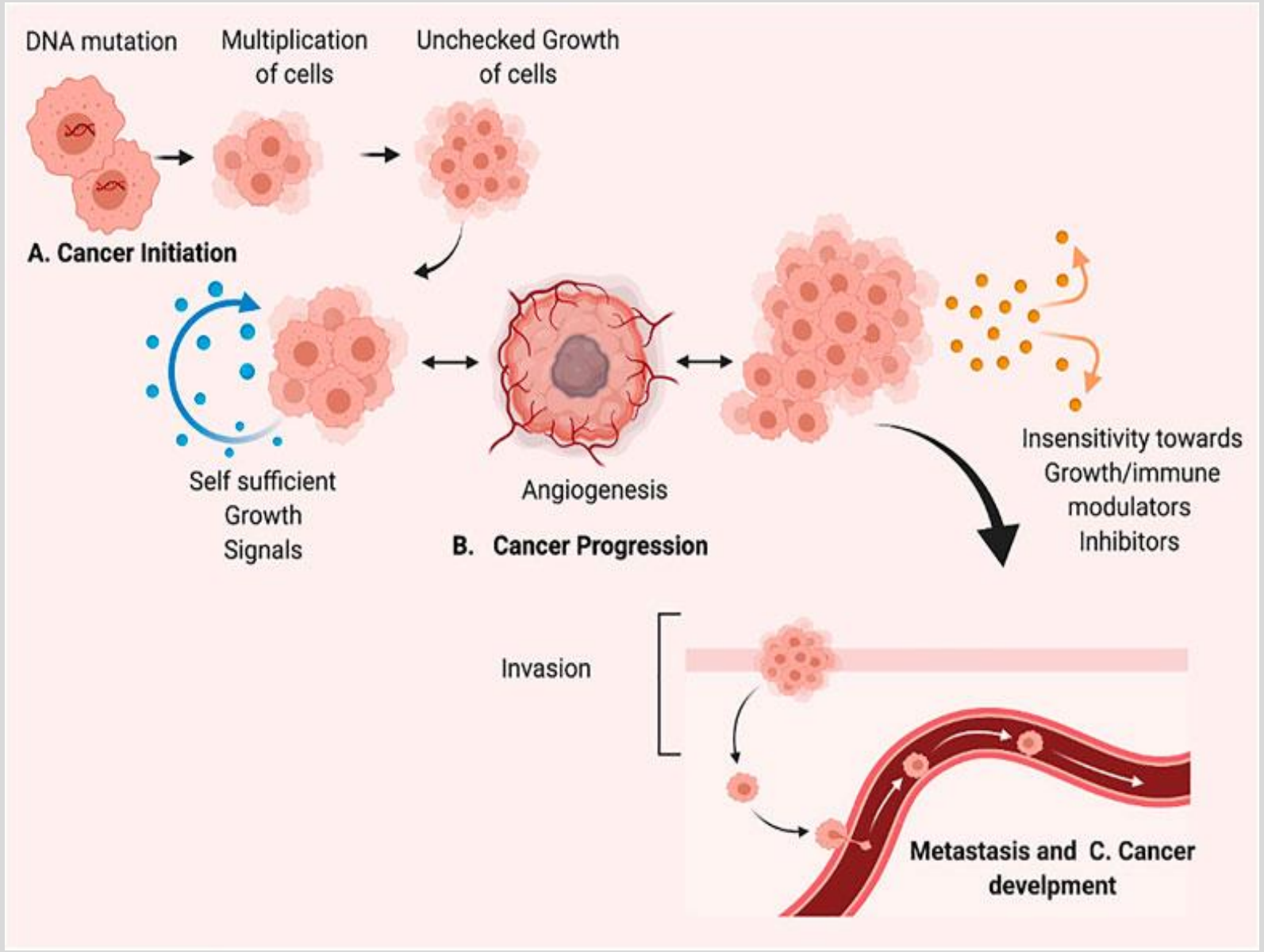
- **What is neoplasia?**
- **Neoplasia is “new growth”.**

A neoplasm: is an abnormal growth of mass of tissue due to excessive cell proliferation that has escaped normal limitations and regulation and persists in the same excessive manner even after cessation of the stimuli.

- Monoclonal growth is the whole mark of malignancy

The process of cancer development/carcinogenesis:

(A) Cancer initiation
(B)Cancer Progression
(C)Metastasis.



Head and neck cancer

- Head and neck cancer accounts for about 4% of all cancers
- in the United States. In 2023, an estimated 66,920 people (49,190 men and 17,730 women) will be diagnosed with head and neck cancer.

- Worldwide, an estimated 562,328 people were diagnosed with head and neck cancer in 2020.
- Head and neck cancers are more than twice as common among men as they are among women . Head and neck cancers are also diagnosed more often among people over age 50 than they are among younger people.

Causes of head and neck cancer

- **Alcohol and tobacco use** (including smoke and smokeless tobacco, sometimes called “chewing tobacco” or “snuff”) are the two most important risk factors for head and neck cancers, especially cancers of the oral cavity, hypopharynx, and voice box .
- **Infection with cancer-causing types of human papillomavirus (HPV), especially HPV type 16**, is a risk factor for oropharyngeal cancers that involve the tonsils or the base of the tongue

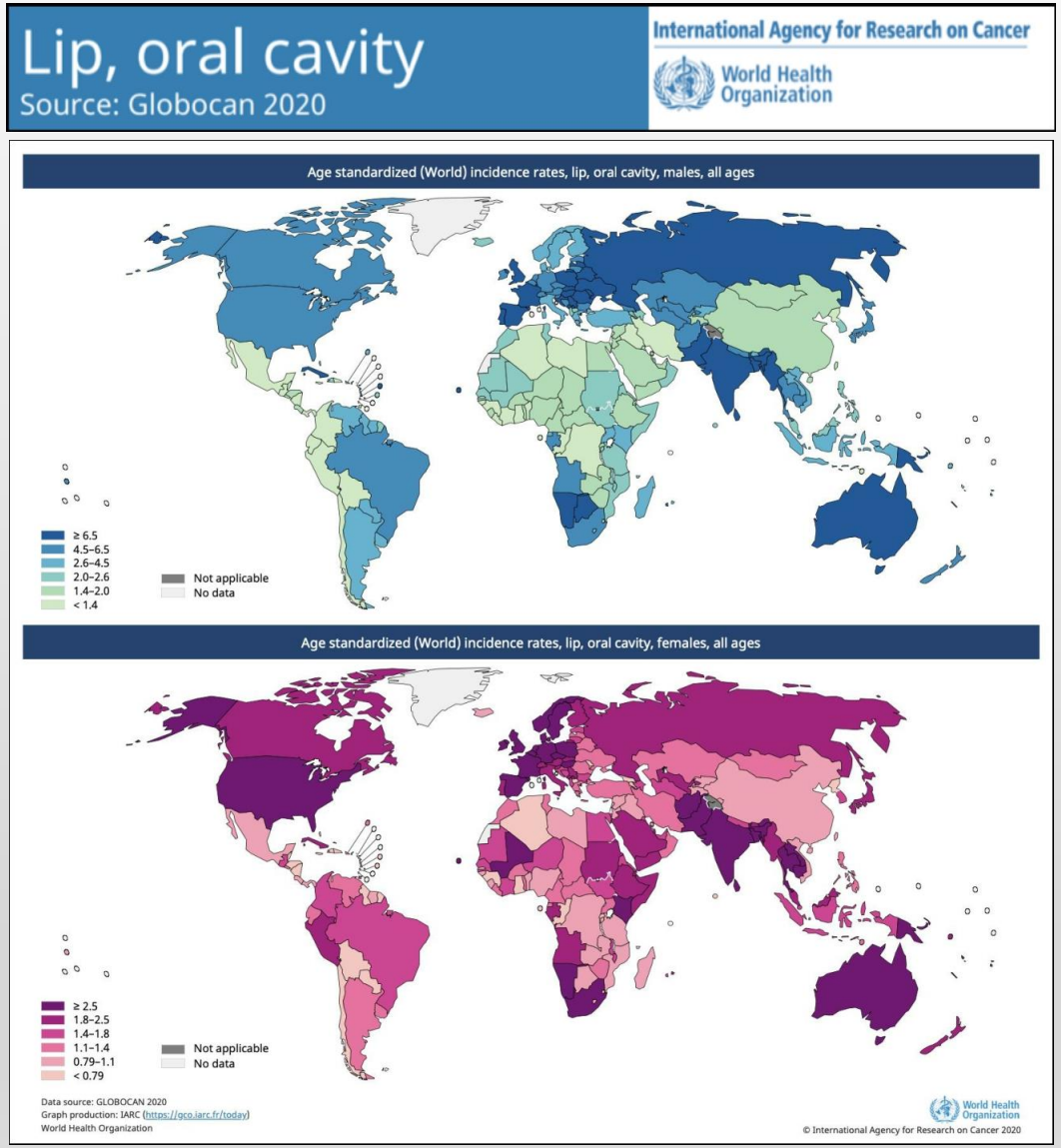
- **Paan (betel quid).** The use of paan (betel quid) in the mouth, a common custom in Southeast Asia, is strongly associated with an increased risk of mouth cancers
- **Occupational exposure.**
- Occupational exposure to wood dust is a risk factor for nasopharyngeal cancer .
- Certain industrial exposures to asbestos and synthetic fibers, have been associated with cancer of the voice box.
- People working in certain jobs in the construction, metal, textile, ceramic, and food industries may have an increased risk of cancer of the voice box .
- Industrial exposure to wood dust, nickel dust, or formaldehydeis a risk factor for cancers of the paranasal sinuses and nasal cavity

- **Radiation exposure.** Radiation to the head and neck is a risk factor for cancer of the salivary glands, sarcoma and squamous cell cancers .
- **Epstein-Barr virus infection.** is a risk factor for nasopharyngeal cancer and cancer of the salivary glands .
- **Ancestry.** Asian ancestry, particularly Chinese ancestry, is a risk factor for nasopharyngeal cancer.
- **Underlying genetic disorders.** Some genetic disorders, such as Fanconi anemia, can increase the risk of developing precancerous lesions and cancers early in life .

- **How can I reduce my risk of developing head and neck cancers?**
- Smoking cessation education and program
- Avoiding oral HPV infection (oral sex)can reduce the risk of HPV-associated head and neck cancers.
- In June 2020, the Food and Drug Administration granted accelerated approval of the HPV vaccine Gardasil 9 for the prevention of oropharyngeal and other head and neck cancers caused by HPV types 16, 18, 31, 33, 45, 52, and 58 in persons aged 9 through 45 years.
- Although there is no standard or routine screening test for head and neck cancers, dentists GP may check the oral cavity for signs of cancer during a routine checkup.

Lip and Oral cavity

EPIDEMIOLOGY

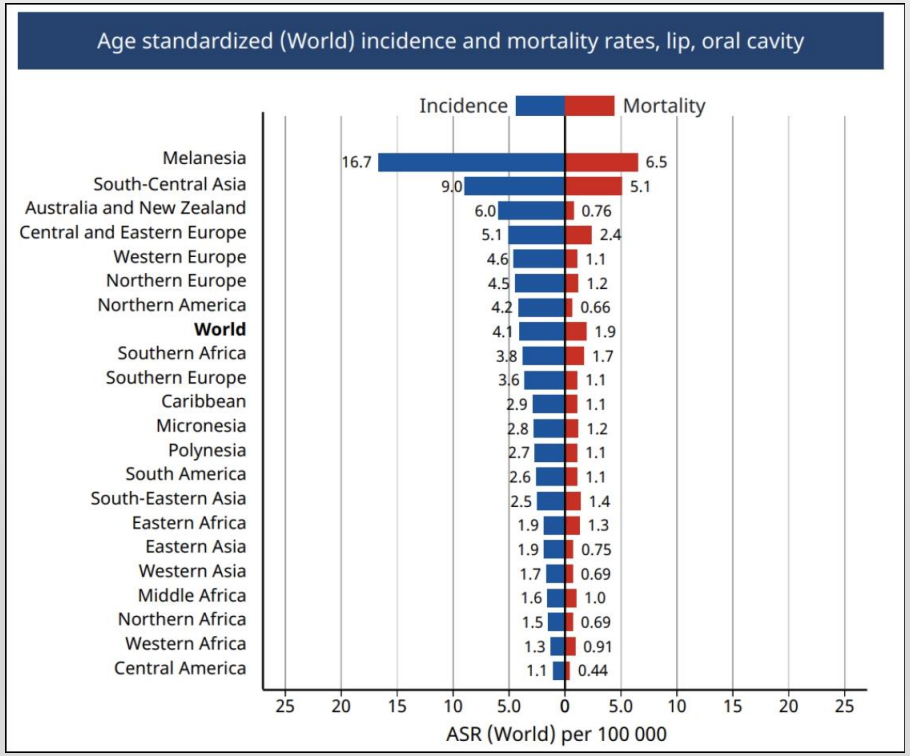


Global patterns and trends in cancers of the lip, tongue and mouth

Miranda-Filho et al, Oral Oncology 2020

- Globally 2.9% of all cancers in males, 1% in females
- Highest prevalence reported in Asian countries (64.2%)
- Most common form of cancer in males in India (16.2% of all cancers)
- Lip and oral cancer show different epidemiology
- Incidence in young adults (< 45 yo) rises worldwide
- 5-year survival rate lower than 50%

New cases in 2020, both sexes, all ages: 377 713
Number of deaths in 2020, both sexes, all ages: 177 757

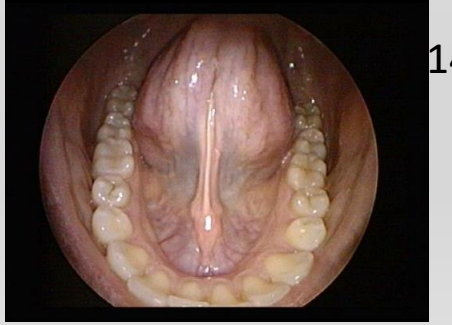


Epidemiologic aspects of oral cancer

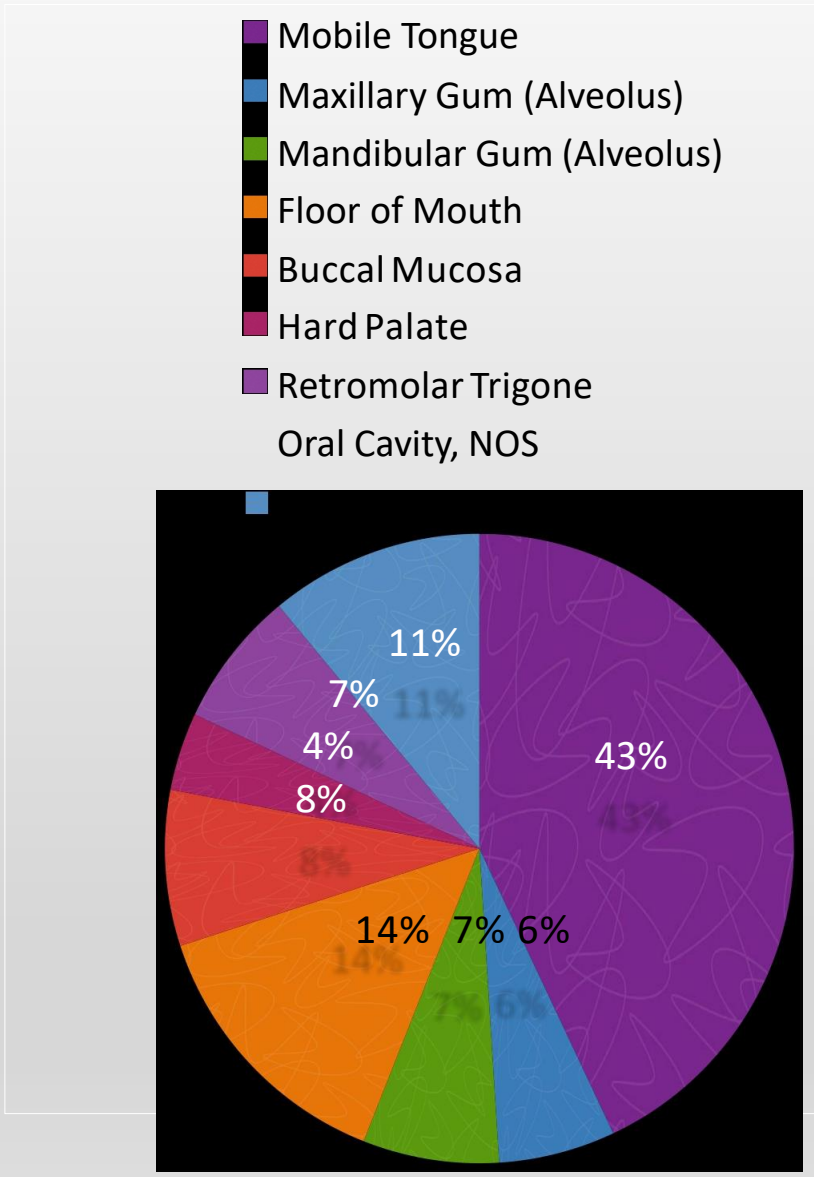
Sarode et al, Disease-a-month 2020

SUBSITES

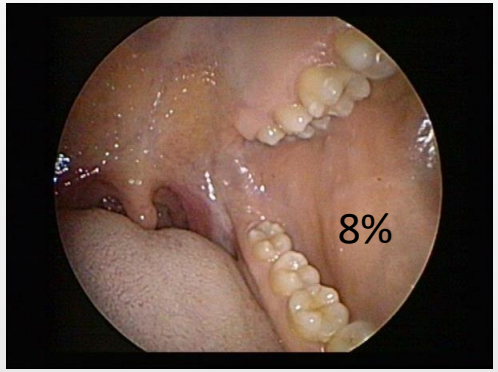
Mobile tongue



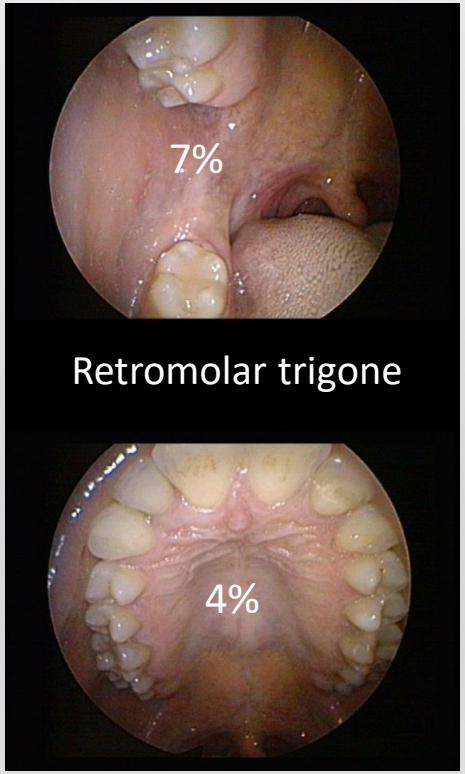
Floor of mouth



Data from
Memorial Sloan-Kettering Cancer Center, New York



Buccal mucosa

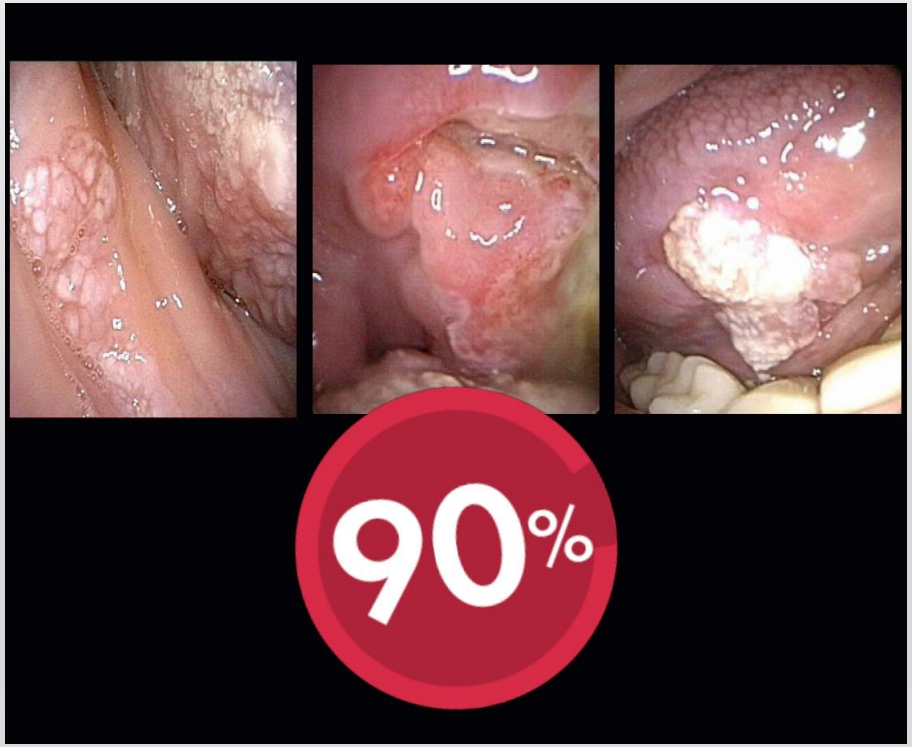


Hard palate

HISTOLOGY

Squamous cell carcinoma

(conventional and subtypes)



Unconventional

Oral mucosal melanoma

Soft tissue and neural tumors

Salivary type tumors

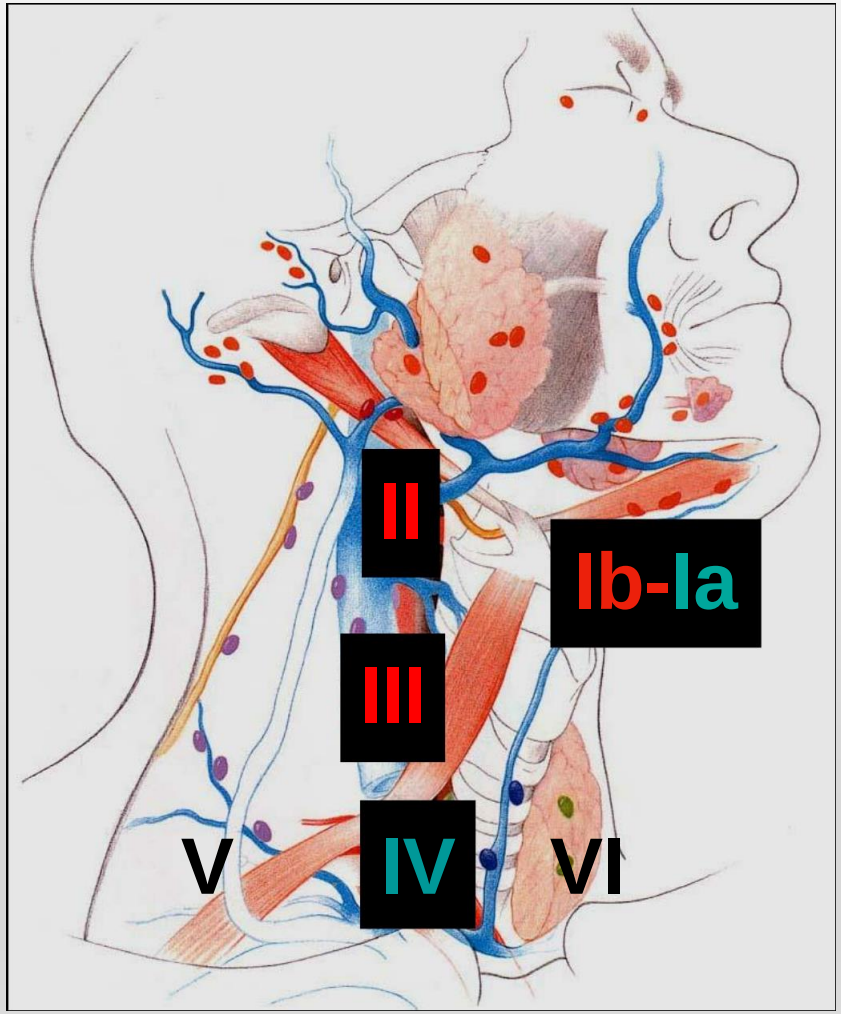
Haematolymphoid tumors

Secondary tumors (kidney, lung)

WHO Classification Head and Neck 2022

METASTATIC SPREAD

NODAL METASTASIS



761 T1-T2 N0 pts

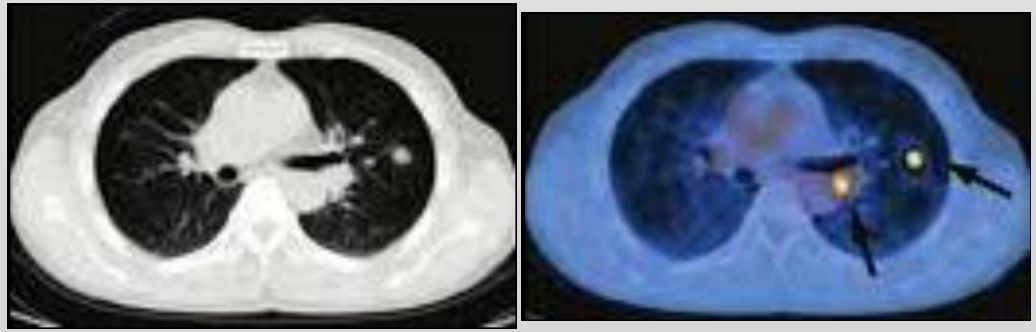
High grade tumor and PNI: increased rate of occult nodal metastases
—> decreased 5y OS

Negligible rate of skip metastases to levels III-IV (around 1%) and Ia (around 0.5%) in clinically negative neck
—> risk of overtreatment?

Incidence and impact of skip metastasis in the neck in early oral cancer: Reality or a myth?
Singh et al,Oral Oncol. 2022

DISTANT METASTASIS

The incidence of distant metastasis for oral cavity SCC has been reported to occur in **10% to 18% of patients at the time of initial diagnosis**



Senft et al, Radiother Oncol 2008
Rohde et al, J Nucl Med 2017
Lu et al, 2022

Oral cancer
CLINICAL WORK-UP

CLINICAL WORK-UP

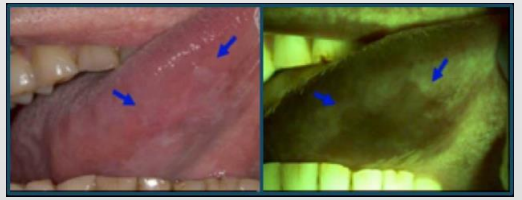
History

Symptoms, tobacco, alcohol, betel, sun exposure (lip), comorbidities

Clinical evaluation

Site(s) of the lesion, trismus, dentition, lymphnodes

endoscopic evaluation



Outpatient biopsy

Imaging

Loco-regional: CE-MRI *or* CE-CT*,* intraoral US, neck US +/- FNAC, lymphoscintigraphy (sentinel node)

- **Systemic**: PET-CT *or* total body CE-CT *or* PET-MRI

3-D EVALUATION: IMAGING

CT/MRI

Lingual US

Depth of invasion (DOI)

Soft tissue extension

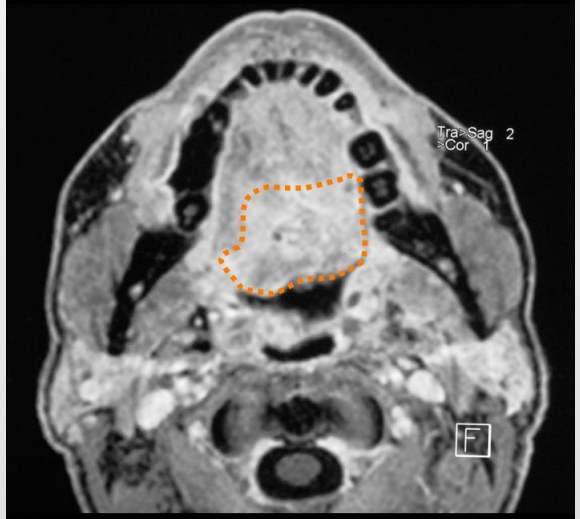
Mandibular involvement

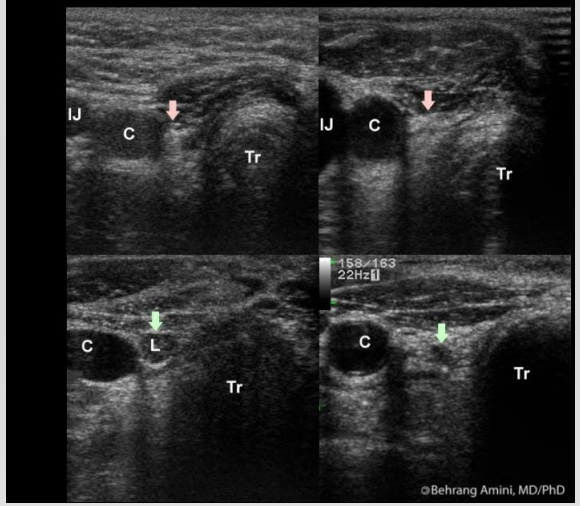
Pterygoid muscles and plates, styloid muscles

Perineural spread along major nerves

N status

Neck US





Oral cancer
STAGING AND PROGNOSIS

AJCC/UICC TNM for oral cancer

8^ Ed. (2017)

T

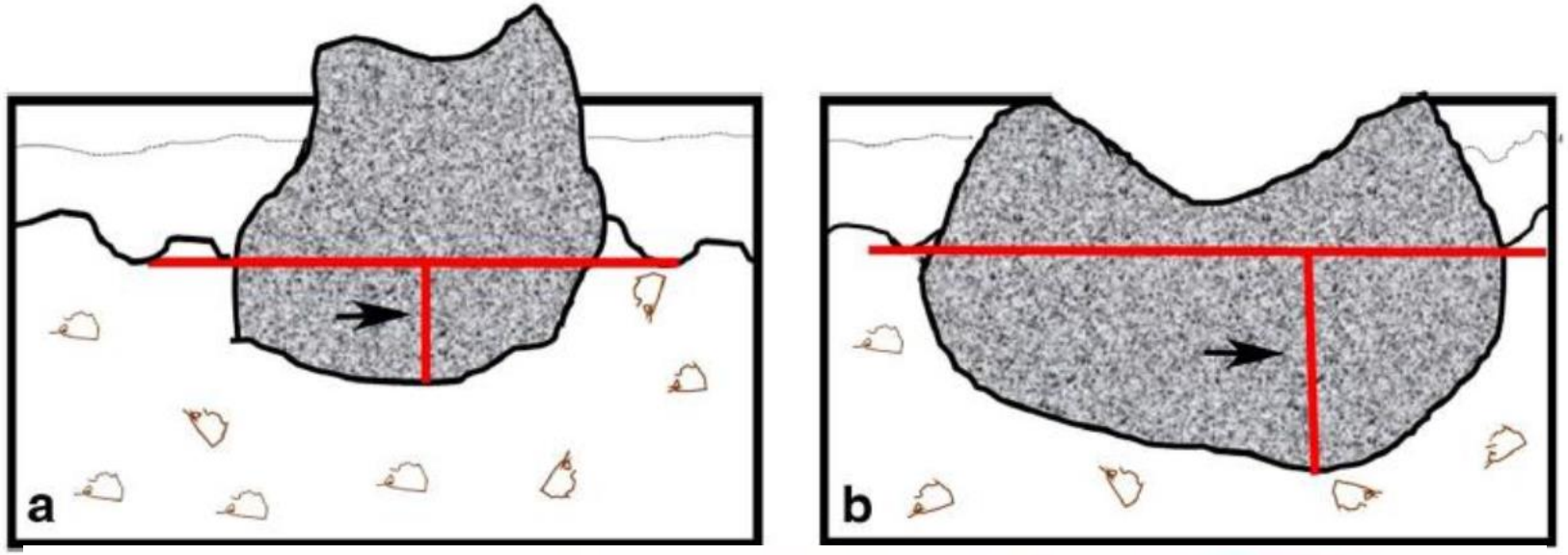
Primary Tumor (T)		
TX		Primary tumor cannot be assessed
Tis		Carcinoma *in situ*
T1		Tumor ≤2 cm with depth of invasion (DOI)* ≤5 mm
T2		Tumor ≤2 cm, with DOI* >5 mm and ≤10 mm *or* tumor >2 cm and ≤4 cm, with DOI* ≤10 mm
T3		Tumor >2 cm and ≤4 cm, with DOI* >10 mm *or* tumor >4 cm, with DOI* ≤10 mm
T4		Moderately advanced or very advanced local disease
	T4a	Moderately advanced local disease Tumor >4 cm, with DOI* >10 mm *or* tumor invades adjacent structures only (eg, through cortical bone of the mandible or maxilla, or involves the maxillary sinus or skin of the face) Note: Superficial erosion of bone/tooth socket (alone) by a gingival primary is not sufficient to classify a tumor as T4.
	T4b	Very advanced local disease Tumor invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery

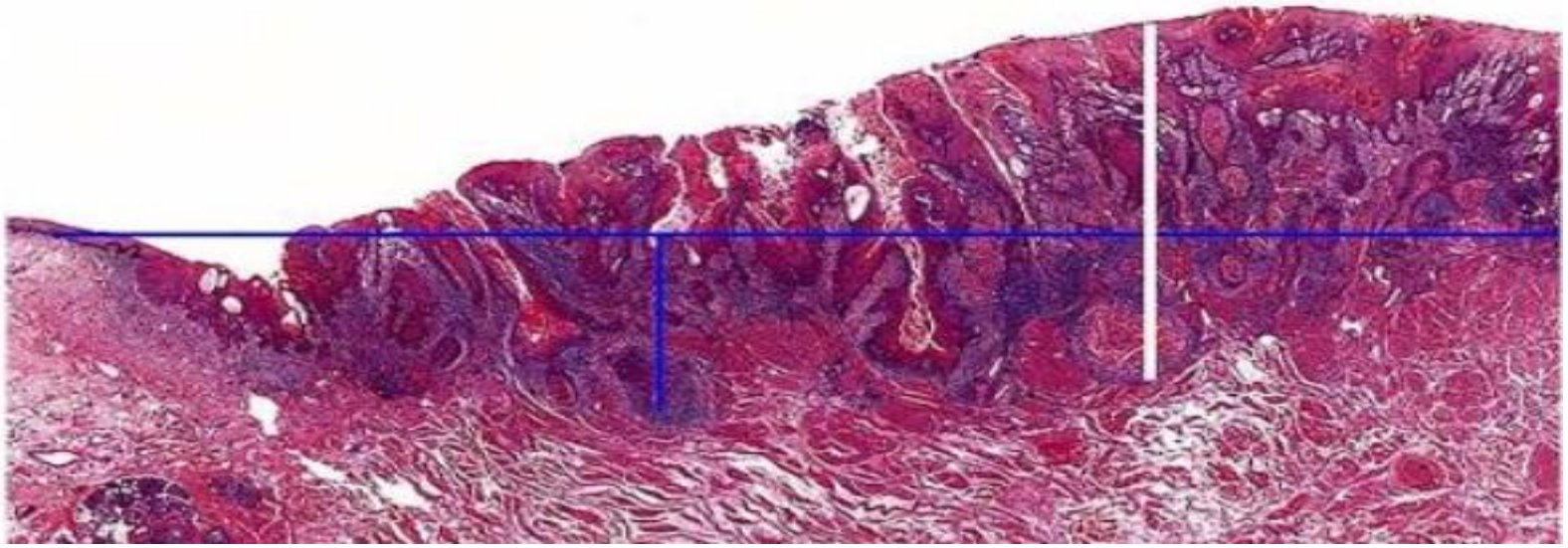
*DOI is depth of invasion and *not* tumor thickness.

Depth of invasion as a classifying criterion T1-T3

Extensive involvement of further structures to define locally advanced tumors T4

Depth of invasion and tumor thickness





STAGING

AJCC/UICC TNM for oral cancer

8^ Ed. (2017)

cN

Regional Lymph Nodes (N)

Clinical N (cN)

NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension ENE(–)
N2		Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–); *or* metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(–); *or* in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(–)
	N2a	Metastasis in a single ipsilateral lymph node larger than 3 cm but not larger than 6 cm in greatest dimension, and ENE(–)
	N2b	Metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(–)
	N2c	Metastases in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(–)
N3		Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−); *or* metastasis in any node(s) and clinically overt ENE(+)
	N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−)
	N3b	Metastasis in any node(s) and clinically overt ENE(+)

Note: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(−) or ENE(+).

pN

Regional Lymph Nodes (N)

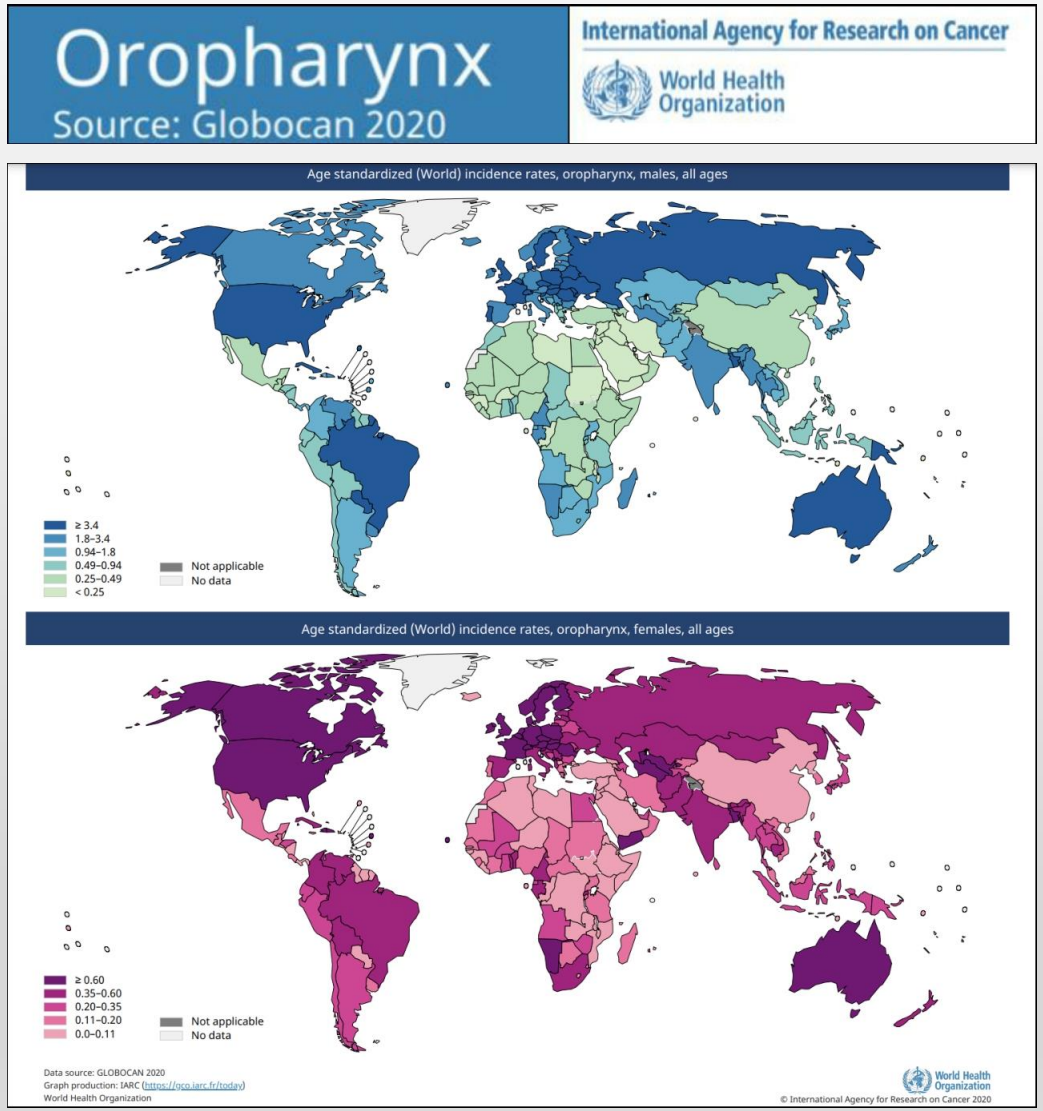
Pathological N (pN)

NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(–)
N2		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(+); *or* larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–); *or* metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−); *or* in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension, ENE(−)
	N2a	Metastasis in single ipsilateral node 3 cm or smaller in greatest dimension, and ENE(+); *or* a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–)
	N2b	Metastases in multiple ipsilateral node(s), none larger than 6 cm in greatest dimension and ENE(−)
	N2c	Metastases in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension, and ENE(–)
N3		Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−); *or* metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); *or* multiple ipsilateral, contralateral or bilateral nodes any with ENE(+); *or* a single contralateral node of any size and ENE (+)
	N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−)
	N3b	Metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); *or* multiple ipsilateral, contralateral or bilateral nodes any with ENE(+); *or* a single contralateral node of any size and ENE (+)

cN3b in case of extranodal extension (regardless of the lymph node side, site, number, and/or dimension)

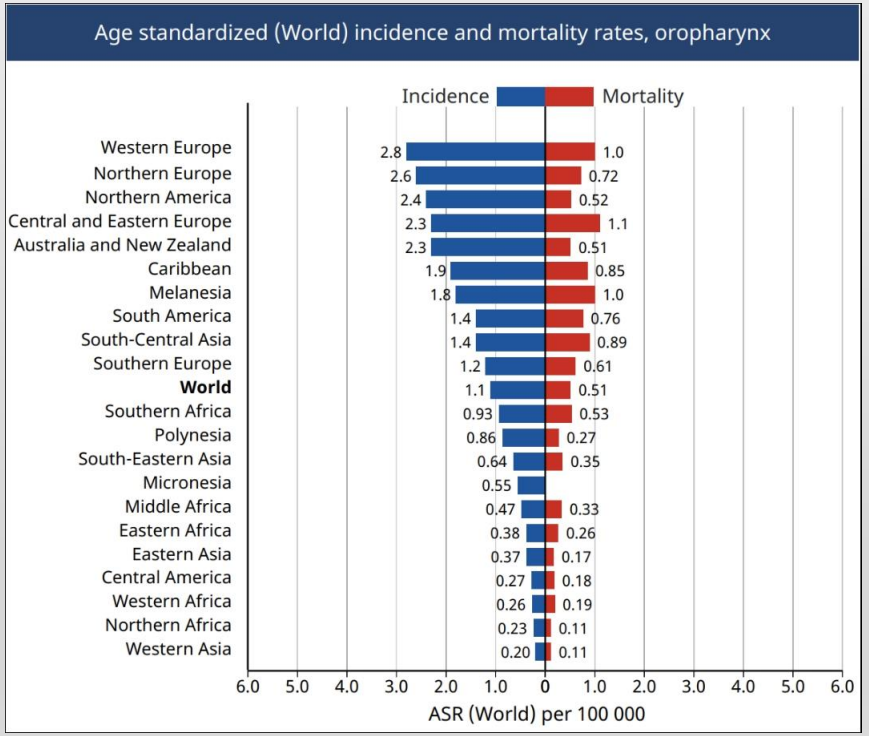
Oropharyngeal cancer

EPIDEMIOLOGY



- Global ASR of 1.1 per 100,000 for both sexes
- Rates were elevated in North America and Europe, notably in Hungary, Slovakia, Germany, and France
- 80% OPSCC are HPV driven in the USA

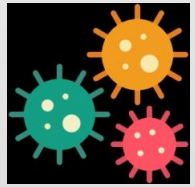
New cases in 2020, both sexes, all ages: 98 412
Number of death in 2020, both sexes, all ages: 48 143



OROPHARYNGEAL SCC AND HPV

MALE
55-65 YEAR-OLD
TOBACCO AND/OR
ALCOHOL ABUSE
NON-HPV RELATED CANCER

MALE
YOUNG/MIDDLE AGE
SMOKING LESS FREQUENT
HPV RELATED CANCER

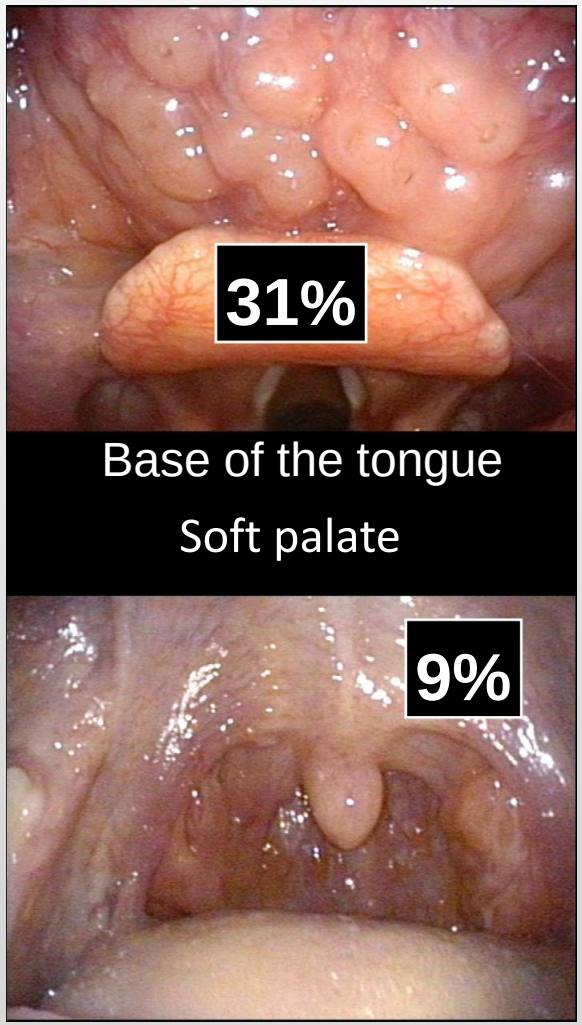


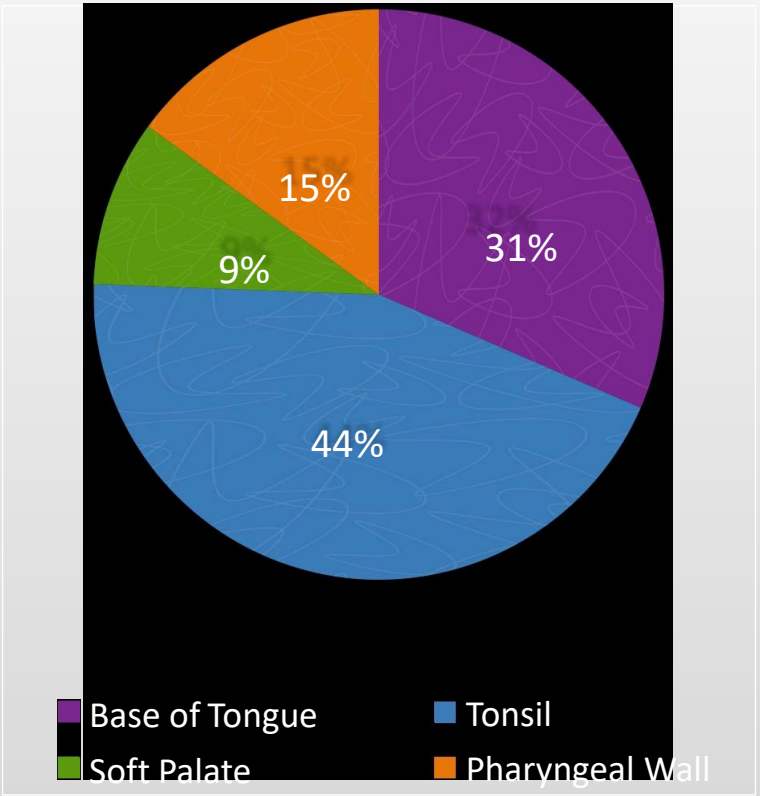
HPV+ SCC ARE GENERALLY DIAGNOSED WITH <u>EARLIER T CATEGORY</u> AND MORE <u>ADVANCED N CATEGORY</u>

95% OF SCC HPV+ ARE <u>NON KERATINIZING</u>
85% OF SCC KERATINIZING ARE HPV -

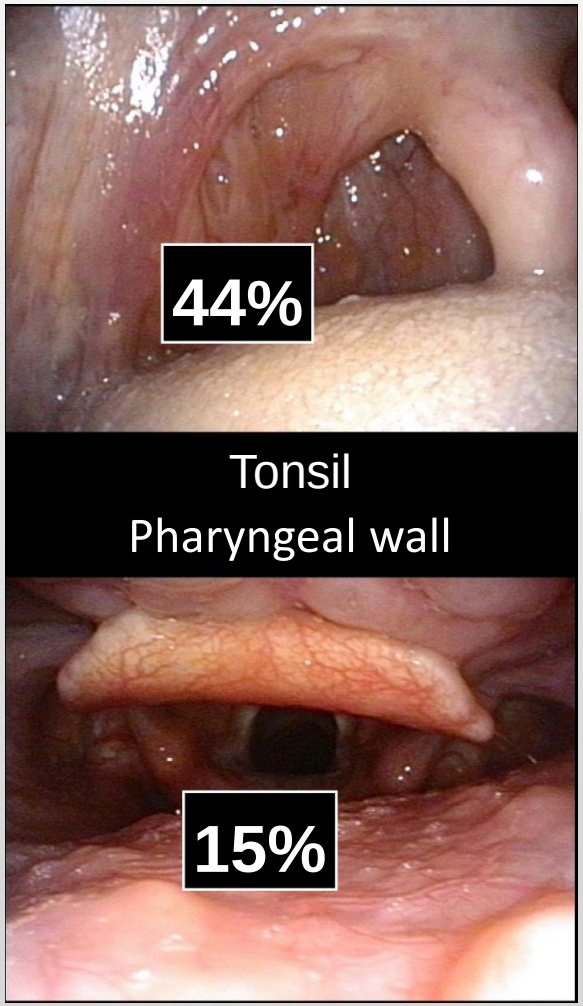
SUBSITES IN HPV NEGATIVE OPSCC

Base of tongue



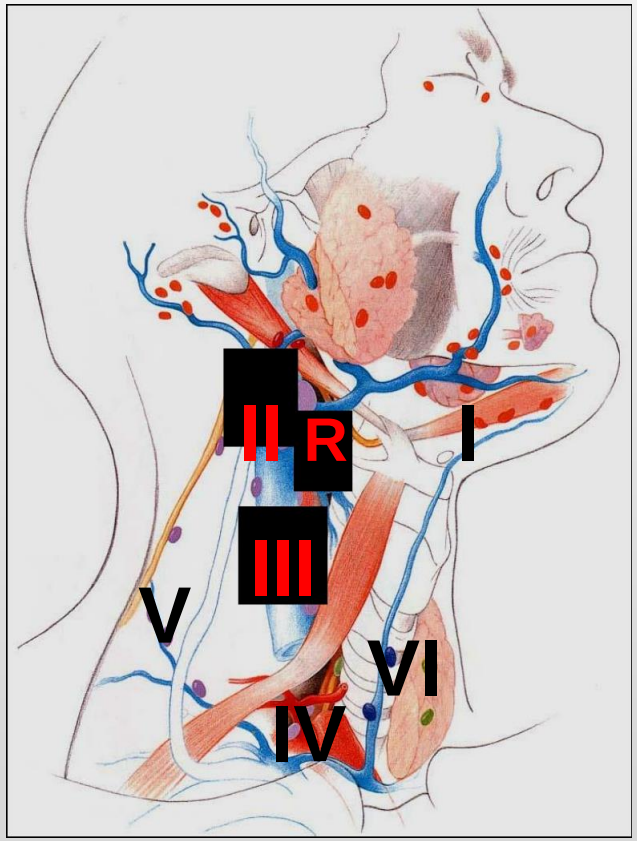


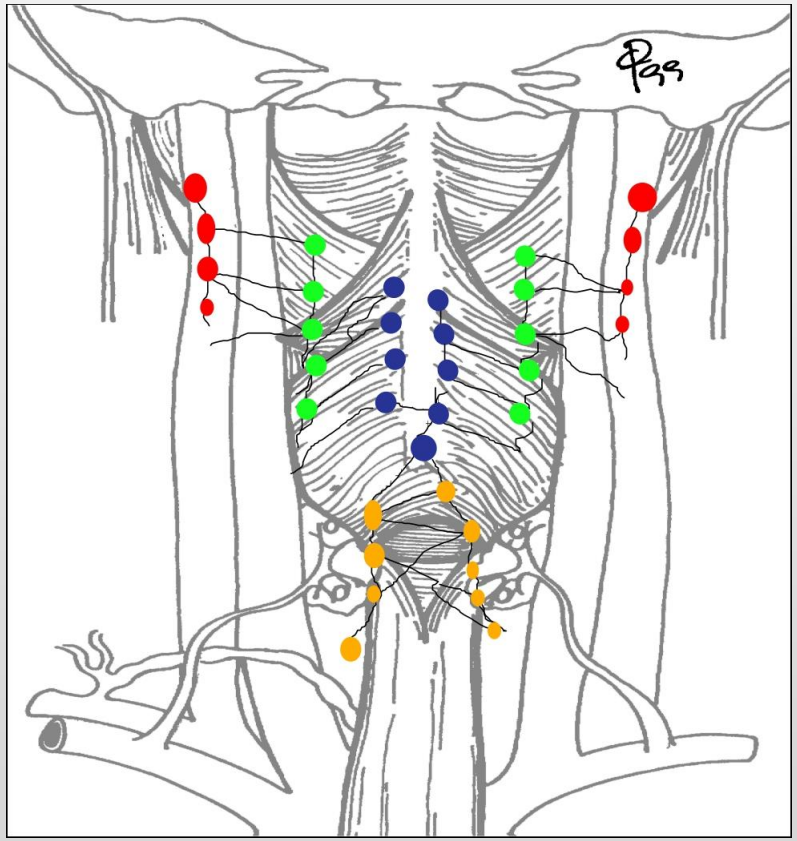
Tonsil



METASTATIC SPREAD

NODAL METASTASIS





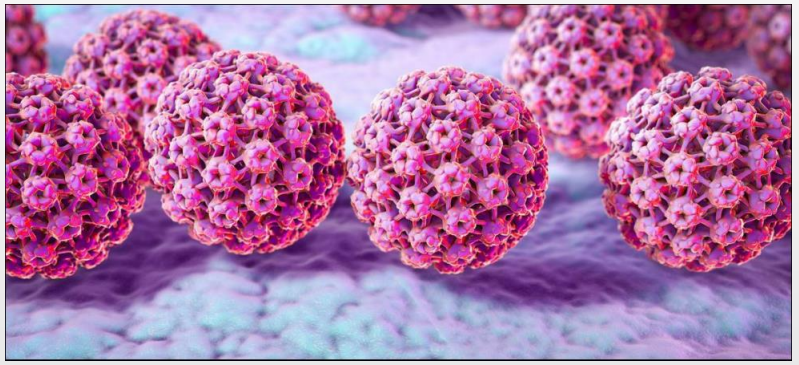
DISTANT METASTASIS

Rare at diagnosis
(1% at diagnosis, 7% during follow up in HPV+)
(Brkic et al 2021)

Lung (80%)
Bone
Liver

Oropharyngeal cancer
CLINICAL WORK-UP

CLINICAL WORK-UP



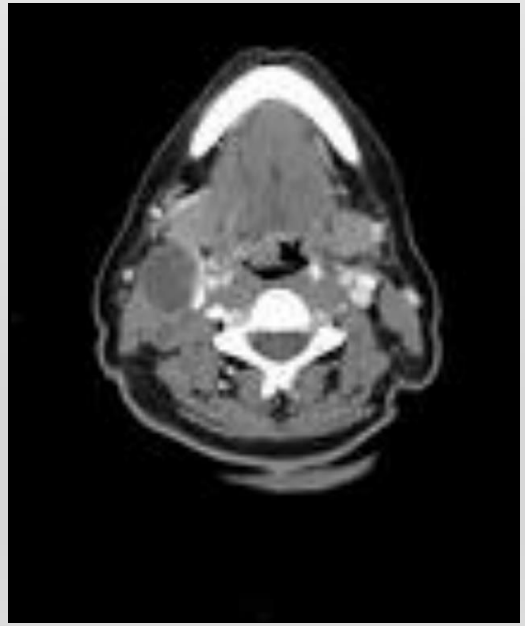
History
Symptoms, tobacco, alcohol, ,

Clinical evaluation
Site(s) of the lesion, palpation, lymphnodes

Endoscopic evaluation

Fiberoptic examination

Outpatient biopsy, HPV status (p16, HPV)



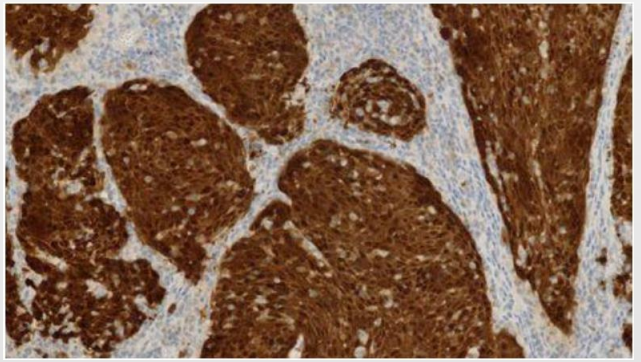
Imaging

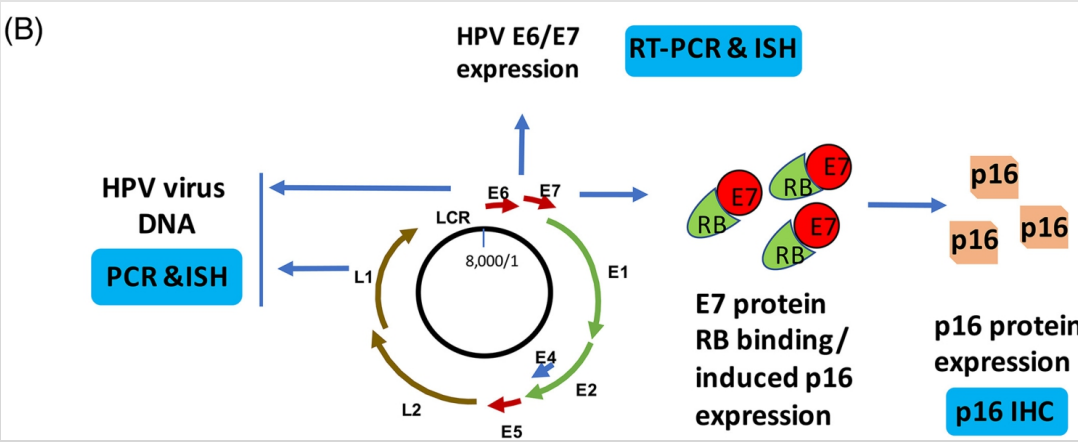
Loco-regional: CE-MRI *or* CE-CT*,* neck US +/- FNAC (risk of false negatives in cystic N)
Systemic: PET-CT *or* total body CE-CT

DIAGNOSIS OF HPV-RELATED LESIONS

The mere detection of HPV-DNA is not sufficient to establish causality in HNCs!!!

IHC/ISH/PCR	PROS	CONS
p16 (IHC)	*routinely used, cost-effective surrogate marker*	p16 overexpression may occur independently of HPV
DNA in situ hybridization (ISH)	high specificity for detecting active viruses	less sensitive when there are low viral copy numbers
RNAscope (ISH)	97% sensitivity and relatively inexpensive	
HPV-DNA PCR	high sensitivity, can detect low viral copy numbers	it does not identify whether the virus is transcriptionally active or a passenger infection
E6/E7 HPV-mRNA PCR	*specific and sensitive - GOLD STANDARD*	high costs





Oropharyngeal cancer
STAGING AND PROGNOSIS

STAGING

AJCC/UICC TNM for oropharyngeal cancer

8^ Ed. (2017)

p16 -

T

Oropharynx (p16-)

TX		Primary tumor cannot be assessed
Tis		Carcinoma *in situ*
T1		Tumor 2 cm or smaller in greatest dimension
T2		Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
T3		Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4		Moderately advanced or very advanced local disease
	T4a	Moderately advanced local disease Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible*
	T4b	Very advanced local disease Tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery

**Note:* Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.*

cN

Regional Lymph Nodes (N)

Clinical N (cN)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in

pN

Regional Lymph Nodes (N)

Pathological N (pN)

NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(–)
N2		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(+); *or* larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–); *or* metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−); *or* in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension, ENE(−)
	N2a	Metastasis in single ipsilateral node 3 cm or smaller in greatest dimension, and ENE(+); *or* a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–)
	N2b	Metastases in multiple ipsilateral node(s), none larger than 6 cm in greatest dimension and ENE(−)
	N2c	Metastases in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension, and ENE(–)
N3		Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−); *or* metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); *or* multiple ipsilateral, contralateral or bilateral nodes any with ENE(+); *or* a single contralateral node of any size and ENE (+)
	N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−)
	N3b	Metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); *or* multiple ipsilateral, contralateral or bilateral nodes any with ENE(+); *or* a single contralateral node of any size and ENE (+)

AJCC/UICC TNM for oropharyngeal cancer

8^ Ed. (2017)

p16+

TNM Staging System for HPV-Mediated (p16+) Oropharyngeal Cancer (8th ed., 2017)
(Not including: P16-negative (p16-) cancers of the oropharynx)

Primary Tumor (T)

T

T0 No primary identified
T1 Tumor 2 cm or smaller in greatest dimension
T2 Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
T3 Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4 Moderately advanced local disease
Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible or beyond*

Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.

Regional Lymph Nodes (N)

Clinical N (cN)

cN

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 One or more ipsilateral lymph nodes, none larger than 6 cm
N2 Contralateral or bilateral lymph nodes, none larger than 6 cm
N3 Lymph node(s) larger than 6 cm

Pathological N (pN)

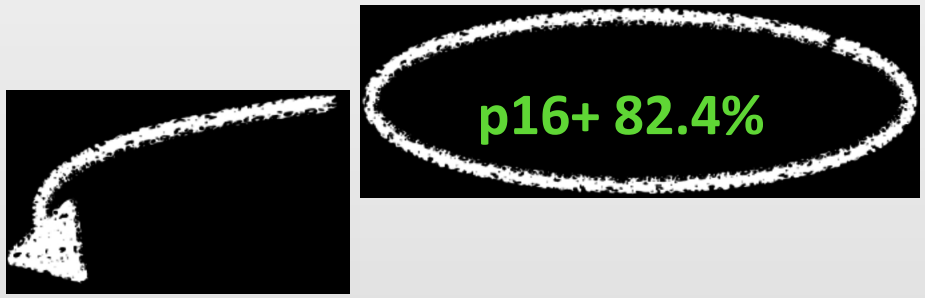
pN

NX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in 4 or fewer lymph nodes
pN2 Metastasis in more than 4 lymph nodes

PROGNOSIS

DIFFERENT PATIENTS, DIFFERENT PROGNOSIS

5-year OS



p16- 44.0%

- lower risk of disease progression (7.8% vs 21.2%),
- lower 5y-disease recurrence (5.6% vs 20.5%)
- lower death because of OPC
- fewer second primaries (16.1% vs. 49.9%)

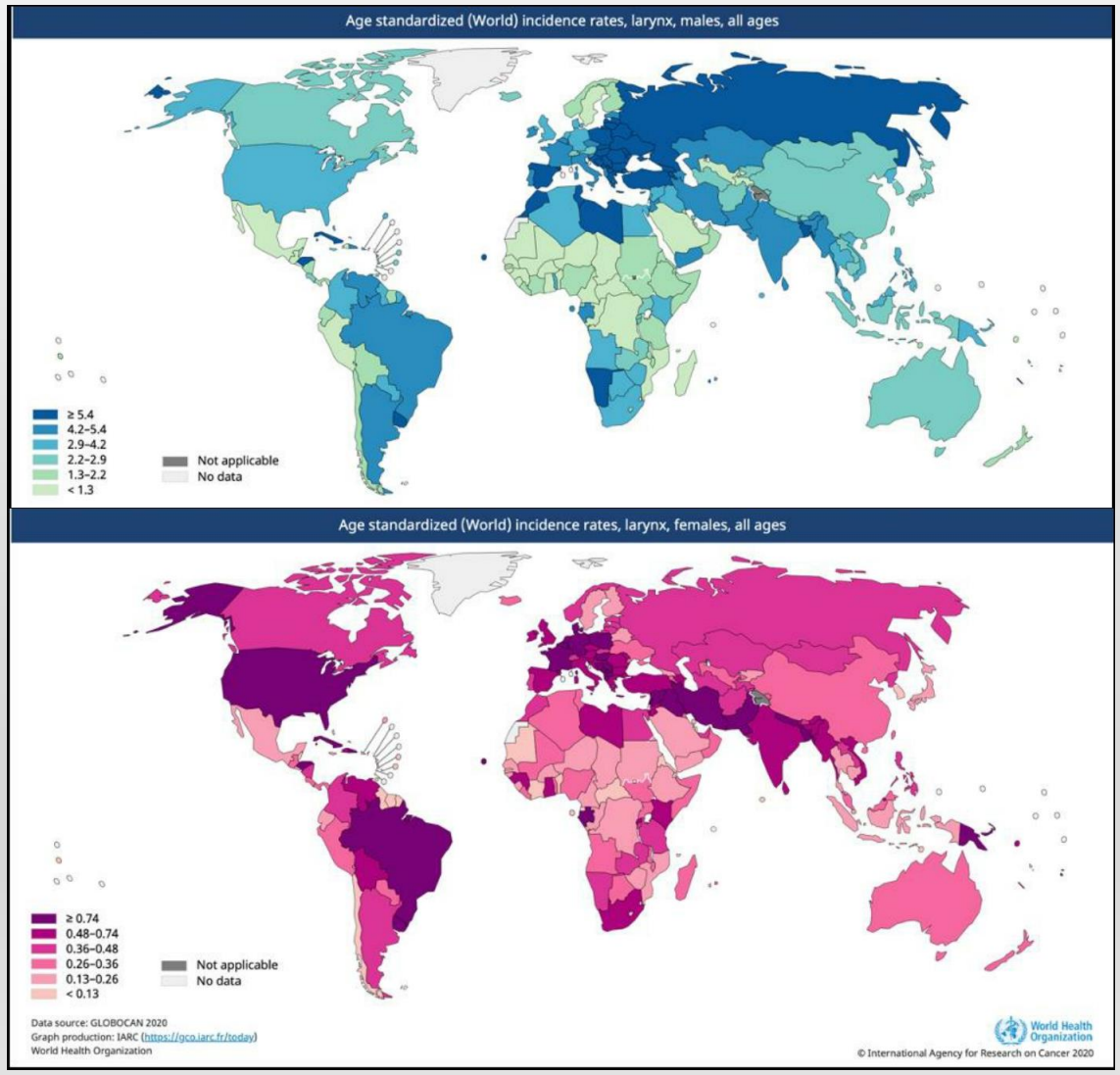
Gorphe et al, Radiother Oncol 2022

Laryngeal and hypopharyngeal cancer

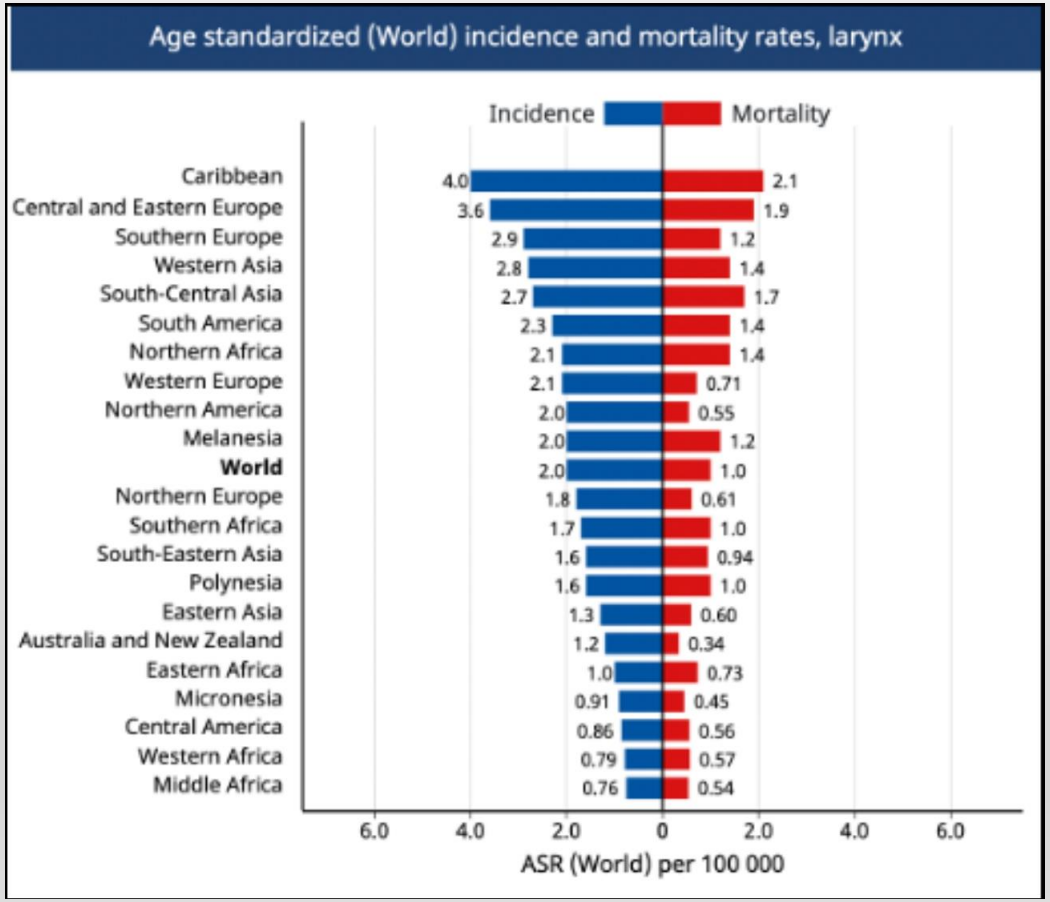
EPIDEMIOLOGY: LARYNX

Larynx
Source: Globocan 2020

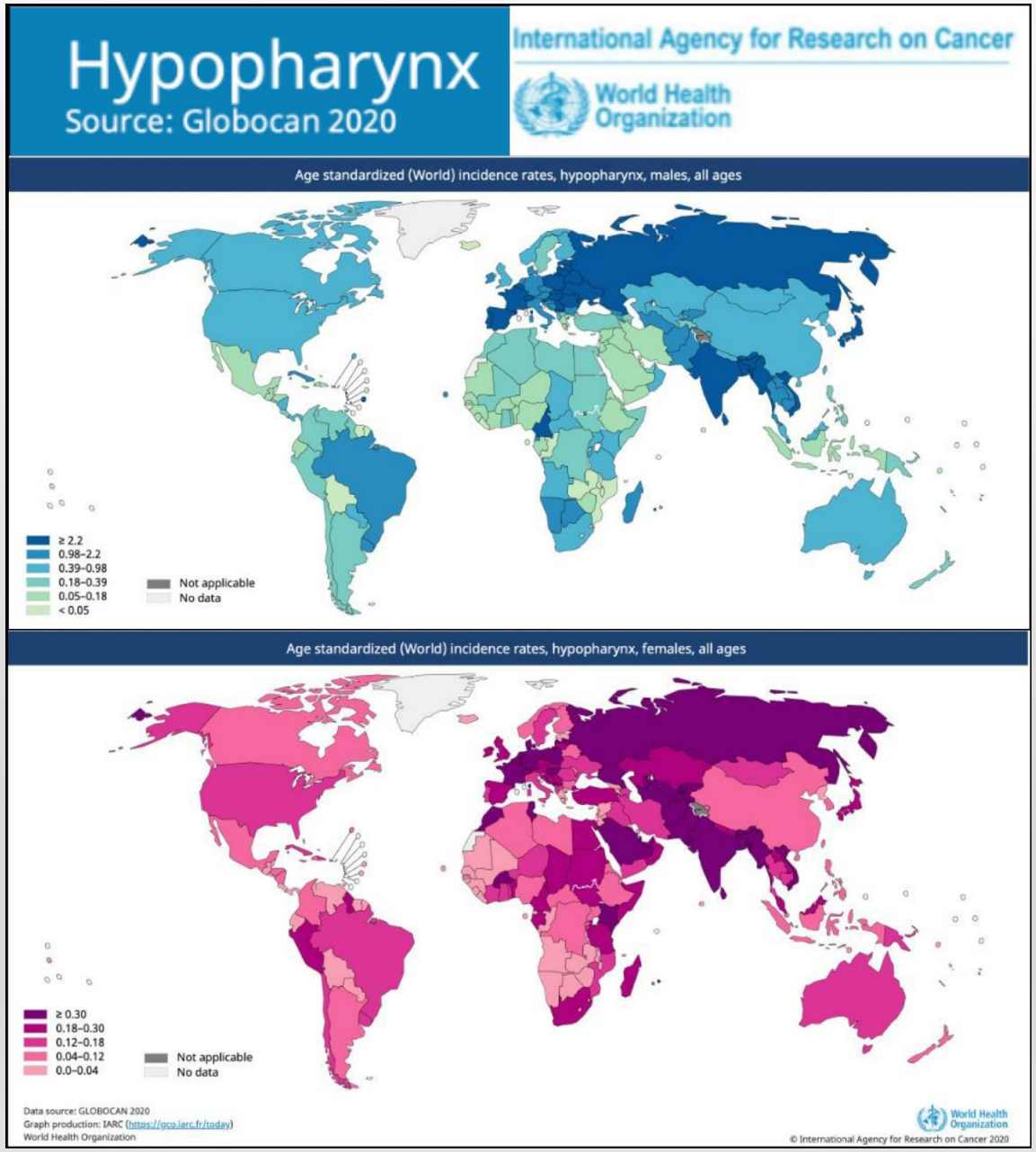
International Agency for Research on Cancer
World Health Organization



New cases in 2020, both sexes, all ages: 184 615
Number of death in 2020, both sexes, all ages: 99 840

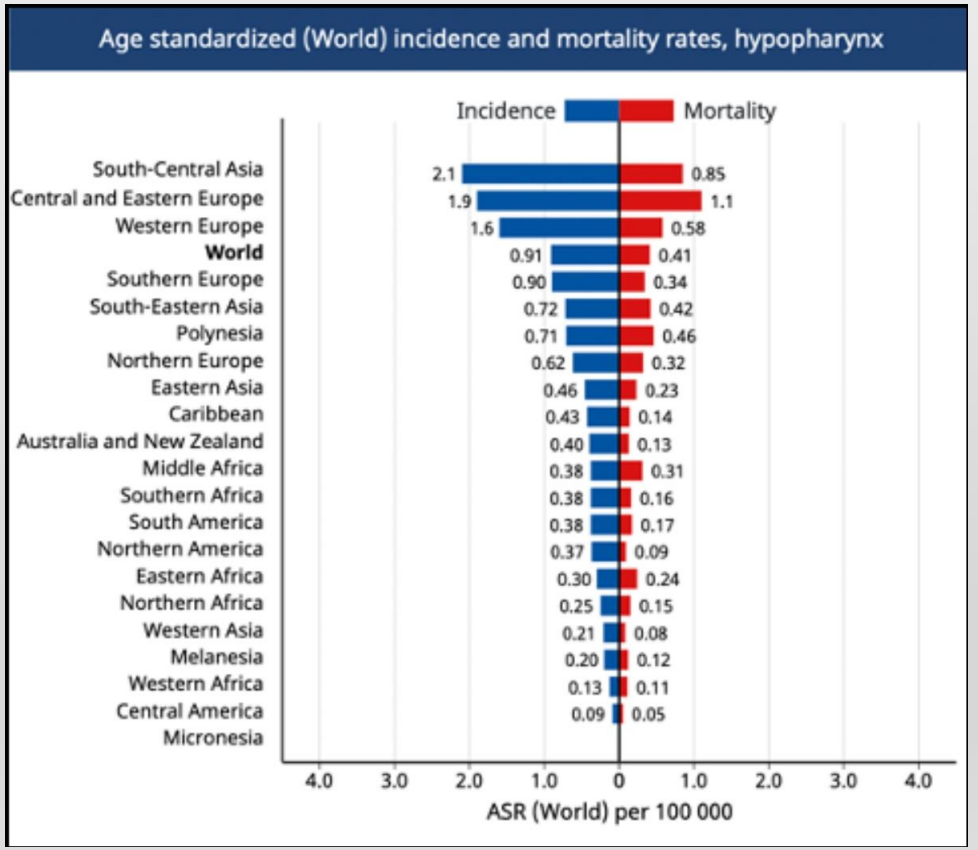


EPIDEMIOLOGY: HYPOPHARYNX



The global incidence rates is averaged at 0.91 per 100,000
1.6 in M, 0.29 in F

New cases in 2020, both sexes, all ages: 84 254
Number of death in 2020, both sexes, all ages: 38 599



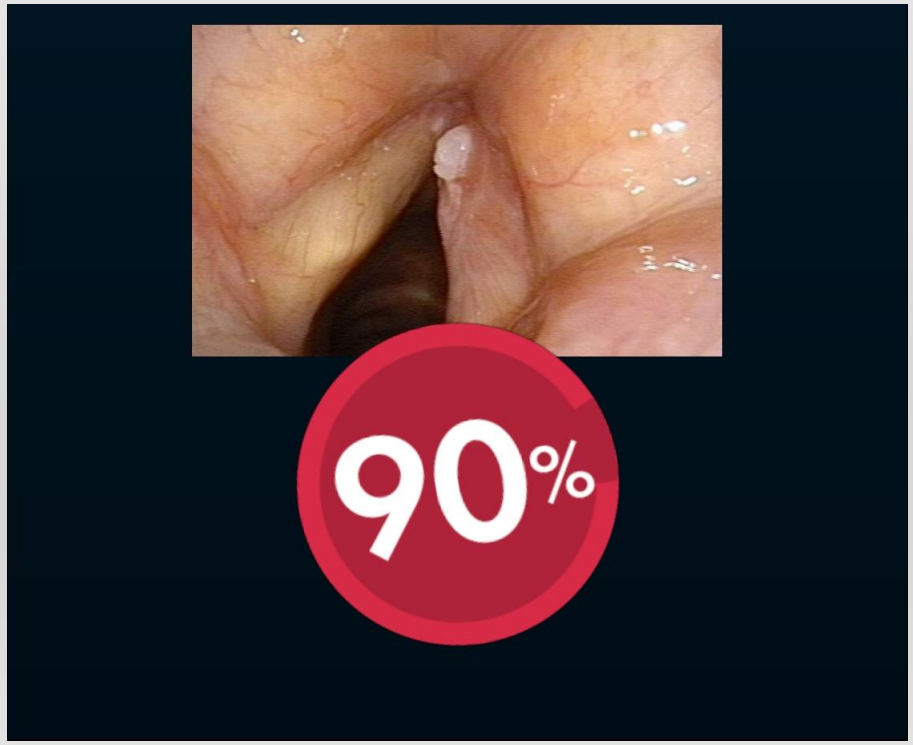
HISTOLOGY

Malignant surface epithelial

Conventional SCC

SCC subtypes spindle cell, adenosquamous, basaloid, verrucous, papillary, acantholytic

Lymphoepithelial



WHO Classification Head and Neck Tumours 2022

Unconventional

Neuroendocrine tumors

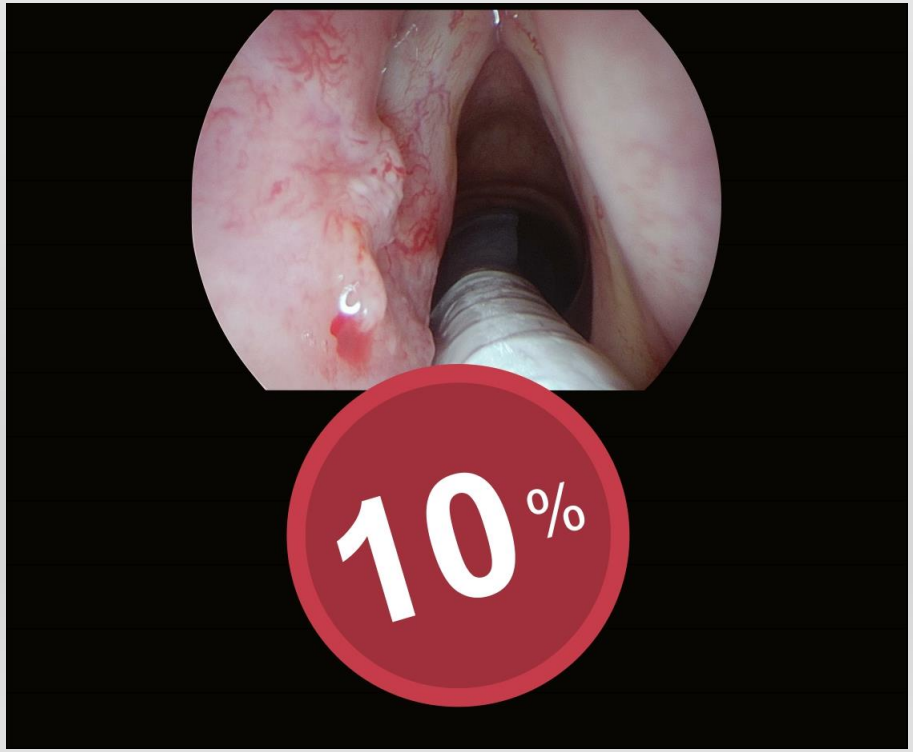
Salivary gland tumors

Soft tissues tumors

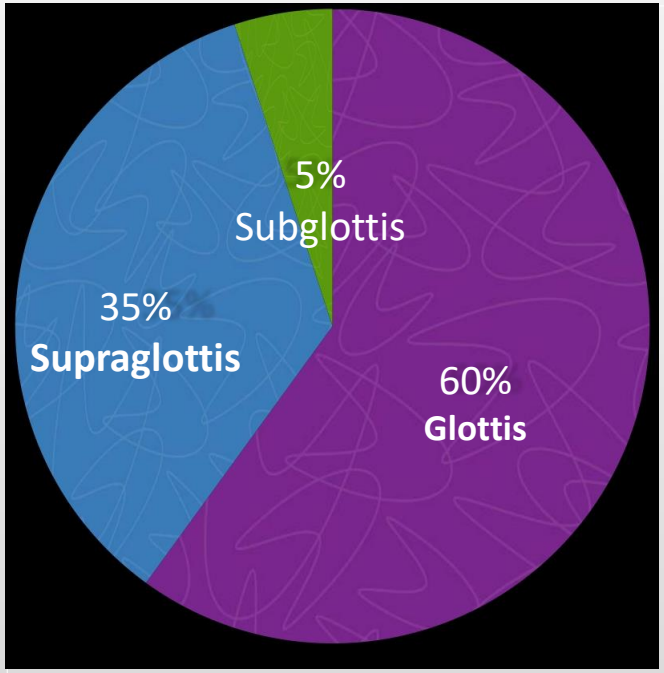
Cartilage tumors

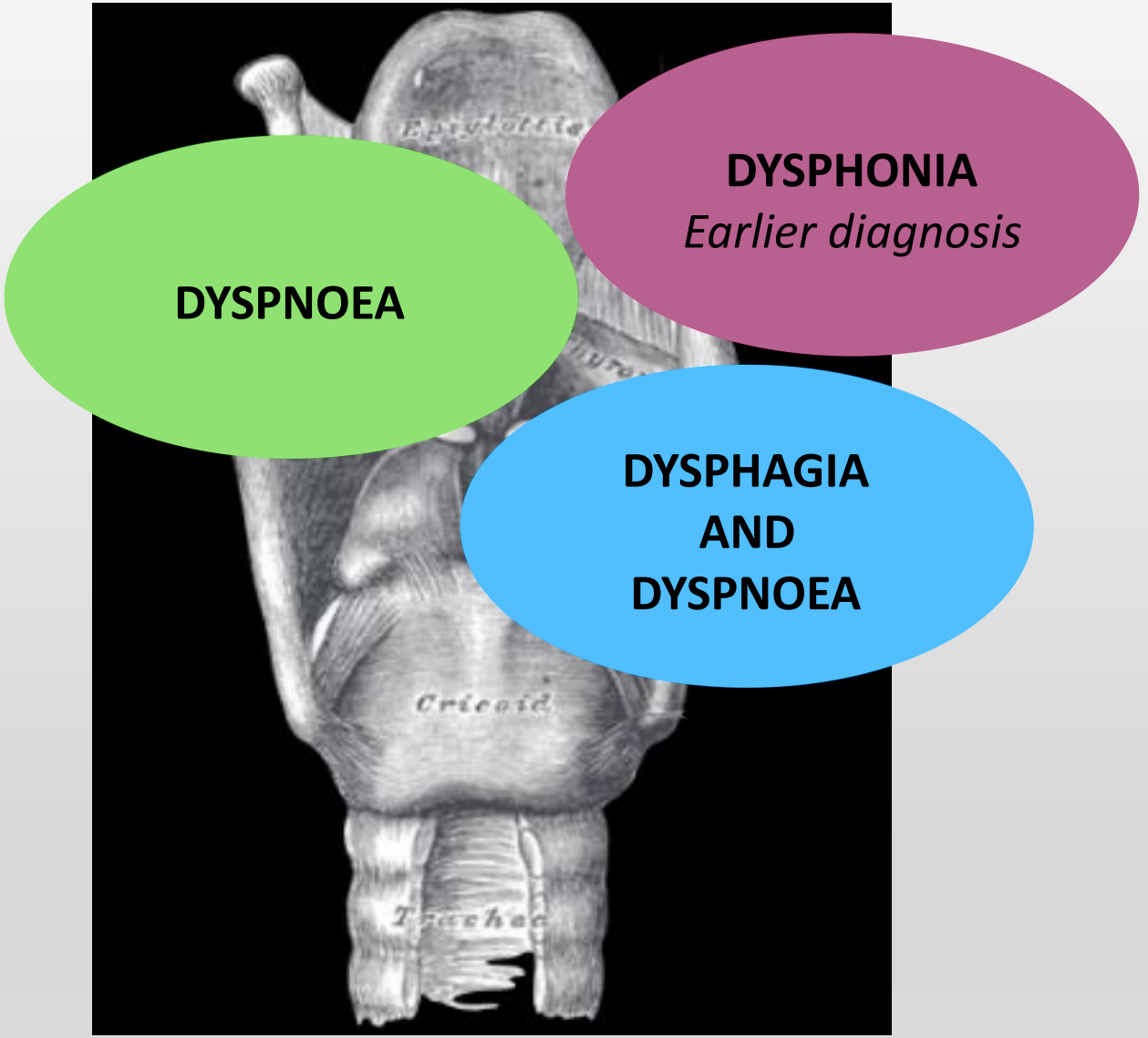
Haematolymphoid tumors

Secondary tumors (kidney, lung)

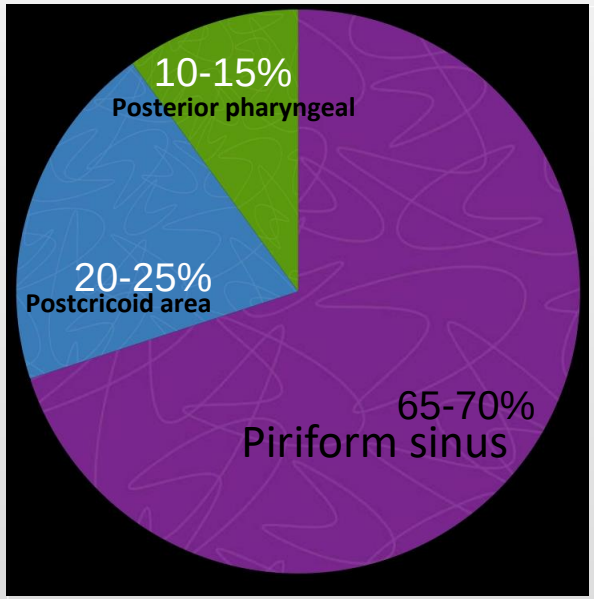


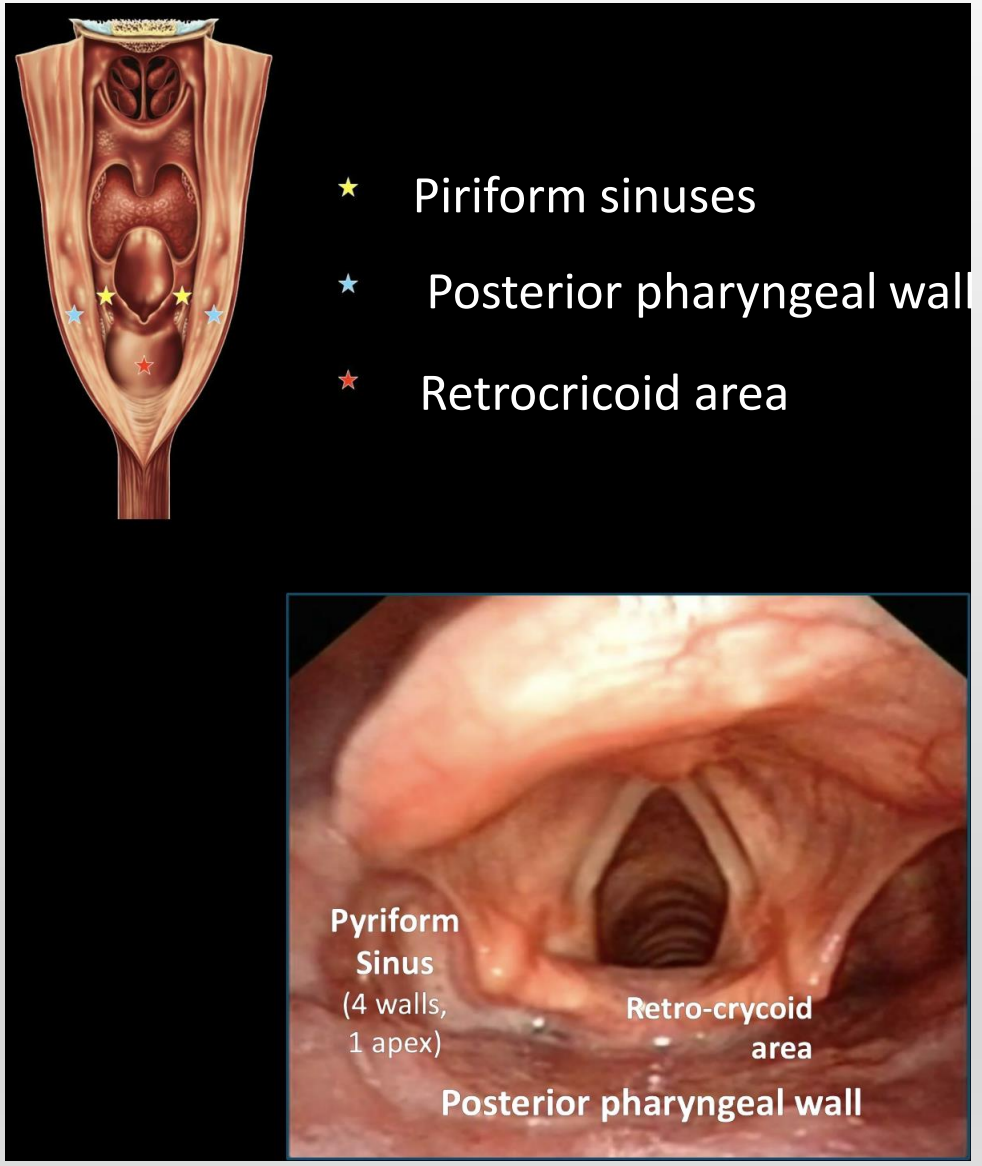
LARYNGEAL CANCER: SUBSITES AND SYMPTOMS





HYPOPHARYNGEAL CANCER: SUBSITES





HYPOPHARYNGEAL CANCER: SYMPTOMS

LATE DIAGNOSIS…
70-85% III-IV stage

Neck mass/lump (uni- or bilateral, single or multiple)

Submucosal spread

Pain in the throat or ear

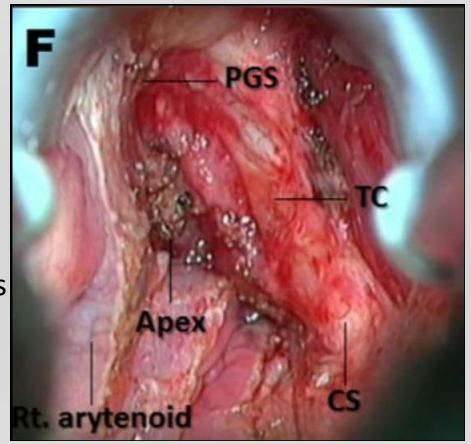
Dysphagia, odynophagia

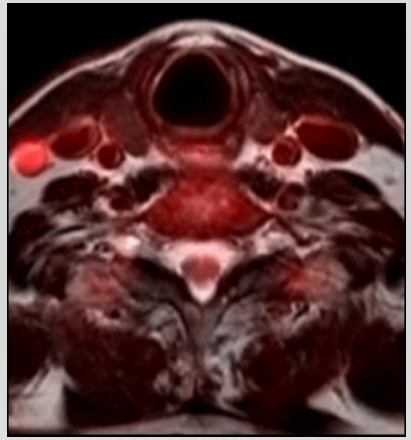
Hoarsness

Recent weight loss (past 6 months)

Field cancerization and second primary

Early infiltration of PGS and esophagus

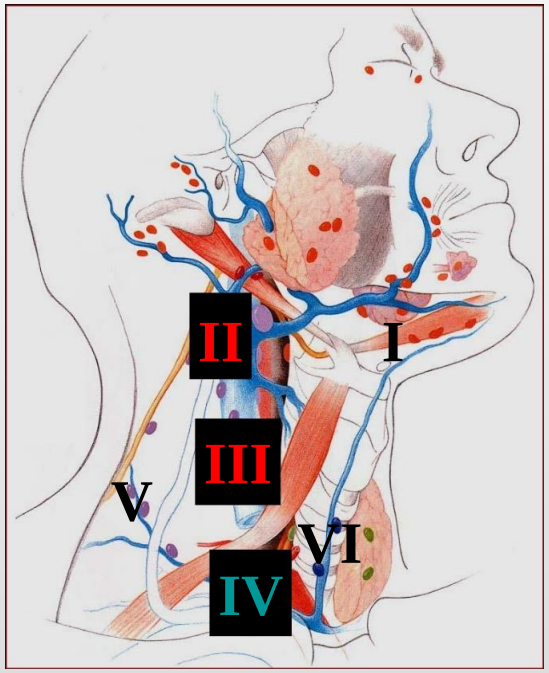




High rates of N+ and M+

METASTATIC SPREAD

Supraglottis

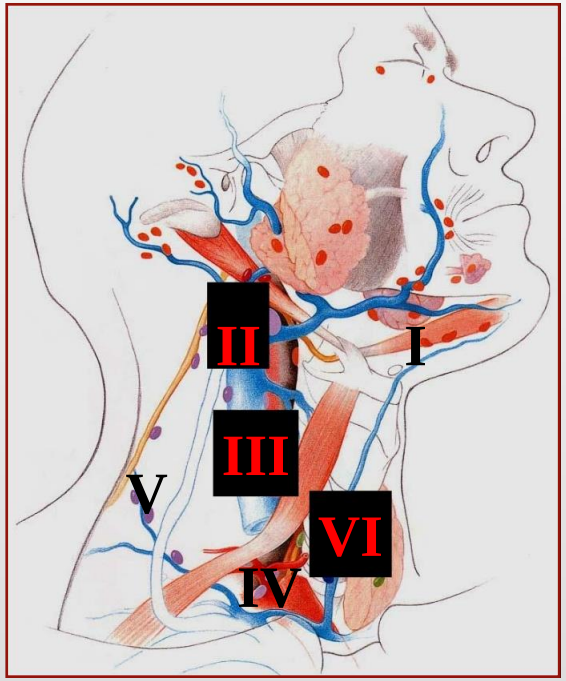


30-70% N+ at diagnosis

23% occult metastasis

2.7% at diagnosis (lung, liver)

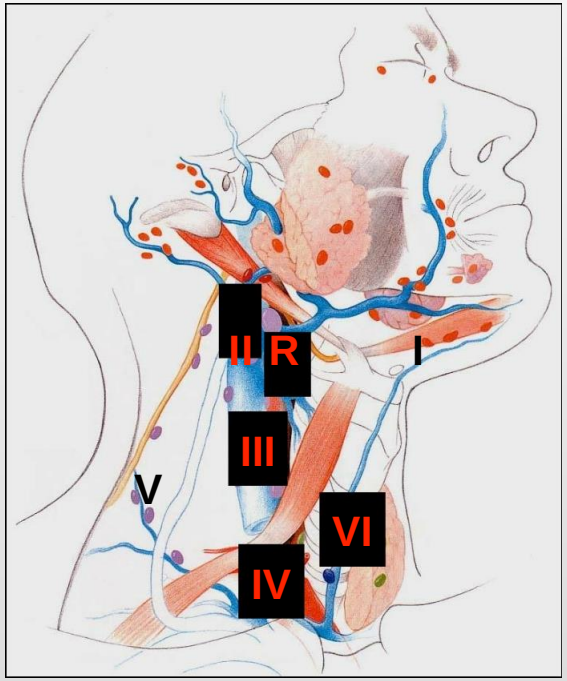
Glottis



4% N+ at diagnosis

12% occult

Hypopharynx



60-75% N+ at diagnosis

20% controlateral occult N

7.3% at diagnosis (lung, liver, brain, bone)

N

M

Laryngeal and hypopharyngeal cancer

CLINICAL WORK-UP

CLINICAL WORK-UP

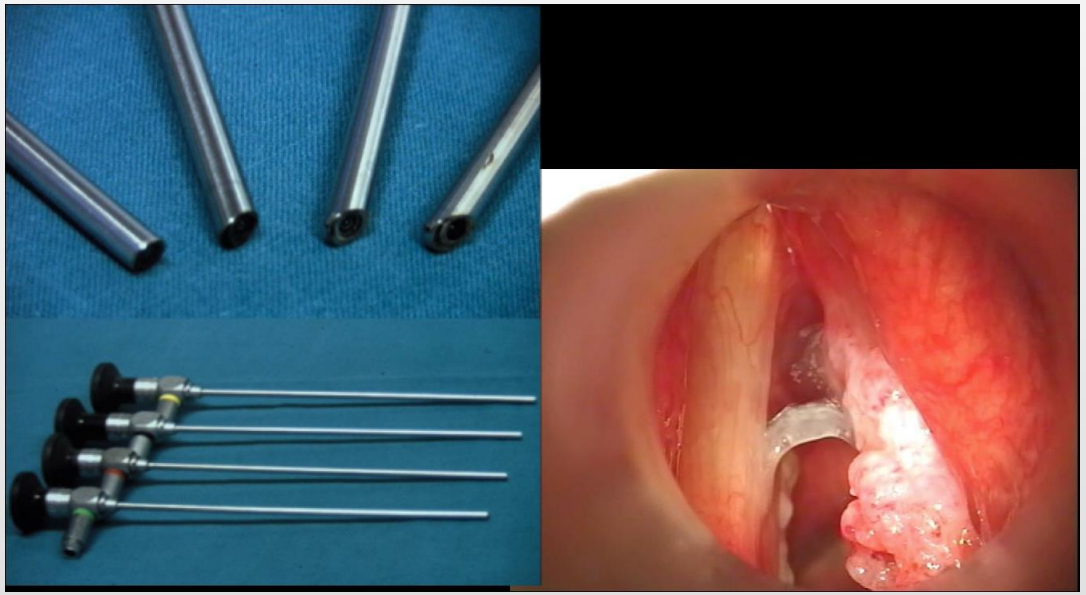
History
Symptoms, tobacco, alcohol, laryngeal conditions (e.g. RRP), comorbidities

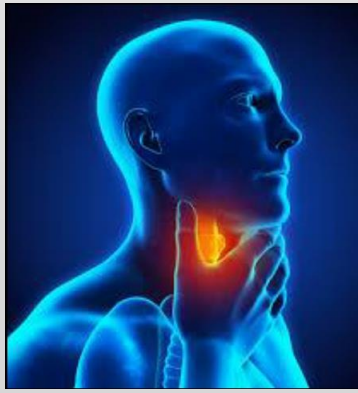
Clinical evaluation
Site(s) of the lesion, airway patency, adenopathies

Endoscopic evaluation
Fiberoptic examination

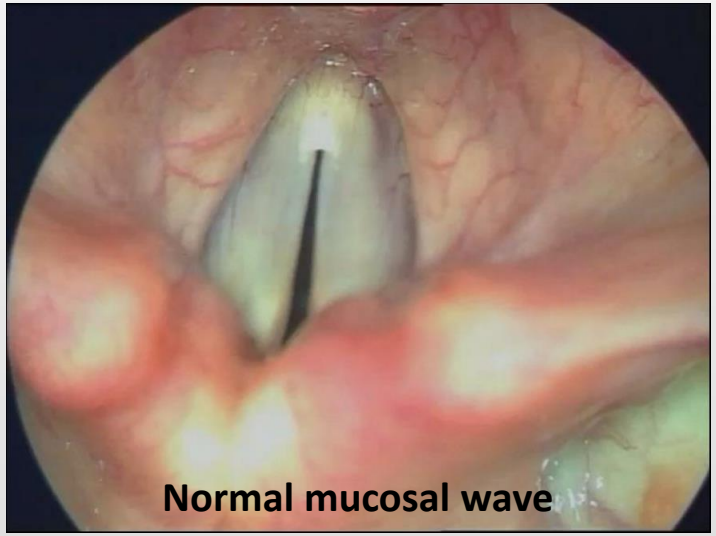
Biopsy
Excisional biopsy (very selected early stage)
Biopsy under general ansthesia

Imaging
Loco-regional: CE-CT or CE-MRI (w/o surface coils), neck US +/- FNAC
Systemic: PET-CT *or* total body CE-CT *or* PET-MRI



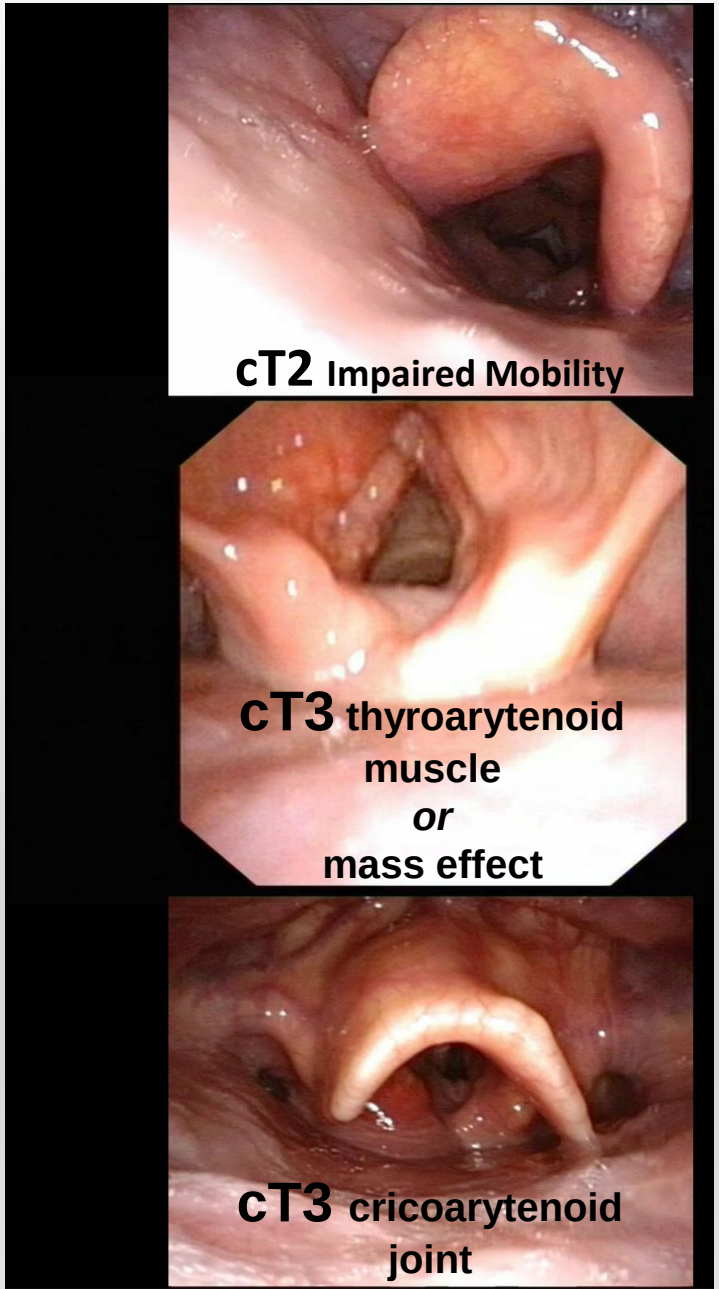


OFFICE BASED ENDOSCOPY



Flexible Panendoscopy

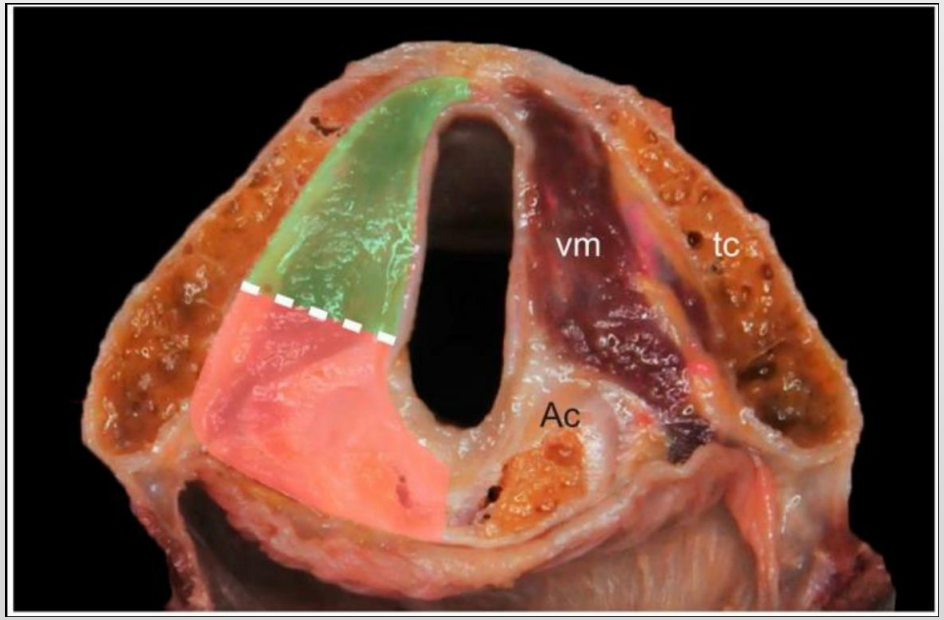
Videolaryngostroboscopy



IMAGING: ROLE OF CT

Imaging Accuracy in Preoperative Staging of T3-T4 Laryngeal Cancers

Benazzo et al., Cancers 2020



CT scan is an accurate method to stage laryngeal cancer

When the lesion extends posteriorly beyond the "**magic plane**" (line tangential to the vocal process and perpendicular to the thyroid lamina) CT scan loses accuracy in evaluating pPGS and extra-laryngeal extension: **MRI should be performed**

Succo et al, Head and Neck 2018
Ravanelli et al, Cancers 2019
Benazzo et al, Cancers 2020

Laryngeal and hypopharyngeal cancer

STAGING AND PROGNOSIS

STAGING

T

Primary Tumor (T)

TX Primary tumor cannot be assessed

Tis Carcinoma *in situ*

Supraglottis

T1 Tumor limited to one subsite of supraglottis with normal vocal cord mobility

T2 Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (eg, mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx

T3 Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, preepiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage

T4 Moderately advanced or very advanced

T4a Moderately advanced local disease
Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)

T4b Very advanced local disease
Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Glottis

T1 Tumor limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility

T1a Tumor limited to one vocal cord

T1b Tumor involves both vocal cords

T2 Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility

T3 Tumor limited to the larynx with vocal cord fixation and/or invasion of paraglottic space and/or inner cortex of the thyroid cartilage

T4 Moderately advanced or very advanced

T4a Moderately advanced local disease
Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, cricoid cartilage, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)

T4b Very advanced local disease
Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Subglottis

T1 Tumor limited to the subglottis

T2 Tumor extends to vocal cord(s) with normal or impaired mobility

T3 Tumor limited to larynx with vocal cord fixation and/or inner cortex of the thyroid cartilage

T4 Moderately advanced or very advanced

T4a Moderately advanced local disease
Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)

T4b Very advanced local disease
Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Hypopharynx

TX Primary tumor cannot be assessed

Tis Carcinoma *in situ*

T1 Tumor limited to one subsite of hypopharynx and/or 2 cm or smaller in greatest dimension

T2 Tumor invades more than one subsite of hypopharynx or an adjacent site, or measures larger than 2 cm but not larger than 4 cm in greatest dimension without fixation of hemilarynx

T3 Tumor larger than 4 cm in greatest dimension or with fixation of hemilarynx or extension to esophageal mucosa

T4 Moderately advanced or very advanced local disease

T4a Moderately advanced local disease
Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, esophageal muscle or central compartment soft tissue*

T4b Very advanced local disease
Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

STAGING

cN

Regional Lymph Nodes (N)

Clinical N (cN)

NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension ENE(–)
N2		Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–); *or* metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(–); *or* in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(–)
	N2a	Metastasis in a single ipsilateral lymph node larger than 3 cm but not larger than 6 cm in greatest dimension, and ENE(–)
	N2b	Metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(–)
	N2c	Metastases in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(–)
N3		Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−); *or* metastasis in any node(s) and clinically overt ENE(+)
	N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−)
	N3b	Metastasis in any node(s) and clinically overt ENE(+)

Note: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(−) or ENE(+).

pN

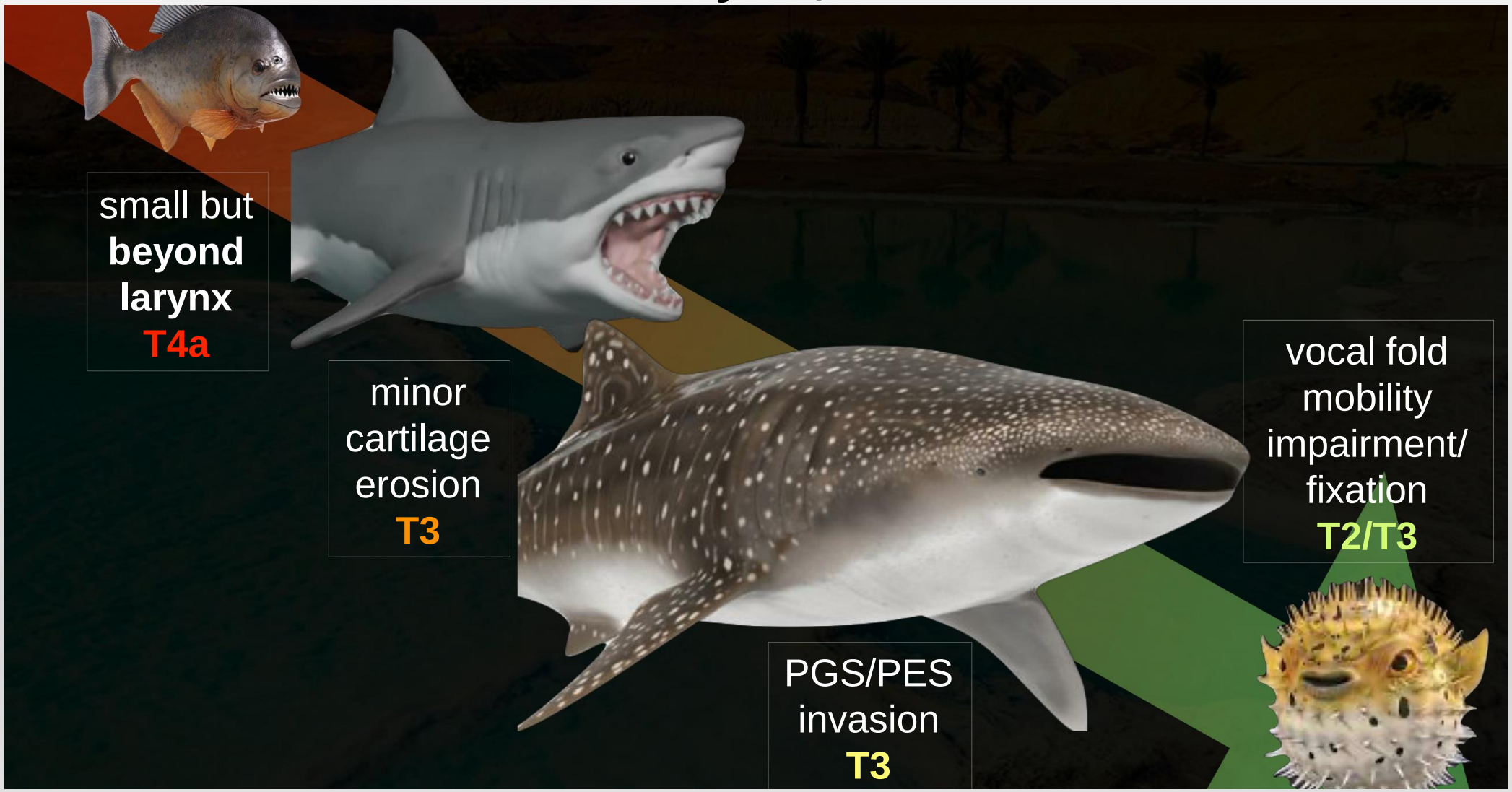
Regional Lymph Nodes (N)

Pathological N (pN)

NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(–)
N2		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(+); *or* larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–); *or* metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−); *or* in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension, ENE(−)
	N2a	Metastasis in single ipsilateral node 3 cm or smaller in greatest dimension, and ENE(+); *or* a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–)
	N2b	Metastases in multiple ipsilateral node(s), none larger than 6 cm in greatest dimension and ENE(−)
	N2c	Metastases in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension, and ENE(–)
N3		Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−); *or* metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); *or* multiple ipsilateral, contralateral or bilateral nodes any with ENE(+); *or* a single contralateral node of any size and ENE (+)
	N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−)
	N3b	Metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); *or* multiple ipsilateral, contralateral or bilateral nodes any with ENE(+); *or* a single contralateral node of any size and ENE (+)

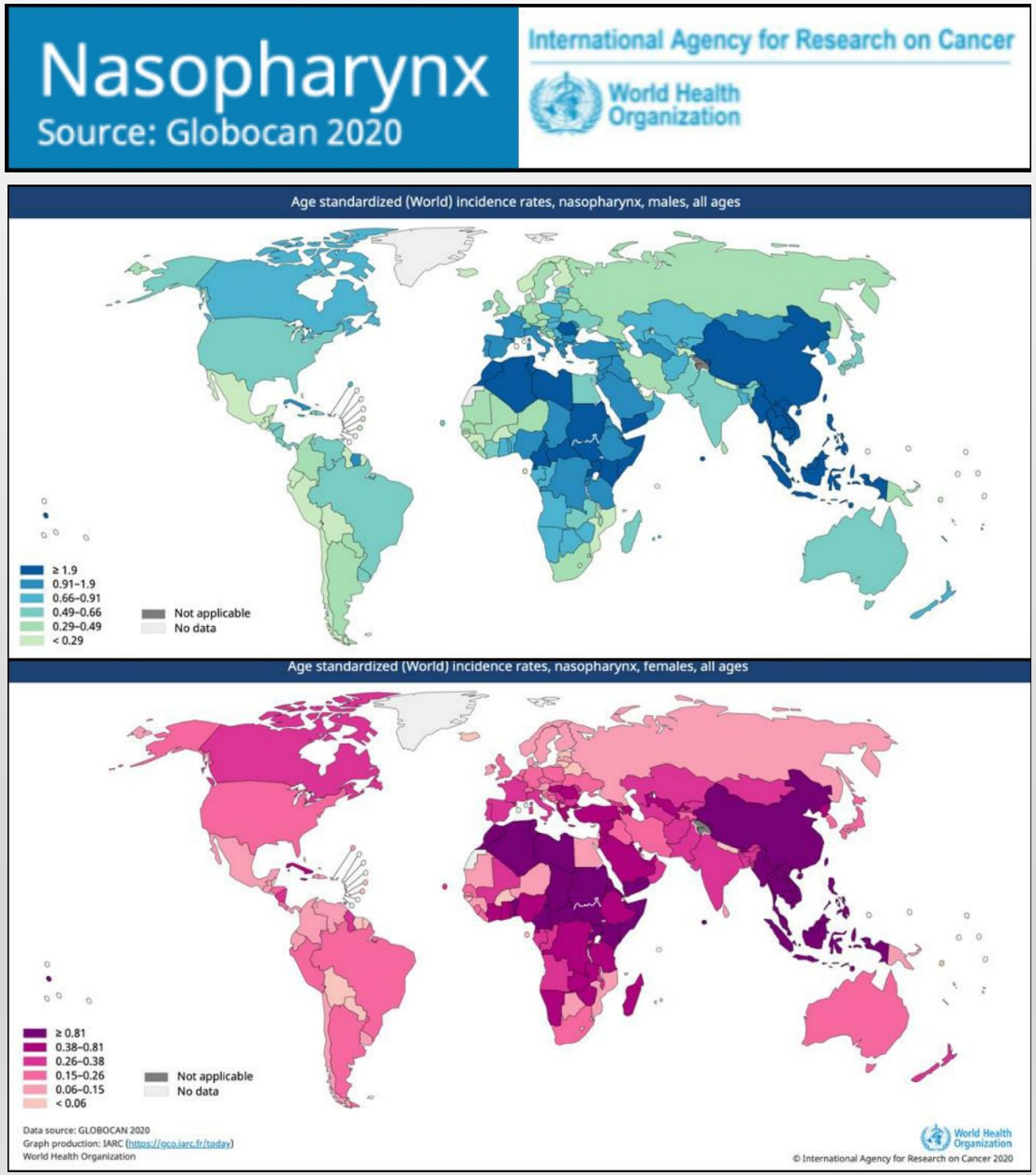
ADVANCED LARYNGEAL CANCER

Many T3, T4…



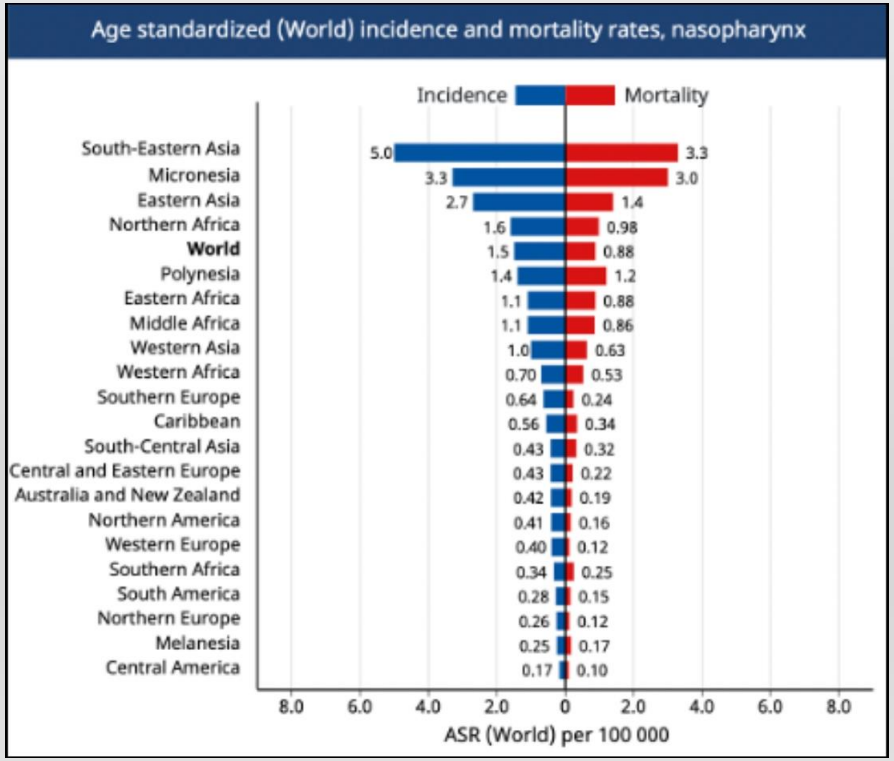
NASOPHARYNX

EPIDEMIOLOGY



Nonkeratinizing undifferentiated carcinoma
Annual incidence in USA and Europe: <1/100,000
Annual incidence in **Southern China: 30/100,000**
Global ASR 1.5 per 100 000: 2.2 in males, 0.82 in females

New cases in 2020: 133 354
Number of death in 2020: 80 008



HISTOPATHOLOGY

WHO CLASSIFICATION 2017

Carcinomas

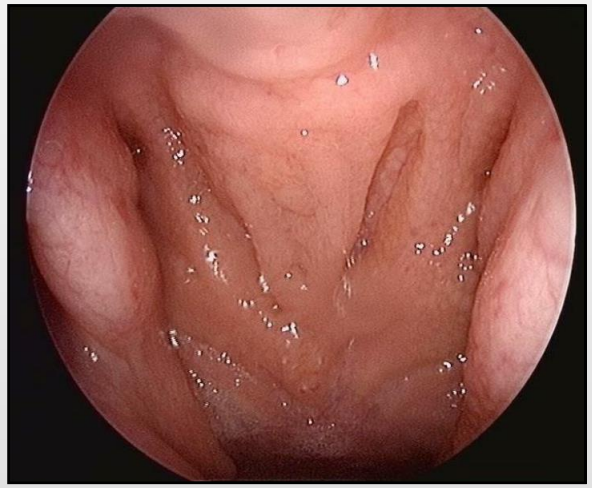
Nasopharyngeal carcinoma

Non-keratinizing SCC

Keratinizing SCC

Basaloid SCC

Nasopharyngeal papillary adenocarcinoma



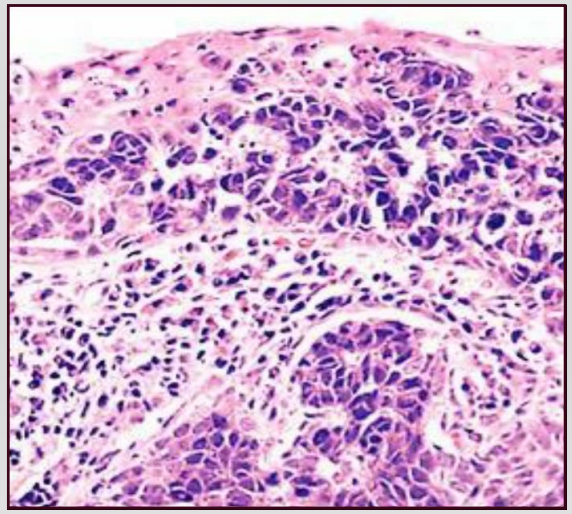
Salivary gland tumors

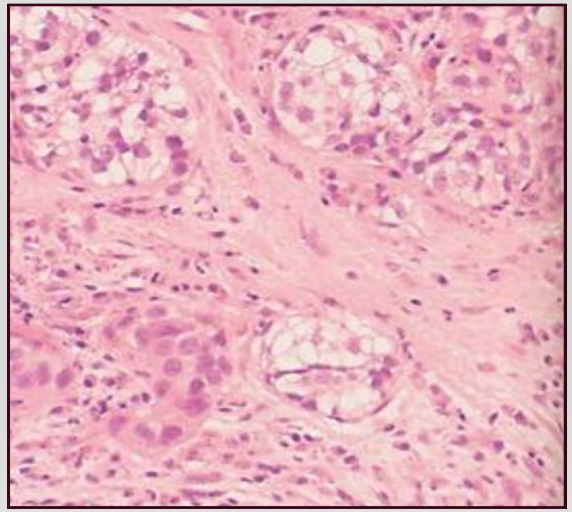
Adenoid cystic carcinoma

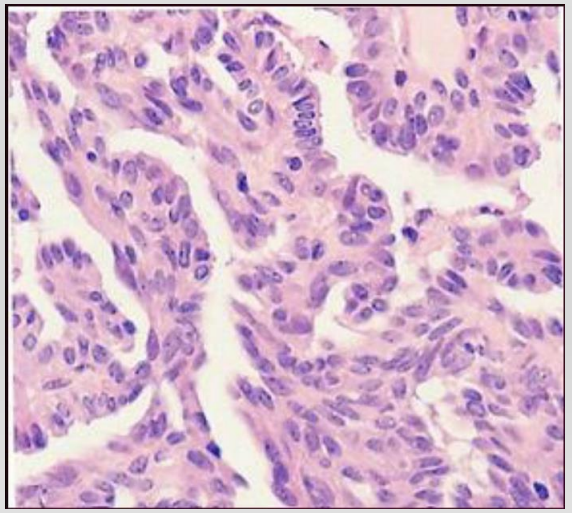
Salivary gland anlage tumor

Haematolymphoid tumors

Notochordal tumours







SIGNS and SYMPTOMS

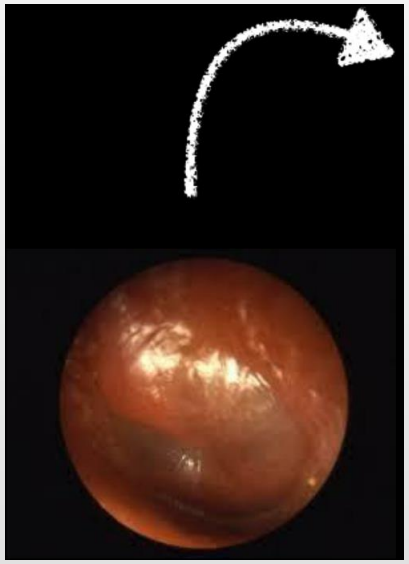
NECK LUMP

At diagnosis: 60.3 - 75.8%

NASAL

At diagnosis: 40.3 - 73.4%

Epistaxis
Nasal obstruction
Mucopurulent discharge
Olfaction impairment



OTOLOGIC

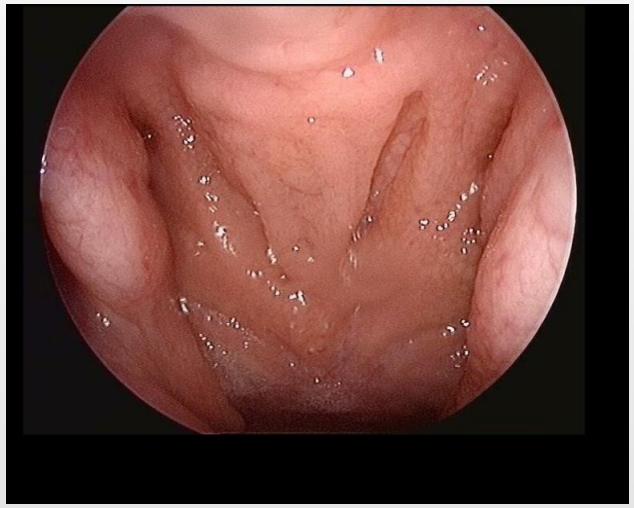
At diagnosis: 43.9 - 62.

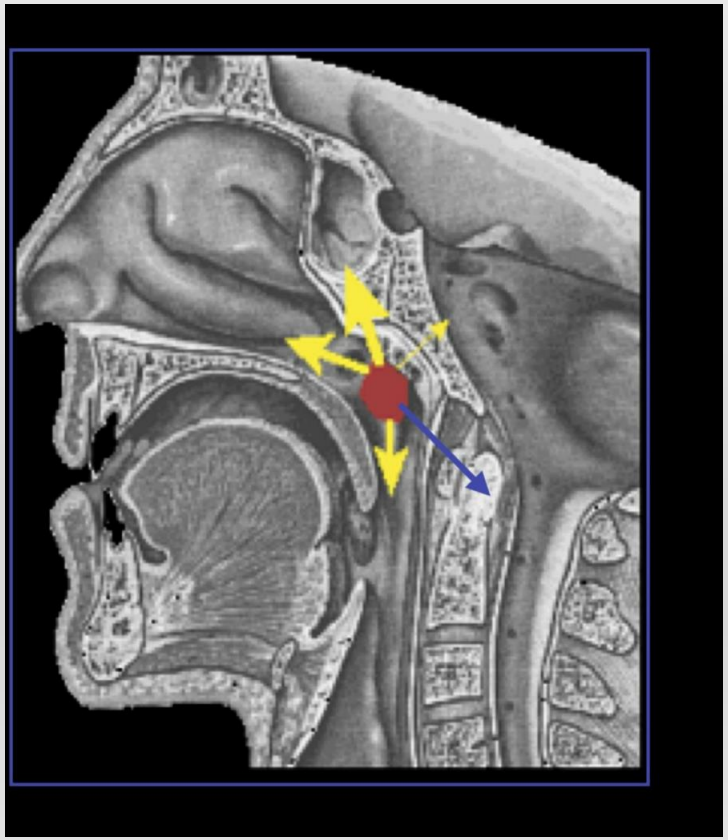
Otitis media
Hearing loss
Fullness
Tinnitus

NEUROLOGIC

III, IV, and VI CN: ophthalmoplegia
V CN: facial pain
Greater petrosal superficial nerve: xerophtalmy
IX, X, and XI CN: different jugular foramen syndromes
XII CN: hemitongue palsy, atrophy, and deviation
Sympathetic cervical trunk: Claude-Bernard-Horner syndrome

LOCAL SPREAD





Eustachian tube

Nasal cavity

Parapharyngeal space

Paranasal sinuses

Oropharynx

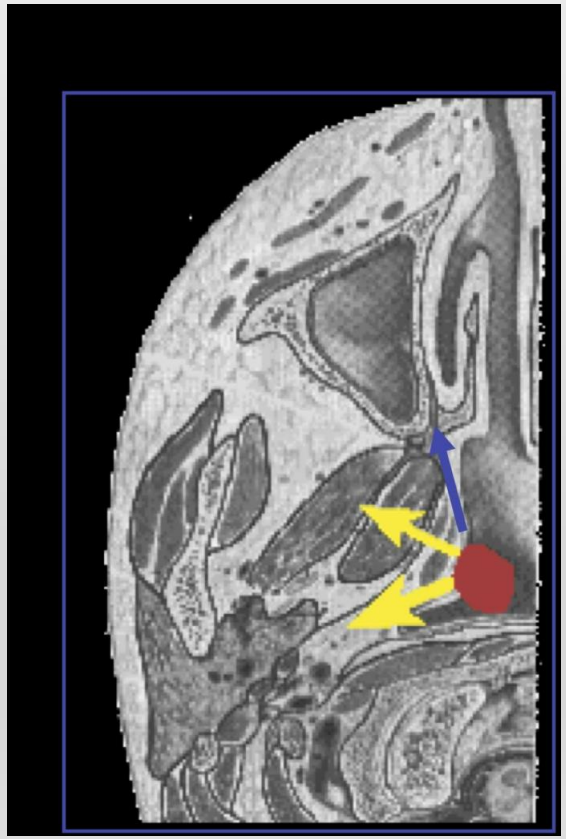
Pterygo-palatine/Infratemporal fossa

Skull base

Cavernous sinus

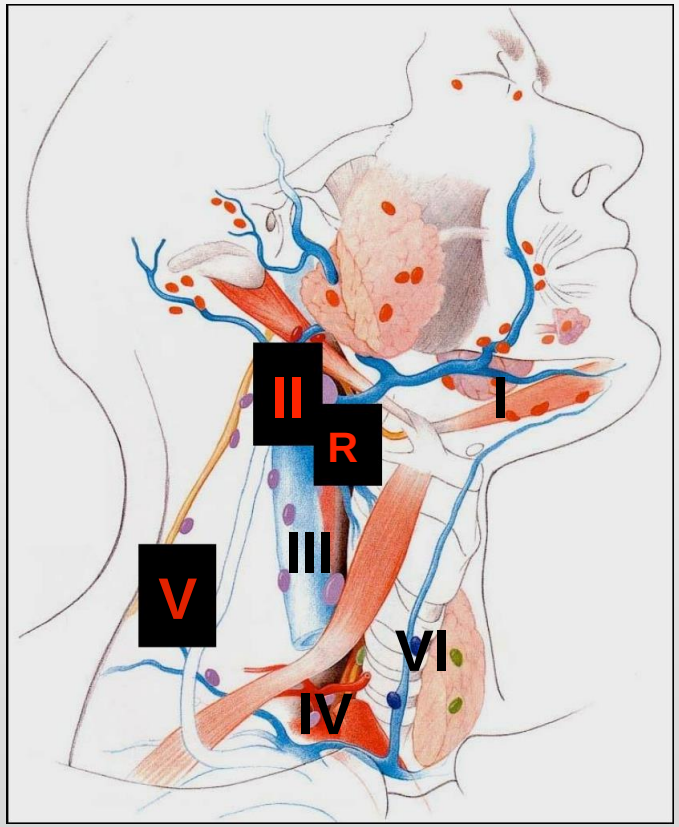
Cranial cavity

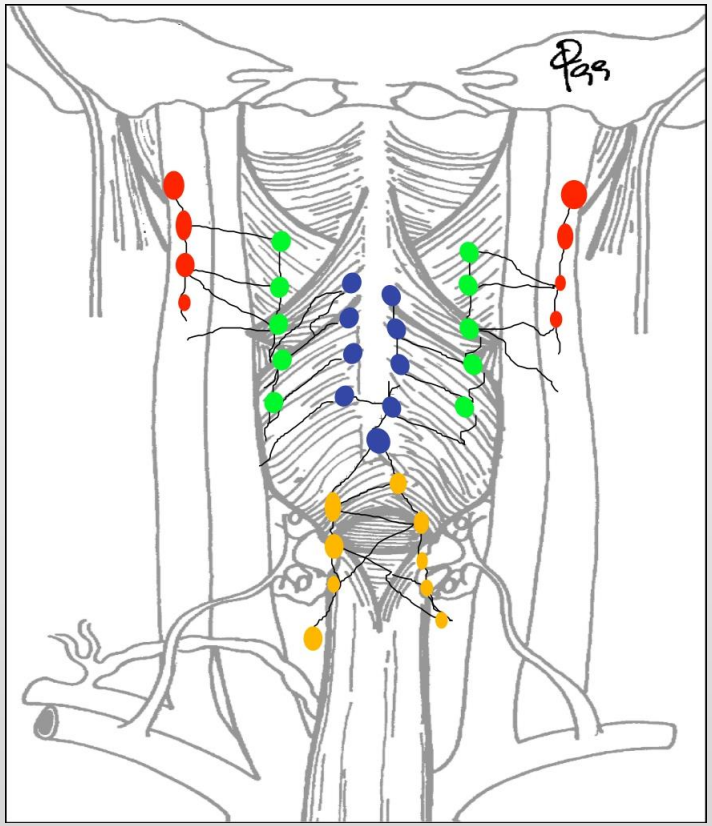
Cervical spine



METASTATIC SPREAD

NODAL METASTASIS





Clinically evident N+ at diagnosis: 60.3 - 75.8%

DISTANT METASTASIS

At diagnosis: 9%

Bone (50%)
Lung
Liver

Nasopharyngeal cancer
CLINICAL WORK-UP

CLINICAL WORK-UP

History
Symptoms, tobacco, alcohol, comorbidities, ethnicity

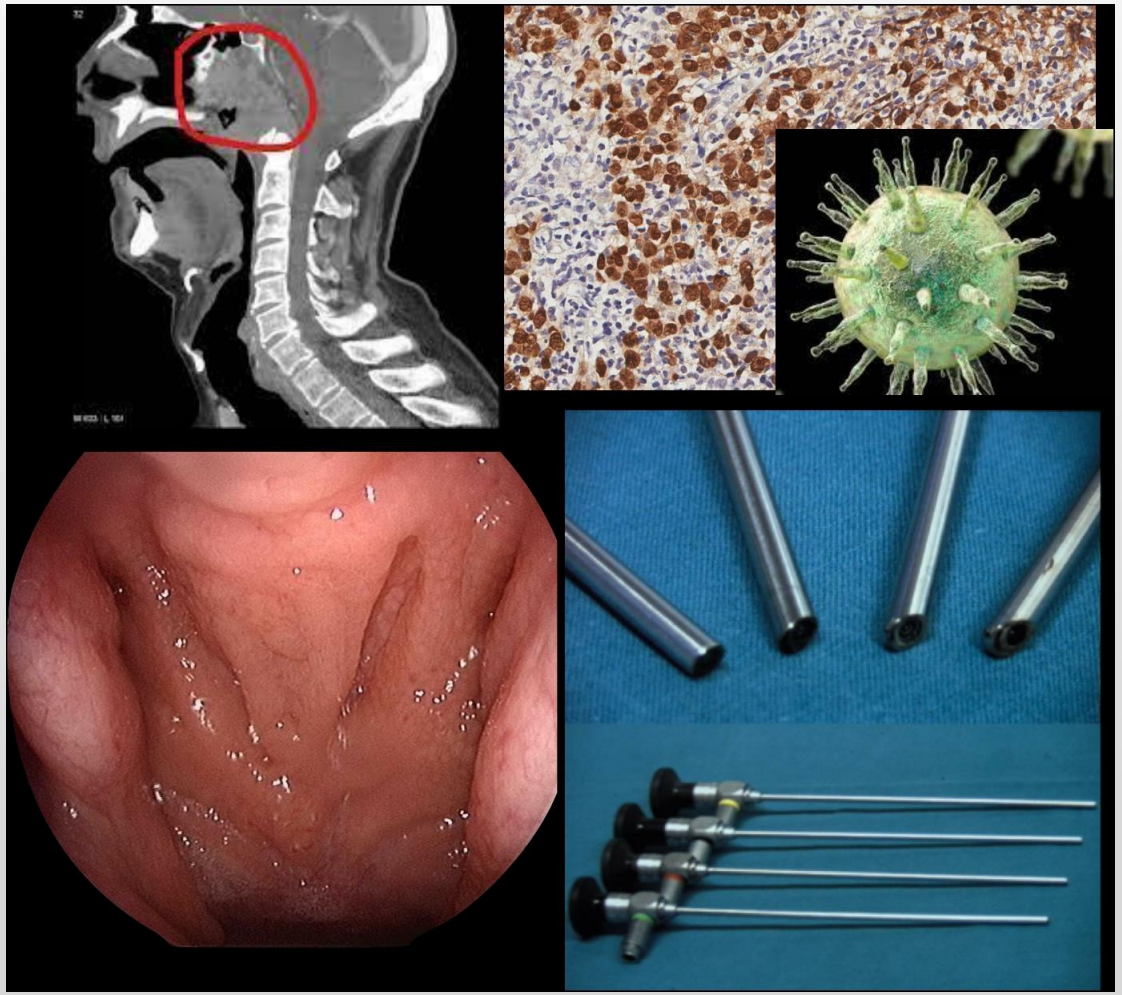
Clinical evaluation
Site(s) of the lesion, adenopathies

Endoscopic evaluation
Fiberoptic examination with NBI

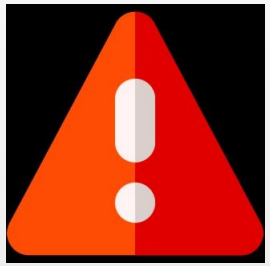
Outpatient endoscopy guided biopsy

EBV status
EBER on biopsy, EBV-DNA plasma levels

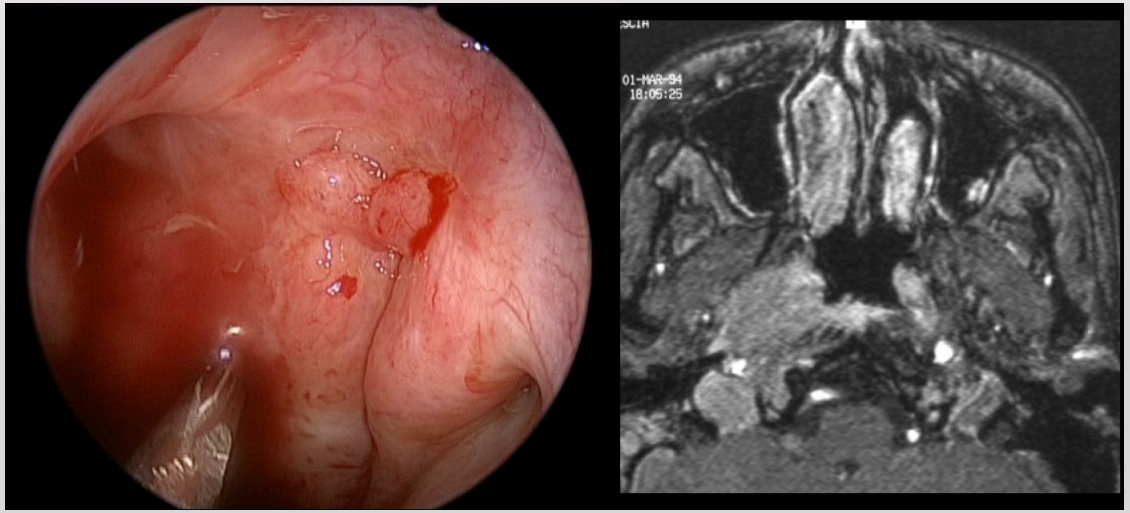
Imaging
- **Loco-regional:** CE-MRI *or* CE-CT, neck US +/- FNAC
- **Systemic**: PET-CT *or* total body CE-CT **Loco-**
- **regional and systemic:** PET-MRI



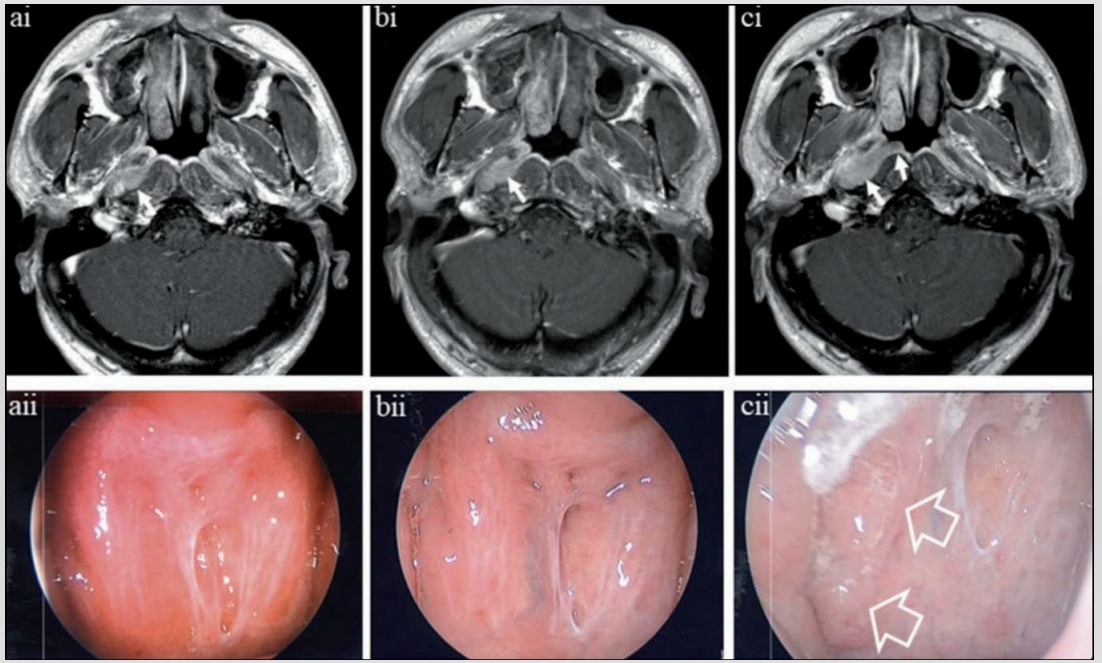
ENDOSCOPY



Endoscopy can be negative (submucosal pattern of growth in 10% of NPC)



Most NPCs arise from the Rosenmüller fossa that is hidden behind the torus tubarius



King et al, Annals of Oncology 2019

ROLE OF EBV PLASMA LEVELS

Plasma Epstein-Barr Viral Deoxyribonucleic Acid Quantitation Complements Tumor-Node-Metastasis Staging Prognostication in Nasopharyngeal Carcinoma

Leung et al, J Clin Oncol 2006

Clinical utility of circulating Epstein-Barr virus DNA analysis for the management of nasopharyngeal carcinoma

Sherwood et al, Chin Clin Oncol 2016

Staging / prognosis

Response to treatment

Follow up

Screening in endemic regions

Unknown primary

5y-Prognostic value

- Stage I, II disease, high DNA (**≥4000 copies/mL**) – **64%**
- Stage III, IVA/IVB disease, low DNA – **66%**
- Stage III, IVA/IVB disease, high DNA – **54%**

Nasopharyngeal cancer
STAGING AND PROGNOSIS

STAGING

T

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No tumor identified, but EBV-positive cervical node(s) involvement
Tis	Carcinoma *in situ*
T1	Tumor confined to nasopharynx, or extension to oropharynx and/or nasal cavity without parapharyngeal involvement
T2	Tumor with extension to parapharyngeal space, and/or adjacent soft tissue involvement (medial pterygoid, lateral pterygoid, prevertebral muscles)
T3	Tumor with infiltration of bony structures at skull base, cervical vertebra, pterygoid structures, and/or paranasal sinuses
T4	Tumor with intracranial extension, involvement of cranial nerves, hypopharynx, orbit, parotid gland, and/ or extensive soft tissue infiltration beyond the lateral surface of the lateral pterygoid muscle

cN = pN

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Unilateral metastasis in cervical lymph node(s) and/or unilateral or bilateral metastasis in retropharyngeal lymph node(s), 6 cm or smaller in greatest dimension, above the caudal border of cricoid cartilage
N2	Bilateral metastasis in cervical lymph node(s), 6 cm or smaller in greatest dimension, above the caudal border of cricoid cartilage
N3	Unilateral or bilateral metastasis in cervical lymph node(s), larger than 6 cm in greatest dimension, and/or extension below the caudal border of cricoid cartilage

Principles of management of head and neck cancer

- MDC (MutiDiscplinary Clinic)
- Diseases factors
- Patient factors

MDC

- Head and neck Surgeon
- Medical oncologist
- Radiation oncologist
- Diagnostic radiology
- Pathologist
- Nutrtionist
- Speech and swallwoing therapist
- Social worker
- Tracheostomy care specilasit
- Head and neck nurse

Therapeutic target :

Good Oncologic Outcome

+

Functional results

Therapeutic target

AVOID AS MUCH AS YOU CAN MULTIMODAL TREATMENT

Disease factors (site)

Nsopharynx:

radiotherapy alone

Chemoradio (induction,concurrent ,adjuvent)

Surgery for salvage

Oral cavity :

Surgery alone

Adjuvant radiotherapy

Adjuvant chemoradio

Larynx :

Radiotherapy

Chemoradiotherapy

Surgery

Oropharynx :

Surgery alone

Adjuvant radiotherapy

Adjuvant chemo radio

Hypopharynx :

Radiotherapy

Chemoradiotherapy

Surgery

Chemotherapy : cisplatinum , 5FU,carboplatinum

Immunotherapy : Pembrolizumab ,cetuximab

Disease factors (stage)

- Stage I: single modality
- Stage II and III : bi-modality
- Stage IV: trimodality

Patient factors

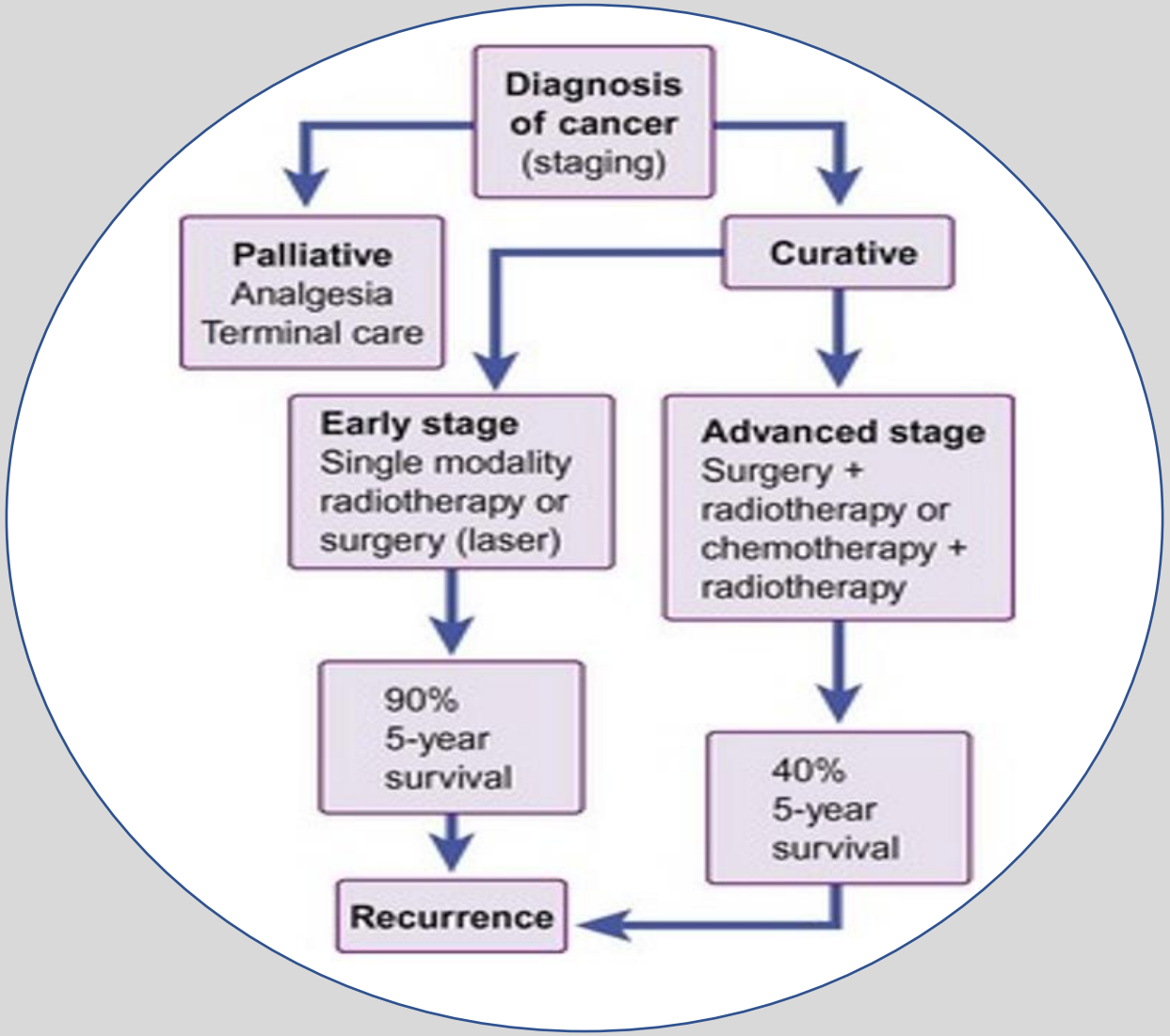
Comorbid diseases :
DM , IHD , anemia

Nutritional status

Age : >70 years

No survival benefits form chemothrapy

Principles of management of head and neck cancer



Indication for adjuvent radiotherapy in head and neck cancer

Absolute indication

I. Positive resction margins (less than 1 mm)
II. ENE (extranodal extension)
III. T4
IV. N2, N3

Relative indication

I. PNI (perineural spread)
II. LVI(lymphovascular invasion)
III. Close resction margins (1-5 mm)
IV. N1

Indication for adjuvent chemotherapy :

1. Positive resction margins
2. ENE

Neck Dissection

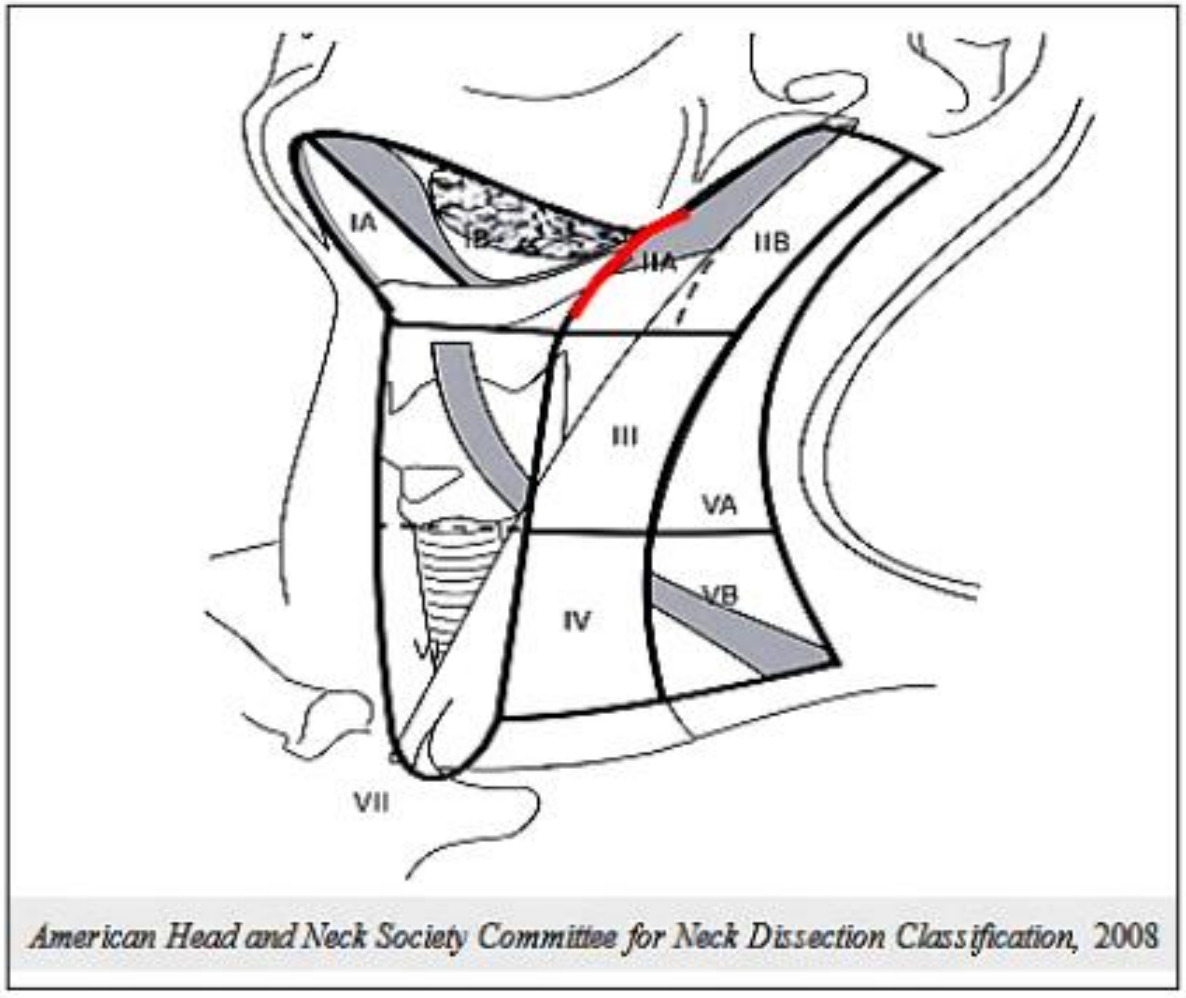
Definition

Neck dissection removes potential or proven metastases to cervical lymph nodes .

Indications

- ✓Elective (END) :when done for clinically occult metastases.
- ✓Therapeutic : when done for clinical metastases .
- ✓Salvage procedure :previously treated neck with(surgery +/ radiation).
- ❖END is indicated when the risk of having occult cervical nodal metastases exceeds 15-20%.(depth of invasion >4mm ,retromolar ,BOT , oral tongue , FOM, supraglottis and hypopharynx)

Nodal Levels



American Head and Neck Society Committee for Neck Dissection Classification, 2008

Neck Dissection Classification

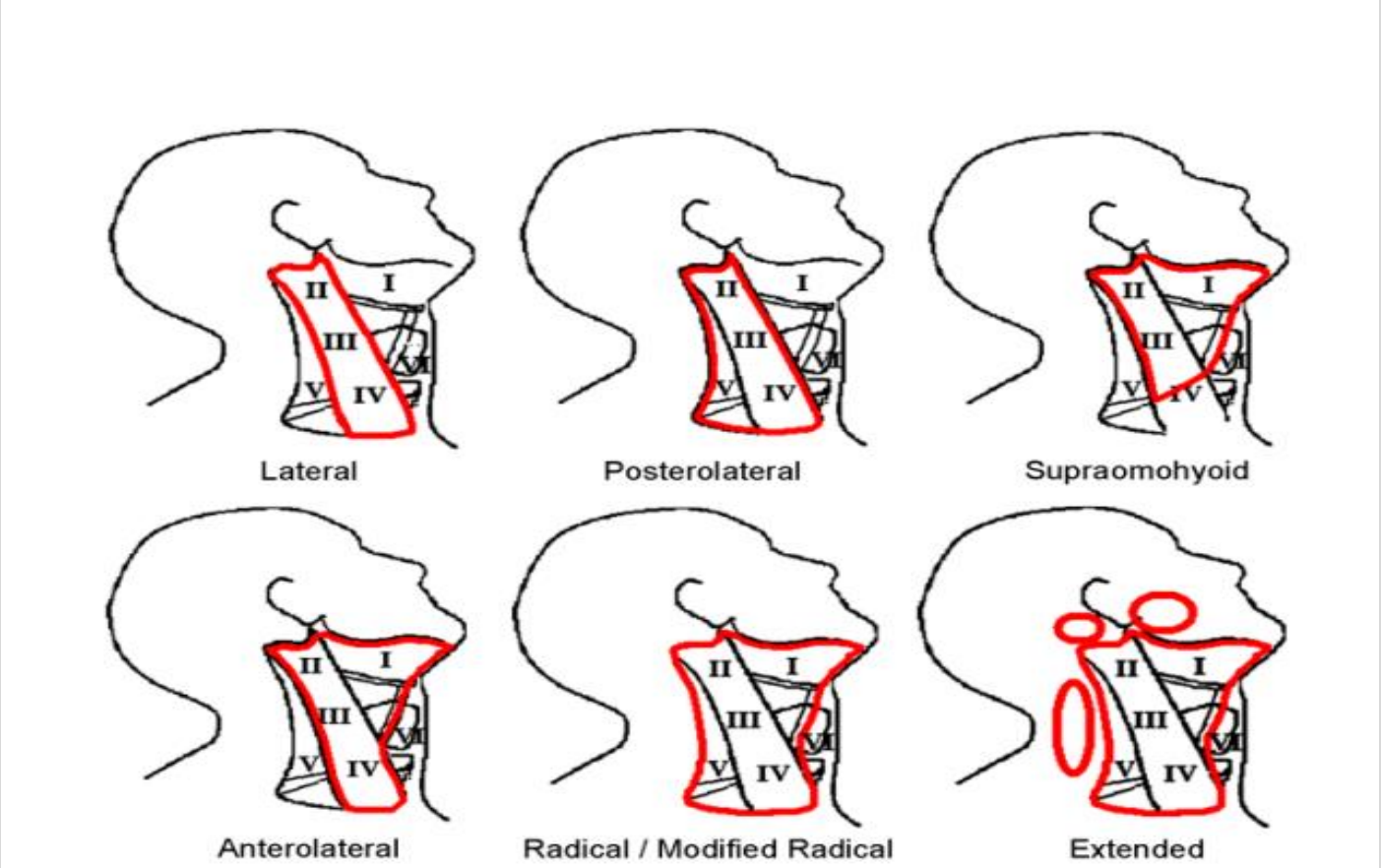


Figure 2: Common types of neck dissection

Skin Incisions

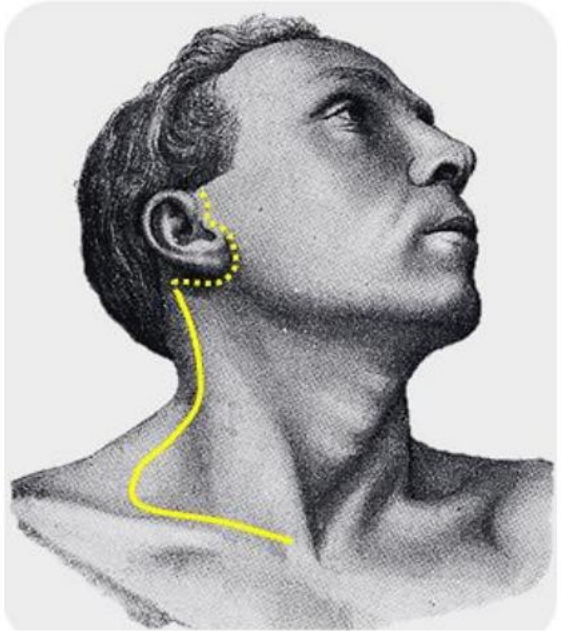


Figure 4: Hockey-stick incision for neck dissection combined with parotidectomy

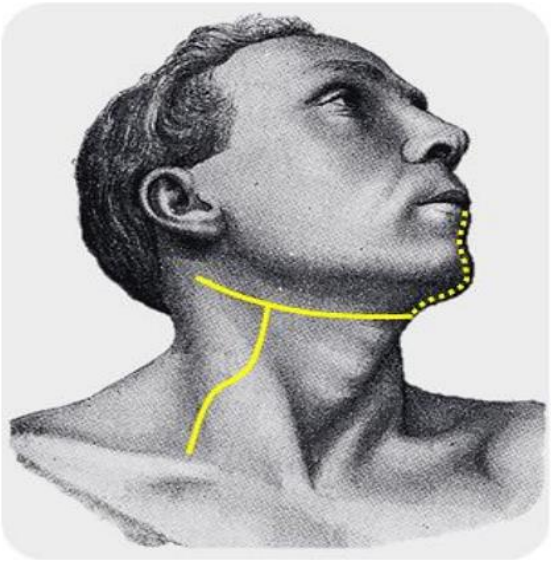
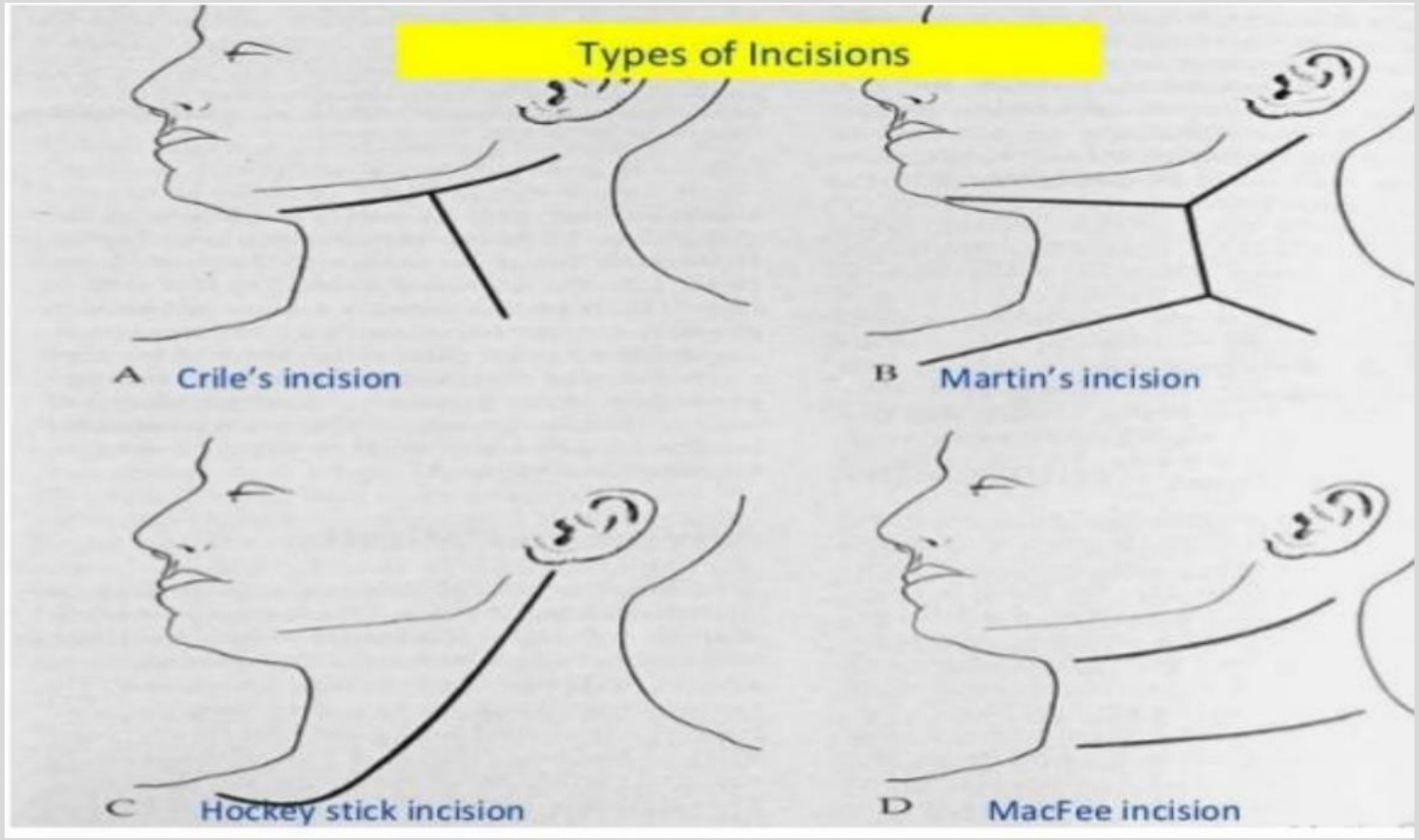


Figure 3: Incisions for neck dissection combined with oral cavity cancer resection

Skin Incisions



THE END