Multidisciplinary approach to head and neck cancer

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Head and neck cancer (H&N)

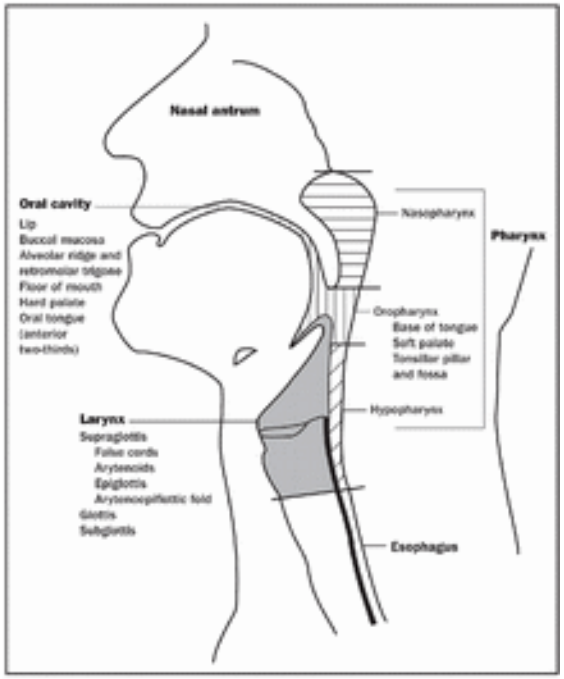


FIGURE 1: Anatomic sites and subsites of the head and neck. The approximate distribution of head and neck cancer is oral cavity, 44%; larynx, 31%; and pharynx, 25%.

What is head & neck cancer?

- Squamous cell carcinoma (90%)
- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Adenocarcinoma (lower esophagus)
- Small-cell carcinoma
- Esthesioneuroblastoma (olfactory neuroblastoma)
- Lymphomas (Hodgkin & non-Hodgkin)
- Sarcomas
- Melanoma
- Thyroid and parathyroid cancers
- Metastases

What is head & neck cancer?

Majority of H&N cancers are of squamus cell origin (90%) and therefore most of clinical guidelines based on EBM apply only to squamus cell cancer.

Special subtypes (sarcomas, melanomas, metastases) treatment guidelines apply both to H&N region and origin site.

Epidemiology

- How can an average patient with H&N cancer be described?

Epidemiology

- Account for about 3% of all cancers
- M/F ratio 3:1
- Avarge age : 50 to 70 y/o.
- Frequency by site:
  - 44% oral cavity
  - 31% larynx
  - 25% pharynx

Etiology

- **Tabbaco and alcohol** (>75%) : effect is synergistic
- **UV light** exposure (cancer of lips)
- **Diet** : poor diet, especially deficient in vit.A, C, chronic iron deficiency
- **Genetic susceptibility**: germline mutations in p53
- **Other enviromental agents**: formaldehyde,wood dust (adenocarcinoma of the ethmoids, nasal cavity, paranasal sinuses), radiation exposure (salivary gland tumors)

Etiology

- **HPV** (mainly oropharyngeal cancer, less often laryngeal and oral cavity cancer)
- **HSV-1, HSV-2** (oral cavity)
- **EBV** (nasopharynx, some salivary gland tumors)

Field cancerization theory

- Diffuse epithelial injury throughout the head and neck, lungs and esophagus that results from chronic exposure to carcinogens .
- Lifetime risk of metachronus H&N cancer is 20-40%.
- Local recurences are far more often than distant metastases.

Anatomy

- Complex anatomy.
- Drainage patterns is systematic and predictable.

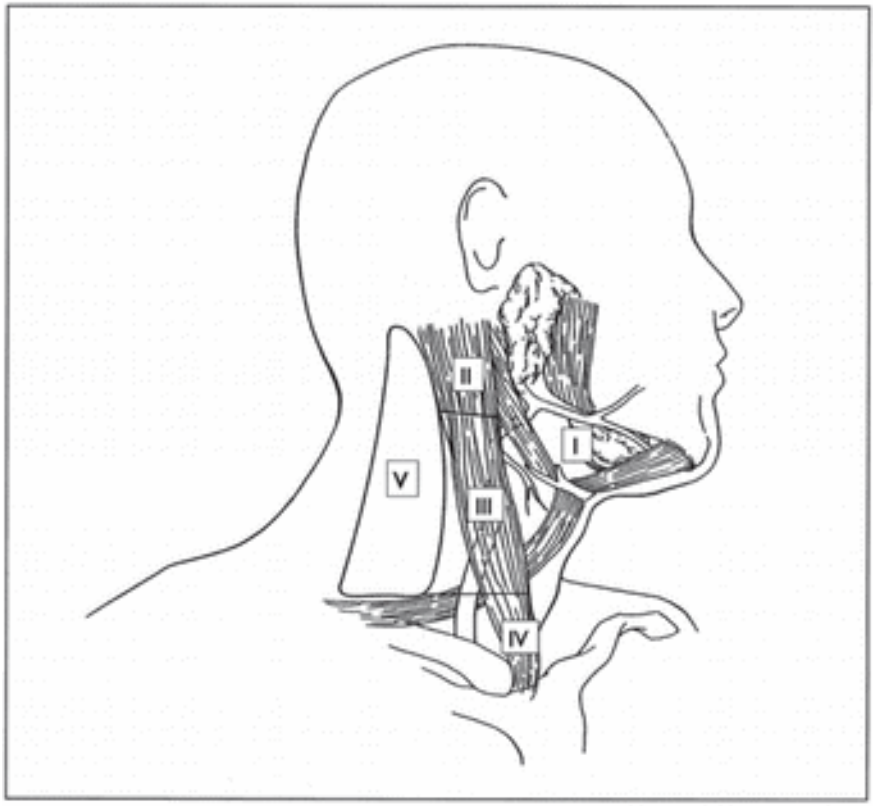


FIGURE 2: Levels of the neck as determined by lymphatic drainage patterns.

Summary

- 3% of all cancers.
- 90% of squamus cell carcinoma
- Male 50-70, tabacco and alcohol abuse.
- HPV infeciton
- Field cancerization
- Complex anatomy

Multidisciplinary team

- Head and neck surgery
- Radiation oncology
- Medical oncology
- Plastic and reconstructive surgery
- Specialized nursing care
- Dentistry/prosthodontics
- Physical medicine and rehabilitation
- Spech and swallowing therapy
- Clinical social work

- Nutrition support
- Pathology (including cytopathology)
- Diagnostic radiology
- Adjunctive services:
  - Neurosurgery
  - Ophtalmology
  - Psychiatry
  - Addiction services
  - Audiology
  - Palliative care

Initial assessment

- Physical examination and history
- Head and neck endoscopy (biopsy)
- Head and neck CT-scan (or MRI, USG)
- Chest X-ray, thoracic CT-scan, abdominal USG/CT
- PET/CT – if high risk of distant metastases

Signs and symptoms

Alterations of deglutition, phonation, hearing, respiration.

- dysphagia,
- odynophagia,
- globus sensation,
- hoarseness,
- a change in the ability to form words,
- epistaxis,
- epiphora,
- otalgia,
- hemoptysis,
- stuffiness of the ears,
- trismus

Signs and symptoms

- **ORAL CAVITY:** swelling or ulcer that fails to heal, ipsilateral otalgia, **leukoplakia and erythroplakia**
- **OROPHARYNX:** silent area (symptoms often delayed), dysphagia, odynophagia, otalgia, neck mass
- **HYPOPHARYNX:** silent area, dysphagia, odynophagia, otalgia, neck mass
- **LARYNX:** persistent hoarsness, pain, otalgia, dyspnea, stridor
- **NASOPHARYNX:** bloody nasal discharge, obstructed nostril, unilateral conductive deafness (eustachian obstruction), neurologic problems (atypical facial pain, diplopia, hoarsness, Horner's syndrome) resulting from cranial nerve involvement, asymptomatic neck mass

Signs and symptoms

- **NOSE AND SINUSES:** bloody nasal discharge, nasal obstruction, facial pain,facial swelling, diplopia (direct orbital extension)
- **PAROTID AND SUBMANDIBULAR GLANDS:** local swelling +/- pain, hemifacial paralysis owing to facial nerve involvement
- **A METASTATIC CERVICAL NODE:** may be part of the clinical presentation of any of the above-mentioned tumours

Signs and symptoms

- **Red flags**
  - Any symptom that lasted for more than 2 weeks
  - Any asymptomatic neck mass

Diagnostic imaging

- X-ray
- **CT**
- MRI
- PET-CT

Biopsy

- Punch or cup forceps biopsy.
- FNA
- Open biopsy

Pathology

- Staging
- Histologic grade

Grade

- G1 : >75% keratinization
- G2 : 25-50% keratinization
- G3 : <25% keratinization

Not a consistent predictor of clinical behavior.

Markers of agresive behaviour:

- Perineural spread
- Lymphatic invasion
- Extracapsular extension

Staging

- T score based on clinical/pathological characteristics of primary tumor
  - Different for every site
- N/M score – similar for all sites

Staging

- High impact on survival rates
  - Stage I >80%
  - Stage III/IV <40%

Involvement of single lymph nodes decrease survival rate by 50%.

Principles of treatment

- **GOALS OF TREATMENT:**

  a)Eradication of cancer

  b)Maintenance of adequate physiologic function of:

  -special senses (vision, hearing, balance, taste, smell)

  -mastication-deglutition (mandible, teeth, tongue, saliva, palate, pharynx, larynx)

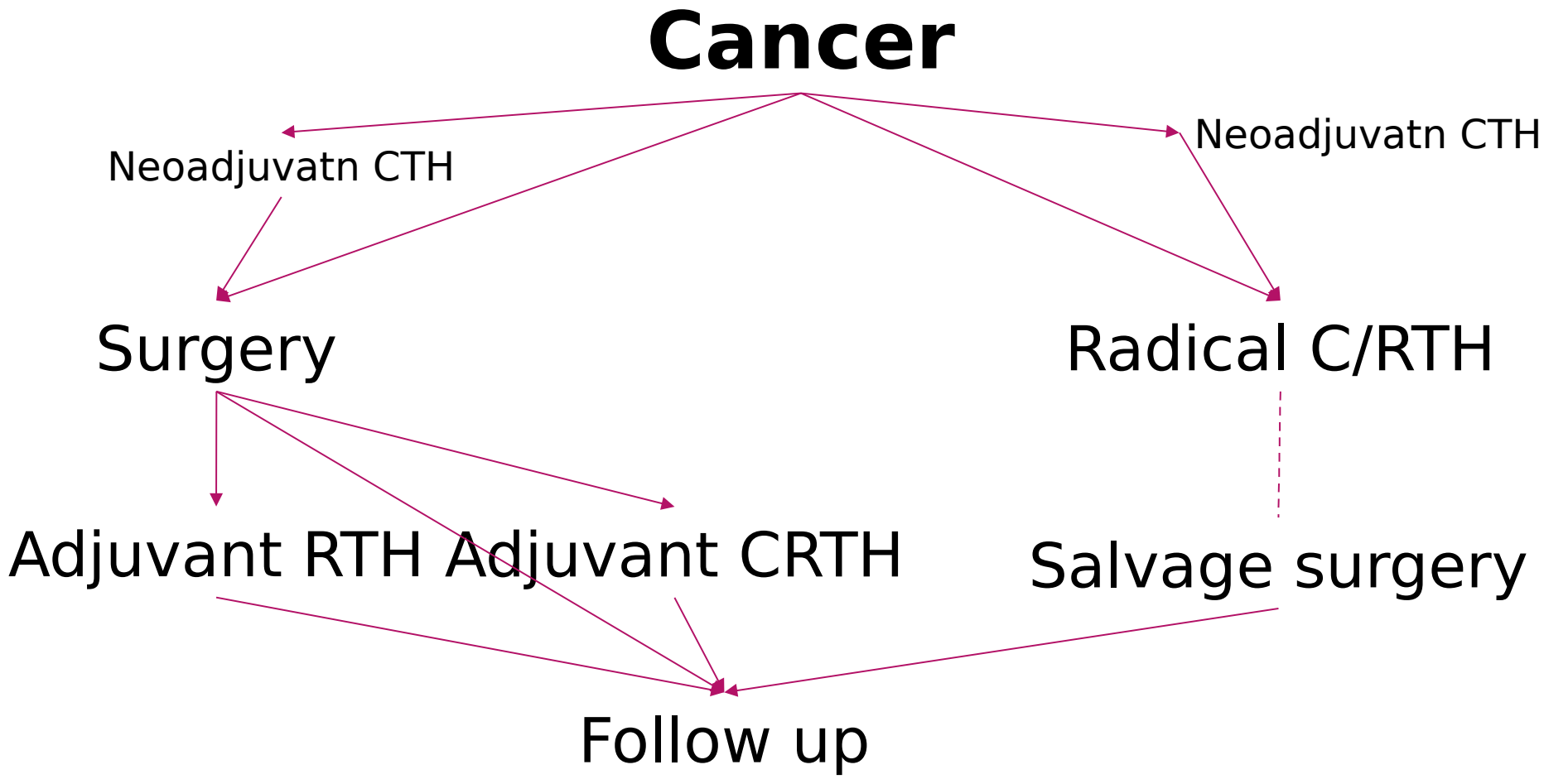
  -respiration (larynx, trachea)

  -speech (larynx, tongue)

  c)acceptable cosmesis requires necessary but sufficient surgery, reconstructive surgical and prothesis rehabilitation

MULTIDISCIPLINARY APPROACH HIGHLY RECOMMENDED

Treatment algorithm (oversimplified)



Principles of treatment:

- EARLY STAGE DISEASE I, II (T1,T2,N0,M0)

  SINGLE MODALITY TREATMENT :

SURGERY

OR RADIOTHERAPY (brachytherapy)

results achieved are equivalent

Principles of treatment

- Decision on which modality should be choose is based on mainly on localization of tumor
  - Surgery : oral cavity
  - Radiotherapy : oropharynx, larynx, nasopharynx

Principles of treatment:

ADVANTAGES OF SURGERY :

-complete pathological staging of disease

-quick local clearance of disease

-avoidiance of toxicity of radiotherapy, including the risk of radiotherapy induced second malignancies

ADVANTAGES OF RADIOTHERAPY:

-avoidance of operative mortality in patients with significant comorbidities

-organ conservation is more likely including preservation of the voice and swallowing

-possibility of treatment of multiple synchronous primaries

Principles of treatment:

- LATE STAGE DISEASE III and IV, RESECTABLE

  Combined treatment:

SURGERY with adjuvant C/RTH

or

CHEMORADIOTHERAPY

Principles of treatment:

COMBINED SURGERY + RADIOTHERAPY:

1. **SURGERY + postsurgical RADIOTHERAPY**

-T3 – T4 primary tumour

->= N2 disease

-perineural or vascular invasion

-poorly differentiated tumor

-short margins

2. **SURGERY + postsurgical CHEMORADIOTHERAPY**

- positive surgical margins (cancer cells in surgical margin)

- extracapsular extension

Principles of treatment:

- LOCALLY ADVANCED UNRESECTABLE DISEASE –STAGE III, IV (M0)

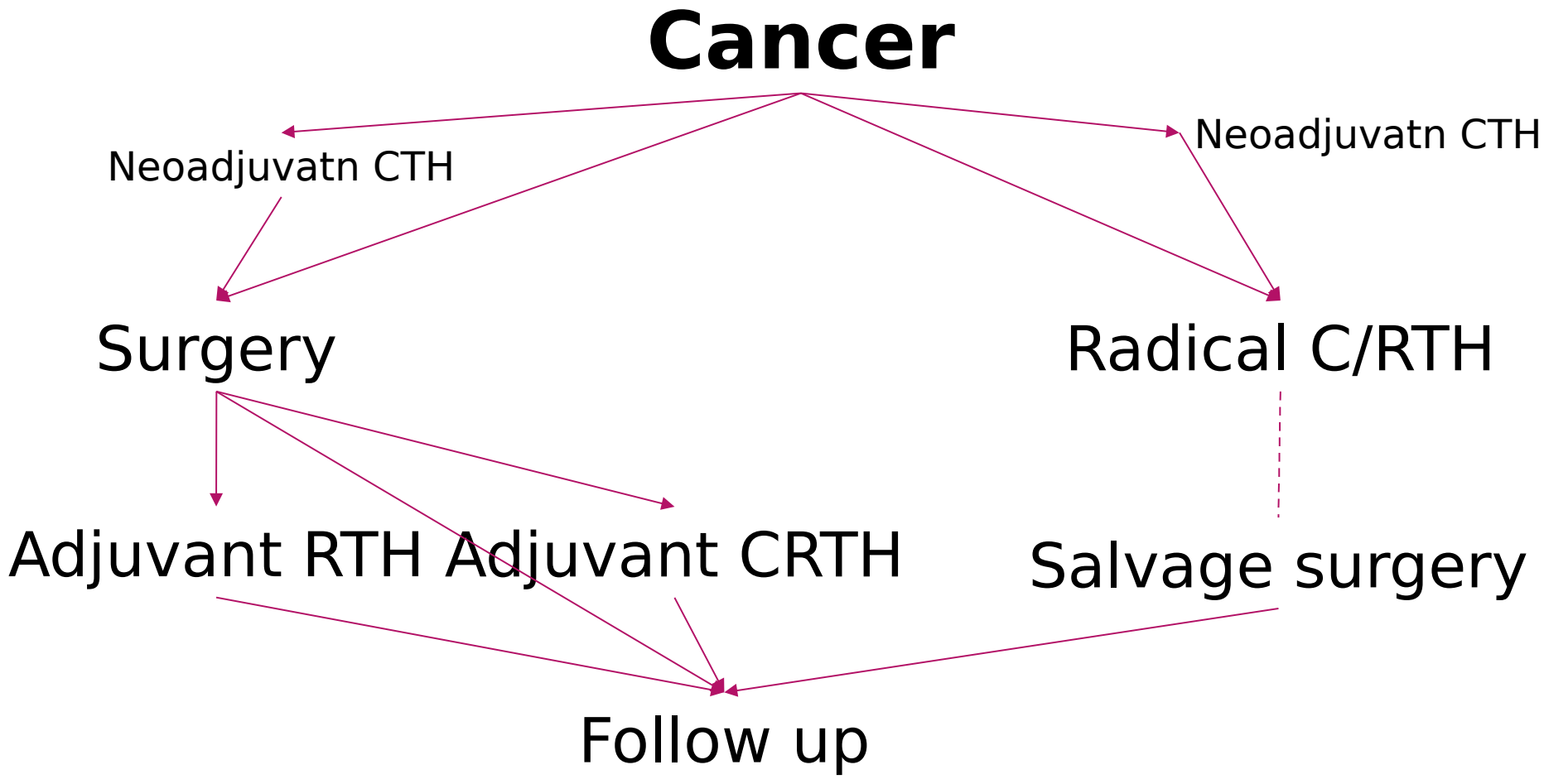
RADIOTHERAPY + CONCURRENT CHEMOTHERAPY

-cisplatin most widely studied

-modest survival advantage over RTH alone

-increased toxicity especially mucositis

Treatment algorithm (oversimplified)



Principles of treatment:

- **CHEMOTHERAPY IN H&N TUMOURS:**

a)palliative treatment for metastatic or recurrent disease

b)neoadjuvant chemotherapy

c)concurrent with RTH in locally advanced H&N tumours:

-improvement in locoregional control of the tumour

d)Adjuvant chemotherapy (rarely)

Impact on survial – 8%

Neoadjuvant chemotherapy

- Performend before surgery or RTH in locally advanced disease.

  -reduction in distant metastases

  -shrinkage of tumour

  -organ preservation

PF (cisplatin + 5FU)

TPF (cisplatin + 5FU + paclitaxel)

Recent studies : negative

Biologic agent

- Way to overcome toxicity of clasic cytotoxic drugs (i.e. cisplatin)
- Most widely studied cetuximab (anty-EGFR antibody)
  - Used in conjunction with radiotherapy
  - Similar outcomes to cisplatin, but much lower morbidity
  - Less evidence than cisplatin.

H&N cancer – recurrent and metastatic disease

- Goal of treatment – curative/**palliative**
- Combined chemotherapy (2 cytotoxics) – platin-based (cisplatin, carboplatin)
- Most frequently used chemotherapy regimen: cisplatin + 5-fluorouracil
- Addition of cetuximab to cispl/5FU chemotherapy improves survival
- For patients in worse general state: monotherapy (metothrexat)
  - **Response rate 30% and survival of 6-12 months**

Optimal way

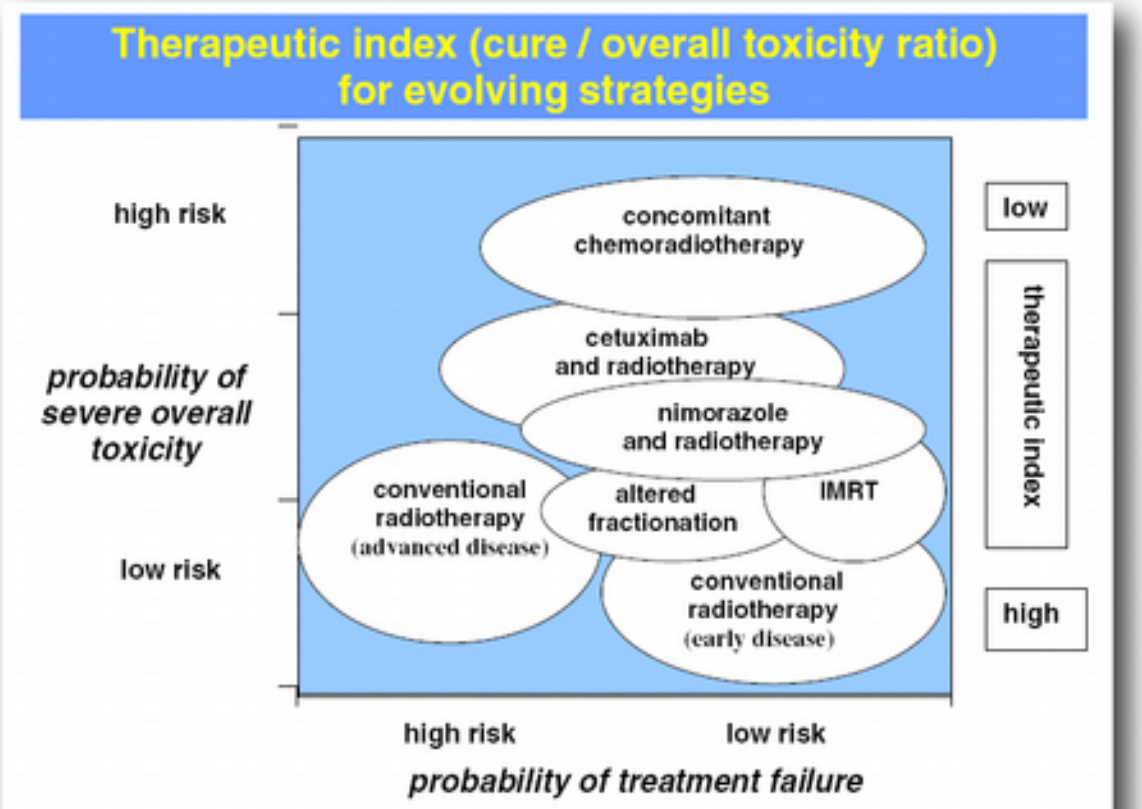


Fig. 1. Potential therapeutic index in HNSCC management as deduced from EBM data interpretation.

HPV in H&N

- Emerging data are clearly indicating that in a subset with positive Human Papilloma Virus (HPV) the **prognosis** may be **better** than for the ordinary patient with HNSCC

- There are data underway which indicate that **HPV infection** is the **most prognostic factor** which outnumbers both Tumor and Nodal status, but this evidence yet needs to be better investigated

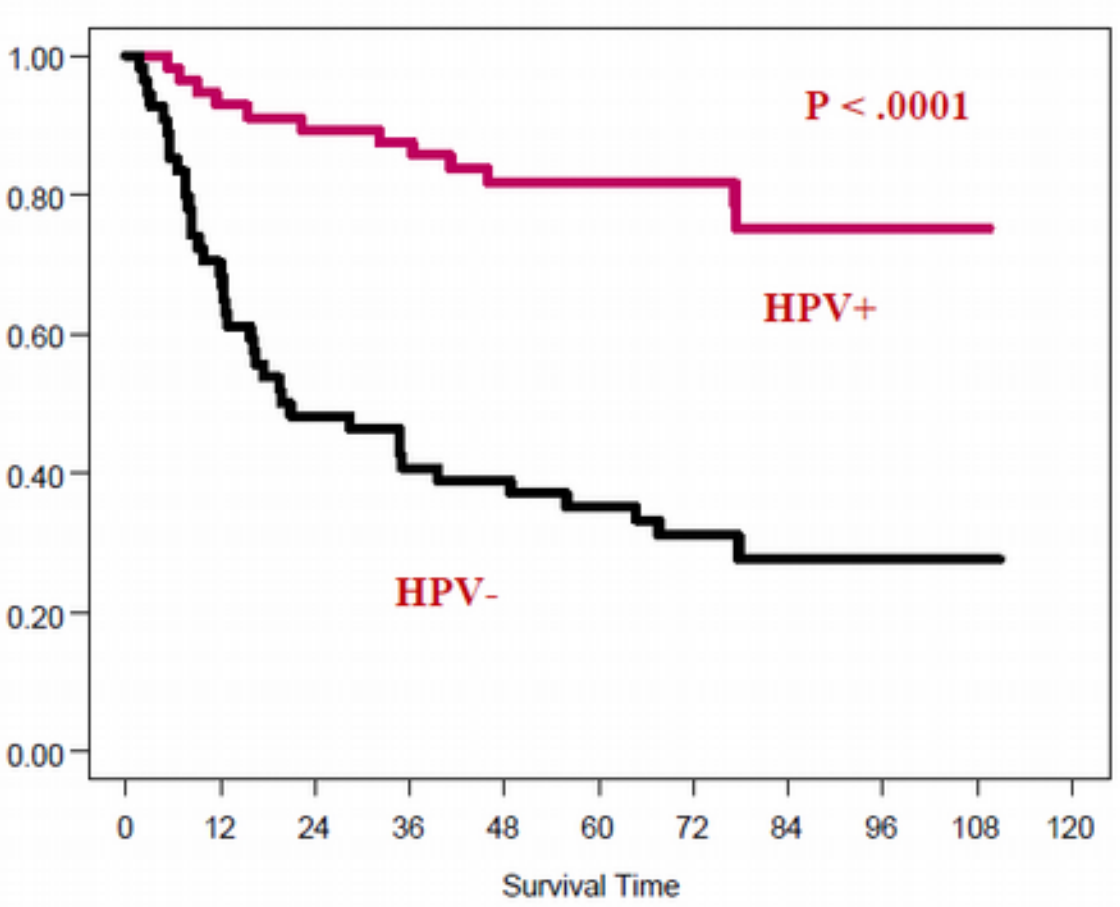
HPV-associated head and neck cancer: a virus-related cancer epidemic. *Lancet Oncol* 2010; 11: 781–89

	HPV-positive tumours	HPV-negative tumours
Anatomical site	Tonsil and base of tongue	All sites
Histology	Non-keratinised	Keratinised
Age	Younger cohorts	Older cohorts
Sex ratio	3:1 men	3:1 men
Stage	Tx, T1–2	Variable
Risk factors	Sexual behaviour	Alcohol and tobacco
Incidence	Increasing	Decreasing
Survival	Improved	Unchanging

Table 2: Differences between HPV-positive and HPV-negative head and neck squamous-cell carcinomas

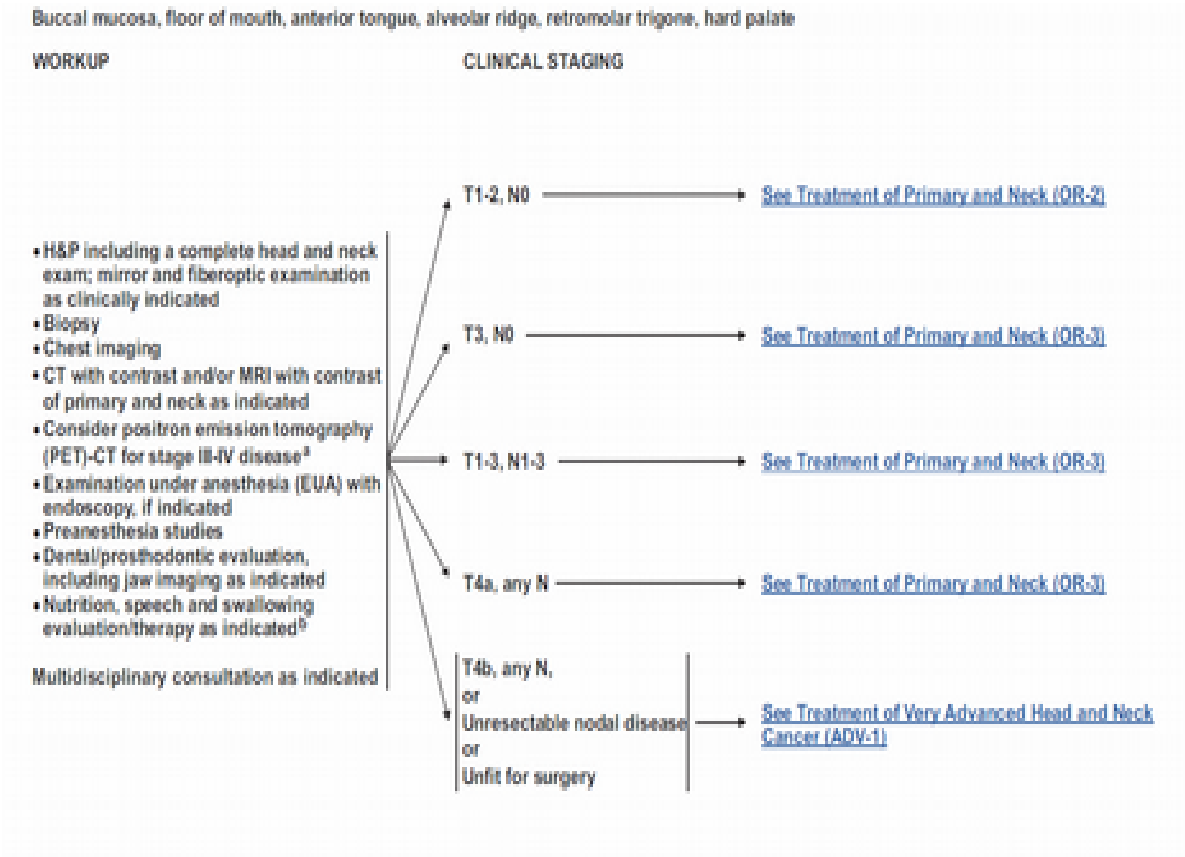
TAX 324 trial:

induction chemotherapy TPF vs PF chemo-radiotherapy



Example

- 58-year-old male patient with history of alcohol and tabacco abuse
- Enlarged, palpable lymph nodes on posterior border of SCM muscle.
- Palpable, ulcerated tumor in anterior 2/3 of tongue
- Problems with swallowing, pain
- Weight loss of 10 kg in last 4 months


Buccal mucosa, floor of mouth, anterior tongue, alveolar ridge, retromolar trigone, hard palate
WORKUP
CLINICAL STAGING
• H&P including a complete head and neck exam; mirror and fiberoptic examination as clinically indicated
• Biopsy
• Chest imaging
• CT with contrast and/or MRI with contrast of primary and neck as indicated
• Consider positron emission tomography (PET)-CT for stage III-IV disease[a]
• Examination under anesthesia (EUA) with endoscopy, if indicated
• Preanesthesia studies
• Dental/prosthodontic evaluation, including jaw imaging as indicated
• Nutrition, speech and swallowing evaluation/therapy as indicated[g]
Multidisciplinary consultation as indicated
T1-2, N0
See Treatment of Primary and Neck (OR-2)
T3, N0
See Treatment of Primary and Neck (OR-3)
T1-3, N1-3
See Treatment of Primary and Neck (OR-3)
T4a, any N
See Treatment of Primary and Neck (OR-3)
T4b, any N,
or
Unresectable nodal disease
or
Unfit for surgery
See Treatment of Very Advanced Head and Neck Cancer (ADV-1)

Staging

- CT scan of H&N : primary tumor : 3 cm
- Single ipsilateral lymph nodes 2 cm.
- Chest X-ray, USG : negative.
- FNA : squamous cell carcinoma G2
- PS 0
- No serious comorbidites

Table 1

American Joint Committee on Cancer (AJCC)

TNM Staging Classification for the Lip and Oral Cavity

(7th ed., 2010)

(Nonepithelial tumors such as those of lymphoid tissue, soft tissue, bone, and cartilage are not included)

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumor more than 4 cm in greatest dimension
T4a	Moderately advanced local disease* (lip) Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, that is, chin or nose (oral cavity) Tumor invades adjacent structures (eg, through cortical bone [mandible or maxilla] into deep [extrinsic] muscle of tongue [genioglossus, hyoglossus, palatoglossus, and styloglossus], maxillary sinus, skin of face)
T4b	Very advanced local disease Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

*Note: Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumor as T4.

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
N2	Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N2a	Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3	Metastasis in a lymph node more than 6 cm in greatest dimension

Distant Metastasis (M)

M0	No distant metastasis
M1	Distant metastasis

Histologic Grade (G)

GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

Continued...

Table 1 - Continued

American Joint Committee on Cancer (AJCC)

TNM Staging Classification for the Lip and Oral Cavity

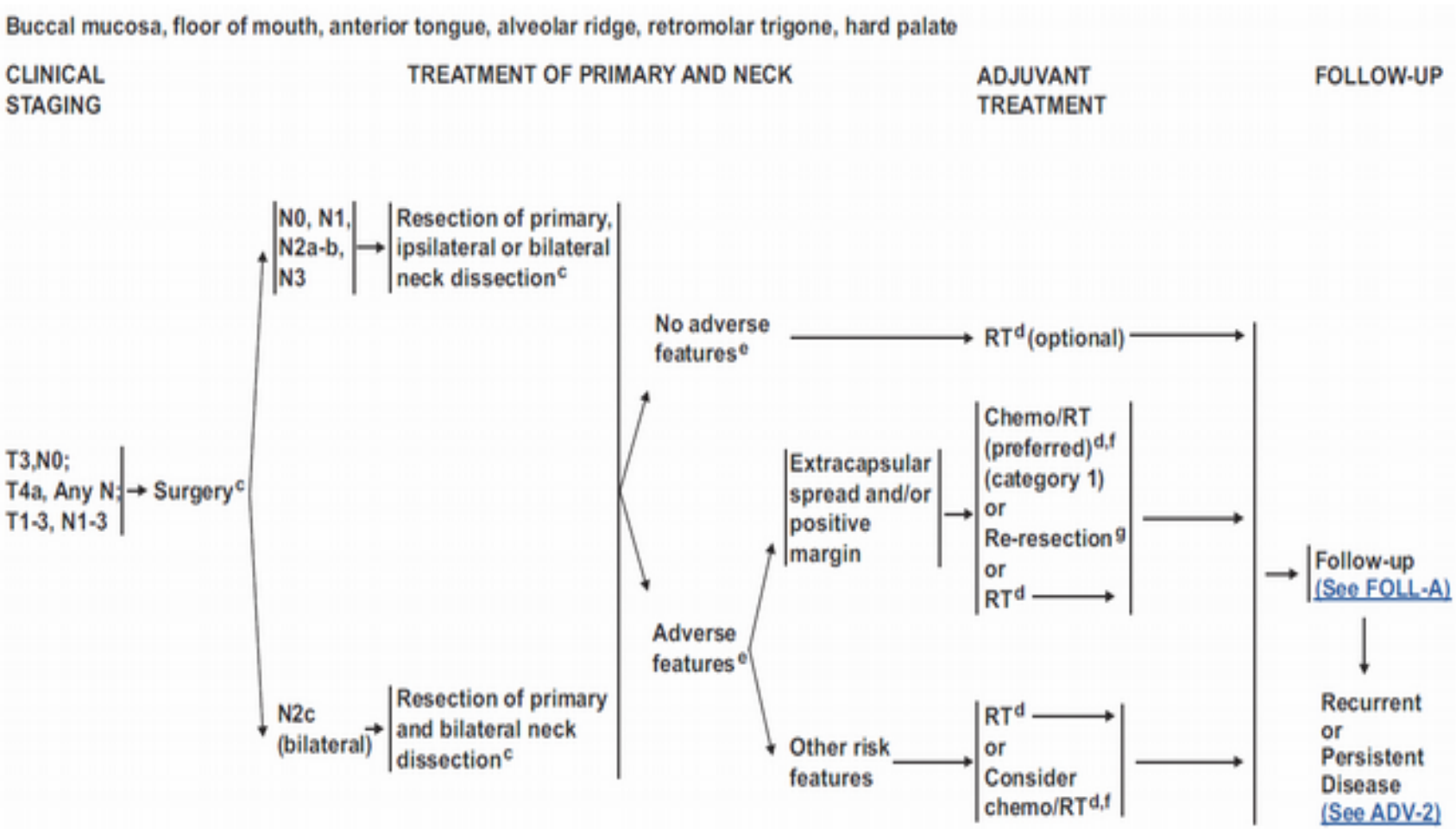
(7th ed., 2010)

(Nonepithelial tumors such as those of lymphoid tissue, soft tissue, bone, and cartilage are not included)

Anatomic Stage/Prognostic Groups			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

Pretreatment :

- Locoregional H&N squamous cell carcinoma
- T2N1M0G2
- PS 0


Buccal mucosa, floor of mouth, anterior tongue, alveolar ridge, retromolar trigone, hard palate
CLINICAL STAGING
TREATMENT OF PRIMARY AND NECK
ADJUVANT TREATMENT
FOLLOW-UP
T3,N0; T4a, Any N; T1-3, N1-3
Surgery[c]
N0, N1, N2a-b, N3
Resection of primary, ipsilateral or bilateral neck dissection[c]
N2c (bilateral)
Resection of primary and bilateral neck dissection[c]
No adverse features[e]
RT[d] (optional)
Adverse features[e]
Extracapsular spread and/or positive margin
Chemo/RT (preferred)[d,f] (category 1) or Re-resection[g] or RT[d]
Other risk features
RT[d] or Consider chemo/RT[d,f]
Follow-up (See FOLL-A)
Recurrent or Persistent Disease (See ADV-2)

Pathological report

- pT3N2aG2
- Positive margins
- 4 lymph nodes removed (1/4)
- No additional risk factors

What now?

- Second surgery (total glossectomy)
- Radiochemiotherapy
- Radiotherapy
- Observation
- ???

- Patient recevied full RCTH treatment with 3 cycles of cisplatin 100 mg/m2 every 3 weeks and 60 Gy (2.0Gy/fraction) on primary site and neck.
- During treatment : mucositis G2, xerostomia G2.

Follow-up

FOLLOW-UP RECOMMENDATIONS
(based on risk of relapse, second primaries, treatment sequalae, and toxicities)

- H&P exam[1]:
  - Year 1, every 1-3 mo
  - Year 2, every 2-6 mo
  - Years 3-5, every 4-8 mo
  - >5 years, every 12 mo
- Post-treatment baseline imaging of primary (and neck, if treated) recommended within 6 mo of treatment[2] (category 2B)
  - Further reimaging as indicated based on signs/symptoms; not routinely recommended for asymptomatic patients
- Chest imaging as clinically indicated (See NCCN Guidelines for Lung Cancer Screening)
- Thyroid-stimulating hormone (TSH) every 6-12 mo if neck irradiated
- Speech/hearing and swallowing evaluation and rehabilitation as clinically indicated
- Smoking cessation and alcohol counseling as clinically indicated
- Dental evaluation
  - Recommended for oral cavity
  - As indicated for oropharynx, hypopharynx, and nasopharynx
  - As indicated for other sites, if significant intraoral radiation
- Consider EBV monitoring for nasopharynx

Q&A

- **Thank you all for your attention!**