Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over

NICE guideline
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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.
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This guideline covers assessing and managing cancers of the upper aerodigestive tract in young people (aged 16 and over) and adults. It aims to reduce variation in practice and improve survival.

Who is it for?

- People aged 16 and over with cancer of the upper aerodigestive tract, and their families and carers
- Healthcare professionals working in secondary and tertiary care
Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Information and support

Information needs

1.1.1 For people with cancer of the upper aerodigestive tract and their carers:

- provide consistent information and support at diagnosis
- review their needs throughout the care pathway including at the end of treatment
- tailor information and support to the person's needs (including the benefits and side effects of treatment, psychosocial and long-term functional issues).

1.1.2 Give people contact details for their allocated key worker, in line with the NICE service guidance on improving outcomes in head and neck cancer and recommendations of the National Peer Review Programme.

1.1.3 Give people details of peer support services that can help them throughout their care pathway.

1.1.4 Offer information about human papillomavirus (HPV) to people with HPV-related cancer of the upper aerodigestive tract.

Smoking cessation

1.1.5 Inform patients and carers at the point of diagnosis about how continuing to smoke adversely affects outcomes such as:

- treatment-related side effects
• risk of recurrence

• risk of second primary cancers.

1.1.6 Offer help to people to stop smoking, in line with the NICE guideline on stop smoking services.

1.2 **Investigation**

**Assessment of neck lumps**

1.2.1 Consider adding ultrasound-guidance to fine-needle aspiration cytology or core biopsy for people with a neck lump that is suspected of being cancer of the upper aerodigestive tract.

1.2.2 Consider having a cytopathologist or biomedical scientist assess the cytology sample adequacy when the procedure is carried out.

**Identifying the occult primary**

1.2.3 Consider a fluorodeoxyglucose positron emission tomography (FDG PET)-CT scan as the first investigation to detect the primary site in people with metastatic nodal squamous cell carcinoma of unknown origin that is thought to arise from the upper aerodigestive tract.

1.2.4 Consider using narrow-band imaging endoscopy to identify a possible primary site when it has not been possible to do so using FDG PET-CT.

1.2.5 Offer a biopsy to confirm a possible primary site.

1.2.6 Offer surgical diagnostic assessment if FDG PET-CT does not identify a possible primary site. This may include:

• guided biopsies

• tonsillectomy

• tongue base mucosectomy.
1.2.7 Consider an MRI or CT scan before diagnostic surgery to help with radiotherapy treatment planning.

Clinical staging – who and how?

1.2.8 Offer systemic staging (see recommendations 1.2.9–1.2.11) to all people with cancer of the upper aerodigestive tract except those with T1N0 or T2N0 disease.

1.2.9 Offer FDG PET-CT to people with T4 cancer of the hypopharynx or nasopharynx.

1.2.10 Offer FDG PET-CT to people with N3 cancer of the upper aerodigestive tract.

1.2.11 Offer conventional imaging (for example, chest CT) to people with cancer of the upper aerodigestive tract who require systemic staging (see recommendation 1.2.8) but FDG PET-CT is not indicated for them.

1.3 Treatment of early stage disease

Squamous cell carcinoma of the larynx

1.3.1 Offer transoral laser microsurgery to people with newly-diagnosed T1a squamous cell carcinoma of the glottic larynx.

1.3.2 Offer a choice of transoral laser microsurgery or radiotherapy to people with newly-diagnosed T1b–T2 squamous cell carcinoma of the glottic larynx.

1.3.3 Offer a choice of transoral surgery or radiotherapy to people with newly-diagnosed T1–T2 squamous cell carcinoma of the supraglottic larynx.

Management of the N0 neck in T1–2 squamous cell carcinoma of the oral cavity

1.3.4 Offer surgical management of the neck to all people with early oral cavity cancer (T1–T2, N0).

1.3.5 Offer sentinel lymph node biopsy instead of elective neck dissection to people with early oral cavity cancer (T1–T2, N0), unless they need cervical access at the same time (for example, free-flap reconstruction).
Squamous cell carcinoma of the oropharynx (T1–2, N0)

1.3.6 Offer people the choice of transoral surgical resection or primary radiotherapy for T1–2 N0 tumours of the oropharynx.

1.3.7 Consider postoperative radiotherapy, with or without concomitant chemotherapy, for T1–2 N0 tumours of the oropharynx if pathologically adverse risk factors have been identified.

1.4 Treatment of advanced disease

Squamous cell carcinoma of the larynx

1.4.1 Offer people with T3 squamous cell carcinoma of the larynx a choice of:

- radiotherapy with concomitant chemotherapy, or
- surgery with adjuvant radiotherapy, with or without concomitant chemotherapy.

1.4.2 Discuss the following with people with T3 squamous cell carcinoma of the larynx and their carers, to inform their choice of treatment:

- the potential advantages of laryngeal preservation
- the risk of needing salvage laryngectomy (and its associated complications)
- the benefits of primary surgery in people with existing compromised swallowing and airway function
- likely voice and swallowing function after treatment (including the need for a long-term feeding tube).

1.4.3 For people with T4a squamous cell carcinoma of the larynx consider surgery with adjuvant radiotherapy, with or without concomitant chemotherapy.

Squamous cell carcinoma of the hypopharynx

1.4.4 Offer larynx-preserving treatment to people with locally-advanced squamous cell carcinoma of the hypopharynx if radiation and neo-adjuvant and/or concomitant chemotherapy would be suitable for them and they do not have:
• tumour-related dysphagia needing a feeding tube
• a compromised airway
• recurrent aspiration pneumonias.

1.4.5 Offer radiotherapy with neo-adjuvant and/or concomitant chemotherapy if larynx-preserving treatment is suitable for the person.

1.4.6 Offer primary surgery followed by adjuvant radiotherapy to people if chemotherapy is not a suitable treatment for them.

1.4.7 Offer adjuvant radiotherapy to people having surgery as their primary treatment. Add concomitant chemotherapy if appropriate.

Palliation of breathing difficulties

1.4.8 Identify people at risk of airways obstruction for whom intervention is appropriate. Think about:

• their performance status
• treatment side effects and length of hospital stay
• involving the palliative care team and other specialists when appropriate.

1.4.9 Consider endoluminal debulking in preference to tracheostomy.

1.4.10 Establish a management plan if surgical intervention is not appropriate, in conjunction with the person, carers and clinical staff.

1.4.11 Assess and treat other causes of breathlessness in people with incurable upper aerodigestive tract cancer.

1.5 HPV-related disease

HPV testing

1.5.1 Test all squamous cell carcinomas of the oropharynx using p16 immunohistochemistry. Regard the p16 test result as positive only if there is strong nuclear and cytoplasmic staining in more than 70% of tumour cells.
1.5.2 Consider high-risk HPV DNA or RNA in-situ hybridisation in all p16-positive cancers of the oropharynx to confirm HPV status.

De-intensification of treatment

1.5.3 Do not offer de-intensification of curative treatment to people with HPV-positive cancer of the oropharynx, unless it is part of a clinical trial.

1.6 Less common upper aerodigestive tract cancers

Carcinoma of the nasopharynx

1.6.1 Offer intensity-modulated radiation therapy with concomitant chemotherapy to people with locally-advanced (stage II and above) nasopharyngeal cancer.

1.6.2 Consider adjuvant or neo-adjuvant chemotherapy for people with locally-advanced (stage II and above) nasopharyngeal cancer.

Carcinoma of the paranasal sinuses

1.6.3 Offer surgery as the first treatment for carcinoma of the paranasal sinuses if complete resection is possible.

1.6.4 Consider radiotherapy with or without concomitant chemotherapy before planned surgical resection of the paranasal sinuses if complete resection is not initially possible.

Unknown primary of presumed upper aerodigestive tract origin

1.6.5 Offer people with squamous cell carcinoma in the cervical lymph nodes with an unknown primary the choice of:

- neck dissection and adjuvant radiation with or without chemotherapy, or
- primary radiation with or without chemotherapy, with surgery for persistent disease.

1.6.6 Consider no further treatment as an option in people with pN1 disease without extracapsular spread after neck dissection.
1.6.7 Consider including potential primary tumour sites when selecting the volume to be treated with radiotherapy.

Mucosal melanoma

1.6.8 Consider surgery and adjuvant radiotherapy for people with newly-diagnosed upper aerodigestive tract mucosal melanoma without systemic metastases.

1.7 Optimising rehabilitation and function

Enteral nutrition support

1.7.1 Assess people's need for enteral nutrition at diagnosis, including prophylactic tube placement. The multidisciplinary team should take into account:

- performance status and social factors
- nutritional status (weight loss, high or low BMI, ability to meet estimated nutritional needs)
- tumour stage
- tumour site
- pre-existing dysphagia
- impact of planned treatment (such as radiation treatment volume and dose-fractionation, concomitant chemotherapy, and extent and site of surgery).

1.7.2 Follow the recommendations in NICE's guideline on nutrition support for adults for people aged 18 years and over.

Speech and language therapy interventions

1.7.3 Consider swallowing-exercise programmes for people having radiotherapy.

1.7.4 Consider mouth-opening exercises for people having radiotherapy who are at risk of reduced mouth opening.

1.7.5 Consider voice therapy for people whose voice has changed because of their treatment.
Shoulder rehabilitation

1.7.6 Consider progressive resistance training for people with impaired shoulder function, as soon as possible after neck dissection.

1.8 Follow-up of people with cancer of the upper aerodigestive tract and management of osteoradionecrosis

Follow-up

1.8.1 Ensure people with cancer of the upper aerodigestive tract and their carers have tailored information about the symptoms of recurrence and late effects of treatment at the end of curative therapy.

1.8.2 Consider structured, risk-adapted follow-up using locally-agreed protocols for people who have had curative treatment for cancer of the upper aerodigestive tract. Use the follow-up protocols to:

- help improve quality of life, including discussing psychosocial issues
- detect disease recurrence or second primary cancer, possibly including narrow-band imaging to improve detection.

Management of osteoradionecrosis

1.8.3 Consider surgery to remove necrotic bone and to establish soft tissue coverage in people with osteoradionecrosis.

1.8.4 Only consider hyperbaric oxygen therapy or medical management for treating osteoradionecrosis as part of a clinical trial.

Stages of upper aerodigestive tract cancer

The stages of upper aerodigestive tract cancer referred to in this guideline are listed below.

- T0: this means there is no primary tumour, but there may be abnormal cells that are precancerous.
- T1 to T4: this refers to the increasing size and/or extent of the primary tumour, with 1 being smallest and 4 largest.
- **N0**: no lymph nodes contain cancer cells.

- **N1 and upwards**: increasing involvement of lymph nodes by cancer cells.
Upper aerodigestive tract cancers are found at various sites in the airways of the head and neck: the oral cavity, oropharynx, nasopharynx, hypopharynx, larynx and nasal sinuses. The majority are squamous cell cancers. The major risk factors for upper aerodigestive tract squamous cell cancer in the UK are tobacco smoking and alcohol consumption.

There is currently variation or uncertainty in the investigations used to assess neck lumps; who needs systemic staging, the most effective treatment for early stage and advanced disease, how to best identify HPV-positive disease, how to optimise function and rehabilitation, the most effective follow-up and the management of osteoradionecrosis of the jaw. This guideline aims to make recommendations that address these areas of variation/uncertainty.

This guideline will cover adults and young people (16 years and older):

- referred from primary care with suspected cancer of the upper aerodigestive tract
- with newly-diagnosed or recurrent cancer of the upper aerodigestive tract.

It will not cover:

- adults and young people with cancers of the thyroid, orbit, middle ear, cutaneous lip, skull base or salivary gland

- adults and young people with sarcoma or lymphoma

- children and young people under 16 years.
Recommendations for research

The Guideline Committee has made the following recommendations for research. The Guideline Committee's full set of research recommendations is detailed in the full guideline.

1 Systemic imaging – who and why?

What factors determine the risk of a person presenting with CUADT having metastasis or a second primary cancer?

Why this is important

Outcomes of interest include prevalence, predictive value and how the abnormalities identified influence patient management. The presence of metastasis or a synchronous second primary cancer at presentation is rare in patients with CUADT. Subgroups of patients have been identified in whom the risk is clearly elevated. However, it is not clear at which level of risk detailed staging investigations are justified and the impact the results of these would have on decision making by the clinicians and the patient. Health economic modelling is needed to inform this process.

2 HPV testing

What is the comparative effectiveness of single-step laboratory diagnostic tests to identify human papillomavirus (HPV) against current diagnostic test algorithms and reference standards in people with cancer of the oropharynx?

Why this is important

Outcomes of interest are sensitivity, specificity and resource use. HPV testing is currently recommended in cancer of the oropharynx because it has significant prognostic implication. Current methods use a 2-step procedure that is not widely available in all treatment centres. A single-step test is likely to be more widely adopted and could have significant budgetary implications for the NHS. The study should also consider the prognostic value and the economic benefits of novel tests.

3 Unknown primary of presumed upper aerodigestive tract origin

In people with CUADT of unknown primary, can radiotherapy target volumes be selected based on clinical and pathological factors?
Why this is important

Outcomes of interest include local control, progression-free survival, overall survival, and treatment-related morbidity and mortality. In a very small percentage of patients with squamous carcinoma involving a cervical lymph node the primary site remains occult despite intensive investigations. The optimum treatment for these patients is uncertain. Some clinical teams will treat the neck disease alone and others will treat some or all potential primary sites with the radiotherapy with or without chemotherapy. The latter strategy is associated with a high level of side effects that may have lifelong consequences, for example xerostomia. A better understanding of the clinic-pathological factors associated with treatment outcomes would improve treatment selection with the potential to reduce these side effects.

4 Enteral nutrition support

What specific clinical and non-clinical factors allow risk stratification when selecting which people with CUADT would benefit from short- or long-term enteral nutrition?

Why this is important

Outcomes of interest include resource use, morbidity of tube placement, duration of enteral feeding and nutritional status. There are no nationally agreed selection criteria for the type of feeding tube placed at diagnosis for people who need enteral nutrition support during curative treatment. Variation across the UK exists as a result of clinician-led practices and local policy. The systematic review by NICE in 2015 found some evidence but no specific list was identified because of limitations with study design, and inability to stratify clinical and non-clinical factors meaningfully. These factors included restricted populations for tumour staging, patient demographics, treatment plan and intent, definitions of malnutrition, timing and method of tube placement, and duration of enteral nutrition.

5 Follow-up

What is the optimal method, frequency and duration of follow-up for people who are disease-free after treatment for CUADT?

Why this is important

Outcomes of interest include quality of life, local control and overall survival. The optimal methods, frequency, and duration of follow-up in people who are clinically disease-free and who have undergone treatment for squamous cell cancer of the upper aerodigestive tract with curative
intent are not known. Considerable resources are expended throughout the country on the follow-up of people who have completed potentially curative treatment. Local follow-up protocols are based more on historical practice than evidence and are often disease- rather than patient-centred. Research to investigate how and when follow-up should optimally be carried out could improve clinical outcomes and the use of resources.

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