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Diagnostic Work-up and Staging of Head and Neck Cancer

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Cancer Care Alberta

Clinical Practice Guideline HN-008 – Version 1
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Background

Head and neck cancer includes a variety of tumours that originate in the oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses, thyroid, and salivary glands. Worldwide, it represents the 6th most common type of cancer and accounts for about 6% of all cancers. Smoking, alcohol, age and sex are some of the most common factors for the development of head and neck cancer[1].

Head and neck cancers are considered among the most complex types of cancers where treatment decisions are made by a multidisciplinary team which includes both oncologists and allied health care professionals such as dietitians, dentists, and speech-language pathologists[2]. The initial evaluation of patient tumour is the most critical step for treating the cancer; it provides information that is essential to making decision on optimal treatment plans. The initial assessment includes indirect mirror and direct endoscopy however the advanced assessment is done by imaging and biopsies. Imaging tools (CT, MRI, PET or PET/CT) are important for determining the local infiltration, regional spread, distant metastases or second primary tumours.

The purpose of this guideline is to outline the diagnosis, and staging recommendations for patients with head and neck cancer in Alberta.

Guideline Questions

1. What are the diagnostic investigation and recommendations for patients with Head and Neck cancer?
2. What is the clinical impact of different imaging tools on management of patients with Head and Neck cancer?
3. What are the diagnostic criteria for biopsy and panendoscopy?

Search Strategy

The National Guideline Clearinghouse and individual cancer agencies' websites were searched for clinical practice guidelines related to Workup and staging for Head and Neck cancer. A systematic literature review was performed by using the Pubmed, EMBASE, and MEDLINE databases. The detailed literature search strategy is outlined in Appendix A, and the evidence tables are available upon request.

Target Population

The recommendations outlined in this guideline are intended for adults over the age of 18 years with suspected malignancies arising in the mucosal surfaces of the upper aerodigestive tract, including the oral cavity, pharynx, larynx, and paranasal sinuses. Different principles may apply to pediatric patients or patients with thyroid/salivary gland pathology.

Recommendations

The following recommendations should be applied in the context of the recommendations outlined in the Alberta Health Services guideline, 'The Organization and Delivery of Healthcare Services for Head and Neck Cancer Patients.'

I. Initial Assessment by Primary Care Physicians and Dental Practitioners

Factors that Increase the Risk of Head and Neck Cancer

The following factors have been shown to increase the risk of head and neck cancer:

- Geography (i.e. Southeast Asia)
- Smoking (including chewing tobacco, betel nut, paan, pituri)
- Alcohol consumption
- Age (over 40 years)
- Sex (male)
- HPV exposure (orogenital)
- UV / sunlight for mucosa (red portion) of lip

Recommendations

History:

1. The following signs/symptoms should be considered highly suspicious for head and neck cancer, especially if there is more than 1 symptom, persisting for more than 3 weeks:
   - Neck lump
   - Change in voice, usually persistent hoarseness
   - Non-healing oral lesions-mass or ulcer
   - Dysphagia for solids
   - Persistent sore throat, particularly if associated with otalgia
   - Unusual/persistent oral bleeding or epistaxis
   - Other non-specific features, including numbness of the tongue, or other areas of the mouth, and swelling of the jaws

2. Associated risk factors should be inquired about and documented.

3. Inquire about HPV vaccination history.

Physical Exam:

4. Physical examination should include: inspection of the neck for lymph nodes, inspection of the facial and scalp skin; inspection of the oral cavity for ulceration of mucosa, swellings, and red or white patches and inspection of the anterior nasal cavities.

Referral to Specialist:

5. For ulcerative lesions or masses that are initially treated as potential infections, or bleeding nasal lesions that are treated with moisturizing ointments and humidification, establish time limit for follow-up to ensure early referral for specialty care (i.e. if lesion is not resolved or dramatically improved after 3 weeks of therapy, refer for urgent specialty review).

II. Workup at Cancer Centre

General

6. Once biopsy proven head and neck cancer identified, newly diagnosed cases should be referred to an appropriate head and neck oncologist (with affiliations to a regional cancer centre) to develop an appropriate treatment plan as soon as possible.

7. All patients should undergo tumour classification and staging prior to treatment. Staging of head and neck cancers are usually based on two classifications, namely cTNM and pTNM described in detail in the 8th edition of the AJCC Cancer Staging Manual.

8. A complete head and neck examination should be completed and documented (i.e. nose, post-nasal space, oral cavity, oropharynx, larynx and hypopharynx, including palpation of neck, oral cavity and tongue base, using endoscopy as appropriate).

9. When feasible, radiological investigations should be performed prior to biopsy to avoid the effect of upstaging from the edema caused by biopsy.

10. When examination under general anesthesia including endoscopy and biopsy is indicated, that procedure should be performed by the surgeon who is responsible for any future procedures

Imaging

CT Scan:

11. In all cases, CT of the neck with contrast is recommended for locoregional staging. If tumour extent is unclear on CT, and if clarification would alter management, then further evaluation with MRI is recommended.

MRI Scan:

12. MRI may be particularly helpful for assessing infiltration of surrounding soft tissues (e.g. extrinsic tongue muscles, parapharyngeal space, and masticator space), perineural spread, and intracranial/ intraorbital extension.

FDG-PET Scan:

13. If nodal status is unclear on CT (+/- MRI), and if clarification would alter management, then further evaluation with FDG-PET is recommended.

14. In a patient with an unknown primary site of tumour after head and neck examination and CT (+/- MRI), FDG-PET should be performed prior to panendoscopy and biopsy so that sites of biopsy will not lead to a false-positive.

15. Chest imaging is recommended for all newly diagnosed head and neck cancers to detect lung metastases and synchronous lung cancers. Both chest CT and PET-CT are superior to chest x-ray in detecting synchronous primary cancers and distant metastases[3]. In cases of N2-N3 disease, patients with a history of smoking and those otherwise at higher risk for second primary tumours and distant metastases (supraglottic and hypopharyngeal cancer), CT of the chest or PET-CT is strongly recommended[3,4].

16. In cases of stage III-IV disease, FDG-PET should be considered for screening for distant metastases and second primary cancers[3]. Interpretation should consider the relatively high false positive rate with PET-CT and the possible need for confirmatory diagnostic tests[5].

Diagnostic Biopsy

17. It is essential that mucosal lesions of the oral cavity, oropharynx, nasopharynx, hypopharynx and larynx that are clinically suspicious for malignancy, primarily squamous cell carcinoma, be appropriately and adequately biopsied in an expedited manner. The approach and method of biopsy are dependent on the site and size of the lesion, the level of suspicion of malignancy, the resources available and experience of the clinician.

18. Oral lesions over 2 cm in maximum dimension, highly suspicious oral lesions and ulcerated or clearly invasive oral lesions should be sampled with an incisional or punch biopsy. The biopsy site should not be in a necrotic or friable area. Generally, a biopsy near the edge of the tumour is ideal. A 4-mm dermatologic punch is a good choice, but scalpel blades or cupped biopsy forceps are acceptable. The biopsy needs to be adequately deep to allow determination of depth of invasion. Excisional biopsies of invasive cancers have a high incidence (62%) of leaving residual cancer requiring repeat excision[6]. This may complicate management but probably does not compromise overall disease control or survival if subsequently appropriately managed. It is suggested that excisional biopsies be reserved for small, superficial lesions that are thought to be benign[7].

19. Incisional biopsies of areas of oral leukoplakia risk false negative results of up to 24-73% in some series mostly due to sampling errors[8]. Small areas of leukoplakia without worrisome clinical features

can be excised under local anesthesia. Excisional biopsies of larger or suspicious areas of leukoplakia should be performed under general anesthesia with adequate margins.

20. All suspicious lesions of the pharynx and supraglottic larynx require biopsies with forceps. Accessible lesions of the soft palate and tonsils may be biopsied transorally without endoscopy. Suspicious lesions of the nasopharynx, oropharynx (base of tongue), hypopharynx and supraglottic larynx may be biopsied using topical anesthesia and endoscopic guidance (rigid or flexible). This requires the appropriate patient positioning, endoscopes, an experienced Otolaryngologist - Head and Neck Surgeon and often a skilled assistant[9]. When these conditions cannot be met then traditional biopsy under general anesthesia via rigid endoscopy is required.

21. Suspected lesions of the tonsils are best sampled by way of an excision of the entire tonsil or tonsils under general anesthesia (diagnostic tonsillectomy). Blind biopsies of the tonsil have a very high false negative rate as cancers often arise deep in the tonsillar crypts and are missed unless they ulcerate through the surface[10]. These tonsillectomies are often done in conjunction with a panendoscopy in the setting of metastatic SCCA in a cervical node without an obvious mucosal lesion on office examination. Larger, ulcerated and clinically obvious cancers of the tonsil may be biopsied with forceps in the clinic.

22. For biopsies of the glottis, in most cases, assessment and biopsy under general anesthesia using rigid laryngoscopes is required (suspension laryngoscopy). Larger lesions may be biopsied without magnification however early T1 cancers, leukoplakia, benign or indeterminate lesions of the glottis usually require adjuvant use of a microscope (suspension microlaryngoscopy). Larger or deeply invasive lesions are sampled with cupped laryngeal forceps. Superficial, benign and indeterminate lesions such as leukoplakia and erythroplasia may be suitable for excisional biopsy using either sharp “cold” instruments or a CO_2 laser. Endoscopic biopsies of the glottis may sometimes be performed in clinic in selected patients by sub-specialist laryngologists in a highly specialized setting (regional voice clinic). Sensitivity and negative predictive values for in office biopsy techniques are reported from 60 – 78% and 74 – 87%, respectively.[11-13]. Lesions involving the anterior commissure of the glottis, bilateral vocal cords or vocal process of the vocal cord should not be excised without prior pathological confirmation and multidisciplinary consultation at a regional cancer centre with discussion of alternative non-surgical options. In performing excisional biopsies of suitable glottic lesions, care must be taken to not violate the vocal ligament or anterior commissure regardless of the instrument used.

23. Panendoscopy as a diagnostic tool for the identification of synchronous tumours is inferior in comparison to CT or PET-CT in most cases[14-16]. Patients at low risk of a secondary lesion have a very low rate of synchronous tumours identified on routine pandendoscopy and esophagoscopy[14,15,17,18] Cancers of the hypopharynx may be an exception in that the incidence of esophageal second primaries is higher and esophagoscopy compares favourably to CT chest[4].

24. Panendoscopy is a useful tool in the workup of patients planned for surgery or potential transoral excision of a head and neck cancer to evaluate feasibility and anatomy.

Occult Primary

25. Fine Needle aspiration cytology of a neck mass or neck node should be performed for occult primaries. When the FNA is non-diagnostic an open biopsy may be required. Special stains including those for lymphoma, EBV and HPV testing should be ordered to help establish the primary tumour.

26. PET-CT imaging is superior to panendoscopy in the identification of an occult primary and should be the initial investigation to establish the primary tumour. **The PET-CT results may direct subsequent confirmatory biopsies.** If PET-CT fails to detect a primary tumour, the patient should be sent for panendoscopy (EUA) for random directed biopsies of potential primary sites including tonsillectomy.

27. The role of total mucosal resection for identification of unknown primaries is currently unclear.

Table 1. Roles of Health Care Providers in the Diagnostic Workup and Staging of Head/Neck Cancers

Recommendation		Primary Care *Family Physicians & Dentists*	Secondary Care *Community ENT & Community OMFS*	Tertiary Care *Regional Head/Neck Core Team Members*
1	symptoms and signs	√	√	
2	risk factors	√	√	
3	HPV vaccination	√	√	√
4	physical examination	√	√	
5	follow-up and referral	√	√	
6	Regional Cancer Centre	√	√	
7	tumour classification/AJCC staging			√
8	complete H&N exam		√	√
9	imaging before biopsy		√	√
10	EUA by primary surgeon			√
11	CT neck with contrast		√	√
12	MRI as required			√
13	PET for nodal status			√
14	PET for PUK (unknown primary)			√
15	chest imaging (CT or PET-CT)		√	√
16	PET for stage III/IV			√
17	biopsy appropriately		√	√
18	punch or incisional biopsy		√	√
19	excisional biopsy of leukoplakia		√	√
20	biopsy of larynx/pharynx		√	√
21	diagnostic tonsillectomy			√
22	biopsy of glottic lesions		√	√
23	synchronous cancers			√
24	pre-surgery endoscopy			√
25	node biopsy in PUK			√
26	PET for PUK (occult primary)		√	√
27	role of mucosal resection in PUK			√

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Appendix A: Literature Search Strategy

Search	Database	Date	Search Strategy	Limits	Results
Biopsies					
FNA, IHC	PubMed	Aug 29	(((("biopsy"[MeSH Terms] OR "biopsy, fine-needle"[MeSH Terms]) OR "incisional biopsy"[All Fields]) OR "excisional biopsy"[All Fields]) AND ("early diagnosis"[MeSH Terms] OR "early detection of cancer"[MeSH Terms])) AND ("head and neck neoplasms"[MeSH Terms] NOT "thyroid neoplasms"[MeSH Terms])	("humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])	82
			(("immunohistochemistry"[MeSH Terms] AND (("early diagnosis"[MeSH Terms] OR "early detection of cancer"[MeSH Terms]) AND (("head and neck neoplasms"[MeSH Terms] NOT "thyroid neoplasms"[MeSH Terms])	("humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])	39
			("fine-needle aspiration"[All Fields] AND "head and neck cancer"[All Fields]) AND "immunohistochemistry"[All Fields]	None	7
			((("early diagnosis"[MeSH Terms] OR ("early"[All Fields] AND "diagnosis"[All Fields]) OR "early diagnosis"[All Fields]) OR ("early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("head and neck neoplasms"[MeSH Terms] NOT "thyroid neoplasms"[MeSH Terms])) AND "epstein-barr virus infections"[MeSH Terms]	("humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])	48
Oral, incisional/ excisional	PubMed	Aug 30	(("early diagnosis"[MeSH Terms] OR "early detection of cancer"[MeSH Terms]) AND ("incisional biopsy"[All Fields] OR "excisional biopsy"[All Fields])) AND "mouth neoplasms"[MeSH Terms]	None	7
			("incisional biopsy"[All Fields] OR "excisional biopsy"[All Fields]) AND "oral cancer"[All Fields]	None	35
Pharynx and larynx	PubMed	Sept 5	"biopsy, fine-needle"[MeSH Terms] AND ("pharyngeal neoplasms"[MeSH Terms] OR "laryngeal neoplasms"[MeSH Terms])	("humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])	79
Imaging					
MRI/CT	PubMed	24 Aug	(((((("head and neck neoplasms"[MeSH Terms] NOT "thyroid neoplasms"[MeSH Terms]))) AND (("computerized tomography"[MeSH Terms] OR "Magnetic resonance imaging"[MeSH Terms]))) AND (("Diagnosis" OR "Staging")))	(("2007/08/27"[PDat] : "2017/08/24"[PDat] AND "humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])) Only the following article types: Clinical trials, comparative studies, controlled clinical trials, meta-analyses, multicenter studies, observational studies, and randomized controlled trials	175

Search	Database	Date	Search Strategy	Limits	Results
				Other limits: sample size greater than or equal to 20	
CT T1a glottic Ca	PubMed	5 Sep	(("computerized tomography"[MeSH Terms] AND "glottis"[MeSH Terms]))		0
PET CT	PubMed	27 Aug	(("head and neck neoplasms"[MeSH Terms] NOT "thyroid neoplasms"[MeSH Terms])) AND "Positron Emission Tomography Computed Tomography"[MeSH Terms] AND (("Diagnosis" OR "Staging"))	(("2007/08/27"[PDat] : "2017/08/24"[PDat] AND "humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])) Other limits: sample size greater than or equal to 20; excluded comparisons of PET-CT and PET-MRI	77
Panendoscopy					
	PubMed	6 Sep	(("head and neck neoplasms"[MeSH Terms] NOT "thyroid neoplasms"[MeSH Terms]) AND Panendoscopy)	("2007/08/27"[PDat] : "2017/09/06"[PDat] AND "humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])	45
Occult Primary					
Biopsy	PubMed	Sept 6	("biopsy"[MeSH Terms] AND ("head and neck neoplasms"[MeSH Terms] NOT "thyroid neoplasms"[MeSH Terms])) AND "neoplasms, unknown primary"[MeSH Terms]	("humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])	46
Wait Times					
	PubMed	7 Sep	((wait times) AND ("head and neck neoplasms"[MeSH Terms] NOT "thyroid neoplasms"[MeSH Terms]))	("2007/08/27"[PDat] : "2017/09/07"[PDat] AND "humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms])	26
	Medline	7 Sep	Keywords: Wait times AND head and neck neoplasms		5
	CINAHL	7 Sep	Keywords: Wait times AND head and neck neoplasms	English Language, publication year between 2007 and 2017	3
	Cochrane	7 Sep	Head and neck neoplasms wait times	English Language, publication year between 2007 and 2017	2
	Embase	7 Sep	Keywords: Wait times AND head and neck neoplasms	N/A English Language, publication year between 2007 and 2017	0

Development and Revision History

This guideline was reviewed and endorsed by the Alberta Provincial Head and Neck Tumour Team. Members include otolaryngology–head and neck surgeons, reconstructive surgeons, dentists, oral surgeons, radiation oncologists, medical oncologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Head and Neck Tumour Team, external participants identified by the Working Group Lead, and a methodologist from the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

This guideline was originally developed in 2019.

Levels of Evidence

I	Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
II	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies
V	Studies without control group, case reports, expert opinion

Strength of Recommendations

A	Strong evidence for efficacy with a substantial clinical benefit; strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit; generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.); optional
D	Moderate evidence against efficacy or for adverse outcome; generally not recommended
E	Strong evidence against efficacy or for adverse outcome; never recommended

Maintenance

A formal review of the guideline will be conducted in 2024 If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations

AJCC, American Joint Committee on Cancer; CT, computed tomography; EBV, Epstein-Barr virus; ENT, ear nose throat; EUA, examination under anesthesia; FDG-PET, fluoro-deoxyglucose positron emission tomography; FNA, fine needle aspiration; HPV, human papilloma virus; MRI, magnetic resonance imaging; OMFS, oral and maxillofacial surgery; PET, positron emission tomography; PUK, primary unknown; TNM, tumour node metastasis.

Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Head and Neck Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

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