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Review

Multidisciplinary management of head and neck cancer: First expert consensus using Delphi methodology from the Spanish Society for Head and Neck Cancer (part 2)

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ABSTRACT

Head and neck cancer is one of the most frequent malignances worldwide. Despite the site-specific multimodality therapy, up to half of the patients will develop recurrence. Treatment selection based on a multidisciplinary tumor board represents the cornerstone of head and neck cancer, as it is essential for achieving the best results, not only in terms of outcome, but also in terms of organ-function preservation and quality of life. Evidence-based international and national clinical practice guidelines for head and neck cancer not always provide answers in terms of decision-making that specialists have to deal with in their daily practice. This is the first Expert Consensus on the Multidisciplinary Approach for Head and Neck Squamous Cell Carcinoma (HNSCC) elaborated by the Spanish Society for Head and Neck Cancer and based on a Delphi methodology. It offers a number of specific recommendations based on the available evidence and the expertise of our specialists to facilitate decision-making of all health-care specialists involved.

Introduction and methods

Introduction and Methodology has been described in the first part of this article.

(QUOTE first article* Ref. [1])

This second article focuses on recurrent/metastatic disease, second primary tumors and squamous cell carcinoma metastatic to cervical nodes with an unknown primary site including categories (C) 3, 4, 5 and 6.

Results and discussion

C3. Evaluation of response after CRT (see Table 1)

Evaluation of response in head and neck after an organ-preservation approach is crucial. Its complexity is based on three main questions. The first question is when exactly we should

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Table 1
Summary of Recommendations on the evaluation of response after non-surgical treatment.

Recommendation	Phase	Accepted consensus (% of agreement)
Evaluation of response should be performed after the resolution of the inflammatory effect caused by concurrent chemo or bioradiotherapy to avoid doubtful residual disease that could hinder decision-making and lead to unnecessary salvage surgery	1	YES (100)
Evaluation of response should be assessed at least 12 weeks (1 week variation is accepted) after completion of radiotherapy	1	YES (88)
Authors do not recommend the evaluation of response at 8 weeks		
Evaluation of response should first be based on clinical assessment, followed by an imaging test (CT or MRI) according to each center protocol, but always considering the initial imaging test (basal)	1	YES (88)
In case of suspected residual disease by CT/MRI, a PET/CT should be performed	2	YES
– Primary Tumor		(76)
– Residual neck disease		(71)
After conservative treatment, salvage surgery of the primary tumor is recommended if it was considered resectable at the initial staging. In the absence of residual neck disease, neck dissection is not recommended	1	YES (72)
Planned neck dissection is not recommended in patients with N-positive disease (including N3) when complete response is achieved after conservative treatment	2	YES (96)
If a complete response of the primary tumor is achieved, but there is evidence of residual neck disease, an elective neck dissection based on the initial N stage is recommended. Radical neck dissection should be avoided	1	YES (90)

assess the response. Classically, the choice of a time frame depended on the optimal timing for neck dissection (ND) in case of residual neck disease (RND), which is considered between 4 and 12 weeks after CRT to allow for resolution of acute effects while preceding late fibrosis [2,3]. For many years, 8 weeks has been taken as the optimal time to perform it, however, since de introduction of PET/CT for the evaluation of response, most authors and international guidelines recommend 12 weeks, to minimize the rate of false positives caused by radiation-induced delayed inflammatory changes [4]. In this regard, the experts agree that response assessment should be performed after the resolution of the inflammatory effect caused by radiation to avoid doubtful residual disease that could lead to unnecessary salvage surgery. The optimal recommended time is 12 weeks (1 week variation is accepted) after completion of CRT. The second question is how to assess the response after CRT. Although clinical assessment might be unreliable, it is essential to evaluate symptoms and signs that might indicate progression. Many studies have documented the accuracy and high sensitivity of CT and MRI [2,3], however, their specificity is low, especially to evaluate neck response, as not all patients who undergo salvage surgery when RND is suspected by CT evidence disease on pathologic examination [5]. In the last decade, retrospective studies evaluating the role of PET/CT have reported high negative predictive values of 94.5–96.0% in patients who have received CRT and bioradiotherapy, leading to a lower number of NDs [6–8]. A recently published phase III trial evaluating the role of PET/CT confirmed these results [9]. In the light of this evidence, NCCN guidelines recommend PET/CT at 12 weeks as the new standard of care for the evaluation of response after an organ-preserving approach [4]. However, CT and MRI are still considered valid imaging techniques and are still the standard of care in many institutions. In this regard, the authors of this consensus agree that evaluation of response should first be based on clinical assessment, followed by an imaging test (CT or MRI), according to each center protocol, but always considering the initial imaging test (basal). The authors did not reach consensus on whether PET/CT should be the initial imaging test, however, they recommend its use upfront of a FNA or ND when RND is suspected by CT.

The third question is what to do once having assessed the response. Planned ND after an organ-preservation approach is still debated. When nodal CR is achieved, no differences in recurrence rates have been reported between planned ND and observation [10–13]. ND entails considerable comorbidity, with a complication rate of up to 35% [14,15]. Balancing the benefit with the increased morbidity of post-CRT surgery, current evidence suggests that ND should be limited to patients with RND after an organ-preservation protocol [9]. International guidelines recommend observation of patients who achieve CR after CRT. In case of confirmed RND, selective neck dissection (SND) has become widely accepted and is currently the procedure most frequently used by head and neck surgeons. The authors reached consensus in this regard, whereas after conservative treatment, salvage surgery of the primary tumor is recommended if it was considered resectable at initial staging and they do not recommend planned ND in patients with N-positive disease (including N3) when CR is achieved. In case of partial response of the primary tumor but no evidence of RND, ND is not recommended either. Conversely, in case of CR of the primary tumor but RND, an elective ND based on the initial N stage is recommended. Radical ND should be avoided, as it entails comorbidity without improvement of survival.

C4. Recurrent/metastatic disease (see Table 2)

Most patients with HNSCC are diagnosed with locally advanced disease whereas initial metastatic disease is rare [16]. Despite multimodality therapy, 60% will develop locoregional or distant recurrence [17]. Most patients with recurrence and ineligible for salvage therapy with radical intent, palliative systemic therapies remain the only treatment option. However, some patients, especially those with locoregional recurrence, might benefit from a radical approach, as some series have reported prolonged survival in patients amenable for salvage surgery or reirradiation [18–20]. In oligometastatic disease, prolonged survival has also been reported for patients with resected metachronous pulmonary metastases [21]. Sacco et al. suggested that an aggressive approach removing all known sites of disease might be beneficial for selected patients. When surgery is not feasible, stereotactic radiotherapy (SBRT) might be an alternative, although due to the lack of prospective trials, this approach cannot be routinely recommended and should be weighed against treatment-related toxicity [22]. Incomplete resections with positive margins are at high risk of recurrence, and reirradiation could entail high toxicity that must be balanced within the potential clinical benefit [19]. Some authors have suggested clinical factors that might predict the benefit of local therapies [23]. The panel of experts suggests that all patients diagnosed with HNSCC presenting local, regional or distant recurrence should be evaluated by a multidisciplinary tumor board to decide the best therapeutic approach, either radical or palliative. In the decision-making process for patients with locoregional recurrence, patients' general condition and comorbidities, localization and disease burden, resectability (odds of achieving a R0/1 resection), time to