

RECOMMENDATIONS OF FSO

Posttreatment surveillance of adults with squamous-cell carcinoma of the upper aerodigestive tract.

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Clinical practice recommendations

METHODOLOGY

The recommendations were graded A, B, or C as follows:

- Grade A recommendations were based on consistent level 1 studies;
- Grade B recommendations were based on consistent level 2 or 3 studies or on extrapolations from level 1 studies;
- Grade C recommendations were based on level 4 studies or extrapolations from level 2 or 3 studies;
- Recommendations for which no grade is given were based on expert opinion (developed during exchanges among Task Force members).

This grading system is intended to clarify the bases for the recommendations. When no proof is available, every effort should be made to conduct further studies. However, the absence of proof does not mean that a recommendation is irrelevant or unhelpful (e.g., no proof is available for mastectomy in breast cancer or antibiotic therapy in tonsillitis).

The Task Force used the guide for reviewing the literature and grading recommendations issued in January 2000 by the ANAES (French Agency for Accreditation and Evaluation in Healthcare) to evaluate the level of proof supplied by the literature, based on the criteria below.

INTRODUCTION

Framework of the recommendations

Posttreatment surveillance is a key component of the management of patients with upper aerodigestive tract cancer. The surgeons, radiotherapists, and oncologists who contributed to the evaluation and treatment of the patient must work together to provide follow-up. Numerous healthcare providers have a role to play in the rehabilitation and global management of these patients.

In the vast majority of cases, patients recognize the need for posttreatment follow-up and are aware of the adverse effect a tumor recurrence would have on their hopes for survival. Detection of recurrences is not the only purpose of follow-up: other goals include evaluation of disease control, evaluation and treatment of residual pain and functional loss related to cancer therapy, assessment of psychological effects and of their impact on quality of life, and detection of metastases and second primaries. The co-morbidities, alcohol abuse, and heavy smoking often present in these patients require specific surveillance measures, which are best orchestrated by the primary care practitioner. These recommendations were developed by a multi-disciplinary panel of experts (including otorhinolaryngologists, radiotherapists, and radiologists). They specify the modalities follow-up, based on data from the literature or, when no data are available, on expert opinion.

Level of proof supplied by the literature	Grade of the recommendation
Level 1 Randomized controlled trials with high statistical power Meta-analysis of randomized controlled trials Decision analysis based on well-conducted studies	Grade A Definitive scientific proof
Level 2 Randomized controlled trials with low statistical power Well-conducted non-randomized comparative trials Cohort studies	Grade B Scientific presumption
Level 3 Case-control studies Comparison with historical controls	Grade C Low level of scientific proof
Level 4 Comparative studies with major sources of bias Retrospective studies Case-series Descriptive epidemiological studies (cross-sectional, longitudinal)	

Clinical practice recommendations

To ensure that the recommendations would apply to a homogeneous patient population, only squamous cell carcinomas of the upper aerodigestive tract were considered; Cancers of the nasopharynx, paranasal sinuses, salivary glands, and thyroid were excluded. The present recommendations are intended for the physicians involved in managing patients with upper aerodigestive tract cancer, namely, otorhinolaryngologists, maxillofacial surgeons, radiotherapists, and oncologists.

The recommendations deal with the four questions selected by the steering committee and task force:

- Modalities and timeline for posttreatment oncological evaluation
- Detection of local and regional recurrences and of metachronous primary cancers of the upper aerodigestive tract
- Detection of metastases and of metachronous primaries of the esophagus and lung
- Non-oncological objectives of posttreatment surveillance

Although this separation into four areas may seem arbitrary, it echoes the logical clinical approach. There is some temporal overlap between the four areas. Nevertheless, the separation results in a more cogent discussion of the approach to surveillance. The conclusion to these recommendations contains a surveillance timeline showing the period corresponding to each recommendation.

POSTTREATMENT ONCOLOGICAL EVALUATION

RECOMMENDATIONS

- The first clinical evaluation should take place 4 to 8 weeks after treatment completion (expert opinion).
- It should consist in a meticulous and thorough clinical examination including a detailed medical history to look for symptoms, an examination of the upper aerodigestive tract with nasal endoscopy if needed, and palpation of cervical lymph node sites.
- Endoscopy limited to the upper aerodigestive tract should be reserved for patients with symptoms that remain unexplained after the physical examination and to those with doubtful or incomplete physical findings.
- Laboratory tests: no reliable serum tumor markers are available (grade A).
- Computed tomography and/or magnetic resonance

imaging can be obtained routinely after 3 months to provide a point of reference. Imaging is advisable when the physical examination is difficult or the treatment did not include surgery.

- Positron-emission tomography is optional and should be considered when discrepancies exist between the physical findings and the results of computed tomography or magnetic resonance imaging.
- The only indication for cervical ultrasonography is evaluation of lymph node sites in untreated N0 necks, in combination with fine-needle aspiration. The operator must be highly experienced.
- A standard chest radiograph should be obtained in patients with pulmonary complications.
- Computed tomography of the chest and abdomen should be reserved for symptomatic patients.
- Independently from these recommendations, advice on hygiene and diet, as well as support in reducing risk factors, are integral to the initial follow-up evaluation (expert opinion).

Posttreatment evaluation is a key component of cancer management. The objectives of the first posttreatment visit are:

- to evaluate the treatment response and healing stage;
- to detect persistent malignant tissue in the primary or nodes;
- to prevent, to detect, and to treat the adverse effects of cancer treatment;
- to assess treatment tolerance and the physiological and psychological impact of cancer treatment;
- and to initiate measures aimed at helping the patient abstain from alcohol and smoking.

Posttreatment evaluations are made difficult by the morphological and tissue changes induced by surgery and/or radiation therapy.

The physical otorhinolaryngological examination is crucial, given the high local and regional failure rates and the need to assess sequelae and treatment-related complications.

Patient education about warning signs and close cooperation with the primary care practitioner are essential to improve the likelihood of early detection. Persistent and/or worsening symptoms should lead to a strong suspicion of active malignancy.

Endoscopy under general anesthesia

This investigation is costly and burdensome for the patient. In addition, its yield is low in patients who have no warning signs. Therefore, the need for endoscopy under general anesthesia should be determined in the light of findings from the clinical evaluation.

Clinical practice recommendations

This investigation should be reserved for patients who have symptoms or cannot be examined, whenever there is a suspicion of active malignancy.

Routinely performing bronchoscopy and esophagoscopy as part of the first follow-up evaluation is unhelpful.

Prospective studies are ongoing to determine the role for **positron-emission tomography (PET)** in the posttreatment surveillance program by answering the following questions:

- when should PET be performed?
- and what benefits to the patient would result from routine PET?

This extremely promising investigation is costly and not yet universally available.

DETECTION OF LOCAL AND REGIONAL RECURRENCES AND OF SECOND PRIMARY HEAD AND NECK CANCER

RECOMMENDATIONS

- The risk for local and node recurrence is greatest during the first 3 years, requiring appropriate surveillance (grade A).
- Surveillance should include routine visits and patient education about warning signs that must prompt an immediate additional visit (grade A).
- Surveillance should be of higher intensity in patients for whom further treatment with curative intent may be available (grade A).
- Serum tumor markers should not be assayed routinely in patients with cancer of the upper aerodigestive tract (grade A).
- Computed tomography and/or magnetic resonance imaging should be performed as indicated by the clinical setting. When clinical surveillance is difficult and further treatment with curative intent may be available, imaging studies are advisable.
- Positron-emission tomography should not be performed routinely for detecting local and regional recurrences of upper aerodigestive tract carcinomas. This investigation is recommended in difficult cases, most notably when computed tomography or magnetic resonance imaging is inconclusive (grade B).

- The contribution of ultrasonography has been investigated only in patients with T1 or T2 cancer of the oral cavity or oropharynx and no treatment to the lymph nodes. In this population, ultrasonography done once a month throughout the first year by an experienced operator is effective in detecting clinically silent node metastases (grade B).

- The detection of second primaries of the upper aerodigestive tract rests on the clinical evaluation. Patients with a history of alcohol abuse and smoking have a lifelong increase in the risk of upper aerodigestive tract cancer. Imaging studies and endoscopy under general anesthesia should be performed at the slightest suspicion (expert opinion).

Local and regional recurrences

Early detection of **local recurrences** and node metastases, as well as of **second primaries**, is a key goal of surveillance in patients treated for upper aerodigestive tract cancer, as curative treatment may be possible at an early stage. Early detection efforts should be started at completion of the initial treatment.

Several **risk factors for local recurrence** have been identified.

- *Characteristics of the primary:*

The risk is chiefly dependent on the characteristics of the initial primary (location, stage, and histology) and on the treatment modalities (decision to refrain from treating node sites, surgery or radiotherapy used alone, surgical excision margins).

- *Histology:* the recurrence rate may be lower in patients with well-differentiated squamous cell carcinomas. Positive excision margins are associated with a significant increase in the local recurrence rate (grade A).

Survival rates are very low in patients with recurrences.

Rates of successful treatment are highest when a recurrence is detected early in a patient initially treated using a single modality.

Routine evaluation visits should include a medical history focusing on symptoms that suggest a local or regional recurrence and a physical examination.

Whenever possible, the routine evaluation visits should be performed by a physician specialized in diseases of the upper aerodigestive tract.

Panendoscopy under general anesthesia is not performed routinely as a part of the surveillance strategy. This investigation is performed after imaging studies, to guide the collection of biopsy specimens.

Clinical practice recommendations

Second primaries of the head and neck

All patients with a history of upper aerodigestive tract cancer are considered at high risk for a second primary of the head and neck. Given that upper aerodigestive tract cancers can be detected by physical examination, prolonged follow-up to detect metachronous cancer is appropriate. Cancer of the oral cavity or oropharynx is associated with the highest rate of second primaries arising in the upper aerodigestive tract. The rate of second primaries of the upper aerodigestive tract is not influenced by the modalities used to treat the first primary.

Follow-up visits are best performed by the specialists who managed the patient initially and should include:

- a medical history focusing on recent events,
- a thorough physical examination of the upper aerodigestive tract with palpation of the neck,
- and nasal endoscopy at the slightest doubt.

Follow-up visits ensure the diagnosis of small tumors. Patients should be educated about the warning signs that require an immediate visit in addition to the routine follow-up visits.

Imaging studies are not required routinely. They should be performed as indicated by the physical findings, as tumors confined to the mucosa are not well visualized by computed tomography or magnetic resonance imaging.

DETECTION OF METASTASES AND OF METACHRONOUS ESOPHAGEAL AND LUNG CANCER

RECOMMENDATIONS

Detection of metastases

- Laboratory tests are not useful for detecting metastases (grade A).
- The task force recommends that chest radiographs be obtained routinely, at 6-month intervals for the first year then once a year (grade C).
- When the chest radiograph is abnormal, computed tomography of the chest should be performed.
 - normal findings : chest radiograph once a year
 - abnormal :
 - nodule > 1 cm and/or progression: multidisciplinary discussion

- nodule < 1 cm: computed tomography 3 months later
 - no progression: surveillance
 - progression: multidisciplinary discussion
- multiple nodules: no further investigations
- Investigations to detect bone and liver metastases should be decided only on the basis of clinical data (expert opinion).
- Detection of metastases more than 3 years after initial treatment should prompt investigations for a second primary.

RECOMMENDATIONS

Detection of metachronous primaries of the esophagus and lung

- Routine radiography or computed tomography of the chest cannot be considered standard practice.
- Nevertheless, the task force recommends that a chest radiograph be obtained once a year, since this investigation is widely available, inexpensive, and capable of detecting other conditions.
- No validated biological markers are available for detecting cancer of the lung or esophagus (grade A).
- The patient should be informed about the risk of a second primary of the lung or esophagus and about warning signs (expert opinion).
- Routine screening by esophageal endoscopy at 2-year intervals is simply an option. When this investigation is performed, iodine staining can be used (expert opinion).

The risk of a **second primary** is higher among patients who continue to use alcohol and cigarettes after the treatment of the first tumor. The risk persists over time.

The risk of a second primary is not meaningful in patients with no history of alcohol abuse or smoking (grade C).

Location of the first primary in the larynx is associated with an increased risk of metachronous lung cancer.

Location of the first primary in the oral cavity or pharynx is associated with an increased risk of metachronous esophageal cancer.

Cancer of the upper aerodigestive tract and metastases

The **most common targets**, by order of decreasing frequency, are the lungs, the bone, and the liver.

Clinical practice recommendations

In 80% of cases, the lung is the only organ involved. In 85% of cases, the metastases are diagnosed within **2 years** after the diagnosis of the primary (grade C). In 50% of cases, the metastases occur against a background of local and regional progression. The initial node status is significantly associated with the incidence of metastatic disease (grade C).

Many **nodular images** are detected by computed tomography of the chest. These images do not necessarily indicate malignant disease. A solitary nodule less than 1 cm in diameter can be managed by watchful waiting, with repeat computed tomography at 3-month intervals. Enlarging nodules and nodules measuring more than 1 cm in diameter can be investigated by fine-needle biopsy under computed tomography guidance, by PET, or by surgery.

Routine **PET** for metastasis detection is useful only when curative treatment for a recurrence or second primary of the head and neck is being considered.

Investigations for **bone metastases** should be reserved for patients with bone pain or hypercalcemia. First-line investigations include radiographs and computed tomography, although magnetic resonance imaging may be performed. Radionuclide bone scanning should be performed in patients with isolated hypercalcemia (expert opinion).

Investigations for **liver metastases** should be reserved for patients with liver pain and/or liver enlargement. Ultrasonography is the preferred first-line investigation and can be completed by computed tomography where appropriate.

In patients with lung metastases, investigations for bone and/or liver metastases should not be performed routinely. Instead, investigations should be selected according to the clinical setting.

Cancer of the upper aerodigestive tract and second cancer of the lung

Over 95% of lung cancer diagnoses occur in asymptomatic patients.

There is general agreement that routine screening for lung cancer by chest radiographs in high-risk populations is unhelpful.

Computed tomography has very high sensitivity but low specificity for lung cancer screening in high-risk patients.

Screening has not been shown to decrease mortality due to lung cancer. Thus, computed tomography has not been found effective as a screening tool.

Metachronous esophageal cancer

Clinical manifestations, when present, indicate fairly advanced disease. Therefore, it is important that patients be informed about warning signs (grade C and expert opinion).

Fiberoptic endoscopy

- should be performed immediately in patients with warning signs,
- is included by some groups in the routine surveillance strategy. In this situation, staining with 2% iodine increases the diagnostic yield. However, routine screening has not been shown to improve survival.

NON-ONCOLOGICAL OBJECTIVES OF FOLLOW-UP

RECOMMENDATIONS

Attention should be given to the following:

- posttreatment pain should be evaluated and its mechanism determined, in order to allow appropriate treatment,
- shoulder function should be evaluated routinely in patients treated with neck dissection, and rehabilitation therapy should be offered if needed,
- specific treatment should be given to improve abnormalities in voice, speech, and swallowing. Speech therapists and physical therapists must contribute to this multidisciplinary management program,
- body weight should be measured at each visit. Patients who lose weight should be referred to the nutritionist,
- discontinuation of alcohol and cigarette use should be facilitated, if needed via referrals to specialized clinics,
- the impact of the disease and treatment on quality of life, family life, work, and social activities should be evaluated. If needed, the patient should be informed about relevant volunteer organizations and self-help groups.

In patients treated with radiation therapy:

- obtain a TSH assay once a year (if the thyroid gland was in the field),
- obtain a cervical Doppler sonogram at the slightest indication of carotid artery stenosis,
- recommend once or twice yearly visits to the dentist,

Clinical practice recommendations

and reinforce the importance of lifelong fluoride applications.

The non-oncological component of posttreatment surveillance in patients with squamous cell cancer of the upper aerodigestive tract includes assessments of lung function, swallowing, phonation, morphological changes, neuro muscular alterations, and cosmetic sequelae.

The goals of this component are:

- to evaluate physiological functions and sequelae of cancer treatment,
- to suggest treatments for sequelae,
- to meet the patient's needs for psychological support, and to provide the follow-up required by the underprivileged socioeconomic background, alcohol abuse, and smoking that are prevalent in this patient population.

Regardless of the site of the initial upper aerodigestive tract cancer, surgical treatment and/or radiotherapy may cause **respiratory impairments** manifesting as dyspnea. All tracheotomized or tracheostomized patients should receive appropriate humidification and tracheal protection.

Careful history-taking is crucial to assess the degree of **communication** impairment and the type of **swallowing** disorders.

Swallowing can be assessed by nasal endoscopy during the ingestion of foods of various consistencies and of liquids, in order to detect aspiration. Videofluoroscopy improves barium swallow analysis. Dental or palatal prostheses may improve chewing, swallowing, and speech. The management of swallowing and phonation disorders requires the involvement of a multidisciplinary team including speech therapists, physical therapists, and nutritionists...

Complications of radiotherapy

The time to development of **carotid stenosis** ranges from a few months to more than 20 years. No proof is available that regular screening by Doppler sonography or computed tomography is beneficial. A high index of suspicion should be maintained, and Doppler sonography should be performed at the slightest clinical sign.

Hypothyroidism occurs chiefly during the first 2 years but may be delayed.

No effective treatment is available for **hyposalivation**.

Dental extractions during and after radiotherapy should be kept to a minimum and performed under medical supervision.

A **decrease in mouth aperture** develops 3 to 6 months after treatment. This abnormality is irreversible. Mechanical therapy can be offered.

Subcutaneous edema can be treated with manual lymphatic drainage of the neck.

An important precaution is to remind patients that they should not expose irradiated areas to sunlight.

Monitoring general health and nutritional status

Posttreatment surveillance should include:

- lung function tests,
- cardiovascular evaluations.

Special attention should be directed to the patient's general health, most notably as reflected by body weight.

Psychological help should be offered immediately if mood disorders develop.

Numerous tools are available for evaluating **quality of life**. Some of these tools, however, have not been validated.

CONCLUSION / PERSPECTIVES

The need for non-oncological follow-up is probably greatest in those patients with the least favorable prognoses (sequelae, resumption of activities ...).

Surveillance timeline

The posttreatment follow-up of patients with upper aerodigestive tract cancer requires that numerous problems be managed simultaneously :

1. Recurrences should be looked for during routine visits and via patient education about signs that should prompt an additional visit. Closer surveillance is recommended in patients treated with a single modality and for whom further curative treatment is available.
2. Second primaries of the upper aerodigestive tract should be looked for by physical examination during routine follow-up visits. Imaging studies and endoscopy should be performed at the slightest doubt. Investigations for second primaries of the lung and esophagus should be performed in patients with suggestive symptoms.
3. Metastases should be looked for by performing a chest radiograph routinely once a year and by obtaining additional imaging studies and laboratory tests in patients with clinical manifestations suggesting bone or liver metastases.

Clinical practice recommendations

4. Pain should be evaluated and managed appropriately.
5. Residual impairments in swallowing, voice, and speech should be evaluated and managed by appropriate rehabilitation and multidisciplinary care.
6. Nutritional status should be assessed by history taking and body weight measurements.
7. Psychological disorders should be evaluated.
8. Patients should receive treatment aimed at discontinuing the use of alcohol and cigarettes.
9. In addition, after radiotherapy:
 - a. Patients should be educated about proper oral hygiene and the need for daily fluoride prophylaxis. Twice yearly visits to the dentist are recommended.
 - b. Thyroid function should be monitored.

Posttreatment surveillance requires the co-operation of all the physicians involved in diagnosing and treating upper aerodigestive tract cancer, including surgeons, upper aerodigestive tract specialists, oncologists, and radiotherapists.

The primary care physician also plays a major role, most notably regarding the management of co-morbidities, pain, psychological disorders, and cessation of alcohol and cigarette use.

Below is a surveillance timeline, which should be tailored to the needs of each patient.

