Latin American Consensus on the Treatment of Head and Neck Cancer

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ABSTRACT

Head and neck squamous cell carcinoma (HNSCC) is well known as a serious health problem worldwide, especially in low-income countries or those with limited resources, such as most countries in Latin America. International guidelines cannot always be applied to a population from a large region with specific conditions. This study established a Latin American guideline for care of patients with head and neck cancer and presented evidence of HNSCC management considering availability and oncologic benefit. A panel composed of 41 head and neck cancer experts systematically worked according to a modified Delphi process on (1) document compilation of evidence-based answers to different questions contextualized by resource availability and oncologic benefit regarding Latin America (region of limited resources and/or without access to all necessary health care system infrastructure), (2) revision of the answers and the classification of levels of evidence and degrees of recommendations of all recommendations, (3) validation of the consensus through two rounds of online surveys, and (4) manuscript composition. The consensus consists of 12 sections: Head and neck cancer staging, Histopathologic evaluation of head and neck cancer, Head and neck surgery—oral cavity, Clinical oncology—oral cavity, Head and neck surgery—oropharynx, Clinical oncology—oropharynx, Head and neck surgery—larynx, Head and neck surgery—larynx/hypopharynx, Clinical oncology—larynx/hypopharynx, Clinical oncology—recurrent and metastatic head and neck cancer, Head and neck surgery—reconstruction and rehabilitation, and Radiation therapy. The present consensus established 48 recommendations on HNSCC patient care considering the availability of resources and focusing on oncologic benefit. These recommendations could also be used to formulate strategies in other regions like Latin America countries.

ACCOMPANYING CONTENT

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INTRODUCTION

Head and neck cancer is a global health problem. Squamous cell carcinoma (SCC) is the main histologic type and accounts for more than 90% of cases, and smoking, alcohol abuse, and human papillomavirus (HPV) infection remain the most relevant risk factors.[1,2] The oral cavity, pharynx, and larynx are the most prevalent subsites of the disease with high incidences worldwide.[3]

The problem is even worse in lesser developed regions where 65% of all patients with head and neck squamous cell carcinoma (HNSCC) and 75% of the deaths caused by the disease occur in the world.[4] Access to specialized health care facilities, early diagnosis, treatment, or even best supportive care is challenging in countries with scarce resources, such as most Latin America countries.[5] Multidisciplinary teams often have considerable structural problems and must treat patients under nonstandard conditions. The adaptation of published guidelines, which are mainly from developed countries, to real-world reality is challenging but extremely necessary.[6]

On the basis of this scenario, the aim of the present study was to establish Latin American guidelines for

the care of patients with HNSCC considering availability of resources and focusing on oncologic benefit to provide a guide for other countries worldwide facing the same reality. Because of the inequity that is unfortunately a reality in Latin America, the panel also demonstrated the best level of evidence in some questions and included recommendations sometimes on gold-standard approaches to provide a definitive guide for specialists in the field in the region and in other similar realities worldwide.

DESIGN

Panel

The panel was composed of 41 head and neck cancer experts in different fields related to head and neck cancer treatment, chosen as some of the different national leaders on the field. All of them were coauthors of this study. The interaction between the panel was performed exclusively online through e-mail correspondence during all the different stages of the guidelines' conduction.

Guidelines

In a modified Delphi process,[7] two invited specialists, part of the 41-panel expert, were assigned to answer a specific group of questions on the basis of the relevant sections of the consensus and individual expertise. These authors were asked to write the answers to the questions, evaluating the standard of care and establishing, wherever possible, the minimum requirements necessary for adequate patient management, considering the availability of resources and oncologic benefit in the context of Latin America (region of limited resources and/or without access to the necessary health care system infrastructure). The answers should be contextualized with the main international guidelines, considering the availability of resources and oncologic benefits as in Latin America.

First Stage: Document Writing, Search Strategy, Reference Selection Criteria, and Evidence Classification

A short answer that cited appropriate references and explained the main results of the selected studies and the rationale for their selection was requested for each question.

The two specialists designated to answer each specific book of questions were free to select the relevant references in the literature, without any reference selection, criteria, or search strategy. To ensure an evidence-based consensus, each reference included in the support of the answer to each specific question was classified according to the level of evidence and degree of recommendation, as described in Table 1.

After the description of the literature, the authors ended their essays with a summary paragraph objectively answering each question.

Second Stage: Review from the Executive Board

The answers to all consensus questions were reviewed by the entire executive board (L.L.M., L.P.K., A.L.F.C., T.B.d.O., G.N.M., and M.P.C. coauthors). During this analysis period, alternative answers were forwarded to the coauthors, and requests for reviews were also forwarded to them when necessary. The level of evidence and degree of recommendations were also determined by a health research methodology expert (L.L.M. author) at this stage, and the list of references used to answer each question was also reviewed to just stratify those with high-quality evidence, wherever possible.

Third Stage: Consensus (validation)

The executive board produced an online survey recorded using Research Electronic Data Capture software (REDCap 11.2.5—2022 Vanderbilt University). The survey was composed of 116 questions divided into the 12 sections of

TABLE 1. Classification System for the Level of Evidence and Degree of Recommendation Applied to All References Selected for the Study

Level of Evidence	Study Design	Degree of Recommendation	Description
1	Systematic review with a meta-analysis or randomized study with adequate sample (strait 95% CI)	A (very strong)	The evidence is reliable, the uncertainties are small, and the research can be used to guide clinical practice
2	Randomized study with uncalculated or inadequate sample (large 95% CI)	B (strong)	The existing evidence is reliable and can be used to guide clinical practice in most cases, but there are some uncertainties to consider
3	Prospective, nonrandomized study or randomized study with a nonstandard comparator	C (moderate)	The existing evidence provides some support for the recommendations, but their application may be debatable
4	Retrospective study	D (weak)	The existing evidence is weak, or the uncertainties are too great. Recommendations should be applied carefully

NOTE. The level of evidence and degree of recommendation are different and independent parameters.

this study. The survey was then sent to all coauthors, whose responses were mandatory. The objective answers to all questions were voted on by the entire group with a binary system of agreement ("I agree" or "I do not agree"). It was also possible to allow the responders to choose not to answer a question if it was not in their area of expertise. In cases of disagreement with any statement, the coauthors were asked to justify their answers to facilitate the review of each point. At this point, all coauthors could suggest missing references to improve the evidence-based quality of the consensus.

A consensus was considered when agreement about the survey responses was obtained from more than two thirds of the coauthors. In this situation, there was no need for further discussion.

There was a lack of consensus regarding seven questions. The executive board reviewed the sentences and the recommendations, and another survey was built and sent to all the coauthors for a new round of vote, displaying all received inputs in an anonymized manner that allowed every panel member to view each comment from their peers.[7] Again, it was considered a consensus when agreement regarding the answers of the new vote round was reached by more than two thirds of the coauthors. In cases of persistent disagreement, the answer to the question was published with a notation that there was no consensus reached among the coauthors regarding that statement.

The two surveys and agreement rates are demonstrated in the Supplement.

Fourth Stage: Approval of the Manuscript

The drafting of the consensus was written by the executive board and based on the document sent by all coauthors and agreed upon by the votes of the surveys. The final manuscript was approved by all participants.

CONSENSUS

This study was divided into 12 sections regarding the management and treatment of patients with HNSCC, according to 48 different questions, as described in Table 2. To facilitate understanding of the recommendations, the different sites were grouped as head and neck cancer when the management and treatment were similar regardless of the specific site; otherwise, specific recommendations were determined for oral, oropharyngeal, laryngeal, or hypopharyngeal SCC, but not with substratification into subsites, where there are main controversies.

All data regarding the literature review that sustains each recommendation are available in the Supplement.

TABLE 2. Consensus Content and Corresponding Recommendations

Content	Recommendation No.
SECTION 1. Head and Neck Cancer Staging	
1.1. Is a clinical examination alone or panoramic radiography acceptable for the evaluation of a tumor next to the bone?	1
1.2. Is neck ultrasound sufficient for the evaluation of nonpalpable lymph nodes?	2
1.3. For locoregional staging, when is a CT scan or MRI indicated?	3
1.4. When should chest radiography, tomography, or PET-CT be performed for distant disease evaluation?	4
1.5. When should a second primary tumor be screened for? How?	5
SECTION 2. Histopathological evaluation—Head and Neck cancer	
2.1. Should frozen sections be mandatory for negative margin evaluation? Should the margins be evaluated on a tumor specimen or on separate fragments?	6
2.2. What is the appropriate margin for the surgical treatment of tumors of the oral cavity, oropharynx, larynx, and hypopharynx?	7
2.3. When is p16 evaluation necessary? How should staging be performed if this exam is unavailable?	8
2.4. When should we consider close margins? Should close margins be considered positive margins?	9
SECTION 3. Head and Neck Surgery—Oral Cavity	
3.1. Can sentinel lymph node biopsy be considered the standard of care in the neck evaluation of stage I and II tumors? What should be the approach when this methodology is not available?	10
3.2. What is the recommended number of lymph nodes for a neck dissection specimen to consider the specimen representative?	11
3.3. When is radical neck dissection (modified, classic, or extended) the recommended option for treating a positive neck?	12
SECTION 4. Clinical Oncology—Oral Cavity	
4.1. What factors should be considered indications for adjuvant chemotherapy associated with radiation therapy, outside positive margins, and extracapsular spread?	13
4.2. Would you consider once a week cisplatin (40 mg/m^2) concurrent with adjuvant radiation instead of the high-dose regimen (100 mg/m^2) once every 3 weeks?	14
4.3. Is there any indication for induction (neoadjuvant) chemotherapy in resectable oral cavity tumors? For unresectable or "borderline" resectable oral cavity tumors, would you consider induction (neoadjuvant) chemotherapy followed by surgery in any scenario? Would you consider this followed by chemotherapy plus radiation?	15
4.4. For patients with locally advanced unresectable disease who are unfit for cisplatin, would you consider once a week concurrent (concomitant) cetuximab?	16

(continued on following page)

TABLE 2. Consensus Content and Corresponding Recommendations (continued)

Content	Recommendation No.
SECTION 5. Head and Neck Surgery—Oropharynx	
5.1. When should transoral approaches (robot, laser, or conventional transoral) be used?	17
5.2. When should surgery be indicated as the initial treatment for T3 or T4 tumors?	18
5.3. Should neck dissection be performed at the same time as transoral surgery or at another time?	19
5.4. What neck levels should be included in negative neck dissection?	20
5.5. When does neck dissection need to be bilateral in a negative neck?	21
SECTION 6. Clinical Oncology—Oropharynx	
6.1. For surgically treated HPV-positive patients with locally advanced disease (T3/T4 and/or node-positive disease), would you consider de-escalating adjuvant treatment (omitting radiation, reducing the dose of radiation, or omitting concurrent chemotherapy for high-risk patients) in any subgroup of patients?	22
6.2. For patients with locally advanced HPV-positive disease who are candidates for a nonsurgical approach, would you consider de-escalation strategies in any subgroup of patients?	23
6.3. Would you consider trimodality treatment (surgery followed by chemoradiation) in any subgroup of patients with oropharyngeal cancer?	24
6.4. For locally advanced HPV-positive or HPV-negative disease, would you consider induction (neoadjuvant) chemotherapy before chemoradiation or surgery in any subgroup of patients?	25
SECTION 7. Head and Neck Surgery—Larynx	
7.1. When should surgical treatment be performed for T1 and T2 tumors?	26
7.2. When indicated, what is the preferred surgical treatment for T1b tumors?	27
7.3. When is endoscopic resection or open partial laryngectomy indicated?	28
SECTION 8. Head and Neck Surgery—Larynx/Hypopharynx	
8.1. When are age and respiratory condition contraindications for partial laryngectomies?	29
8.2. What are the absolute indications for total laryngectomy as the primary treatment for laryngeal or hypopharyngeal tumors?	30
8.3. What cervical levels should be included in negative neck dissection for supraglottic tumors?	31
8.4. When should thyroidectomy and central compartment dissection be indicated in laryngeal and hypopharyngeal tumors?	32
SECTION 9. Clinical Oncology—Larynx/Hypopharynx	
9.1. Would you consider concurrent chemoradiation as definitive treatment for high-risk T2 hypopharyngeal carcinoma?	33
9.2. Is once a week cisplatin concurrent with radiation therapy a good strategy for organ preservation in T3 laryngeal/hypopharyngeal carcinoma?	34
9.3. Would you consider a nonsurgical organ preservation strategy for any subgroup of patients with T4 laryngeal and hypopharyngeal carcinoma?	35
9.4. Would you consider induction chemotherapy followed by radiation therapy or concurrent radiation plus chemotherapy as an organ preservation strategy for locally advanced laryngeal/hypopharyngeal carcinoma?	36
9.5. Would you consider cetuximab plus radiation therapy as an organ preservation strategy for patients with laryngeal and hypopharyngeal carcinoma who are unfit for cisplatin?	37
SECTION 10. Clinical Oncology—Recurrent and metastatic Head and Neck Cancer	
10.1. What is the preferred regimen for first-line treatment for patients with an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1 recurrent and metastatic HNSCC who are not amenable for local therapies according to PD-L1 combined positive score (CPS) expression (PD-L1–negative, 1-19, or higher than 20)? What is the second-line treatment recommended after progression in these situations?	38
10.2. For patients with an ECOG PS of 2 and HNSCC, what is the recommended systemic first-line treatment? Should PD-L1 CPS expression be considered when choosing the regimen?	39
SECTION 11. Head and Neck Surgery—Reconstruction and Rehabilitation	
11.1. When is free-flap reconstruction indispensable in reconstruction?	40
11.2. When should pharyngeal reconstruction be indicated in laryngeal and hypopharyngeal tumors?	41
11.3. What are the indications for the different phonatory rehabilitation methods?	42
SECTION 12. Radiation Therapy	
12.1. Technique. Is IMRT the most appropriate technique for the treatment of patients with HNSCC? Is the 3D conformal technique (3DCRT) an acceptable option for the treatment of patients with HNSCC? Is 3DCRT a well-suited technique for the treatment of patients with early-stage glottic laryngeal cancer? Is conventional two-dimensional radiation therapy (2DRT) an acceptable technique option for the treatment of patients with HNSCC?	43
12.2. Simulation. Should CT simulation be performed using a slice thickness of 3 mm or less? Is intravenous contrast needed for target delineation, mostly with respect to identification of the cervical lymph nodes?	44
12.3. Target volumes and treatment deintensification. Should target volumes and organs at risk be defined based on international guidelines (eg, ASTRO and/or	45

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TABLE 2. Consensus Content and Corresponding Recommendations (continued)

Content	Recommendation No.
ESTRO)? Can treatment deintensification reducing target volumes and/or total radiation dose for HPV-related oropharyngeal cancer be considered the standard of care? Should target volumes and organs at risk be peer reviewed by an additional radiation oncology staff?	
12.4. Treatment dose and treatment planning. Could moderately hypofractionated radiation therapy (eg, 44-48 Gy/20 fractions) be considered a treatment option for patients with HNSCC in a curative setting? Should altered fractionation (ie, 6 fractions per week) be strongly considered in patients with locally advanced HNSCC in whom exclusive radiation therapy is indicated? Should altered fractionation (ie, 6 fractions per week) be strongly considered in patients with locally advanced HNSCC when concurrent chemotherapy and radiation therapy are indicated? For early-stage glottic laryngeal cancer, should moderately hypofractionated radiation therapy with 63 Gy in 28 fractions and 65.25 Gy in 29 fractions (2.25 Gy/fraction) for T1N0 and T2N0 tumors, respectively, be recommended? Regarding radiation therapy planning, should 95% of the planning target volume (PTV) for each dose level receive the prescription dose? Should the final plans be peer reviewed by an additional radiation oncology staff before final approval?	46
12.5. Image-Guided Radiation Therapy. Is it recommended to perform IGRT with a CB prior to a radiation session to ensure accuracy? Is it recommended to perform IGRT with planar imaging (2D) prior to a radiation session to ensure accuracy? Must IGRT (CB/2D imaging) be performed daily? Must IGRT (CB/2D imaging) be performed on the first 3 days of treatment and then once a week?	47
12.6 Time to initiate treatment and physician evaluation. Is it recommended to initiate radical radiation therapy within 6-8 weeks of diagnosis? Is it recommended to initiate postoperative radiation therapy within 6-8 weeks of surgery? Must the indications for postoperative radiation therapy be maintained even whether treatment starts 8 weeks postoperatively? During radiation therapy treatment, must the patient be evaluated by the physician at least once a week? Should discontinuation of or breaks in radiation therapy be avoided (unless it is clinically necessary)?	48

Abbreviations: ASTRO, American Society for Therapeutic Radiology and Oncology; 2DRT, two-dimensional radiation therapy; 3D, three-dimensional; CB, cone beam; CPS, combined positive score; CRT, conformal technique; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; ESTRO, European Society for Radiotherapy and Oncology; HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; IGRT, image-guided radiation therapy; IMRT, intensity modulated radiotherapy; MRI, magnetic resonance imaging; PET-CT, positron emission tomography-computed tomography; PTV, planning target volume.

Section 1. Head and Neck Cancer Staging

The aim of this section is to establish the minimum pretreatment evaluation for clinical staging considering the standard of care. All recommendations regarding head and neck cancer staging are described in Table 3.

Clinical examination, with or without panoramic radiography, may be sufficient for assessing cancer near bone in cases of large, clearly bone-compromising lesions, especially those requiring segmental mandibulectomy. However, its accuracy is limited. Ideally, sectional imaging methods like computed tomography (CT) scan or magnetic resonance imaging (MRI) should be used, particularly for patients with gingival or maxillofacial tumors lacking evident bone involvement. When bone involvement is uncertain, both CT scan and MRI are essential as they offer comparable accuracy in detecting mandibular invasion.[8-11]

Neck ultrasound, on its own, is inadequate for a thorough assessment of nonpalpable lymph nodes in head and neck cancer staging. Nevertheless, it could serve as the sole imaging option in low-resource settings when elective neck dissection (END) is programmed although it relies heavily on the operator's skill. Its accuracy increases when combined with a fine-needle aspiration biopsy, but its diagnostic effectiveness remains comparable with that of a more convenient CT scan.[12,13]

Given the greater availability and lower cost of CT scans compared with MRI in many centers, it is advisable to opt for CT scans rather than MRI when dealing with resource limitations for locoregional staging of head and neck cancer. In addition, recent evidence does not suggest a significant difference in accuracy between the two methods.[14-16]

At a minimum, chest radiography should be conducted for all patients to assess distant disease in head and neck cancer staging. Nevertheless, for patients with advanced disease, particularly those with N2 or N3 neck disease, a CT scan is recommended. Positron emission tomography-computed tomography provides the highest accuracy in detecting distant metastasis and should be considered especially for high-risk patients, such as those with HPV-related carcinomas, as these cancers may metastasize to atypical sites.[17-25]

Patients with tobacco-related head and neck cancer should undergo a thorough assessment for additional primary malignancies in the upper aerodigestive tract. This assessment should encompass a comprehensive locoregional examination, including nasopharyngolaryngoscopy, upper GI endoscopy, and chest imaging.[22,26-30]

TABLE 3. Recommendations Regarding Head Neck Cancer Staging Histopathologic Evaluation

Recommendation	Level of Evidence	Degree of Recommendation
SECTION 1. Head and Neck Cancer Staging		
Recommendation 1		
Clinical examination, with or without a panoramic radiography, could be sufficient to evaluate a cancer near the bone in cases of bulky lesions clearly compromising the bone, especially in cases with indications for segmental mandibulectomy, but with inferior accuracy	4	C
In an ideal scenario, a sectional imaging method should be employed, such as a CT scan or MRI, mainly in patients with gingival tumors or tumors located close to the mandible or maxilla without gross bone involvement	1	C
In cases of questionable bone involvement, a CT scan and/or MRI is required, and both exams have similar accuracy to detect mandibular invasion	1	B
Recommendation 2		
Neck ultrasound alone is insufficient to properly evaluate nonpalpable lymph nodes in head and neck cancer staging. However, it could be the unique imaging modality if an elective neck dissection is planned in low-resource settings, but it is highly operator-dependent. The accuracy of the method is improved when performed with a fine-needle aspiration biopsy, but the diagnostic power is similar to a CT scan, which is much easier to perform	3	C
Recommendation 3		
As CT scan is a method that is much more readily available in several centers than MRI, and it has a lower cost than MRI, therefore, in a scenario of limited resources, CT should be employed instead of MRI for locoregional staging of head and neck cancer. Furthermore, the most recent evidence does not support accuracy improvement from one method over another	1	C
Recommendation 4		
At minimum, chest radiography should be performed for all patients to evaluate distant disease in head and neck cancer staging; however, a CT scan should be performed in patients with advanced disease, mainly those with N2 or N3 neck disease	4	C
PET-CT has the best accuracy in the detection of distant metastasis and should be considered in high-risk patients, especially for HPV-related carcinomas, due to the risk of distant metastasis at unusual sites	2	C
Recommendation 5		
All patients with tobacco-associated head and neck cancer should be carefully evaluated to exclude a synchronous and metachronous second primary malignancy of the upper aerodigestive tract. This evaluation should include a detailed locoregional examination combined with nasopharyngolaryngoscopy, upper gastrointestinal endoscopy, and chest imaging	1	C
SECTION 2. Head and Neck Cancer—Histopathologic evaluation		
Recommendation 6		
Frozen section examination is an important tool to assure a complete and oncological tumor resection	1	D
Margin evaluation at the specimen level is the best strategy to decrease local recurrence, and it is a more accepted practice	3	C
Recommendation 7		
Margins >5 mm based on the surgical specimen can be considered negative for oral, oropharyngeal, supraglottic, and hypopharyngeal tumors. Exclusively for glottic tumors, margins >1 mm are considered negative	3	C
Recommendation 8		
Margins between 1 and 5 mm are classified as close and <1 mm as positive for oral, oropharyngeal, supraglottic, and hypopharyngeal tumors. Exclusively for glottic tumors, margins <1 mm are considered close margins for these cases	1	C
In general, close margins for HNSCC should not be considered positive margins based on the current evidence, and their correct prognosis and management should be better determined	1	D
Recommendation 9		
All patients with oropharyngeal SCC should have an HPV status evaluation, and p16 immunostaining is the easiest way to first perform this evaluation. Once, until now, there is no change at treatment, and if unavailable, HPV evaluation should not delay treatment initiation	2	B

Abbreviations: CT, computed tomography; HPV, human papillomavirus; MRI, magnetic resonance imaging; PET-CT, positron emission tomography-computed tomography; SCC, squamous cell carcinoma.

TABLE 4. Recommendations Regarding the Management of Patients With Oral Cavity or Oropharynx Squamous Cell Carcinoma

Recommendation	Level of Evidence	Degree of Recommendation
SECTION 3. Head and Neck Surgery—Oral Cavity		
Recommendation 10		
SLNB should be employed in patients with stages I and II oral SCC when all the resources, such as appropriate preoperative imaging, specialized head and neck cancer radiologist, nuclear medicine services, radiolabeled markers, an adequate pathologist, and immunohistochemistry techniques, are available. Otherwise, SND should continue to be the standard of care for those patients. Active surveillance of the neck should not be recommended	1	A
Recommendation 11		
A LNY higher than 18 is a quality metric in head and neck surgery, specifically in patients undergoing elective neck dissection. The surgical technique can significantly impact the LNY, but also it is possible to improve this evaluation with the application of more rigorous specimen processing by the pathology team. Subsequently, this measure could yield more accurate nodal staging and ultimately drive more appropriate use of adjuvant therapy	4	B
Recommendation 12		
SND is an acceptable alternative to CND or RND in patients with stage T1 or T2 and cN1 oral cavity SCC and for very selected cN2 cases, sited at levels I or II. However, RND and CND are still the standard of care in patients with oral cancer with advanced T-stage disease (T3 or T4) or cN2 and cN3 disease, which require primary surgical treatment	1	B
SECTION 4. Clinical Oncology—Oral Cavity		
Recommendation 13		
There is a strong recommendation for adjuvant concurrent chemoradiation over adjuvant radiation therapy alone primarily for patients with positive surgical margins and/or metastatic lymph nodes with ENE.	1	A
The presence of more than two positive lymph nodes is also an indication for postoperative chemoradiation	4	B
The presence of perineural invasion, perivascular invasion, involvement of multiple lymph nodes, and lymph node involvement at low cervical levels (IV and V) could, in highly selected cases and after multidisciplinary discussion, be considered for concurrent chemoradiation	1	C
Recommendation 14		
Adjuvant (postoperative) concurrent chemoradiation with once a week cisplatin (40 mg/m^2) can be used instead of the high-dose regimen (100 mg/m^2) once every 3 weeks	1	A
Recommendation 15		
Induction (neoadjuvant) chemotherapy may be considered in unresectable or borderline resectable oral cavity tumors in highly selected cases with multidisciplinary input	4	C
Recommendation 16		
There is no evidence to prescribe cetuximab concurrent with radiation therapy in patients with oral cavity unsuitable to receive cisplatin	4	D
For these patients, radiation therapy concurrent with docetaxel is an option	1	B
SECTION 5. Head and Neck Surgery—Oropharynx		
Recommendation 17		
Transoral approaches (TORS or TLM) with or without neck dissection and adjuvant radiotherapy or chemoradiation should be used in T1-2 N0-2 oropharyngeal SCC and could be used in selected cases of T3 N0-2 oropharyngeal SCC, regardless of HPV status. Conventional transoral surgery should be used in cases without availability of robotic tools or when an expert transoral endoscopic surgeon is unavailable. Conventional surgical and nonsurgical treatment provides comparable oncologic results	1	C
Recommendation 18		
For selected cases of T3 oropharyngeal SCC, TORS or TLM may be indicated, depending upon the need for reconstruction of the soft palate. Conventional open surgery may be indicated for patients with T3-4a oropharyngeal SCC who are not amenable to chemoradiation with high-dose cisplatin but who are fit for a major surgical procedure with reconstruction and adjuvant treatment, with a reasonable expectation of favorable functional results	3	C
Recommendation 19		
In transoral surgery (TORS or TLM), if the primary oropharyngeal tumor does not require a radical tonsillectomy and the submandibular gland can be preserved during neck dissection, a concurrent approach (transoral surgery with neck dissection) is preferred. On the other hand, if radical tonsillectomy is planned or if the submandibular gland must be removed, staged procedures 10-14 days apart should be advocated, starting with neck dissection with ligation of the branches of the external carotid artery	4	C

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TABLE 4. Recommendations Regarding the Management of Patients With Oral Cavity or Oropharynx Squamous Cell Carcinoma (continued)

Recommendation	Level of Evidence	Degree of Recommendation
Recommendation 20		
Patients with neck-negative oropharyngeal SCC primarily treated with surgery should receive, at least, dissections of levels II-IV. An absolute consensus has not yet been reached, but level I can be omitted in select cases. HPV or p16 status does not require modification of this indication yet.	4	C
Recommendation 21		
Regardless of HPV status, bilateral elective neck dissection is recommended for all cases of oropharyngeal SCC that extend to or approach the midline. For lateralized tumors that involve the tongue base, soft palate, and posterior pharyngeal wall, elective bilateral neck dissection should be considered due to contralateral lymphatic drainage	4	C
SECTION 6. Clinical Oncology—Oropharynx		
Recommendation 22		
Despite the good prognosis of patients with HPV-positive tumors, patients with locally advanced oropharyngeal treated with surgery should receive adjuvant treatment, regardless of HPV status	1	A
Patients with low-risk HPV-positive oropharyngeal SCC, stage T1/T2 disease with free margins, no invasion, and up to one positive lymph node measuring <3 cm and without ENE can be considered for observation after surgery	1	C
There was no consensus if patients with intermediate-risk HPV-positive oropharyngeal SCC (close margins, <1 mm ENE, or 2-4 metastatic nodes, perineural invasion, or lymphovascular invasion) can be considered for treatment de-escalation—mainly with a reduced dose of radiation and omission of chemotherapy	1	C
Recommendation 23		
In a definitive setting, patients with HPV-positive oropharyngeal SCC should be treated the same as those patients with HPV-negative tumors	1	A
Recommendation 24		
Trimodality treatment should be avoided in locally advanced oropharyngeal cancer	1	A
Recommendation 25		
Cisplatin-based concurrent chemoradiation is the standard-of-care nonsurgical treatment for locally advanced oropharyngeal carcinoma	1	A
Induction chemotherapy can be considered in patients with high-volume disease, those with a high risk of distant metastasis, symptomatic patients in need of a rapid response, and those in whom delayed initiation of radiotherapy is expected	1	B

Abbreviations: CND, comprehensive neck dissection; ENE, extranodal extension; HPV, human papillomavirus; LNY, lymph node yield; RND, radical neck dissection; SCC, squamous cell carcinoma; SLNB, sentinel lymph node biopsy; SND, selective neck dissection; TLM, transoral laser microsurgery; TORS, transoral robotic surgery.

Section 2. Head and Neck Cancer—Histopathologic Evaluation

The aim of this section is to present the evidence of the assessment of intraoperative margins and histopathologic evaluation of head and neck cancer considering availability of resources and oncologic benefit, and the recommendations are presented in Table 3.

Frozen section examination plays a crucial role in ensuring an oncologic tumor resection. Evaluating margins at the specimen is considered the most effective strategy for reducing the risk of local recurrence, and it has gained wider acceptance in current practice.[31-54]

Margins >5 mm can be classified as negative for oral, oropharyngeal, supraglottic, and hypopharyngeal tumors, and >1 mm for glottic tumors.[46,53,55-60]

Margins between 1 and 5 mm are categorized as close margins, whereas those measuring <1 mm are classified as positive margins for oral, oropharyngeal, supraglottic, and hypopharyngeal tumors and for glottic tumors, and margins <1 mm are considered close margins. Generally, close margins for HNSCC should not be considered as positive margins on the basis of current evidence. The prognosis and appropriate management of close margins in HNSCC cases should be more precisely determined.[42,56,57,59,61,62]

All patients diagnosed with oropharyngeal SCC should undergo an HPV status evaluation, and p16 immunostaining is a convenient initial method for this assessment. If p16 immunostaining is unavailable, the evaluation of HPV status should not cause any delay in the initiation of treatment.[63-65]

Section 3. Head and Neck Surgery—Oral Cavity

The aim of this section is to present the evidence of the different neck approaches for oral cavity SCC, considering their availability and oncologic benefit, as described in Table 4.

Sentinel lymph node biopsy should be used in patients with stage I and II oral SCC when all the resources, such as appropriate preoperative imaging, a specialized head and neck cancer radiologist, nuclear medicine services, radiolabeled markers, an adequate pathologist, and immunohistochemistry techniques, are available. Otherwise, selective neck dissection (SND) should continue to be the standard of care for those patients. Active surveillance of the neck should not be recommended.[66-74]

A lymph node yield (LNY) higher than 18 is a quality metric in head and neck surgery, specifically in patients undergoing END. Not only the surgical technique can significantly affect the LNY, but also it is possible to improve this evaluation with the application of more rigorous specimen processing by the pathology team. Subsequently, this measure could yield more accurate nodal staging and ultimately drive more appropriate use of adjuvant therapy.[75-80]

SND is an acceptable alternative to comprehensive neck dissection (CND) or radical neck dissection (RND) in patients with stage T1 or T2 and cN1 oral cavity SCC and for very selected cN2 cases, sited at levels I or II. However, RND and CND are still the standard of care in patients with oral cancer with advanced T-stage disease (T3 or T4) or cN2 and cN3 disease, which require primary surgical treatment.[62,81-91]

Section 4. Clinical Oncology—Oral Cavity

The aim of this section is to present the evidence for systemic treatment of locally advanced oral cavity SCC, summarized in Table 4.

A robust recommendation favors adjuvant concurrent chemoradiation over adjuvant radiation therapy alone, particularly for patients with positive surgical margins and/or metastatic lymph nodes showing extranodal extension (ENE). In select cases, chemoradiation may also be given for patients with perineural invasion, perivascular invasion, involvement of multiple lymph nodes, and lymph node involvement at lower cervical levels (IV and V).[92-99]

Adjuvant (postoperative) concurrent chemoradiation with once a week cisplatin (40 mg/m^2) can be used instead of the high-dose regimen (100 mg/m^2) once every 3 weeks.[100]

Induction (neoadjuvant) chemotherapy may be considered in unresectable or borderline resectable oral cavity tumors in highly selected cases with multidisciplinary input.[101-104]

There is no evidence to recommend the use of cetuximab concurrently with radiation therapy for patients with oral cavity SCC who are not suitable for cisplatin. In such cases, an alternative option is concurrent radiation therapy with docetaxel.[105-108]

Section 5. Head and Neck Surgery—Oropharynx

The aim of this section is to present the evidence of different primary tumor and neck approaches in oropharyngeal SCC, considering their availability and oncologic benefit, as shown in Table 4.

Transoral approaches, such as transoral robotic surgery (TORS) or transoral laser microsurgery (TLM), are recommended for T1-2 N0-2 oropharyngeal SCC. In selected cases, they can also be considered for T3 N0-2 tumors, independent of HPV status. In cases where robotic tools are unavailable or when there is a lack of expertise in transoral endoscopic surgery, conventional transoral surgery should be used. Conventional surgical and nonsurgical treatments yield similar oncologic outcomes.[109-130]

In specific cases of T3 tumors, the choice between TORS or TLM may be appropriate, depending on the necessity for soft palate reconstruction. For patients with T3-4a tumors who are not suitable for high-dose cisplatin-based chemoradiation but are fit for a major surgical procedure with reconstruction and subsequent adjuvant treatment, conventional open surgery may be recommended. This approach should be considered when there is a reasonable expectation of achieving favorable functional outcomes.[109,115-117,119,121,124,126,128,130-134]

In transoral surgery (TORS or TLM) when the primary tumor does not need a radical tonsillectomy and the preservation of the submandibular gland is feasible during neck dissection, a concurrent approach is the preferred strategy. Conversely, if radical tonsillectomy is part of the plan or if removal of the submandibular gland is required, a staged approach involving two procedures spaced 10-14 days apart is recommended. The sequence typically starts with neck dissection, which includes ligation of the branches of the external carotid artery.[135-140]

Patients with neck-negative oropharyngeal SCC who are primarily treated with surgery should undergo dissections of, at least, levels II-IV. While there is' not an absolute consensus, in some selected cases, the omission of level I dissection may be considered. HPV or p16 status does not currently necessitate a modification of this guideline.[126,141-152]

Irrespective of HPV status, bilateral END is advised for oropharyngeal SCC cases approaching the midline. In lateralized tumors affecting the tongue base, soft palate, and posterior pharyngeal wall, elective bilateral neck dissection should be considered because of contralateral lymphatic drainage.[126,141-143,148,153-155]

Section 6. Clinical Oncology—Oropharynx

The aim of this section is to present the evidence for systemic treatment in locally advanced HPV-positive and HPV-negative oropharyngeal carcinoma and for de-escalation strategies in HPV-positive disease. The recommendations are presented in Table 4.

Despite the generally favorable prognosis of patients with HPV-positive tumors, patients with locally advanced oropharyngeal cancer treated surgically should still receive adjuvant treatment, regardless of their HPV status. However, for patients with low-risk HPV-positive oropharyngeal SCC (T1/T2 disease with clear margins, minimal invasion, and limited lymph node involvement without ENE), observation after surgery can be considered. In cases of intermediate-risk HPV-positive tumors (involving factors like close margins, <1 mm ENE, 2-4 metastatic nodes, perineural invasion, or lymphovascular invasion), there is no consensus on whether treatment de-escalation, particularly reducing radiation dosage and omitting chemotherapy, can be considered.[111,156-158]

In a definitive setting, patients with HPV-positive oropharyngeal SCC should be treated the same as those patients with HPV-negative tumors.[159-161]

Trimodality treatment (surgery followed by chemoradiation) should be avoided in locally advanced oropharyngeal cancer.[162-167]

The standard-of-care nonsurgical treatment for locally advanced oropharyngeal SCC is cisplatin-based concurrent chemoradiation. However, in certain cases, induction chemotherapy may be considered. This includes patients with high-volume disease and a high risk of distant metastasis, symptomatic patients requiring a rapid response, and those expected to face a delay in starting radiotherapy.[168-182]

Section 7. Head and Neck Surgery—Larynx

The aim of this section is to present the evidence for the different primary tumor approaches in laryngeal SCC, considering their availability and oncologic benefit, and is described in Table 5.

Both surgery and radiotherapy are valid options for T1 and T2 laryngeal SCC with similar outcomes. Surgery, especially TLM, provides low local recurrence and supports larynx preservation, while radiotherapy can improve vocal outcomes. The choice between these treatments should involve a patient-centered discussion considering individual preferences and circumstances.[183-189]

When surgical treatment is considered, the preferred surgical treatment for T1b laryngeal SCC is TLM. In patients with inadequate exposure, frontolateral vertical laryngectomy is an option.[189-191]

Open partial laryngectomies are currently recommended for laryngeal tumors with limited transoral access and specific anterior commissure tumors with vertical extension and also for selected patients who need surgical salvage therapy.[184,187,192,193]

Section 8. Head and Neck Surgery—Larynx/Hypopharynx

The aim of this section is to present the evidence of the different primary tumor and neck approaches in laryngeal and/or hypopharyngeal SCC, considering their availability and oncologic benefit. The recommendations are presented in Table 5.

Elderly patients should receive curative treatment, considering their overall health and disease stage. Chronologic age alone should not determine treatment decisions, but it is essential to recognize that elderly patients often have more comorbidities and are at a higher risk of postoperative complications.[194-205]

Nonsurgical treatments for laryngeal or hypopharyngeal SCC should be considered for patients who cannot undergo partial laryngectomy and those with stage T3 and low-volume stage T4a tumors that still have a preservable larynx but are candidates for total laryngectomy. Total laryngectomy is recommended for cases involving laryngeal dysfunction, extensive infiltrative tumors with cartilage invasion and extralaryngeal spread, or when nonsurgical organ preservation treatments have failed.[206-227]

For stage T1 and T2 N0 supraglottic tumors of the ventricular bands or ventricles that do not approach the midline, it is advised to perform END on the ipsilateral side, encompassing at least levels IIA and III. For those in the epiglottis or aryepiglottic fold and those approaching the midline, it is recommended to opt for bilateral END, covering at least levels IIA and III. In cases of stage T3 and T4 N0 supraglottic tumors, bilateral END involving levels IIa, III, and IV is indicated. In addition, anterior compartment dissection and thyroidectomy are needed if there is extension into the paraglottic space.[126,228-234]

Central compartment dissection (level VI) and thyroidectomy should be considered in the following cases of laryngeal and/or hypopharyngeal cancer: primary or subglottic extension advanced glottic SCC (T3-T4), especially if it involves the anterior commissure, cricoid cartilage, or subglottic extension; advanced supraglottic SCC (T3-T4), especially if it involves the ventricle/paraglottic space, involves anterior commissure, or has lymph node metastases in the lateral neck compartment; and hypopharyngeal SCC.[235-248]

Section 9. Clinical Oncology—Larynx/Hypopharynx

The aim of this section is to establish candidate patients for nonsurgical organ preservation strategies and to present the evidence for systemic treatment in these scenarios including a discussion about patients living in a resource-constrained environment. All statements are summarized in Table 5.

TABLE 5. Recommendations Regarding the Management of Patients With Larynx and/or Hypopharynx Squamous Cell Carcinoma and the Management of Recurrent or Metastatic Head and Neck Cancer

Recommendation	Level of Evidence	Degree of Recommendation
SECTION 7. Head and Neck Surgery—Larynx		
Recommendation 26		
Either surgery or radiotherapy is indicated for T1 and T2 laryngeal SCC, and both have similar oncological results. In general, surgery, especially transoral laser resection (if technically possible), provides a low rate of local recurrence and a high rate of laryngeal preservation; however, radiotherapy may offer better vocal results. The choice of treatment modality for these tumors should be discussed with the patient	1	C
Recommendation 27		
When surgical treatment is considered, the preferred surgical treatment for T1b laryngeal SCC is transoral laser resection. In patients with inadequate exposure, frontolateral vertical laryngectomy is also an option	1	B
Recommendation 28		
The current indications for open partial laryngectomies are laryngeal tumors with inadequate transoral exposure and certain tumors of the anterior commissure with vertical extension. Partial laryngectomy should be used in selected patients requiring salvage surgical therapy for a recurrent or persistent laryngeal tumor after radiotherapy failure	1	B
SECTION 8. Head and Neck Surgery—Larynx/Hypopharynx		
Recommendation 29		
Elderly patients with laryngeal carcinoma should be treated with curative intention. Their general condition and health as well as the stage of disease should be considered. Chronological age itself is not a reason to treat elderly patients differently; however, the elderly is generally affected by more comorbidities than younger patients and are prone to more postoperative complications. A careful preoperative evaluation and adequate communication with the patient are essential	4	B
Recommendation 30		
Nonsurgical organ preservation treatment should be performed in selected cases of laryngeal or hypopharyngeal SCC, ideally, in patients in whom a partial laryngectomy is not possible and in patients with stage T3 and low-volume stage T4a tumors with preserved larynx but candidate to total laryngectomy. Total laryngectomy is indicated in cases of laryngeal dysfunction, extensive highly infiltrative tumors with gross invasion of the cartilage and extralaryngeal extravasation, and local failure after nonsurgical organ preservation protocols. The patient's priorities should always be respected	1	B
Recommendation 31		
For stage T1 and T2 N0 supraglottic tumors in ventricular bands or ventricles and tumors that do not approach the midline, ipsilateral elective neck dissection of at least levels IIA and III is recommended	2	B
For stage T1 and T2 N0 supraglottic tumors in the epiglottis or aryepiglottic fold and tumors that approach the midline, bilateral elective neck dissection of at least levels IIA and III is recommended	2	B
For stage T3 and T4 N0 supraglottic tumors, bilateral elective neck dissection of levels IIa, III, and IV is recommended, and dissection of the anterior compartment and thyroidectomy should be considered in cases with extension to the paraglottic space	1	A
Recommendation 32		
Central compartment dissection (level VI) and thyroidectomy with preservation of the parathyroid glands or autotransplantation should be performed in the following patients with laryngeal and/or hypopharyngeal cancer: (1) Primary or subglottic extension: central compartment dissection of both sides + partial or total thyroidectomy; (2) Advanced glottic SCC (T3-T4), particularly those with involvement of the anterior commissure, cricoid cartilage, and/or subglottic extension: central compartment dissection ipsilateral to the lesion side and ipsilateral partial thyroidectomy or bilateral and total thyroidectomy in tumors extending to both sides; (3) Advanced supraglottic SCC (T3-T4), particularly those with involvement of the ventricle/paraglottic space, anterior commissure, and/or with lymph node metastases in lateral compartment of the neck: central compartment dissection ipsilateral to the lesion side and ipsilateral partial thyroidectomy or bilateral and total thyroidectomy in tumors extending to both sides; (4) Hypopharyngeal SCC: central compartment dissection ipsilateral to the side of the lesion or bilateral in tumors extending to both sides	1	B
SECTION 9. Clinical Oncology—Larynx/Hypopharynx		
Recommendation 33		
Combined chemotherapy and radiation therapy should be offered to patients with T2 hypopharyngeal SCC with lymph node involvement who are candidates for organ preservation	1	B
There is insufficient evidence from randomized studies to support the use of chemotherapy for T2N0 hypopharyngeal carcinomas, and radiation therapy alone remains the standard approach, even though many institutions routinely recommend concurrent chemoradiation therapy in this setting	4	D
Recommendation 34		
Once a week cisplatin at a dose of 40 mg/m^2 may be given concurrently with radiation therapy for stage T3 laryngeal/hypopharyngeal SCCs, but the recommendation is extrapolated from evidence generated in the setting of adjuvant therapy or from studies that were not specifically focused on organ preservation. A more favorable toxicity profile with the once a week approach is applicable for resource-constrained healthcare systems; however, the infrastructure for once a week infusions may not be available to all patients, and the cost-effectiveness of this strategy has not yet been specifically evaluated	2	C

(continued on following page)

TABLE 5. Recommendations Regarding the Management of Patients With Larynx and/or Hypopharynx Squamous Cell Carcinoma and the Management of Recurrent or Metastatic Head and Neck Cancer (continued)

Recommendation	Level of Evidence	Degree of Recommendation
Recommendation 35		
At present, we do not recommend nonsurgical organ preservation strategies for patients with T4 laryngeal or hypopharyngeal carcinomas with gross thyroid cartilage invasion or with > 1-cm tongue base extension	2	A
Patients with T4 tumors due to other features may be candidates for organ preservation strategies on a case-by-case basis after thorough discussion of the goals of care and risks and benefits of surgical versus nonsurgical approaches in the setting of limited data	3	D
Quality of life, contemplating since the beginning what should be offered for rehabilitation, and the presence of comorbidities should be considered, as well as tumor stage, during the management plan	4	D
Recommendation 36		
There is insufficient evidence to support the superiority of concurrent chemoradiation therapy versus induction chemotherapy followed by radiation therapy, and we consider either one of these approaches to be equally reasonable as an organ preservation strategy for locally advanced laryngeal or hypopharyngeal cancers, balancing oncological results, quality of life, and patients' status	1	B
Recommendation 37		
Cetuximab given concurrently with radiation therapy may be considered for patients with laryngeal and hypopharyngeal SCC who are unfit for cisplatin, but it is not mandatory (given lack of robust evidence, the use of cetuximab in this setting should be carefully weighed against its costs in resource-constrained countries)	3	C
SECTION 10. Clinical Oncology—Head and Neck Cancer—Recurrent and metastatic disease		
Recommendation 38		
For patients with HNSCC who have experienced progression or recurrence over 6 months after definitive or adjuvant cisplatin-based chemoradiation and have an ECOG-PS of 0-1, the panel recommends chemotherapy plus cetuximab for patients with a CPS <1, chemotherapy plus pembrolizumab for those with an intermediate CPS (1-19), and pembrolizumab or chemotherapy plus pembrolizumab for those with a high CPS (≥20)	1	A
Second-line therapy options include nivolumab for patients who have progressed with chemotherapy and cetuximab within 6 months (platinum-refractory disease) and are immunotherapy-naïve	1	A
Cetuximab-chemotherapy regimens for immunotherapy experienced patients. In both scenarios, clinical trial enrollment is strongly encouraged based on availability	2	A
Recommendation 39		
There is little evidence regarding treatment of patients with an ECOG PS of 2 and HNSCC. Evaluation of the PD-L1 CPS can be considered. For CPS-positive patients, pembrolizumab monotherapy can be an option. Selected CPS-negative patients can be considered for chemotherapy or cetuximab monotherapy	3	C

Abbreviations: CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; HNSCC, head and neck squamous cell carcinoma; SCC, squamous cell carcinoma.

Combined chemotherapy and radiation therapy are recommended for patients with T2 tumors with lymph node involvement who are eligible for organ preservation. For T2N0 hypopharyngeal carcinomas, there are not enough data to endorse chemotherapy. Standard practice continues to be radiation therapy alone although some institutions routinely advise concurrent chemoradiation therapy in such cases.[206,207,249-256]

For stage T3 tumors, concurrent once a week cisplatin at a dose of 40 mg/m^2 with radiation therapy is the recommended treatment. The once a week approach offers a more favorable toxicity profile.[100,207,257,258]

Currently, we do not recommend nonsurgical organ preservation strategies for patients with T4 carcinomas that exhibit gross thyroid cartilage invasion or tongue base extension exceeding 1 cm.[206,207,259-263]

There is insufficient evidence to establish the superiority of concurrent chemoradiation over induction chemotherapy followed by radiation therapy. Therefore, both approaches are equally reasonable as organ preservation strategies for locally advanced cancers.[206,207,251,252,264]

Cetuximab, combined with radiation therapy, can be an option for patients who cannot tolerate cisplatin, but it is not obligatory. Because of the limited strong evidence, the decision to use cetuximab in such cases should be made thoughtfully, considering the costs.[107,265]

Section 10. Clinical Oncology—Head and Neck Cancer—Recurrent and Metastatic Disease

The aim of this section is to present the evidence of the systemic treatment for recurrent and metastatic HNSCC including a discussion about patients living in a resource-constrained environment, as demonstrated in Table 5.

For patients with HNSCC experiencing recurrence more than 6 months after cisplatin-based chemoradiation with an Eastern Cooperative Oncology Group performance status (ECOG PS) of

0-1, the following recommendations apply: chemotherapy plus cetuximab (combined positive score [CPS] <1), chemotherapy plus pembrolizumab (CPS 1-19), and pembrolizumab alone or chemotherapy plus pembrolizumab (CPS ≥20). Second-line therapy options include nivolumab for patients who have progressed with chemotherapy and cetuximab within 6 months (platinum-refractory disease) and are immunotherapy-naïve. Cetuximab-chemotherapy regimens are for immunotherapy-experienced patients.[111,266-269]

Limited evidence exists for treating patients with HNSCC with an ECOG PS of 2. Evaluating the PD-L1 CPS can be helpful. For CPS-positive patients, pembrolizumab as monotherapy can be considered. Selected CPS-negative patients may be candidates for chemotherapy or cetuximab monotherapy.[270-276]

Section 11. Head and Neck Surgery—Reconstruction and Rehabilitation

The aim of this section is to present evidence of reconstruction and rehabilitation after oncologic resection of head and neck cancers, considering the availability of resources. Recommendations are described in Table 6.

Free-flap reconstruction is essential when vital structures need coverage, particularly when reliable local or regional flaps are not viable options. Surgeons should consider free-flap reconstruction in cases such as anterior segmental mandibulectomy, maxillectomy without an obturator prosthesis, implant coverage, reconstruction failure with other flaps, and when aiming for optimal functional and aesthetic outcomes.[277,278]

Pharyngeal reconstruction is imperative in cases of circumferential defects or when primary closure might lead to stenosis. In salvage operations, the use of a muscular flap over the suture line can be considered to minimize the risk of postoperative complications.[279,280] Phonatory rehabilitation is essential for all total laryngectomy patients.[281]

Section 12. Radiation Therapy

The aim of this section is to describe the evolution of external radiation therapy techniques, simulation, target volumes and treatment deintensification, dose and treatment planning, time to initiate treatment, and physician evaluation, as demonstrated in Table 6.

Intensity modulated radiotherapy (IMRT) is the standard treatment because of its significant reduction in radiation exposure to nearby healthy tissue, minimizing side effects. For early-stage laryngeal cancer, the standard approach is still the three-dimensional conformal technique.[282-285]

CT scan thickness should not exceed 3 mm. Outside the target volume, a slice thickness of up to 5 mm is acceptable. Although not obligatory, the use of intravenous CT contrast agents is recommended.[286-289]

Target volumes and organs at risk should be defined following international guidelines. A crucial step involves the review of target volumes by two radiation oncologists as part of a double-checking process.[288,290-296]

When patients receive chemoradiation, the standard radiation therapy dose follows conventional fractionation. The potential advantages of combining concurrent chemotherapy with altered fractionation are not fully established. Early stage glottic cancer typically adheres to moderate hypofractionation for standard fractionation. The widely accepted dose distribution for the planning target volume (PTV) focuses on D95%/100 of the PTV.[159,297-309]

Image-guided radiation therapy (IGRT) minimizes geometric uncertainties, reducing the risk of undertreating the target and damaging adjacent organs. For departments using a 5-mm clinical target volume-PTV margin expansion, daily and alternate-day IGRTs are advised. Departments not using daily IGRT should consider wider margins, exceeding 5 mm. In cases where residual errors persist in daily/alternate-day IGRT or when there is suspicion of volumetric tumor changes requiring treatment adaptation, three-dimensional volumetric imaging may be necessary.[310-327]

Delays in starting or completing radiation therapy reduce survival and increase local relapse. The recommended timeframe for commencing curative radiotherapy is typically within 30 days of diagnosis. For postoperative radiation therapy, treatment should initiate within 4-6 weeks post-surgery. To prevent treatment disruptions and their impact on oncologic outcomes, weekly evaluations of the patients are essential.[328-334]

In conclusion, this study was conducted on the basis of a consensus using a modified Delphi methodology that has also been applied in similar studies worldwide.[7] However, there are intrinsic limitations that should be addressed.

First, we did not conduct a comparison or an adaptation of already published guidelines. From the outset, the objective of this study was to establish specific recommendations tailored to the context of Latin America and other regions with limited resources, while focusing on the best available evidence. Simply adapting a guideline designed for another context might deviate from our intended focus but could lead to potential pitfalls because of insufficient evidence.

Second, although the stakeholders involved in the process were recognized national leaders in the field, unfortunately, many others were not included in the study. To mitigate any bias in this selection, all recommendations underwent validation by the entire panel, as detailed in the Methods section.

TABLE 6. Recommendations Regarding Reconstruction and Rehabilitation and Radiation Therapy for Patients With Head and Neck Squamous Cancer

Recommendation	Level of Evidence	Degree of Recommendation
SECTION 11. Head and Neck Surgery—Reconstruction and Rehabilitation		
Recommendation 40		
Free-flap reconstruction is indispensable when there is the need for coverage vital structures, especially in the absence of reliable local or regional flaps as alternatives. The surgeon must consider a free-flap reconstruction for anterior segmental mandibulectomy, after a maxillectomy without an obturator prosthesis, to cover implants, in cases of reconstruction failure with other regional or local flaps, and to obtain the best functional and aesthetic results	4	C
Recommendation 41		
Pharyngeal reconstruction is necessary when there is a circumferential defect or when primary closure will result in stenosis that can increase the risk of salivary fistula formation, especially in salvage surgeries. The interposition of a muscular flap over the suture line could also be performed to reduce the risk of major postoperative complications, mainly in salvage operations	1	B
Recommendation 42		
All patients should receive phonatory rehabilitation after a total laryngectomy. The valved voice prosthesis is the best method to achieve improved quality and fluency of speech. An electrolarynx is an option for immediate rehabilitation, and esophageal speech could also be tried, especially when there is no other resource available	4	B
SECTION 12. Radiation Therapy		
Recommendation 43		
IMRT is the standard of care as it notably reduces the dose to neighboring normal tissue and reduces side effect	1	A
For early-stage laryngeal cancer, 3DCRT remains the standard approach	4	B
Recommendation 44		
The CT scan thickness must be ≤ 3 mm throughout the region that contains the target volumes at simulation. Regions outside the target volume may be scanned with a slice thickness ≤5 mm. The use of intravenous CT contrast agents is not mandatory but is recommended	4	C
Recommendation 45		
Target volumes and organs at risk should be defined based on international guidelines. It is essential that the target volumes be reviewed by two different radiation oncologists (double-checking process)	4	C
There are no available phase 3 studies to support these deintensification strategies in clinical practice	1	A
Recommendation 46		
When patients are treated with radiation therapy concomitant with chemotherapy for both, radical or postoperative settings, the standard radiation therapy dose is the conventional fractionation	1	A
The benefit of the association of concurrent chemotherapy with altered fractionation has not yet been completely defined	1	B
The standard fractionation for early-stage glottic cancer is moderate hypofractionation	1	A
The most accepted dose distribution to the PTV is D95%/100 of the PTV	4	C
The peer review process is an essential part of quality assurance	4	C
Recommendation 47		
IGRT is an essential component for delivering radiation therapy due to its ability to reduce geometric uncertainties and the risk of undertreating the target volume and overtreating adjacent organs at risk. Daily and alternate-day IGRTs are recommended for services that apply a 5-mm CTV-PTV margins expansion. Margins larger than 5 mm are recommended for departments that avoid daily IGRT. Three-dimensional volumetric imaging may be necessary to remove residual errors in daily/alternating IGRT or when there is a suspicion of volumetric tumor changes, and some action to adapt the treatment is necessary	4	C
Recommendation 48		
Delays in starting or completing radiation therapy have been associated with decreased survival and increased local relapse. The most accepted time for starting curative radiotherapy is 30 days after the diagnosis. In the setting of postoperative radiation therapy, the treatment should begin within four or 6 weeks postoperatively. Each day of treatment interruption can be associated with a 1.4% decrease in local control. Moreover, 5 days of prolonged OTT was associated with a 3.5% decline in the 2-year local control rate. To avoid treatment interruptions and their impact on the oncological outcomes, it is essential to evaluate patients with head and neck cancer weekly	4	C

Abbreviations: 3DCRT, three-dimensional conformal technique; CT, computed tomography; CTV, clinical target volume; IGRT, image-guided radiation therapy; IMRT, intensity modulated radiotherapy; OTT, overall treatment time; PTV, planning target volume.

Third, no patients or patients' representatives were directly included in the study. However, the GBCP (Brazilian Group of Head and Neck Cancer) is a multidisciplinary organization of health care professionals specializing in assisting patients with head and neck cancer and advocating for patient rights. The entire board of GBCP directors contributed to this study's authorship, ensuring consideration for the patients' best interests in adapting the best evidence to the Latin American context and aiming to minimize potential biases.

Finally, we established 48 recommendations on the basis of the Latin American context without aiming to provide a stratification of different possibilities according to resource settings or other variables such as availability or physicians' expertise, for example. Readers should consider these limitations when applying the recommendations to their clinical scenarios.

The present consensus established 48 recommendations on care of patients with HNSCC considering the availability of resources and focusing on oncologic benefit in the reality of Latin America. These recommendations could also be used to formulate treatment strategies for other regions with similar situations to Latin America countries.

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DISCLAIMER

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