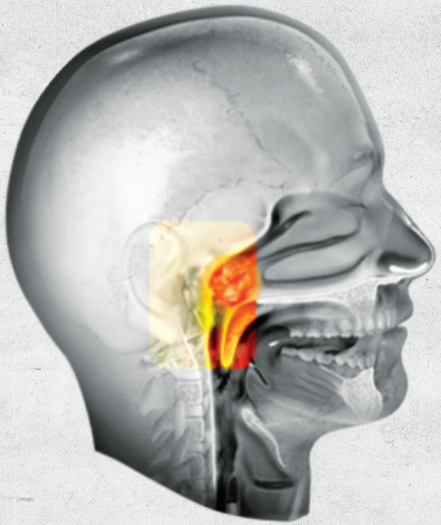
QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MANAGEMENT OF NASOPHARYNGEAL CARCINOMA



Ministry of Health Malaysia

Malaysian Society of Otorhinolaryngologist - Head & Neck Surgeons (MSO-HNS)

Academy of Medicine Malaysia

KEY MESSAGES

1. In Malaysia, nasopharyngeal carcinoma (NPC) is the fourth most common cancer. NPC is predominant among Chinese, followed by natives of Sabah and Sarawak (especially Bidayuh) and Malay.
2. Tobacco smoking is one of the important risk factors for NPC.
3. NPC is usually diagnosed late due to trivial presentation which leads to poor survival outcome.
4. In patients presenting with cervical lymphadenopathy, full head and neck assessment and fine needle aspiration cytological examination of the nodes should be done.
5. NPC should be diagnosed by histopathological examination of the nasopharynx.
6. Staging of NPC is by using the tumour node metastasis (TNM) system American Joint Committee on Cancer or AJCC Cancer Staging Manual 2010 (7th Edition).
7. Primary treatment for NPC is radiotherapy. Intensity modulated radiotherapy is the preferred radiation technique.
8. Concurrent chemoradiotherapy should be offered in Stage II, III, IVA and IVB.
9. In recurrent NPC, nasopharyngectomy or re-irradiation may be offered.
10. Multimodality treatment including dental, supportive and palliative care should be considered in the management of NPC.

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Nasopharyngeal Carcinoma.

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

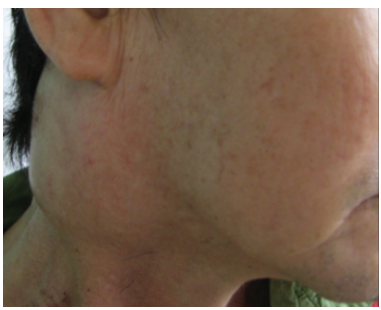
Ministry of Health Malaysia	:www.moh.gov.my
Academy of Medicine Malaysia	:www.acadmed.org.my
Malaysian Society of Otorhinolaryngologists Head & Neck Surgeons	:www.msohns.com

Also available as a mobile app for Android & IOS platform: MyMaHTAS

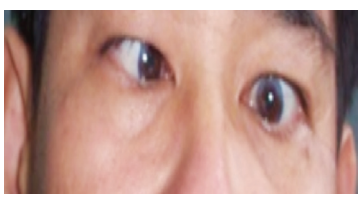
CLINICAL PRACTICE GUIDELINES SECRETARIAT
Health Technology Assessment Section
Medical Development Division, Ministry of Health Malaysia
4th Floor, Block E1, Parcel E, 62590 Putrajaya
Tel: 603-8883 1229 E-mail: htamalaysia@moh.gov.my

CLINICAL PRESENTATIONS AND REFERRAL

- Patients presenting with any of the following symptoms should be referred to Otorhinolaryngologists as soon as possible to rule out NPC :
  - painless neck lump (unilateral/bilateral)
  - blood-stained nasal discharge/saliva
  - unilateral ear block or hearing loss
  - headache
  - facial numbness
  - diplopia



Painless neck lump



NPC with ophthalmoplegia

RISK FACTORS OF NASOPHARYNGEAL CARCINOMA

- Ethnicity (especially Chinese and natives of Sabah & Sarawak)
- Gender (male to female ratio is 3:1)
- Family history of NPC
- Lifestyle and environment
  - Tobacco smoking
  - Consumption of salted fish
  - Exposure to domestic wood cooking fires
  - Exposure to occupational solvents
  - Occupational exposure to wood dust

AJCC CANCER STAGING MANUAL 2010 (7TH EDITION)

Nasopharynx	
T1	Tumour confined to the nasopharynx, or tumor extends to oropharynx and/or nasal cavity without parapharyngeal extension*
T2	Tumour with parapharyngeal extension*
T3	Tumour involves bony structures of skull base and/or paranasal sinuses
T4	Tumour with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, or with extension to the infratemporal fossa/masticator space
*Note: Parapharyngeal extension denotes posterolateral infiltration of tumour.	
N1	Unilateral metastasis in cervical lymph node(s), ≤6 cm in greatest dimension, above the supraclavicular fossa, and/or unilateral or bilateral, retropharyngeal lymph nodes, 6 cm or less, in greatest dimension*
N2	Bilateral metastasis in cervical lymph node(s), ≤6 cm in greatest dimension, above the supraclavicular fossa*
N3	Metastasis in a lymph node(s)* >6 cm and/or to supraclavicular fossa*
N3a	>6 cm in dimension
N3b	Extension to the supraclavicular fossa**
*Note: Midline nodes are considered ipsilateral nodes.	
**Note: Supraclavicular zone or fossa is defined by three points: (1) the superior margin of the sternal end of the clavicle, (2) the superior margin of the lateral end of the clavicle, (3) the point where the neck meets the shoulder. All cases with lymph nodes (whole or part) in the fossa are considered N3b.	
Distant Metastasis (M) **M0** No distant metastasis **M1** Distant metastasis	

Stage 0	N0		M0
Stage I	T1	N0	M0
Stage II	T1	N1	M0
	T2	N0	M0
	T2	N1	M0
Stage III	T1	N2	M0
	T2	N2	M0
	T3	N0	M0
	T3	N1	M0
	T3	N2	M0
Stage IVA	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IVB	Any T	N3	M0
Stage IVC	Any T	Any N	M1

PROGNOSIS OF DIFFERENT NPC STAGES

Stage	Prognosis
T1-2 N0-1	Relatively good treatment outcome
T3-4 N0-1	Mainly local failure
T1-2 N2-3	Mainly regional and distant failure
T3-4 N2-3	Local, regional and distant failure

FOLLOW-UP SCHEDULE OF NPC WITHOUT RECURRENCE

Year after completion of treatment	Frequency of follow-up
First year	Every 1 to 2 months
Second year	Every 2 to 3 months
Third year	Every 3 to 5 months
Fourth to fifth year	Every 6 months
After fifth year	Every 6 to 12 months

*interval of follow-up may be adjusted based on clinical judgement

TOXICITIES OF RADIOTHERAPY ON HEAD AND NECK

ACUTE TOXICITIES

- Lethargy
- Radiation dermatitis
- Mucositis
- Dysphagia
- Taste changes
- Nausea and vomiting
- Haematological toxicities (neutropaenia)

LATE TOXICITIES

Neurological Complications

- Temporal lobe injuries
- Cranial nerve palsies
- Lhermitte's syndrome

Non-neurological Complications

Tinnitus
Hearing loss
Otorrhea
Trismus
Dysphagia
Subcutaneous fibrosis
Endocrinopathy
- primary hypothyroidism
- hypopituitarism

Xerostomia
Second cancer within radiotherapy fields

ALGORITHM A : MANAGEMENT OF NASOPHARYNGEAL CARCINOMA

- History taking
- Complete physical examination
- Nasopharyngeal examination & biopsy
- +/- FNAC of regional lymph nodes
- Baseline investigations (FBC, renal profile, random blood sugar, liver function test, chest X-ray and electrocardiogram)
- MRI of nasopharynx & neck (from base of skull to thoracic inlet) or CT with contrast
- PET-CT or CT thorax/abdomen or ultrasound and bone scan, as indicated
- Pre-treatment dental assessment
- Nutritional evaluation

Determine disease stage

Stage I (T1N0M0)
Treatment with definitive radiotherapy (RT) to nasopharynx & elective RT to neck

- Definitive RT:-
  - Primary site: total of 66-70 Gy for 33-35 fractions, treated one fraction/day for 6-7 weeks (1.8-2.0 Gy/fraction)
  - Prophylactic neck: 54-60 Gy for 30 fractions, treated one fraction/day for 6 weeks (1.8- 2.0 Gy/fraction)
- IMRT recommended to minimise dose to critical structure

Stage II, III, IVA and IVB
Concurrent chemoradiotherapy

- Cisplatin + RT
- Conventional fractionation:
  - Primary site: total of 66-70 Gy for 33-35 fractions, treated one fraction/day for 6-7 weeks (1.8-2.0 Gy/fraction)
  - Neck: 54-70 Gy for 30-35 fractions, treated one fraction/day for 6-7 weeks (1.8-2.0 Gy/fraction)
- IMRT recommended to minimise dose to critical structures

Stage IVC (distant metastasis)
Palliative treatment

- Consider clinical trial if available
- Palliative chemotherapy to be considered in patients with good ECOG performance status (0-2)
- RT to palliate symptoms
- Referral to palliative care/ palliative home care

Follow-up and Surveillance

- Multidisciplinary team involvement (ENT specialist, oncologist, speech therapist, audiologist, etc)
- Head & neck and systemic examination (including nasopharyngoscopy):

Year	Intervals
First year	Every 1 to 2 months
Second year	Every 2 to 3 months
Third year	Every 3 to 5 months
Fourth to fifth year	Every 6 months
After fifth year	Every 6 to 12 months

- Cross-sectional imaging in the initial 5 years
- Speech/swallowing assessment as clinically indicated
- Hearing evaluation & rehabilitation as clinically indicated
- Post-treatment dental management every 3 to 4 months by trained and experienced dental specialist
- Weight assessment on follow-up
- Annual thyroid function test (TFT) screening

ALGORITHM B : MANAGEMENT OF PERSISTENT DISEASE OR RECURRENT NASOPHARYNGEAL CARCINOMA

- Restage to assess recurrent or persistent disease – MRI or CT scan and PET/CT scan
- Biopsy of recurrent lesion(s), as clinically indicated
- Treatment should be individualised based on patient performance status and extent of disease

Local disease

Options include:

- Nasopharyngectomy OR
- Re-irradiation with external beam RT or brachytherapy

Regional disease

Options include:

- Neck dissection
- Re-irradiation
- Chemotherapy

Distant disease

- Consider clinical trial if available
- Palliative chemotherapy to be considered in patients with good ECOG performance status (0-2)
- RT to palliate symptoms
- Referral to palliative care/ palliative home care

Follow-up and Surveillance

- Multidisciplinary team involvement (ENT specialist, oncologist, speech therapist, audiologist, etc)
- Head & neck and systemic examination (including nasopharyngoscopy):

Year	Intervals
First year	Every 1 to 2 months
Second year	Every 2 to 3 months
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- Cross-sectional imaging in the initial 5 years
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CHEMOTHERAPY DRUGS AND COMMON SIDE EFFECTS

CHEMOTHERAPY DRUGS	COMMON SIDE EFFECTS
Cisplatin	• Nausea and vomiting • Myelosuppression • Renal toxicity • Electrolyte imbalance (hypomagnesaemia, hypocalcaemia, hypokalaemia) • Auditory (tinnitus; with or without hearing loss)
Carboplatin	• Myelosuppression • Nausea and vomiting • Hypersensitivity reaction • Alopecia
Fluorouracil	• Diarrhoea and stomatitis • Myelosuppression • Angina, myocardial infarction, arrhythmia, acute pulmonary oedema (special precaution) • Alopecia
Docetaxel	• Myelosuppression • Fluid retention • Alopecia, cutaneous reaction, nails changes • Stomatitis, diarrhoea, nausea and vomiting • Hypersensitivity reaction