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Review

Clinical Evidence of Methods and Timing of Proper Follow-Up for Head and Neck Cancers

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Simple Summary: Optimal treatment strategies for HNSCC involve multidisciplinary tumor boards considering disease location, stage, and functional outcomes. While early-stage disease may be treated with single-modality approaches, locally advanced cases often require multimodal treatment. Despite aggressive therapies, local and distant recurrences remain a common challenge. Thus, a well-structured follow-up strategy is essential, with a focus on detecting recurrences within the first two years after treatment. However, due to the lack of standardized protocols and clear guidelines, clinical and radiological follow-up practices vary significantly among institutions, and their impact on patient survival remains uncertain.

Abstract: Background: For patients with head and neck squamous cell carcinoma (HNSCC), after a single or multi-modality treatment, a specific follow-up strategy is needed, but there is no agreement between the main international societies on the proper methods and timing of follow-up. **Methods:** We performed a descriptive review to evaluate the available data and compare the main guidelines, giving some practical guidance to perform effective personalized follow-up strategies. **Results and Conclusions:** While clinical and endoscopic follow-up alone seems to be appropriate for early-stage HNSCCs, the addition of close radiologic follow-up in locally advanced HNSCCs is still debated, as there are no data indicating that an earlier detection of recurrence correlates with increased survival, while it is mandatory in the first three-six months to define the response to treatment. For patients who have undergone conservative surgery or have major pathological risk factors, the incidence of locoregional recurrence is higher, and locoregional radiologic follow-up (magnetic resonance imaging is preferred to computed tomography) should be considered. Positron emission tomography may be useful in cases of suspected locoregional persistence of disease, differentiating it from post-irradiation outcomes. Distant radiological follow-up can be considered in the detection of the second primary in cases of specific risk factors and for virus-related tumors. For the latter, the use of circulating DNA should always be considered. A brain scan is not recommended without specific symptoms. For all patients who do not fall into the above categories, clinical and endoscopic follow-up should be proposed, reserving radiological investigations only at the onset of symptoms.

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1. Introduction

Head and neck squamous cell carcinoma (HNSCC) is the seventh most common cancer, accounting for about 700,000 new cases each year worldwide [1]. HNSCC may arise from epithelial cells of the oral cavity, oropharynx, nasal and paranasal cavities, larynx, and hypopharynx. Tobacco use and alcohol consumption are the main risk factors associated with HNSCC diagnosis, and their combined use has a synergistic effect [2–5].

Smoking tobacco also plays a role as a prognostic factor, primarily due to the higher rate of smoking-related second primary tumors. Additionally, the disease-specific mortality is significantly increased in former or active smokers compared to non-smokers [6–8]. Human papilloma virus (HPV) infection is also implicated in the etiopathogenesis of oropharyngeal carcinomas (OPSCCs) [9,10].

An HPV-positive OPSCCs, characterized by distinct histopathological features and an earlier age of onset, is associated with a more favorable prognosis compared to its HPV-negative counterpart [11].

The optimal treatment strategy must be discussed by a multidisciplinary tumor board, and it should be individualized considering the disease location, stage, viral correlation, and the expected functional outcome.

For early-stage HNSCC, a single-modality treatment approach involving either surgery or radiotherapy (such as intensity-modulated radiation therapy or volumetric-modulated arc therapy) is recommended. In contrast, locally advanced diseases can be effectively managed through a combination of surgery followed by adjuvant (chemotherapy)-radiotherapy [(C)RT] or exclusive concurrent CRT [12].

In cases of multimodal treatment failure, local recurrence is the most common presentation of relapse, occurring in approximately 40% of patients, most of which occur within the first 2 years after the initial diagnosis [13–18], while the incidence of distant metastases (DMs) is lower (10–20%) [19] and it is strictly connected to specific risk factors, such as three or more positive pathological nodes, extra nodal invasion, low jugular nodes tumor invasion, previous (loco)regional recurrence, a primary hypopharynx tumor, an advanced T-stage, and nodal metastases of 6 cm or more [20]. The most common site of DMs is the lung, followed by bones, the liver, and skin. Moreover, most of HNSCC DMs (around 50%) occur within the first 8 months after the end of treatment, then gradually decrease until 24 months, reaching a final plateau for the remaining follow-up [21].

All these data suggest the crucial role of follow-up, currently composed of the combination of clinical, endoscopic, and radiologic approaches according to the tumor subsite, clinical stage, and the treatment performed [14–18,22,23].

Unfortunately, given the lack of randomized clinical trials, there is no agreement on the proper follow-up strategy for locally advanced HNSCC, both in terms of timing and methods, and practice recommendations are controversial.

The most debated role involves radiological follow-up, as it could identify locoregional or distant recurrences/second primary tumors earlier than clinical and symptom-guided follow-up, but it is unclear whether this positively impacts patient survival [24].

2. Radiological Techniques

Currently, post-treatment surveillance for HNSCC relies on a combination of morphological and functional imaging techniques. Morphological techniques include computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US), while functional techniques include positron emission tomography (PET)-CT.

CT is the most-used imaging technique for assessing the response to therapy and the onset of distant metastases in oncological radiology, as this constitutes a relatively inexpensive and rapid tool for HNSCC surveillance.

MRI is the first choice for clinical staging for most HNSCC subsites, thanks to its superior contrast resolution among radiological techniques that enables a great soft tissue depiction.

US has a limited role in HNSCC imaging as it is severely limited in the evaluation of deeper structures. However, for its high spatial resolution, it may be useful to discriminate pathological lymph nodes and to evaluate superficial disease in a selected (accessible) subsite, such as, for instance, the oral cavity [25]. Moreover, US is widely used for guiding fine needle aspiration and core biopsy.

CT possesses the capability to evaluate the status of bones, particularly cortical margins, as well as detecting cartilage erosion and destruction with remarkable sensitivity. As a result, CT can effectively contribute to the staging and surveillance of nasopharyngeal, oropharyngeal, and laryngeal cancer [26]. However, MRI offers several advantages over CT: for instance, bone and cartilage permeation may be easily missed on CT and MRI is superior to CT in detecting bone marrow invasion [26]. Therefore, CT and MRI may be considered complementary techniques for assessing bone invasion. For laryngeal cancer, both reactive inflammatory changes and the early invasion of cartilages may appear as sclerosis, and CT is not able to distinguish between them [27]. MRI greatly facilitates cartilage assessment in laryngeal carcinoma, both for staging [28] and surveillance after therapy [29]. However, MRI for laryngeal cancer has strict technical requisites and should be correctly performed (i.e., high resolution sequences, a small FOV, local receive surface coils) [27]. Thanks to its better soft tissue resolution, MRI should always be preferred for sites close to the skull base, such as paranasal sinuses and the nasopharynx, and for tumors prone to perineural extension, such as minor and major salivary gland tumors [30]. A pivotal role in MRI cancer surveillance is played by the diffusion-weighted imaging (DWI) sequence. DWI can identify hypercellular tissue because of the reduction in intracellular and extracellular spaces available for the free diffusion of water molecules. Consequently, the apparent diffusion coefficient decreases and signal intensity increases. DWI showed superior sensitivity for recurrent or residual tumor detection on MRI [31–33], thus several authors proposed to include MRI for Neck Imaging Reporting and Data Systems (NI-RADSs) [34,35].

PET-CT offers cancer functional information with a high specificity but modest sensitivity for post-treatment recurrence, and must be integrated with morphological techniques and clinical investigation [36]. PET-CT is particularly useful for doubtful radiological or clinical findings characterizations, with high negative predictive value [37]. However, PET-CT is widely used for HNSCC surveillance, even if any evidence of survival advantages has been proven.

PET-CT must not be performed immediately after treatment but preferably 8–12 weeks after therapy because an increased (18)F-fluorodeoxyglucose (FDG) uptake is observed both in inflammatory and neoplastic tissue [38–40].

Table 1 summarizes the advantages and disadvantages of commonly used radiological techniques in head and neck cancer surveillance.

Table 1. Advantages and disadvantages of commonly used radiological techniques in head and neck cancer surveillance. US: ultrasound; CT: computed tomography; MRI: magnetic resonance imaging; PET-CT: Positron Emission Tomography–Computed Tomography.

Technique	Advantages	Disadvantages
US	Great spatial resolution, ultrasound-guided fine needle aspiration and core biopsy	Severe limitation for evaluating deeper structures
CT	Inexpensive, rapid	Poor soft tissue resolution
MRI	Great soft tissue resolution, intracranial disease, perineural spreading	Long time of acquisition, expensive
PET-CT	Functional information	Poor morphological information

3. Clinical Follow-Up

Clinical follow-up is of paramount importance for HNSCC patients for several reasons. Firstly, it allows for the assessment of treatment response, enabling healthcare providers to gauge the effectiveness of the chosen therapeutic approach. Secondly, regular follow-up visits facilitate the early detection of late adverse events that may arise because of treatment. Moreover, clinical follow-up serves to provide comprehensive support to both the patient and their caregiver, ensuring their well-being throughout the recovery process [41].

To accomplish this, routine follow-up visits should be conducted by a multidisciplinary team comprising ear, nose, and throat (ENT) surgeons, oncologists, radiation oncologists, nuclear medicine physicians, speech and swallowing therapists, nutritionists, and dentists. This collaborative approach aims to foster a holistic view of the patient's condition, considering various facets of their health and well-being.

Duration and frequency of the follow-up program should always be defined case by case, considering the patient and cancer features. Generally, specialistic follow-up for HNSCC could be stopped 5 years after the diagnosis, while for adenoid-cystic carcinomas, HPV-positive OPSCC, and head and neck neuroblastomas, the follow-up should be continued for 10 years, considering their risk of late recurrence [1,41].

Clinical follow-up should be carried out every 2–3 months for the first 2 years, every 3 to 6 months for years 3–5, and annually thereafter, according to clinical practice guidelines form the European laryngology society (ELS), the European Head and Neck society (EHNS), the European Society for Medical Oncology (ESMO), the European Society for Radiotherapy and Oncology (ESTRO), and the National Comprehensive Cancer Network (NCCN) [1,41,42].

During clinical follow-up it is mandatory to investigate any onset symptoms such as dysphonia, abnormal and persistent throat discomfort and globus, breathing difficulties and local pain, dyspnea, dysphagia, odynophagia, reflex otalgia, weight loss, lockjaw, and local pain. The palpation of the primary site of the tumor (if accessible) and of the neck are required.

Subsequently, a comprehensive endoscopic evaluation is necessary to assess the entire mucosal lining. Depending on the specific location of the disease, a high-resolution flexible endoscope should be used for laryngeal or hypopharyngeal diseases, while a rigid endoscope is suitable for investigating oral cavity, sinonasal, or nasopharyngeal diseases. In the case of oropharyngeal cancer and patients with a history of smoking, both tools may be employed to achieve the optimal visualization of the affected site and to screen for second primary tumors [43]. All endoscopies should be carried out in White and Narrow Band Imaging (NBI) to enhance the visualization of the mucosal and submucosal microvascular pattern vessels [44–46]. NBI uses narrow-band spectrum optical filters to enhance the mucosal view and the microvascular patterns of the submucosal view. Due to the fact that the depth of penetration of light depends on its wavelength, NBI filters select the blue and green light (with wavelengths of 415 and 540 nm, respectively), corresponding to the peaks of absorption of hemoglobin. A well-demarcated brownish area, with thick dark spots and winding vessels and an afferent hypertrophic vessel, is considered to be a suspicious lesion in NBI [45].

Clinical follow-up can detect locoregional recurrences earlier, which increases the chance of performing salvage treatments with locoregional control of the disease: when this occurs, 5-year survival is 77% with an excellent cost-effectiveness ratio [47].

Since only 40% of patients presenting with symptoms have a recurrence (or a second primary), and 72% of all patients reported late effects, clinical follow-up is also useful for the detection and monitoring of treatment sequelae and late toxicities, which can also develop several years after the end of treatment [47].

In early-stage cases, where radical treatment is highly effective and the incidence of recurrence is low, endoscopic follow-up without radiological imaging is adequate.

4. Radiological Follow-Up

A radiological follow-up program is often a theme of debate, given the lack of randomized clinical trials in any solid tumor and the absence of standardized protocols.

Moreover, due to the heterogeneity of head and neck malignancies, including several histotypes and subsites, the follow-up of these tumors is even less standardized compared to that of others (e.g., breast, lung, or colorectal cancers) [48,49].

While the NIRADS guidelines [50] recommend follow-up based on radiological imaging over time in all patients, the ACS guidelines advise against it, regardless of the characteristics of the primary lesion [51].

The guidelines of the ASCO, ESMO and NCCN, which are considered the most authoritative and widely used guidelines, recommend radiological follow-up for patients in whom, after radical treatment, there is suspicion of persistent disease on the initial re-evaluation and in case of disease districts being difficult to explore endoscopically [1,52,53]; however, none of the guidelines [1,39,42,50–52] seem to define with certainty if an earlier diagnosis can positively impact patients' survival endpoints, in particular their overall survival.

Among all the main international guidelines, there seems to be agreement only about the need for a first radiological evaluation after treatment, although there is no agreement on either the timing (between 3 and 6 months) or the modalities of it [1,39,42,50–52].

Table 2 are summarizes the follow-up strategies of the main international guidelines.

Table 2. A comparative table of the most-used international guidelines for head and neck tumors' response evaluation and subsequent follow-up.

	Response Evaluation		Follow-Up	
Guideline	**Selection Criteria**	**Timing**	**Selection Criteria**	**Timing**
NCCN	Locally advanced tumors (T3, T4, N1, N2, or N3), or anatomical areas difficult to explore	PET/CT within 3–6 months. CT and MRI within 3–4 months.	Difficult areas to explore endoscopically. Not indicated for asymptomatic patients with negative clinical exam.	Not defined
ESMO	Locally advanced cancers	≥3 months. PET/CT for N-positive patients.	Symptomatic patients or clinically suspicious of recurrence.	Not defined
ASCO	Locally advanced tumors (T3, T4, N1, N2, or N3), or NO with high risk of occult lymph node metastasis.	PET/CT ≥ 12 weeks after the end of treatment.	Patients with residual lymph nodes (LNs) with mild uptake and ≤1 cm, or residual LNs ≥ 1 cm without uptake on initial post-treatment imaging.	Not defined
AHNS	Locally advanced tumors (T3, T4, N2, or N3) of oro-hypopharynx, glottic/supraglottic larynx, and nasopharynx.	12 weeks post-treatment	Not routinely recommended.	Not defined
NIRADS	All patients with head and neck tumors.	PET/CT 8–12 weeks post-treatment. MRI or CT from 12 weeks to 6 months	All patients	CT/MRI or PET/CT 6 months after first imaging; 12 months after; annually thereafter. Every 3 months for suspicious findings.

In case of suspected regional disease persistence or recurrence, a PET-CT scan may be considered the gold standard examination, assessing the metabolic activity of suspicious lesions as the results of previous treatments (e.g., radiotherapy) or tumor-induced morphological changes [39,53]. For the same reasons, a PET scan seems to be the radiological examination of choice for patients who underwent definitive chemo-radiotherapy treat-

ment, possibly preceded by MRI, and for the evaluation of lymph nodes in patients who underwent adjuvant radiotherapy (alone or with concurrent chemotherapy) [39,53].

Differently from the PET-CT scan, MRI provides a morphological evaluation of the head and neck sites. MRI should not be performed within 60–90 days after the end of treatment, especially after radiotherapy, due to the treatment-related alterations (in particular, edema and other inflammatory findings) that can cause the misinterpretation of radiological images.

In all other circumstances, MRI is to be considered the technique of choice.

For some head and neck subsites or different histologies, due to the high risk of specific recurrences, a different follow-up program is recommended, such as for nasopharyngeal carcinoma, characterized by an higher predilection of liver metastases [54], NOTCH+ ACC which metastasize to the lungs [55,56], and HER2-positive salivary duct carcinoma, in which a brain scan is recommended [57].

Radiological follow-up has some limitations.

Primarily, it has been demonstrated that HNSCC patients have poor adherence to follow-up strategies over time: only one out of two patients is adherent with surveillance, and it is unclear how it impacts survival outcomes, compared to radiologic follow-up adherence. It is also important to consider the stress related to hospital access and the consequent reduction in patients' quality of life [58]

Secondarily, it has been demonstrated that intensive nonsymptom-based radiologic follow-up, albeit with the limitation that each country has different costs, can cost more than $9000 per year, with no clear cost–benefit ratio: only 10–20% of patients who develop a recurrence are asymptomatic [47,59].

Despite this, there are no data indicating that the early detection of recurrence has an impact on patient prognosis, and along with the other limitations seen above, it is paramount to think about less intensive and more symptom-related radiology follow-up strategies [47]. Despite this, in specific cases, radiological follow-up could play a key role, particularly in patients with a primary site of disease that cannot be explored endoscopically, as salvage strategies may be possible with the early detection of recurrence. At present, unfortunately, we are unable to predict any patterns of recurrence.

5. Distant Metastases and Second Primary Tumors

The occurrence of distant metastases in HNSCC during follow-up shows a rapid increase within 8 months after treatment, with a subsequent slow increase between months 8 and 24, followed by a substantial plateau between months 24 and 84, indicating the absence of late metastases [60,61].

The incidence of distant metastases, at least diagnosed, in HNSCC is low: less than 5% at diagnosis [20] and overall occurring in about 10–20% of cases, most of which are asymptomatic [19]. Although in specific cases, such as advanced T, the primary tumor of the pharynx, the presence of a second primary HNSCC, the presence of $\geq$3 neck lymph node metastases, bilateral lymph nodes metastases, low jugular positive lymph nodes radiological or histological extra nodal extension (ENE), nodal metastases $\geq$ 6 cm in size, a high grade tumor, a high volume tumor, lymph vascular invasion, and regional recurrence [15,20,56,57,62–65], the incidence of distant recurrence is higher. There are no data that early diagnosis could impact on prognosis. Although oligometastatic patients might benefit from the treatment of lesion(s), it is impossible to predict who might develop this pattern of recurrence. The most common site of distant metastasis is the lungs (in about 75–80% of cases), followed by bones and the liver in 15–39% and 10–30% of cases, respectively [20,66].

In metastatic patients, it is useful to combine locoregional and distant investigation, with endoscopic and radiological imaging, including that of the chest and abdomen.

Systemic staging is sometimes able to reveal second primary tumors: the incidence of second primaries is 2% and 4% per year [67].

In approximately 75% of cases, HNSCCs are directly related to tobacco smoking and alcohol use, and, in particular, OPSCCs are often related to HPV infection [11]. Both conditions may promote the occurrence of tumors in other districts: tobacco smoking correlates with cervical esophagus, lung, and bladder cancers, while HPV infection correlates with penis, cervix, and anus cancers.

However, there are currently no indications in the guidelines regarding screening for possible second malignancies in patients diagnosed with an HNSCC. The only exception is for heavy smokers (>20 pack/years), for whom even at an early stage, a chest CT scan is recommended [41].

Further examinations for the above-mentioned districts remain at the discretion of the clinician. It is important to consider the possibility of a second primary tumor in patients with risk factors in differential diagnosis if alarming symptoms appear.

6. Circulating Biomarkers

Among HNSCCs, two tumors may be related to viral infection: nasopharyngeal carcinoma (NPCs) and OPSCCs.

NPCs are classified into three different histological types: keratinising, non-keratinising (subdivided into differentiated and undifferentiated), and basaloid carcinomas. A non-keratinising NPC is more frequent in endemic areas and is almost always related to Epstein–Barr virus (EBV) infection, while a keratinising NPC is more frequent in non-endemic areas, and it is less associated with EBV [54].

An OPSCC, on the other hand, may be caused by chronic human papillomavirus (HPV) infection [68].

For NPCs, EBV in tumor cells is detected using in situ hybridization to identify EBV-encoded RNAs (EBER) [69], and for EBER-positive NPCs, EBV-DNA could be found in plasma. A pre-treatment circulating EBV-DNA load is related to both disease stage and cancer-related risk, with lower levels associated with a low stage and better prognosis [70,71]. A post-treatment circulating EBV-DNA load (with a cut-off of 500 copies/mL distinguishing between good and poor prognosis) and the rate of decrease have prognostic significance: the circulating EBV-DNA load continues to change during the first 3 months after treatment, and patients with delayed or no remission of EBV-DNA have a poorer prognosis with an increased risk of persistence/recurrence [71,72].

For HPV-related OPSCCs, HPV infection, and, in particular, HPV-16, could play a significant role in oncogenesis interacting with host–cell proteins involved in tumor suppression and cell cycle regulation [73], and the infection can be detected by in situ hybridization or assessing the expression of the tumor suppressor p16 protein [74].

Regardless of smoking status, HPV-related OPSCCs have a better prognosis than HPV-negative OPSCCs [72].

Similarly to EBER-positive NPCs, in p16-positive OPSCCs, circulating HPV-DNA could be detected by liquid biopsy and is considered to be a sensitive and specific biomarker [75]. In particular for patients with positive pre-treatment circulating HPV-DNA, its remission after radical treatment is associated with an excellent prognosis [75]. Because their detection and/or increase is related to the presence of disease, their assessment should be proposed during follow-up, at least for patients in whom there was a pre-treatment detection.

In patients expressing these markers, it has even been proposed to consider them during follow-up as surrogates for recurrence, implementing follow-up strategies excluding radiological imaging.

However, this has some limitations. Primarily, despite pre-treatment detection, not all disease recurrences, often due to dedifferentiation, express circulating biomarkers: particularly for HPV-related OPSCCs, it has been shown, albeit with low numbers of patients, that in about 30% of recurrences, circulating HPV-DNA had negative results despite clinical disease [76]. Secondly, in patients with circulating DNA detection but no radiologic/clinical correlation, there are no data that initiating treatment can impact prognosis, just as an earlier detection of recurrence (even ascertained by radiologic and/or

clinical investigations) by circulating DNA detection has not yet been shown to positively impact patient survival.

7. Suspicion of Recurrence

After locoregional treatments, in particular after surgery and radiotherapy, the anatomy of the head and neck district and soft tissues can change radically.

For this peculiar complexity, the American College of Radiology (ACR) has compiled a Neck Imaging and reporting Data System (NI-RADS), a standard report template associated with management recommendations, in order to improve communication between radiologists and referring clinicians in an area of such a high clinical impact [49].

It was originally conceived for CT surveillance imaging, with or without PET, and was further adapted for MRI.

The NI-RADS report template classifies radiological findings into five different categories (from zero to four) according to the suspicion of recurrence, given by their characteristics.

Furthermore, NI-RADS is divided into two macro-classes, depending on whether the suspicion of recurrence concerns T or N.

- The NI-RADS 0 category is attributable to incomplete evaluation, often related to the absence of previous radiological examinations with which to compare.
- In the NI-RADS 1 category, there is no suspicion of disease recurrence, i.e., a disappearance of previous findings, no appearance of new ones, a possible presence of post-treatment fibrocystic tissue, reduced enhancement and/or no FDG uptake of previously reported lymph nodes.
- In the NI-RADS 2 category, there is low suspicion of recurrence (the presence of findings with an intermediate signal, soft tissue lesions with MRI features different from pathological tissue, a reduction in tumor mass in the first post-treatment study, residual lymph node tissue with heterogeneous enhancement and/or mild-to-moderate FDG uptake).

In these cases, a strict follow-up at 3 months, or a PET scan if this is not performed, is recommended.

Mucosal lesions are classified as being in the NI-RADS 2a category, as they are easy to assess clinically. They are often post-treatment outcomes. If the changes are superficial mass-like, mucosal or submucosal, and particularly if they develop after the first re-evaluation, they are classified as NI-RADS 3.

- The NI-RADS 3 category is defined as a high level of suspicion and includes the presence/appearance of a nodular lesion with the same features as the primary tumor, including enhancement, high FDG uptake (if a PET scan is performed), a newly found lymph node with necrosis and/or irregular margins and/or intense FDG uptake (if a PET scan is performed), and residual lymph node tissue with high uptake. In these cases, the indication is to proceed with biopsy examination.
- NI-RADS category 4 is a radiological or anatomopathological definite relapse of disease requiring clinical management and multidisciplinary discussion to define the best treatment.

8. Conclusions

While for patients with early-stage malignancies, clinical examination and endoscopic control seem to be appropriate, the role of radiological examinations in patients with locally advanced diseases remains controversial, with no agreement among the major international guidelines, and without any indication of which strategy is better between intensive or symptom-related follow-up.

For patients with locally advanced HNSCC, there is no standard follow-up program: at least 6 months after the end of treatment, a radiological examination of the treated sites is essential to assess the treatment response, the possible outcomes, and to have baseline imaging for possible future investigations. Beyond that, there is no agreement among the

major international guidelines on an unambiguous radiological follow-up plan, which is therefore modulated according to the clinician decisions and to the patient characteristics.

Considering that (1) most of the recurrences are locoregional and detectable with clinical follow-up, (2) about only 10–20% of them are asymptomatic, (3) there are no data (especially for distance recurrences) that an earlier diagnosis improves patients' survival, (4) there are high costs and there is a lack of adherence of HNSCC patients to radiological follow-up, the application of radiological follow-up strategies based on patients' symptoms should be taken into consideration.

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