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SFORL Guidelines

Guidelines of the French Society of Otorhinolaryngology (SFORL), short version. Diagnosis of local recurrence and metachronous locations in head and neck oncology

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ABSTRACT

Surveillance is fundamental to the management of head and neck cancer. The present guidelines of the French ENT society (SFORL) were drawn up by a group of experts in the field, and are intended to specify the modalities of management, based on a review of the literature and, where data are lacking, to provide expert opinion. The present paper deals with guidelines for the diagnosis of local and regional recurrence and metachronous head and neck locations. Locoregional recurrence usually occurs within 3 years of primary treatment and is mainly related to the characteristics of the primary tumor and the treatment measures taken. Laryngeal location, safe primary resection margins, low level of lymph node invasion, unimodal primary treatment and early diagnosis of recurrence are factors of good prognosis. Systematic imaging surveillance may be considered for patients for whom a curative technique exists and when surveillance is difficult. The role of PET-scanning remains to be determined. Metachronous locations are frequent, even in the late course; prolonged surveillance is appropriate. The best preventive measure is cessation of alcohol abuse and smoking. Patient education is primordial.

Surveillance is fundamental to the management of head and neck cancer, and is the responsibility of all practitioners involved in care.

Ninety-seven percent of patients consider it necessary [1] (level of evidence 4).

The present guidelines were drawn up by a multidisciplinary group of experts in the field: ENT specialists, and also radiotherapists and oncologists. They are intended to specify the modalities of management, based on a study of the literature and, where data are lacking, on expert opinion. Nasopharynx, facial sinus, and salivary and thyroid gland cancer were excluded.

The present paper deals with guidelines for the diagnosis of local and regional recurrence and metachronous head and neck locations.

1. Local and regional recurrence

Diagnosis is essential, especially in high-risk patients and those for whom curative measures are available.

Diagnosis of locoregional recurrence begins 6 months after the end of primary treatment and is intended to determine curative treatment [2] (level of evidence 2).

Local recurrence induces lymph node recurrence, which in turn induces metastasis [3,4] (level of evidence 4).

Early diagnosis enables treatment with curative intent and improves survival [3,5] (level of evidence 4), [6] (level of evidence 2).

1.1. Time to onset of local recurrence

Locoregional recurrence, estimated at 15–35%, is usually local. Onset in 90% of cases is within 3 years of primary treatment [2] (level of evidence 2), [1] (level of evidence 2), [3,7,8] (level of

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evidence 4). De Raucourt et al. estimated recurrence rates at 21% by 2 years and 25% by 3 years [9] (level of evidence 4).

Guideline

- Locoregional recurrence should be screened for during the first 3 years (expert opinion).

1.2. Risk factors for locoregional recurrence

Risk factors are mainly related to primary tumor characteristics and treatment modalities.

Recurrence rates are higher in pharyngeal than laryngeal tumor. According to Boysen et al. [2] (level of evidence 2) and Haas et al. [3] (level of evidence 4), recurrence rates are independent of tumor location and are lower only for T1 tumor. N0 tumor shows less lymph node recurrence, which is very high in N3 tumor [3] (level of evidence 4).

Abstention from lymph node surgery incurs a high-risk of lymph node recurrence, especially in oral cavity cancer [10] (level of evidence 2).

Histologically, well-differentiated squamous cell carcinoma shows the lowest rate of local recurrence [1] (level of evidence 2).

Positive margins [11] (level of evidence 4) and perineural invasion [12] (level of evidence 4) increase the risk of local recurrence.

HPV+ tumor shows less local recurrence [13] (level of evidence 2). In oropharyngeal HPV+ tumor, smoking is the main risk factor for local recurrence [14] (level of evidence 2).

1.3. Patients in whom early diagnosis of recurrence may influence survival

Survival rate for patients with recurrence or in whom a second location is discovered is very low: 16% at 5 years according to Haas et al. [3] (level of evidence 4).

In advanced recurrence, treatment is curative in only 5% of cases [15] (level of evidence 4).

Time to onset of recurrence does not correlate with survival [16] (level of evidence 2). Laryngeal primary tumor is associated with optimum survival in case of second location, probably due to primary tumor stage, which is usually T1 or T2N0, managed by exclusive surgery allowing salvage surgery and radiation therapy [3] (level of evidence 4). The success rate for treatment of recurrence of laryngeal tumor is nearly 85%, versus 35% for other locations [16] (level of evidence 2).

Early diagnosis of recurrence influences survival, which is further correlated with the TNr stage rather than with primary stage, Nr stage being more influential than Tr stage [17] (level of evidence 2).

Success of tumor salvage treatment is high only with unimodal primary treatment; authors therefore recommend intensive surveillance following unimodal treatment, as treatment will be with curative intent in case of recurrence [2] (level of evidence 2), [3] (level of evidence 4).

1.4. Contribution of systematic examination in screening for recurrence

Treatment with curative intent is usually feasible in asymptomatic patients [1] (level of evidence 2), arguing strongly for systematic consultation, preferably by a head and neck specialist. Boysen et al. reported a higher rate of tumor detection in case of symptomatic lesion [2] (level of evidence 2), without significant impact on survival. The literature findings are sometimes contradictory; some authors report higher detection rates in control consultations without functional complaint [3] (level of evidence 4), while others, such as Flynn et al. [12] (level of evidence 4), reported much higher recurrence discovery rates in consultations for functional complaints.

Surveillance should certainly be systematic, while informing patients for the possible need of extra consultations in case of onset of symptoms suggestive of recurrence.

1.5. Contribution of endoscopy in recurrence screening

There have been no studies of the contribution of panendoscopy to surveillance. The consensus is that it should be scheduled according to symptoms or examination findings, preferably after imaging, to guide biopsy [18,19] (expert opinion).

1.6. Contribution of biological examination

There are no specific biological markers for the diagnosis and follow-up of head and neck cancer, other than in the nasopharynx.

1.7. Contribution of imaging

1.7.1. Contribution of CT in screening for local and lymph node recurrence

In an organ-sparing protocol, Hermans reported earlier recurrence detection on CT than on clinical or fiberoptic examination, probably due to the submucosal primary location [20] (level of evidence 4). Progression assessment therefore requires baseline imaging as part of the posttreatment check-up.

Jung et al. [8] (level of evidence 4), in a retrospective study of 520 patients, reported that 53% of recurrences were diagnosed by the specialist, 25% by the patient and 22% on systematic imaging following multimodal treatment of advanced tumor; patients receiving surgery showed less local recurrence, and local recurrence was more often detected by specialists whereas regional recurrence and metastasis were more often detected on complementary examination.

Systematic imaging surveillance may be considered for patients for whom a curative treatment is available or in whom clinical and endoscopic surveillance is problematic (e.g., following radiation therapy).

1.7.2. Contribution of PET-CT in screening for local and regional recurrence

Studies using systematic PET-CT in follow-up reported a 30% rate of tumoral events at 1 year's surveillance [21] (level of evidence 4), [22,23] (level of evidence 2). Beswick et al. reported that 95% of recurrences occurred within 24 months, and that there is no interest in continuing PET-CT systematically after that time [21] (level of evidence 4).

In a meta-analysis of 55 studies with more than 2355 patients, Gupta et al. reported insufficient positive predictive value (58%) with PET-CT; the very good negative predictive value (95%), however, helps avoid unnecessary invasive examination [24] (level of evidence 1).

PET-CT is currently recommended in difficult cases with suspected tumor but negative biopsy or when assessment fails to account for symptoms, especially when CT and MTI prove noncontributive. It should be performed late after biopsy, to avoid false positives.

A prospective study of survival and medico-economic aspects could determine the surveillance role of PET-CT and patient selection, frequency of examination and posttreatment interval.

2. Metachronous locations at the level the upper aerodigestive tract (UADT)

Populations at risk of second location: all patients with an initial location at the UADT are at significant risk of second location, estimated at 2–4% per year for 10 years or more [25] (level of evidence 4). In the first 3 years, the main risk is of locoregional recurrence. Surveillance should thereafter focus on secondary locations [9] (level of evidence 4).

Patients with an initial location at the UADT show a cumulative rate of metachronous second head and neck location of 56% by 15 years, on a linear curve not diminishing over time [9] (level of evidence 4).

Prolonged surveillance is therefore mandatory.

Some patients are at higher risk of developing a metachronous second location.

2.1. Risk related to social history for tobacco and alcohol

Smoking and alcohol abuse are risk factors for secondary cancer [26] (level of evidence 2).

Cessation of smoking reduces risk [27] (level of evidence 2) and, according to Murakami et al., withdrawal from smoking and alcohol is the best preventive measure [28] (level of evidence 4).

2.2. Risk related to tumor location

The oropharynx and oral cavity are the sites where second locations are the most frequent [25] (level of evidence 4). Haughey et al., in a meta-analysis including 3706 patients, reported 67%, 53%, 43% and 30% rates of second location for primary cancers of the oropharynx, oral cavity, hypopharynx and larynx, respectively; these rates were inversed for pulmonary secondary locations [29] (level of evidence 2).

2.3. Risk related to tumor characteristics

Tumor stage, histologic type and lymph node status do not seem to affect secondary onset.

Resection margins, likewise, do not affect secondary locations, although they are an essential factor in local recurrence.

Two retrospective studies showed that HPV+ oropharyngeal tumor shows significantly less risk of second location occurrence [30,31] (level of evidence 4).

2.4. Risk related to treatment

Several prospective studies reported similar secondary location rates with radiation therapy and concomitant radio-chemotherapy following surgery [15,32,33] (level of evidence 1).

3. Patient selection for early diagnosis of secondary head and neck location

Second head and neck location is the most frequent and easiest to diagnose, being accessible to clinical examination, and shows the best prognosis: 20% survival, versus 3% for the esophagus and 2% for the lung, according to Schwartz et al. [26] (level of evidence 2). Patients who have never smoked or shown alcohol abuse can be excluded from such surveillance [26,34] (level of evidence 2).

The interest of systematic surveillance is controversial. Boysen et al. insisted on patient education, encouraging consultation for any abnormal sign [2] (level of evidence 2).

de Visscher and Manni, in contrast, in a 1994 study of 428 patients, found better survival after early event screening than after return to consultation for symptoms [1] (level of evidence 4), and therefore considered surveillance, like psychological follow-up, to be indispensable.

Finally, although survival benefit remains unproven, screening for metachronous cancer appears justified in patients at high-risk according to the above-mentioned criteria. This is especially true for secondary head and neck locations, which are most accessible to treatment with curative intent.

3.1. Contribution of systematic clinical examination in screening for secondary head and neck locations

3.1.1. Surveillance consultation

The size of asymptomatic tumors discovered on scheduled consultation is not significantly smaller than that of symptomatic tumors, and survival is identical [9] (level of evidence 2).

Some authors therefore question the usefulness of systematic consultation, highlighting rather the importance of patient education [2] (level of evidence 2).

3.1.2. Contribution of endoscopy in screening for second locations at the level of the UADT

Panendoscopy is not systematic; it should be performed only in the case of a doubtful diagnosis, a particular symptom or to enable biopsy (expert opinion).

Only two reports recommended systematic panendoscopy, but without demonstrating efficacy and benefit: once yearly for Di Martino et al. [25] (level of evidence 4), and twice yearly for Narayana et al. [35] (level of evidence 2).

3.2. Biological examination

Serum tumor markers show poor sensitivity for the diagnosis and follow-up of head and neck cancer.

3.3. Imaging

Imaging should be guided by clinical examination.

Purely mucosal locations are poorly visualized on CT and MRI. PET-CT is mainly useful in screening for recurrence and is not very cost-effective for second cancer: events are infrequent (5% at 6 months and 4% at 1 year) and sensitivity is 29% at 3–6 months and 80% at 1 year. The study by Kim et al. was alone in reporting second (metachronous) cancer, but most cases were not necessarily related to smoking (nasopharynx, thyroid, prostate, stomach) and were therefore sometimes discovered serendipitously; with annual secondary incidence at 4%, the cost of such “screening” becomes problematic [22] (level of evidence 2).

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