

NCG Guidelines Version.3

Management of Head and Neck Cancers

INITIAL REMARKS

- The guidelines have been formulated in line with the latest evidence available at the time they were laid out.

They incorporate available evidence and also the considered opinion of the Expert group.

- All the available treatment options have been considered and resource stratified as Essential, Optimal, and Optional. The definition of the same are given below.

Essential: This would be considered as the minimum treatment that should be provided. The recommendation is based on evidence, practicality (wide availability of expertise and infrastructure), as well as the cost of treatment and the value it offers. If centers do not have the capabilities to implement these, they should refer patients to a higher center.

Optimal: Based on both evidence as well as cost effectiveness.

Optional: Based on the available evidence (some could be standard of care) with no consideration for cost effectiveness. These options should be considered and undertaken when affordable (employer insurance scheme, personal insurance scheme etc.)

- For most situations more than one treatment option is listed.
- It is strongly recommended that Optimal Care includes the constitution of a Tumor Board/ Joint Cancer Clinic with mechanisms for cross- specialty inputs at the basic minimum from Surgical and Radiation specialists, and optimally from Medical oncology specialists and other specialties.

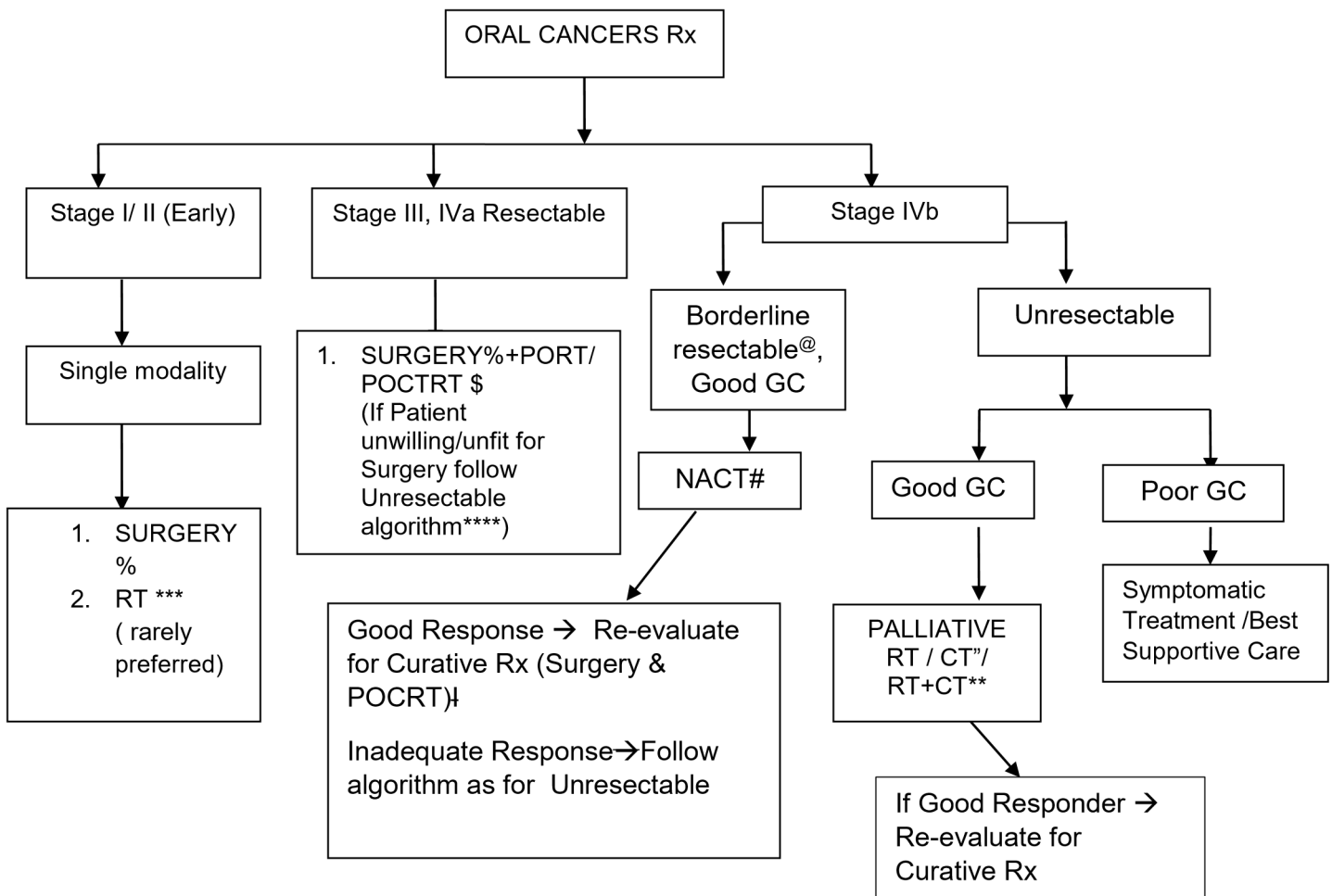
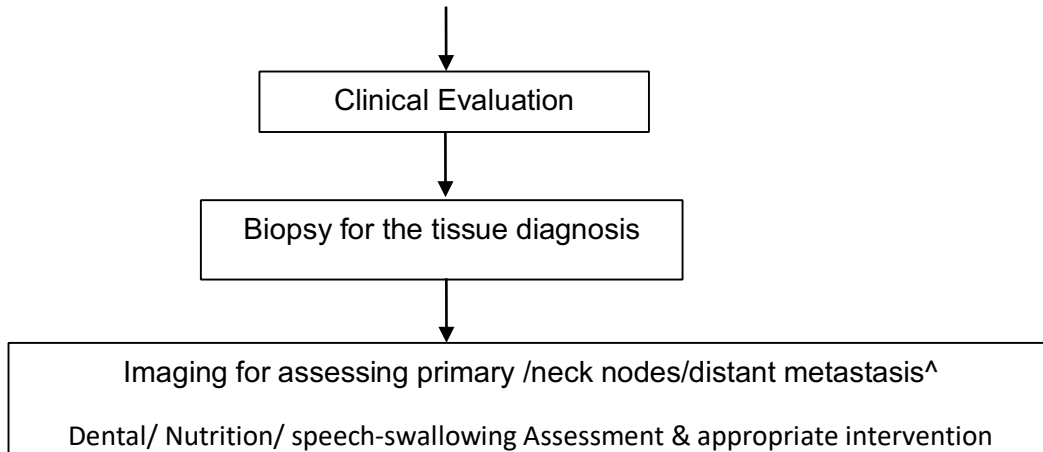
The current guidelines may be taken as guiding principles, but treatment decisions may need to be individualized and to be based on disease status, patient's general health and co-morbidities, social support, treatment center feasibility, circumstances and expertise, and consideration to the patient's expectations and desires.

- Decisions regarding intent of treatment (Curative/ Curative & Organ Preserving / Palliative / Response Assessment and reassess) need to be taken early and communicated to patients. Integration of palliative care must be considered at the earliest for cases where it is deemed appropriate.
- Clinicians must encourage patients to participate in clinical trials. The option of participating in these trials must also be provided to the patients whenever appropriate.
- Post completion of initial treatment, focus should be directed to rehabilitation and survivorship issues for patients.

ORAL CANCER

ORAL CANCER- ASSESSMENT/ Workup-
Non-healing ulcer over the lip/tongue/cheek/gums/palate

Loose teeth/ Earache/ Metastatic Lymph nodes



^- Optimal Imaging modality for tongue lesion is a MRI and for other sites a Contrast enhanced CT scan. Loco regional imaging is for assessment of the primary and the neck. Early stage oral cavity that is amenable to adequate clinical evaluation may not warrant imaging studies of the primary and Ultrasound examination of the neck is an optional alternative to CECT/MRI in this situation.

Chest X-ray is an essential investigation for ruling out lung metastasis and possible aspiration. Either a PET CT(Optional) or CECT Thorax (Optimal) should be preferred in patients being considered for curative therapy but with a high risk for distant metastasis (N3 node (size > 6 cm), multiple bilateral neck nodes, Lower cervical neck nodes , large primary (T4b) and in patients who have symptoms suggestive of distant metastasis.

%- Surgery - Primary tumor- Wide local excision (at least 1 cm gross margin so as to achieve > 5 mm histological tumor free margin) with appropriate Neck Dissection and appropriate reconstruction. For N0 Neck- Selective neck dissection addressing Level I-III (Essential)+/- Level IV. For N+ Neck – Modified neck dissection (Level I-V) with sparing of the XI nerve, IJV, SCM Muscle whenever oncologically feasible (Essential). The minimum optimal number of lymph nodes included in a SND should be >10 and in a MND >14.

***-The option of Radiation therapy for early oral cancers is preferred only for lip tumors and selected other sub sites. Tumors abutting the mandible risk osteoradionecrosis. The treatment should preferably include brachytherapy as a part of treatment. Either complete dose or partial dose should be delivered by brachytherapy.

****The option of Radiation Rx/ Chemo radiation Rx for advanced tumors is applicable only for patients who are unfit and unwilling for surgery, and target volumes that can be safely encompassed by a tumoricidal dose of 70 Gy. Patients with gross mandibular erosion risk osteoradionecrosis and are not suitable for this modality. Tumors abutting the mandible and tumors with gross skin ulceration are also at greater risk of complications.

\$- Indication for adjuvant post-op radiotherapy are T3-T4 primary, Node positivity, perineural invasion, lymphovascular invasion, and poorly differentiated disease. IMRT may be considered (Optional) if affordable (employer insurance scheme, personal insurance schemes) and available. Adjuvant post-op concurrent chemoradiation is indicated for positive margin and presence of extra nodal extension/extracapsular spread, and presence of nodal positivity of 2 or more lymph nodes. The options for adjuvant concurrent chemotherapy are- Cisplatin 100 mg/m² (preferred option) or weekly cisplatin 30-40 mg/m². Audiometry is preferred prior to administration of cisplatin.

@- Borderline Resectable - This is broadly a situation wherein the primary tumor is grossly resectable, but significant concern exists regarding the probability of a positive resection margin or excessive surgical morbidity. The decision regarding borderline resectability should be taken by a surgeon (preferably in a multidisciplinary tumor board). Situations which may be deemed as borderline resectable are-

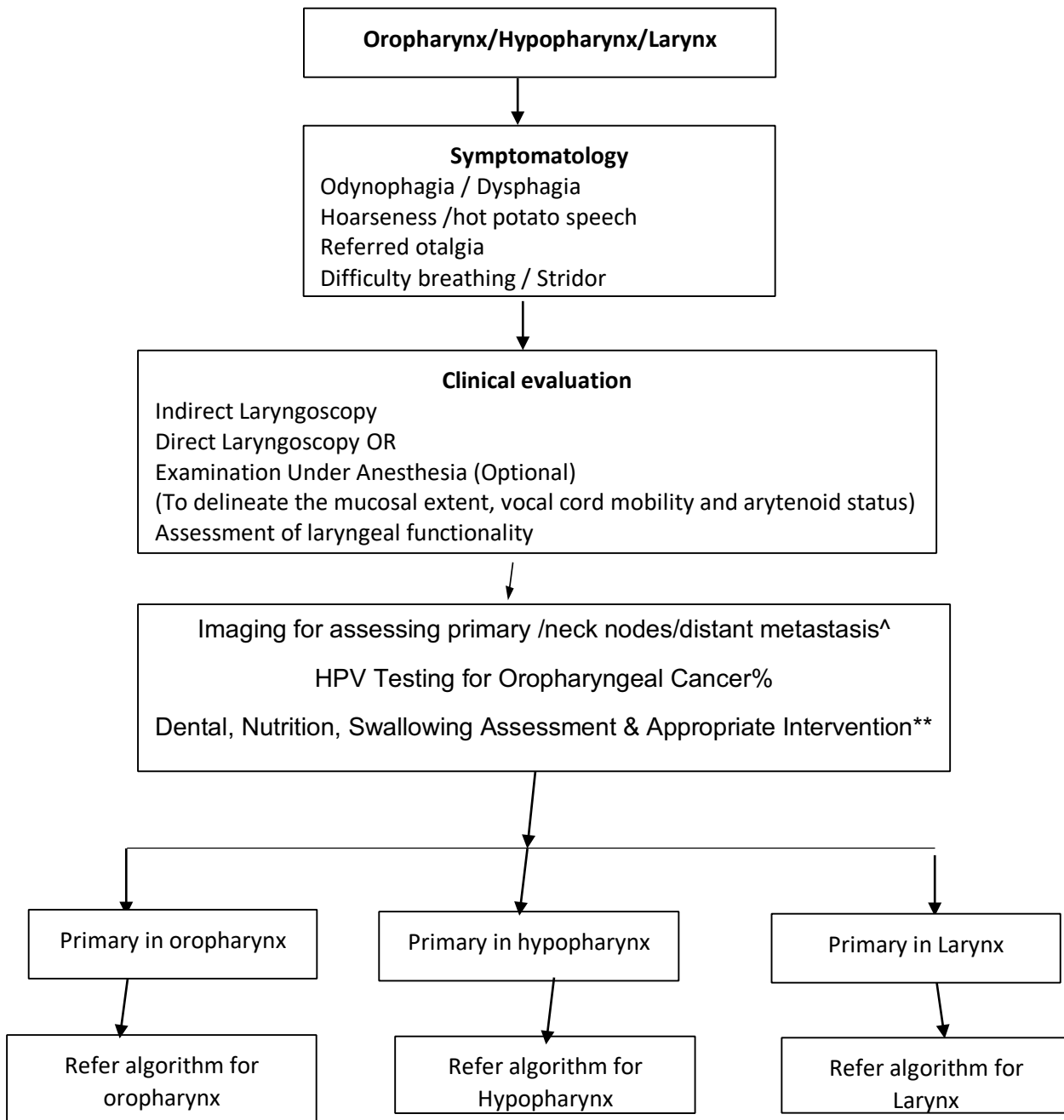
1. Soft tissue swelling up to the zygoma in case of a BM-GBS primary.
2. Disease close to hyoid or valleculae in case of a Tongue primary.
3. Some situations with Extensive skin infiltration and Involvement of (Supra-notch) infratemporal fossa.

Radiological involvement of the infratemporal fossa which is inferior to the level of the mandibular notch is deemed as resectable by current surgical techniques.

If the treating team (surgeon) considers the lesion to be resectable then surgery should be offered as per the algorithm for operable oral cancers.

*Options for first line palliative chemotherapy include-

- Cytotoxic chemotherapy (single agent or combination)- metronomic chemotherapy consisting of weekly methotrexate-celecoxib; or combination Chemotherapy (Platinum, 5-FU, Taxane)
- 5FU– Platinum –Cetuximab - or Paclitaxel -Platinum-Cetuximab - (Optional);
- Pembrolizumab (if deemed appropriate with genetic testing for PDL1 and mutation load) – Optional

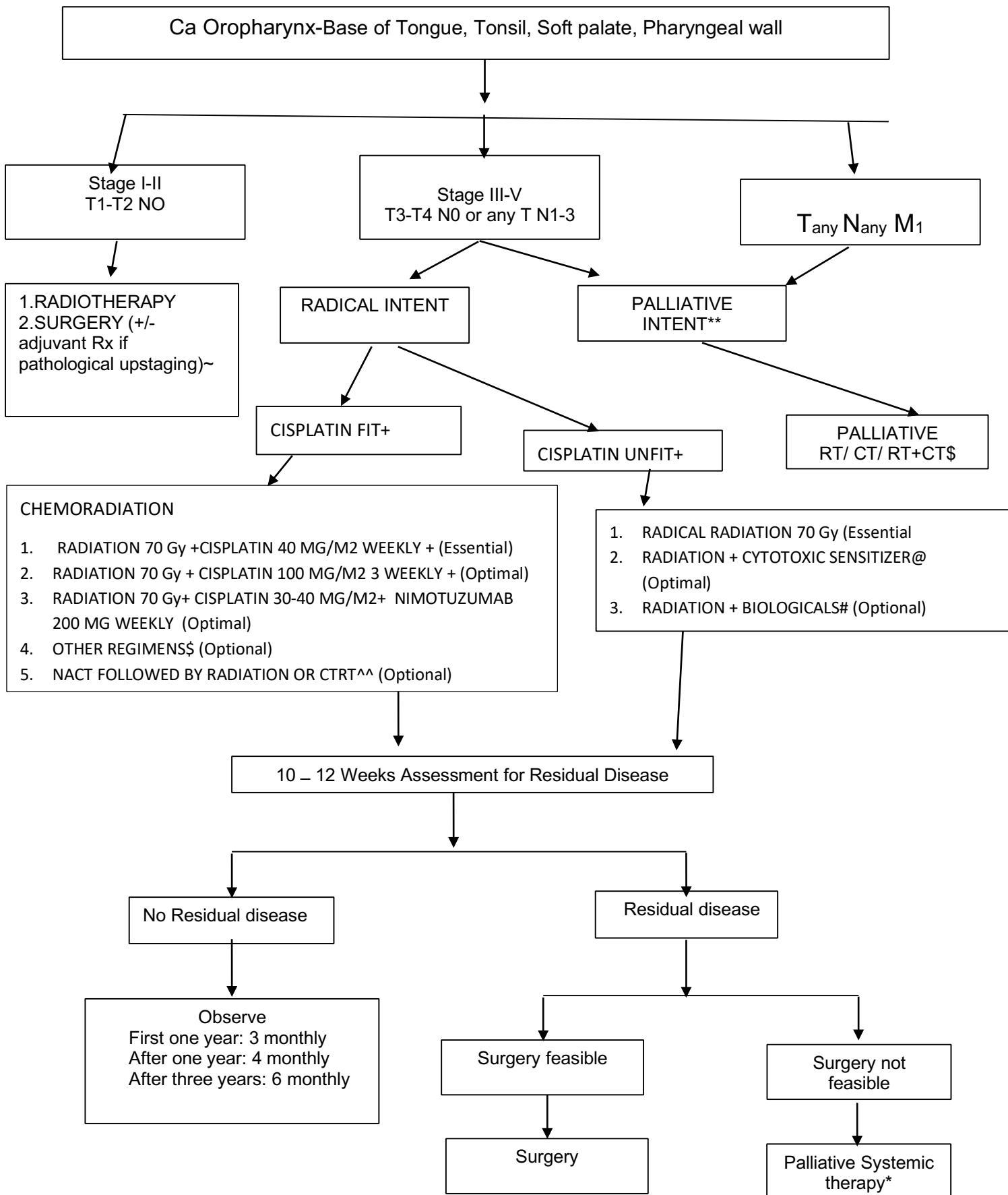


^- Optimal Imaging modality for the primary and the neck may be by a CECT or MR. A MRI may be preferred for the Oropharynx and a CECT for the larynx and hypopharynx.

Chest X-ray is an essential investigation for ruling out lung metastasis and possible aspiration. Either a PET CT(Optional) or CECT Thorax (Optimal) should be preferred in patients being considered for curative therapy but with a high risk for distant metastasis (N3 node (size > 6 cm), multiple bilateral neck nodes, Lower cervical neck nodes , large primary (T4b), advanced hypopharyngeal cancer , and in patients who have symptoms suggestive of distant metastasis.

%- HPV testing is Optimal for all Oropharyngeal Cancers. This may be by p16 (Optimal). If expertise and facilities are available, then HPV mRNA testing is more specific (Optional). HPV+Ve Oropharyngeal Cancer is however currently noted in < 20% as per Indian studies and testing is not yet routine.

** - Assessment for speech and swallowing to evaluate for aspiration is considered Optimal. At least a 100 ml Bed side water swallowing test should be considered (Optimal). If facility available, Fiber optic endoscopic evaluation of swallowing or Videofluoroscopy evaluation of swallowing to be undertaken (Optional)



~- Selected T1-2N0 lesion of tonsil – Base Tongue can be considered for minimally invasive Trans Oral Surgery (Laser/ Robotic) surgery (Optional) to achieve a margin negative resection of the primary (tumour free margin of 3-5 mm). This needs to be accompanied with selective neck dissection and appropriate adjuvant RT/ CTRT as indicated by surgical histology.

\$- carboplatin -5FU or 5FU-Hydroxyurea or paclitaxel-cisplatin. These options were tested in platinum fit patients. Expertise in delivering chemotherapy is required for these regimens.

@- The options in non-cisplatin fit are carboplatin -5FU or 5FU-Hydroxyurea. These options were tested in platinum fit patients and hence while administering them in cisplatin unfit patients caution is mandated. Expertise in delivering chemotherapy is required for these regimens.

#- Either Cetuximab or Nimotuzumab can be used in this setting, Optimal if affordable (employer insurance scheme, personal insurance schemes) and available. However, these options were tested in platinum fit patients and hence while administering them in cisplatin unfit patients caution is mandated. Expertise in delivering chemotherapy is required for these regimens.

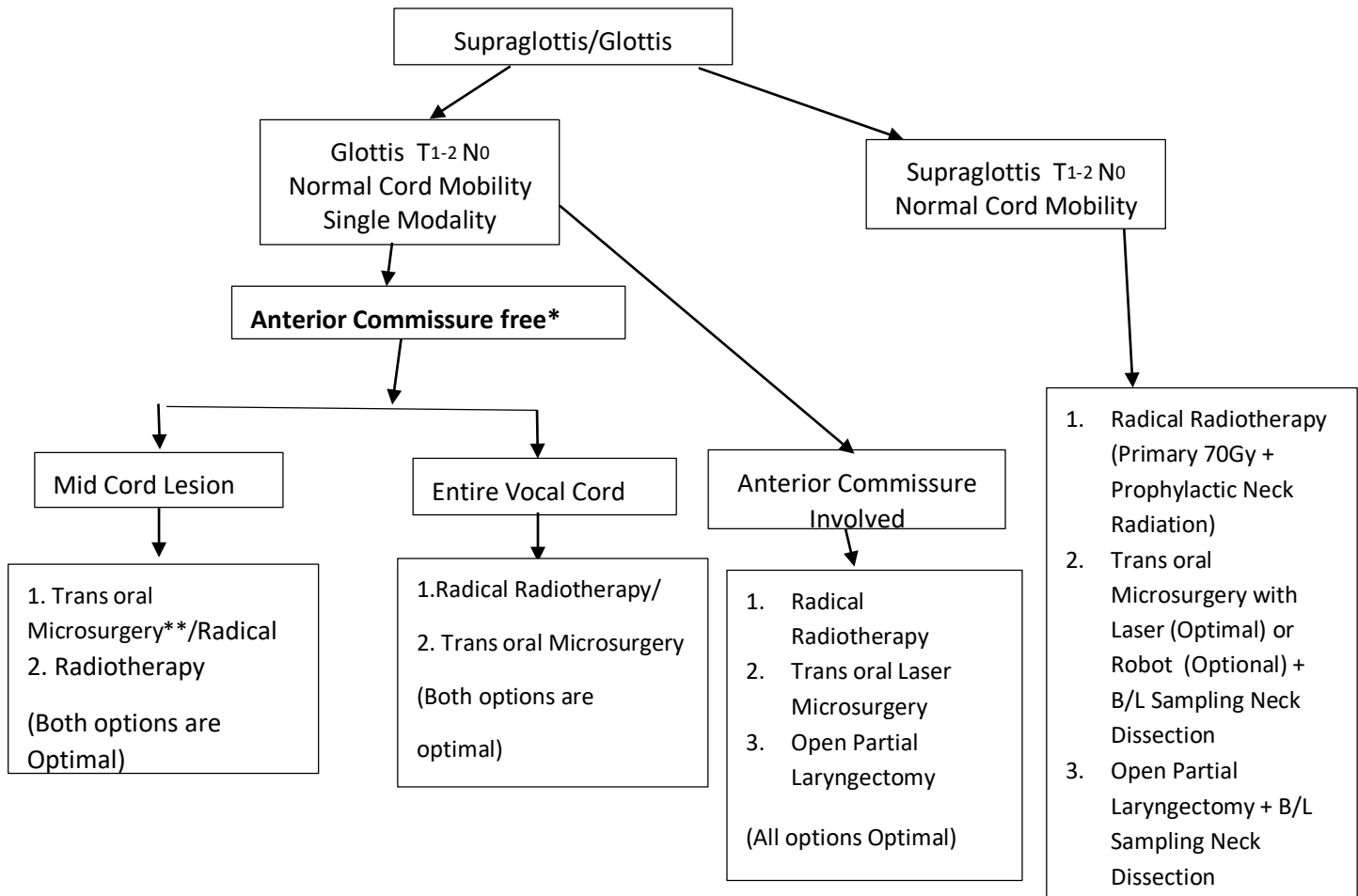
^^- Indications for neoadjuvant chemotherapy are N3 lymph node (> 6 cm) and extensive soft tissue extension, which is difficult to encompass safely in radiation portals. Post induction chemotherapy patients may be routed to Curative therapy or Palliative therapy as per clinical response and reassessment of General Condition.

** - Large T4b lesions or large multiple N3 nodes (> 6 cm) could be considered for palliative therapy. In case of elderly patients or those with poor social support with very advanced disease this option can be considered.

+ - The criteria for cisplatin fitness can be adopted from Ahn et al [Oral Oncol.](#) 2016 Feb;53:106.

doi: 10.1016/j.oraloncology.2015.11.019

\$Options for palliative chemotherapy - As listed in section for Oral Cancer



*At least a 16 slice CT scan with 3 mm cut should be preferred to evaluate involvement of cartilage.

** - Tumor free margin of at least 1-2 mm should be achieved.

*** The risk of occult metastasis to the neck needs to be addressed in all treatments for Supraglottic Cancer.

Glottis/Supraglottis T1-2 N1-3
Normal Cord Mobility

Non-Surgical
Option***

Surgical Option for Primary

Cisplatin
Fit+

Cisplatin
Unfit+

1. Trans oral Surgery with laser or Robot and appropriate neck dissection. Pathology directed adjuvant post op therapy (RT/CT-RT)
2. Open Partial laryngectomy* with appropriate neck dissection and pathology directed adjuvant post op therapy (RT/CT-RT)**

1. RADICAL RADIATION (Essential)
2. RADIATION + CYTOTOXIC SENTIZER@ (Optimal)
3. RADIATION + BIOLOGICALS# (Optional)

- 1 Concurrent CHEMORADIATION
- ☐ RADIATION 70 Gy + CISPLATIN 100 MG/M² 3 WEEKLY (Optimal)
 - ☐ RADIATION 70 Gy + CISPLATIN 40 MG/M² WEEKLY (Essential)
 - ☐ RADIATION 70 Gy + CISPLATIN 30-40 MG/M²+ NIMOTUZUMAB 200 MG WEEKLY (Optimal)
 - ☐ OTHER REGIMENS\$ (Optional)
- 2.NACT FOLLOWED BY CRT / RT^^ (Optional)

*Conservative laryngeal surgeries (Open partial laryngectomy) for Glottic growth / Supraglottic Laryngectomy for Supraglottic growth. Case selection should include considerations of anatomical spread to warrant a reasonable expectation of a R0 resection, and also physiological considerations with regard to pulmonary and swallowing function to minimize post-surgical swallowing dysfunction and aspiration.

** Indication for adjuvant post-op radiotherapy are T3-T4 primary, Node positivity, perineural invasion, lymphovascular invasion, and poorly differentiated disease. Adjuvant post-op concurrent chemoradiation is indicated for positive margin, and presence of extra nodal extension/extracapsular spread. The options for adjuvant concurrent chemotherapy are- Cisplatin 100 mg/m² on day 1,22, 43 or weekly cisplatin 30-40 mg/m². Audiometry is preferred prior to administration of cisplatin.

+ - The criteria for cisplatin fitness can be adopted from Ahn et al [Oral Oncol.](#) 2016 Feb;53:10-6. doi: 10.1016/j.oraloncology.2015.11.019

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^- Post induction chemotherapy the options for concurrent are weekly cisplatin (30 mg/m²), weekly carboplatin or weekly Cetuximab or weekly Nimotuzumab.

Supra Glottis/Glottis T₃ N₀₋₃
 Impaired Cord Mobility / Fixed cord
 CT - SCAN Larynx – Paraglottic Space /Pre-epiglottic
 Space Involvement
 Operable Neck nodes

Laryngeal function intact
 & Cisplatin fit+

Laryngeal function intact
 & cisplatin unfit+

Laryngeal Function
 Compromised

1. CHEMORADIATION

A) Concurrent CHEMORADIATION

- RADIATION 70 Gy + CISPLATIN 100 MG/M² 3 WEEKLY (Optimal)
- RADIATION 70 Gy + CISPLATIN 40 MG/M² WEEKLY (Essential)
- RADIATION 70 Gy + CISPLATIN 30-40 MG/M²+ NIMOTUZUMAB 200 MG WEEKLY (Optimal)
- OTHER REGIMENS\$ (Optional)

B) NACT FOLLOWED BY RT / CTRT^^ (Optimal)

*If CR/PR – consider RT/ CTRT
 *If <PR / stable disease -> surgery followed by RT/CTRT

2. Open Partial laryngectomy* with appropriate neck dissection and pathology directed adjuvant post op therapy (RT/CT-RT)** (Occasionally appropriate)*

- RADICAL RADIATION(Essential)
- RADIATION + CYTOTOXIC SENTIZER@ (Optimal)
- RADIATION + BIOLOGICALS# (Optional)
- Open Partial Laryngectomy* with appropriate neck dissection with adjuvant therapy (RT/CT-RT) (Occasionally appropriate/Optional)*

Near-Total Laryngectomy / Total Laryngectomy with TEP# & bilateral appropriate neck dissection with adjuvant therapy (RT/CT-RT) (Optimal)**

*Conservative laryngeal surgery (Supracricoid Laryngectomy) for Glottic growth / Supraglottic Laryngectomy for Supraglottic growth is occasionally appropriate in the situation of mobile cords but T3 staging in view of paraglottic space/ pre-epiglottic space involvement.

A Tracheo-Esophageal Prosthesis (TEP) for speech rehabilitation is appropriate and optimal for most patients undergoing a Total Laryngectomy

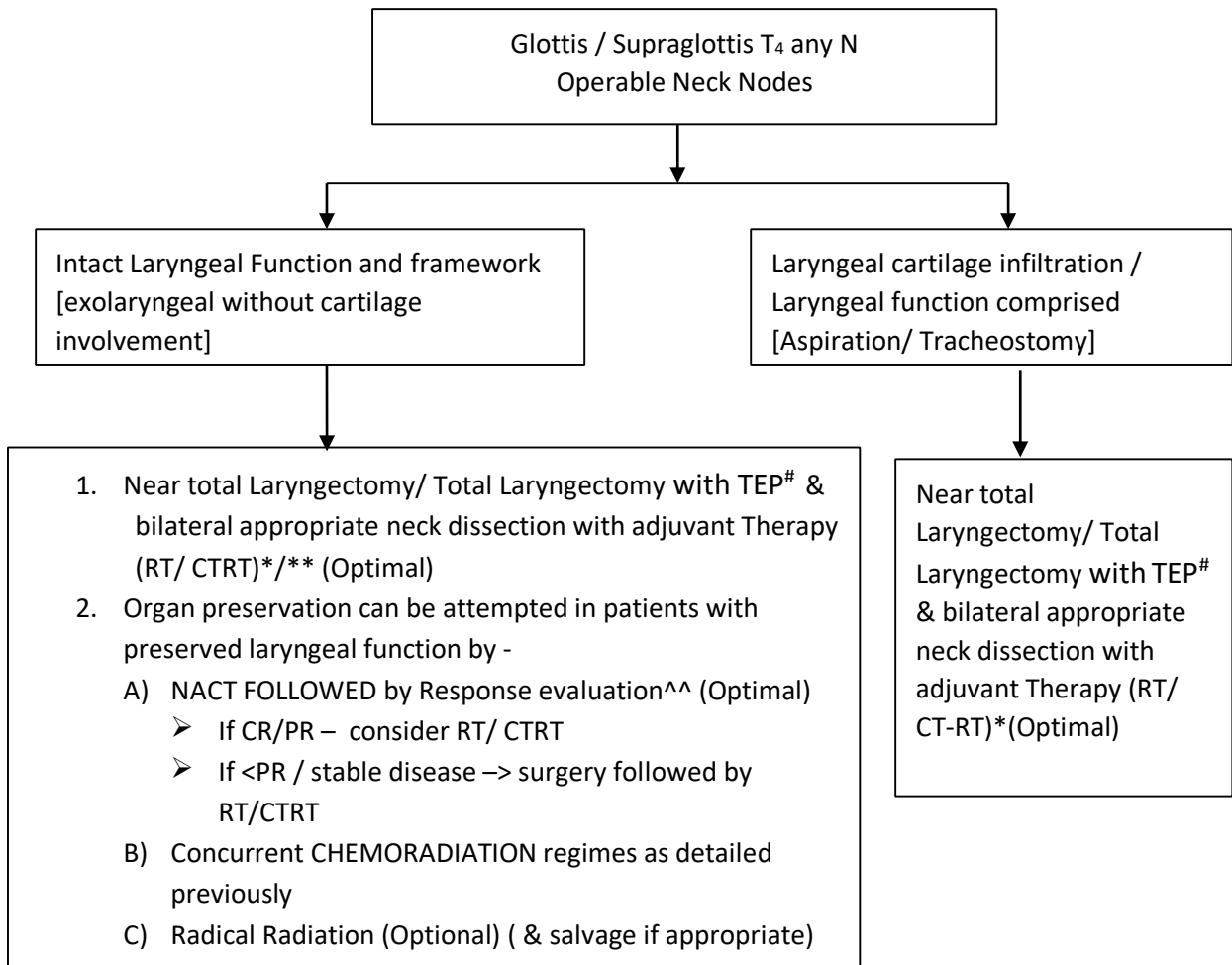
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*- Surgery remains the preferred option. Non-surgical options are likely to compromise cure rates especially in the setting of cartilage erosion. Patients may however choose for a laryngeal preserving non-surgical option despite the risks towards cure.

Some situations with anterior commissure related Thyroid cartilage erosion with mobile cords may be appropriate for surgical organ preservation with partial laryngectomy rather than Total/Near-total laryngectomy.

For patients undergoing Total Laryngectomy, a Tracheo-Esophageal Prosthesis (TEP) for speech rehabilitation is appropriate and optimal

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Hypopharynx T₁/ T₂
Both Cords Mobile

Clinicoradiological N0

Clinicoradiological N+

- Radical Radiotherapy (Optimal)
- Trans oral Laser Microsurgery with selective neck dissection.
* (Optional)

- NACT FOLLOWED BY Response Evaluation^^ (Optimal)
If CR/ PR → Radical RT/ CRTT
If <PR / stable disease → Surgery & post op
RT/CRTT^^

- Concurrent CHEMORADIATION

Cisplatin Fit

- RADIATION 70 Gy + CISPLATIN 40 MG/M² WEEKLY (Essential)
- RADIATION 70 Gy + CISPLATIN 100 MG/M² 3 WEEKLY (Optimal)
- RADIATION 70 Gy + CISPLATIN 30-40 MG/M²+ NIMOTUZUMAB 200 MG WEEKLY (Optimal)
- Other Regimens (Optional)

Cisplatin unfit+

1. Radical Radiation (Essential)
2. Concurrent RT with Biologicals # or other regimens@ (Optional)
3. Conservation laryngeal surgery with appropriate neck dissection & Post op RT/CRTT as appropriate
*/** (Optional)

*Surgical Organ preservation should be considered in select cases as expertise for the same is not widely available.

Case selection should include considerations of anatomical spread to warrant a reasonable expectation of a R0 resection, and also physiological considerations with regard to pulmonary and swallowing function to minimize post-surgical swallowing dysfunction and aspiration.

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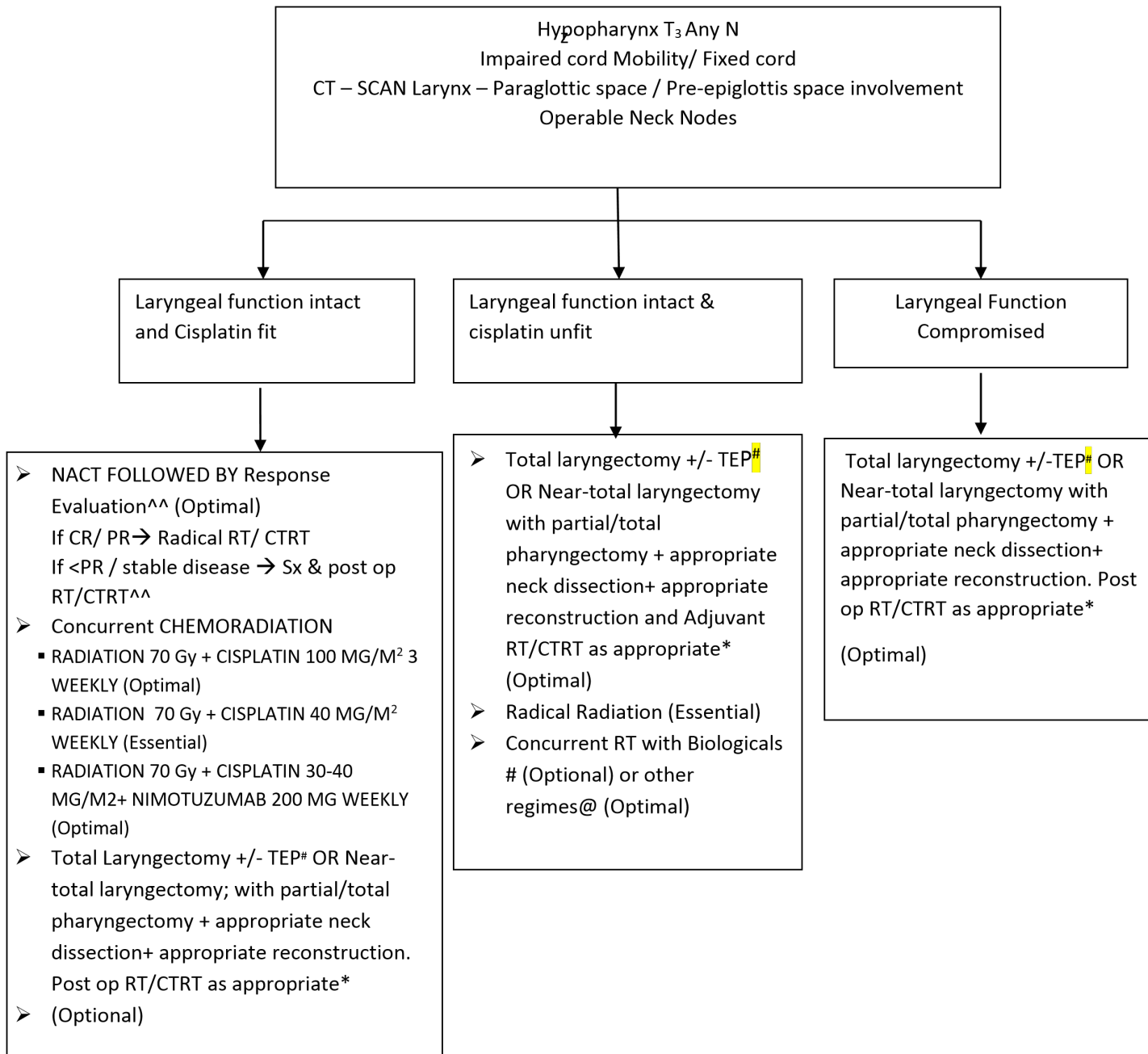
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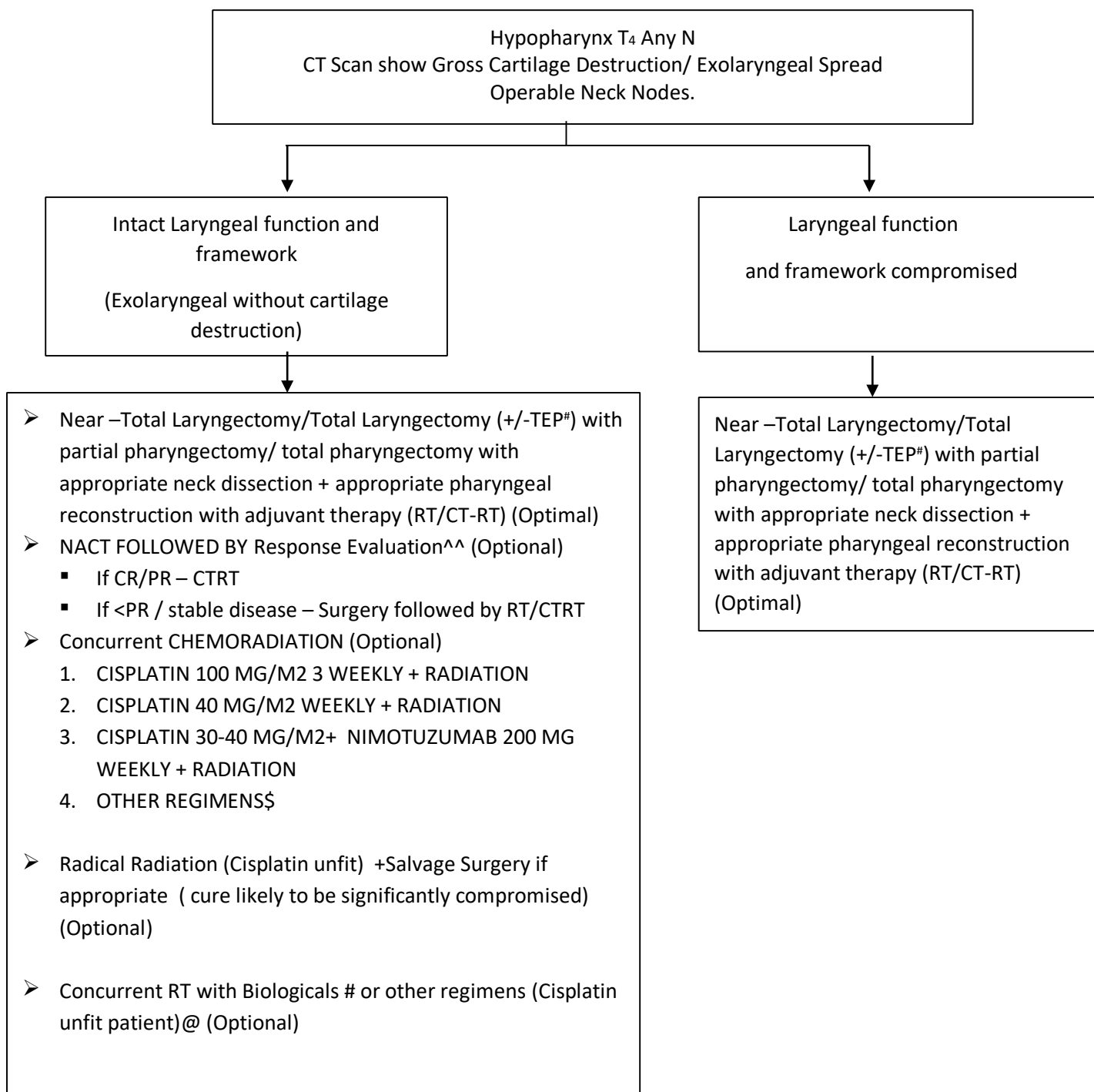
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**Larynx and Hypopharynx
Any T Inoperable Neck Nodes**

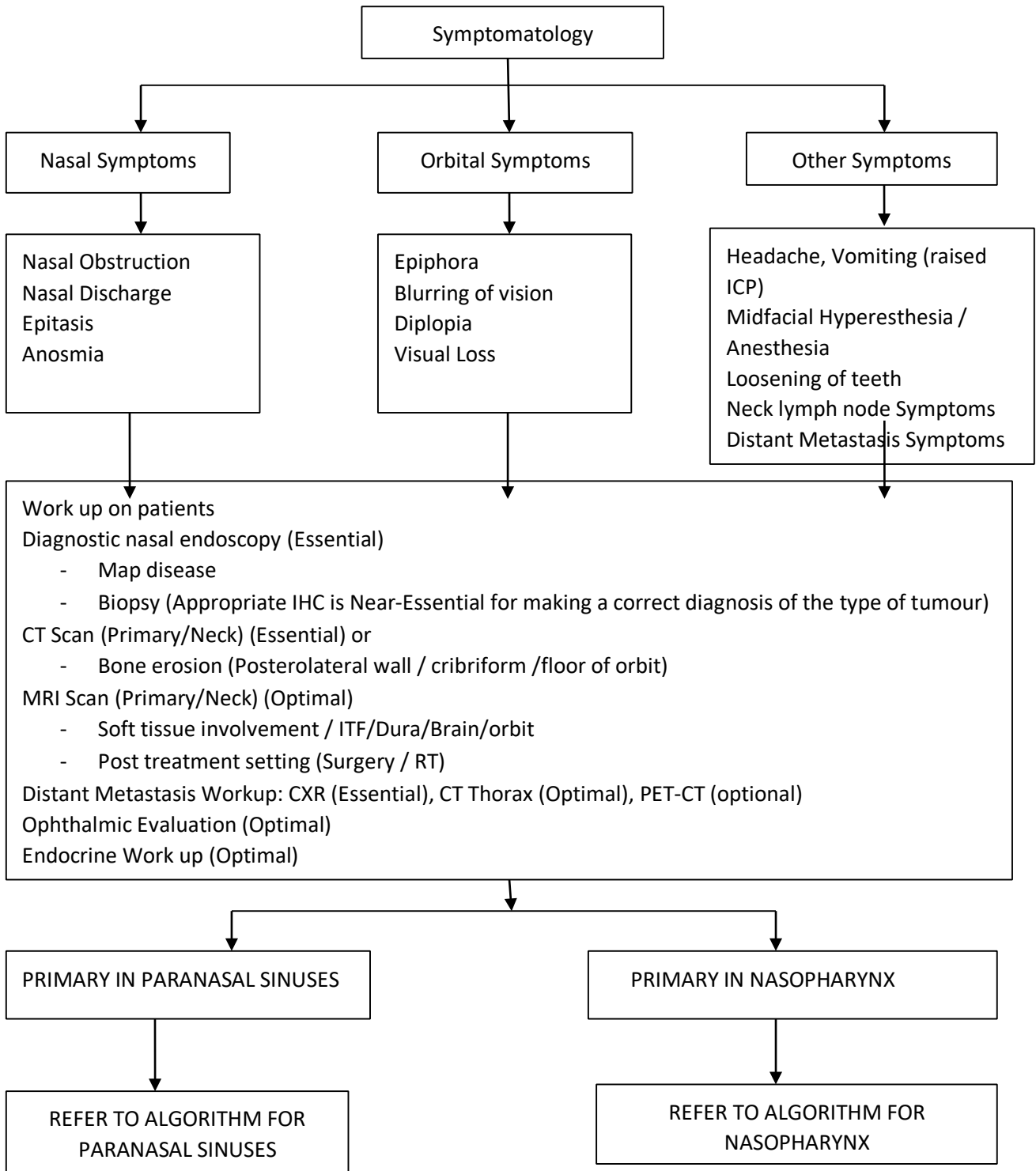
ECOG performance 0-1

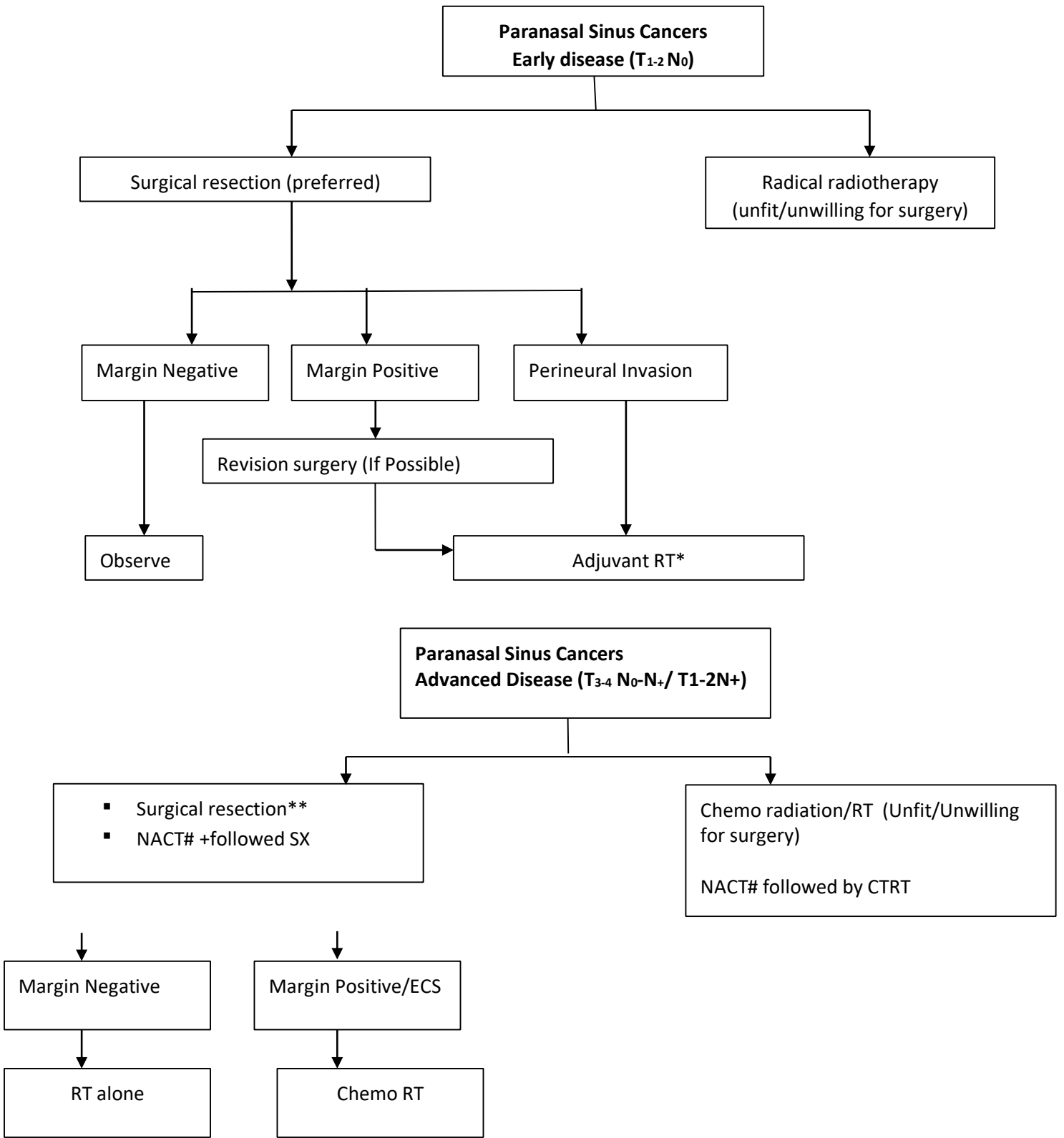
ECOG performance >2

- Cisplatin fit
- NACT FOLLOWED BY Response Assessment^^ (Optimal)
 - ➔ Re-evaluate for Curative treatment
- Concurrent CHEMORADIATION
 - CISPLATIN 100 MG/M2 3 WEEKLY + RADIATION (optimal)
 - CISPLATIN 40 MG/M2 WEEKLY + RADIATION (essential)
 - CISPLATIN 30-40 MG/M2 + NIMOTUZUMAB 200 MG WEEKLY + RADIATION (optimal)
- Cisplatin unfit+
 - Concurrent RT with Biologicals # (Optional) or other regimens@ (Optimal)
 - Radical Radiation (Essential)

Palliative RT/
Chemotherapy / RT+CT
(Optimal) OR
Best Supportive Care
(Essential)

PARANASAL SINUS AND NASAL CAVITY MANAGEMENT ALGORITHM



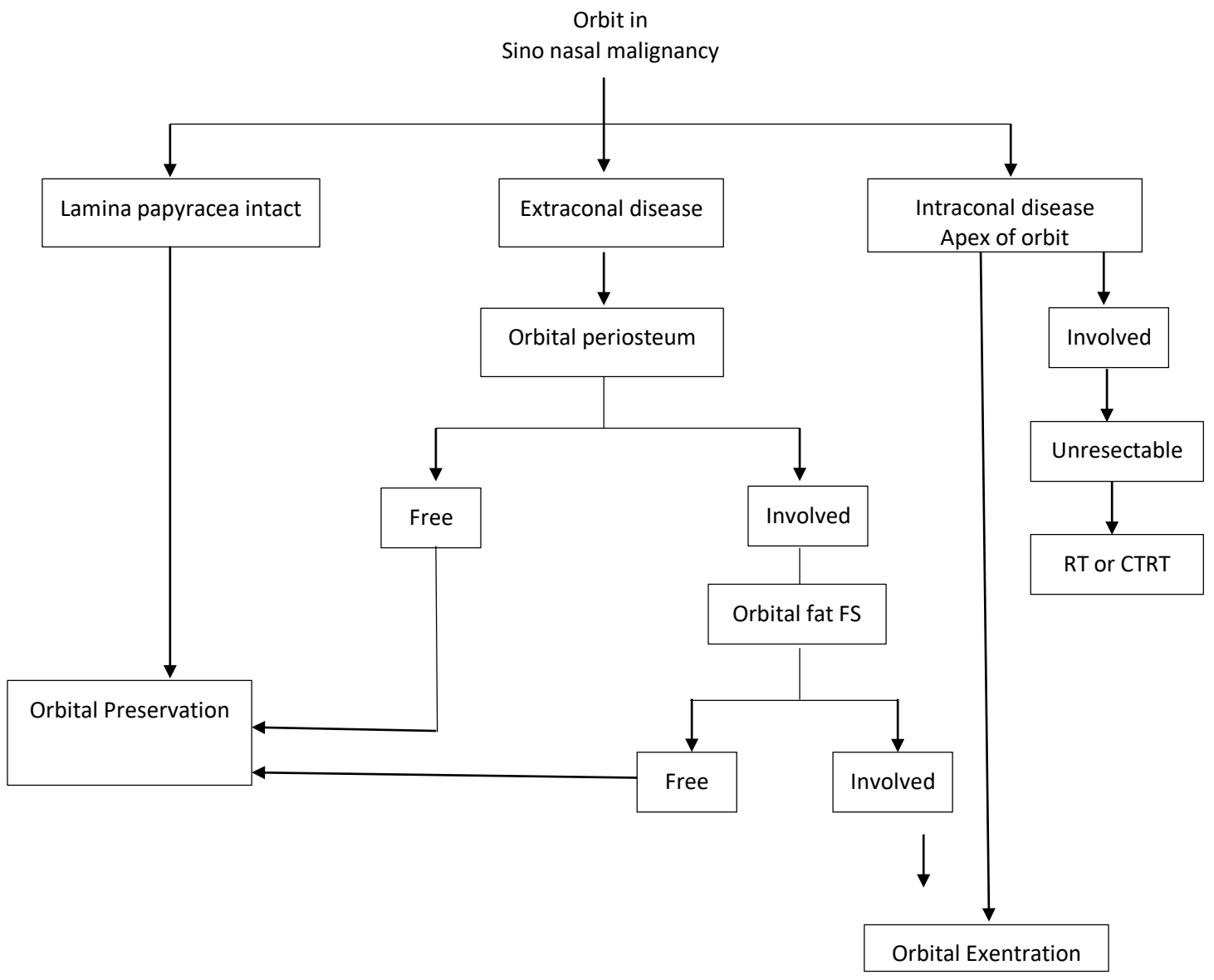


*Radiation In the PNS is optimally delivered with IMRT due to the vicinity of cranial nerves, intracranial contents and orbit. **(IMRT Optimal)**. For advanced tumors and posteriorly positioned tumors radiation therapy should include coverage for the retropharyngeal node.

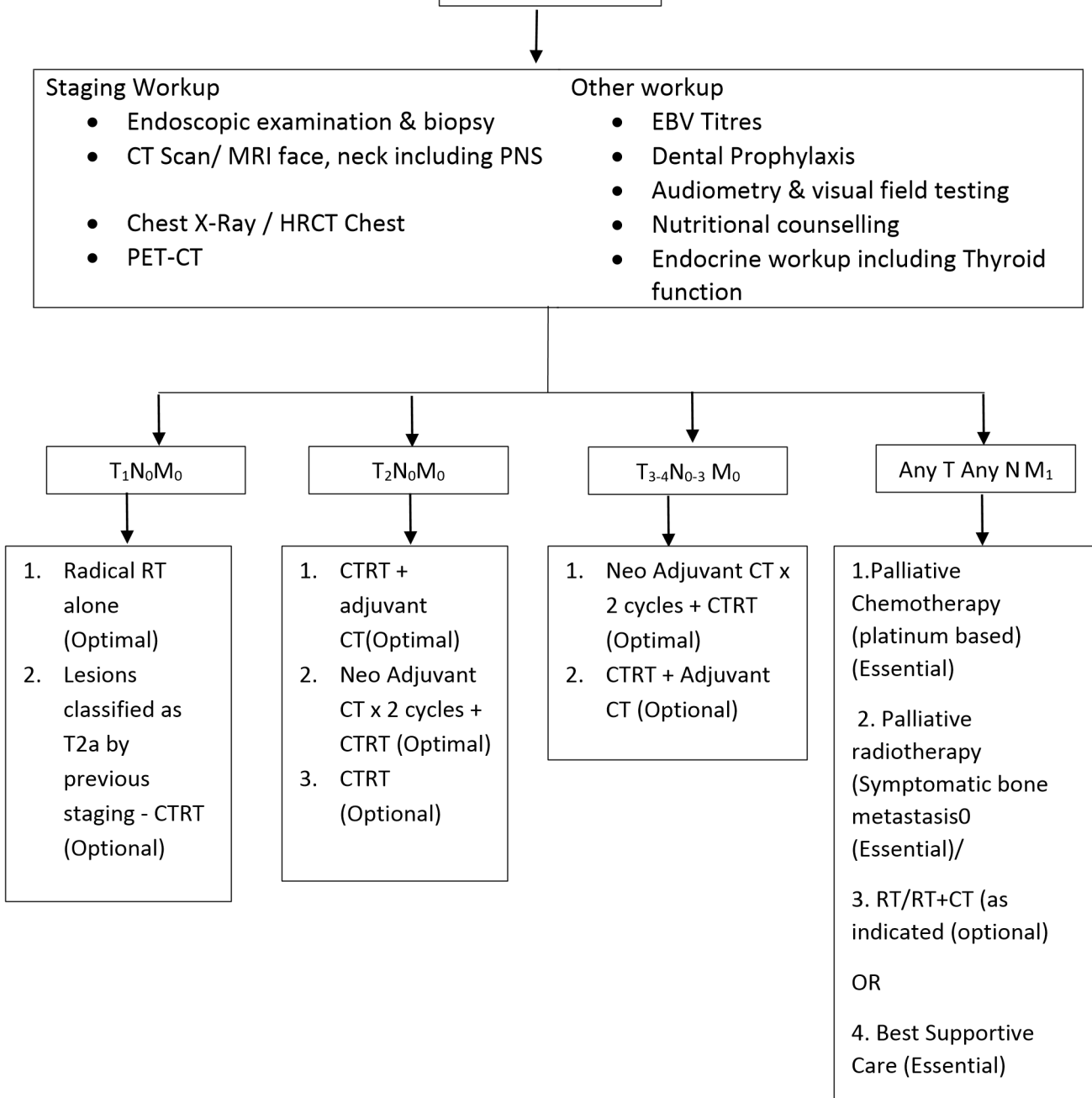
** - Surgery should achieve a R0 Resection. The appropriate surgical technique may be accordingly selected (endoscopic, partial, total or extended maxillectomy, orbital Exentration, craniofacial resection). Neck Dissection is undertaken for a N+ neck. Prognosis is however very guarded for N+ disease except in the situation of Level I nodes related to anterior PNS Tumour/ Skin involvement.

#NACT indication- should be considered optimal for advanced tumors with non-squamous high-grade histology {ENB (Gr3,4)/SNUC/SNEC/NUT/Small cell/Others}.

NACT can be considered for SCC (Optional) in situations wherein surgical resection may not yield a R0 Resection or lead to unacceptable morbidity (Intracranial extension; High ITF involvement; orbital preservation in intraocular extension)

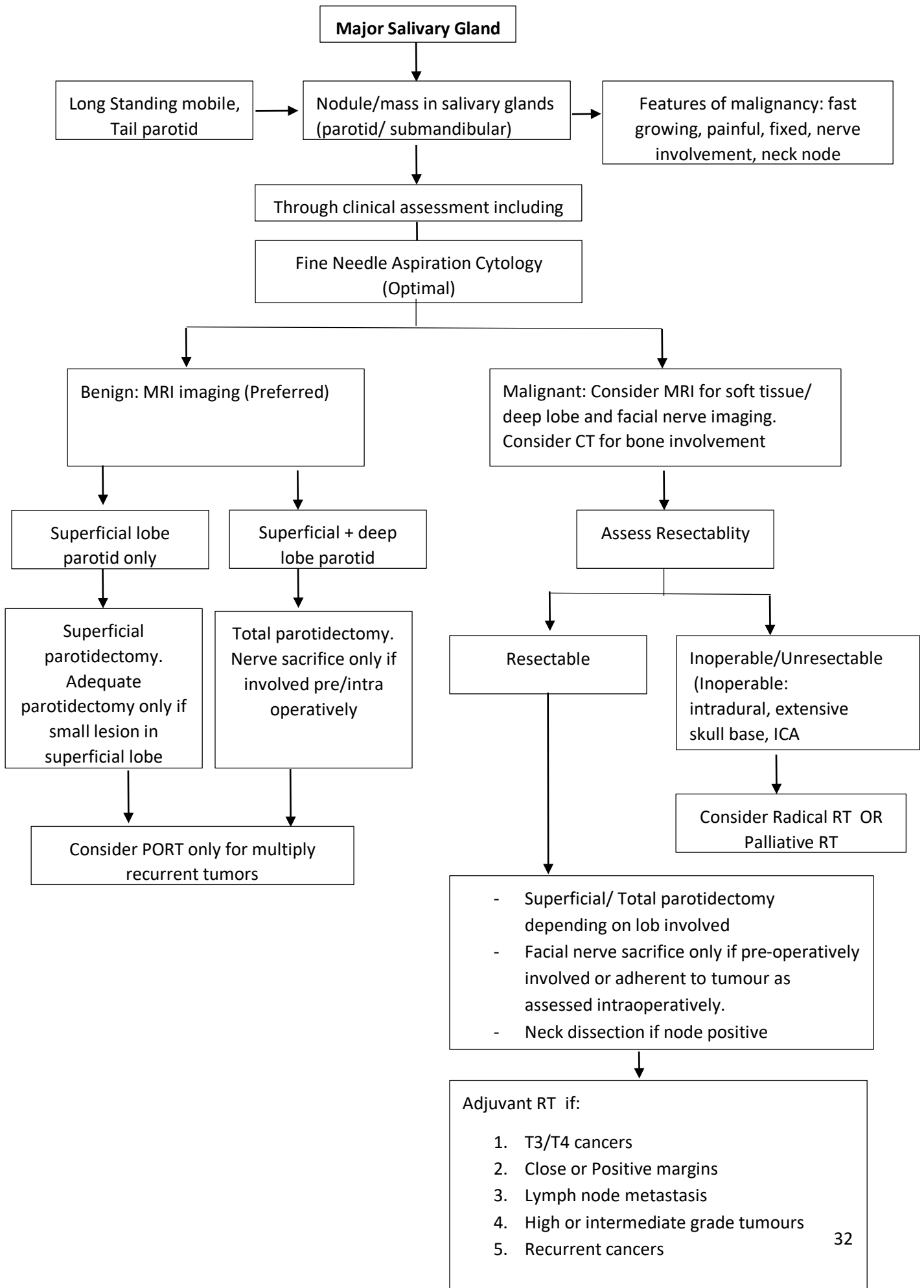


NASOPHARYNX



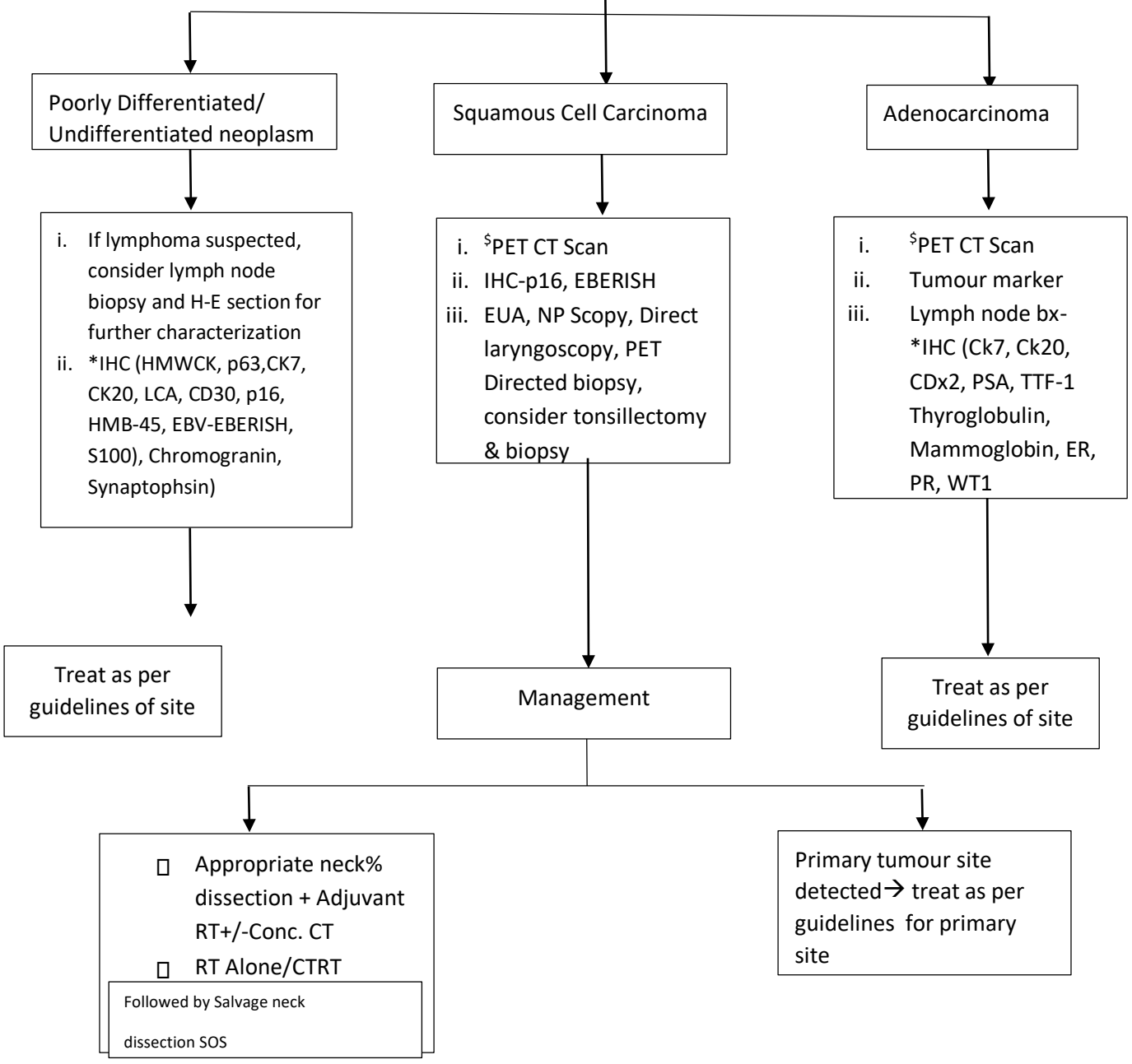
FOLLOW – UP

- PET-CT/MRI for response evaluation
- Examination of the nasopharynx and neck, cranial nerve function
- For T3 and T4 tumours, PET-CT/MRI might be done annually for 5 years
- Thyroid function at 1 year, annually thereafter
- Audiometry
- EBV titres
- **IMRT or 3DCRT are preferred modalities for radiotherapy for Nasopharyngeal Cancer (Optimal)**
- All treatments to be titrated as per patient's general condition and tolerability



Cervical nodes with an unknown primary

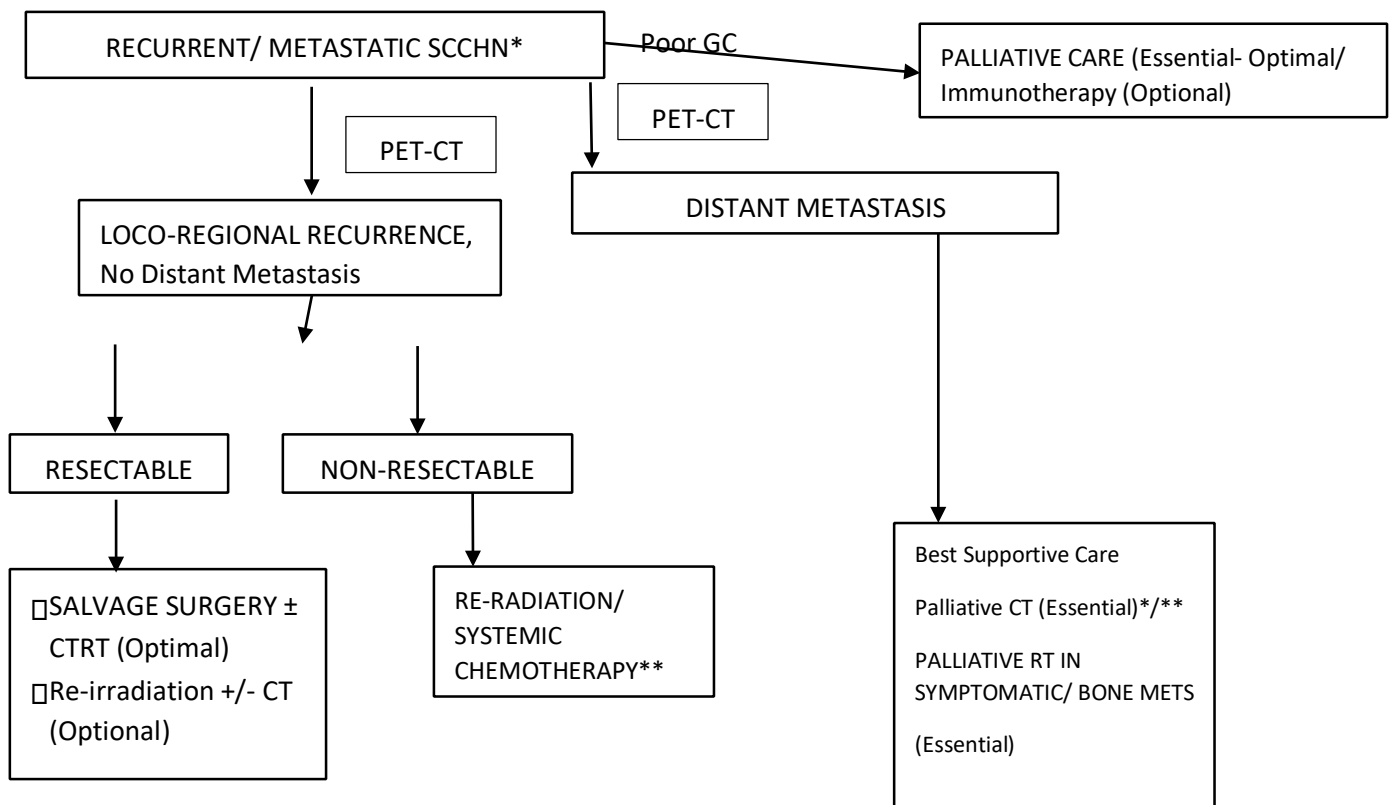
FNAC



*Preferred
 § PET-CT where not available → CECT of the Face & Neck
 CECT thorax
 USG (Abdomen)

%Depending on nodal stage and institutional policy

MANAGEMENT ALGORITHM FOR RECURRENT / METASTATIC SCCHN



*Consider early palliative care.

**Options for first line palliative chemotherapy include-

- Cytotoxic chemotherapy (single agent or combination)- metronomic chemotherapy consisting of weekly methotrexate-celecoxib; or combination Chemotherapy (Platinum, 5-FU, Taxane)
- 5FU– Platinum –Cetuximab - or Paclitaxel -Platinum-Cetuximab - (Optional);
- Pembrolizumab (if deemed appropriate with genetic testing for PDL1 and mutation load) – Optional