Quality Indicators in Oropharyngeal Squamous Cell Carcinoma: Systematic Review of the Literature

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ABSTRACT

Introduction: Oropharyngeal cancer (OPC) has recently gained relevance owing to its increasing incidence in the population. We propose an evaluation of quality indicators for the management of OPC.

Objectives: To analyze studies that evaluated the quality indicators of oropharyngeal cancer.

Data Synthesis: The literature search was carried out in the following databases: Scielo, PubMed, EMBASE and LILACS, incorporating articles in Spanish and English that evaluated quality indicators in oropharyngeal cancer. A systematic review of the literature was conducted using descriptive analysis of the selected articles. Risk of bias analysis was performed using the ROBINS-E tool. Meta-analysis could not be performed because of the heterogeneity of data between the studies. Twelve studies were identified and four articles were selected, all of which had a moderate risk of bias. Two studies evaluated the use of high-quality care and demonstrated an improvement in overall survival (HR = 0.53 [0.39 – 0.71]). The remaining two studies evaluated the delay times between diagnosis and end of treatment, demonstrating that less than 48 and 78 days for patients with oropharyngeal cancer treated with chemoradiotherapy and surgery, respectively, showed improvement in overall survival (HR=1.24 (1.04-1.48) and HR=1.97 [1.39-2.78], respectively).

Conclusions: Quality indicators can be used to homogenize care in patients with head and neck cancer. Currently, there are no accepted quality indicators for oropharyngeal cancer and studies on this topic are scarce. Further studies are needed to determine whether these indicators affect these populations.

Keywords: Oropharyngeal Neoplasms; Quality Indicators, Health Care; Head and Neck Neoplasms

Introduction

Oropharyngeal cancer has recently gained relevance owing to its increasing incidence in the population. Some studies have shown an increase in incidence of up to 225% in the US population, due to the growing increase in oropharyngeal squamous cell carcinoma related to human papillomavirus[1].

Despite its increasing incidence, it remains a rare disease in the general population [2], which leads to the management of this condition being carried out in multiple and diverse health centers, without there being centralization/regionalization of cases that allow for an adequate volume or a homogeneous management in order to ensure an ideal outcome for the patients, risking less adherence to clinical management guidelines in this situation[3].

The association between the volume of management of head and neck cancer patients and oncological outcomes has been demonstrated in several studies, where it has been seen that the greater the volume, the better the oncological outcome, not only in terms of surgical results but also in the overall management of the patient. This is explained by greater experience and coordination regarding the medical and surgical services provided to these patients, complying with current standards of care[4]. This is also observed in the case of academic versus non-academic centers, with a better result in the former [5,6].

The problem of centralization is worldwide, which is why several groups in the world have sought minimum criteria to improve the health care of head and neck cancer patients, not only from the point of view of medical and surgical management, but also from a transdisciplinary structural vision addressing the processes of referral, diagnosis, staging, management, follow-up, survival and palliative care associated with these diagnoses[7]. Among which we could name the following: discussion of cases in a multidisciplinary oncological meeting board, adherence to clinical practice guidelines, start time of adjuvant therapy less than 6 weeks after surgery and adherence to quality criteria for oncological surgery[8]. In the latter case, the American Society of Head and Neck Surgery published two groups of quality indicators in relation to the management of patients with cancer of the larynx and oral cavity in 2007 and 2008, respectively (Table 1 and 2)[9,10].

Table 1. American Head and Neck Society Quality Measures for Squamous Carcinoma of the Oral Cavity.

Measures prior to treatment of carcinoma from the oral cavity:
1.All patients with oral tongue cancer require documentation of pathology using the College of American Pathologists (CAP) criteria with histopathologic confirmation of disease.
2.All patients with oral tongue cancer require documentation of appropriate TNM staging (as defined by the American Joint Committee on Cancer)
a.Assessment of primary tumor size (T)
b.Evaluation of regional nodal groups for metastatic lymphadenopathy (N)
c.Systemic disease evaluation (M)
3. Smoking cessation counseling.
Quality measures related to treatment:
1.All patients with oral cavity cancer with advanced T stage or metastatic lymph nodes should be referred to radiation oncology to consider postoperative radiation therapy.
2.All patients with oral cavity cancer with positive pathologic margins or metastatic lymph nodes showing extracapsular extension should be referred to a medical oncologist or radiation oncologist for consideration for adjuvant chemotherapy and radiation.
Post-treatment quality measures:
1.All patients treated for oral cavity cancer should have follow-up visits for symptom management and monitoring for recurrence and second primary tumors.
2.Patients treated with radiation therapy to the neck should undergo evaluation of serum thyroid-stimulating hormone (TSH) to detect hypothyroidism. Post-treatment serum TSH should be monitored within twelve months of completion of radiotherapy.

Adapted from Chen AY. The development of quality of care measures for oral cavity cancer.*Arch Otolaryngol Head Neck Surg*. 2008;134(6):672

Table 2. American Head and Neck Society Quality Measures for Squamous Carcinoma of the Larynx.

Measures prior to treatment of laryngeal cancer:
All patients with laryngeal cancer require documentation of pathology using the CAP criteria with histopathological confirmation of the disease.
All patients with laryngeal cancer require documentation of appropriate TNM staging (as defined by AJCC)
Assessment of primary tumor size (T)
Evaluation of regional nodal groups for metastatic lymphadenopathy (N)
Systemic disease evaluation (M)
Advice to quit smoking
Pre-laryngectomy counseling for patients undergoing laryngectomy.
Quality measures related to treatment:
All patients with advanced stage T laryngeal cancer should be referred to radiation oncology to consider postoperative radiation therapy.
All patients with postoperative laryngeal cancer with more than one positive lymph node and/or advanced T stage should be referred to radiation oncology for consideration of radiation therapy.
All patients with laryngeal cancer with positive pathologic margins or metastatic lymph nodes showing extracapsular extension should be referred to a medical oncologist or radiation oncologist for consideration for adjuvant chemotherapy and radiation.
All patients undergoing laryngeal surgery (partial or total) should be evaluated and followed by a speech pathologist.
Post-treatment quality measures:
All patients treated for oral cavity cancer should have follow-up visits for symptom management and monitoring for recurrence and second primary tumors.
Patients treated with radiation therapy to the neck should undergo serum TSH evaluation to detect hypothyroidism. Post-treatment serum TSH should be checked within 12 months of completion of radiotherapy.

Adapted from Cramer JD, Speedy SE, Ferris RL, Rademaker AW, Patel UA, Samant S. National evaluation of multidisciplinary quality metrics for head and neck cancer. *Cancer*. 2017;123(22):4372-4381

Cramer et al. evaluated adherence to 5 indicators published by the American Head and Neck Society in relation to oncological management of head and neck cancer in different centers in the United States, where the results, including 76,853 patients, were variable, having 80% adherence for negative surgical margins, 73.1% for cervical dissection, 69% for adjuvant radiotherapy, 42.6% for adjuvant chemotherapy, and 44.5% for adjuvant therapy within 6 weeks[7].

On the other hand, the working group of the RARECAREnet project, in Europe, developed 11 quality indicators that addressed the care of patients with head and neck cancer in a more global way from the diagnostic process to their definitive management (Table 3)[3]. When analyzing compliance of those indicators, there is a regular to moderate level of adherence in European countries varying between 50-70%, depending on the country as well as the indicator analyzed, accounting for an issue that has room for improvement[3].

Table 3. Quality indicators for head and neck cancer.

Diagnosis
Percentage of patients with a defined stage at the time of diagnosis.
Time to start treatment and treatment compliance with clinical guidelines
Time to start treatment (time between definitive pathological diagnosis and start of surgery or radiotherapy <1 month)
Time of initiation of postoperative radiotherapy or concomitant chemotherapy (<8 weeks from surgery)
Percentage of patients with early stages I and II referred for surgery or radiotherapy
Percentage of patients with locally advanced stage III and IV referred for surgery plus postoperative radiotherapy or postoperative chemoradiotherapy or concomitant chemoradiotherapy. Quality of surgery and radiotherapy
Percentage of complete tumor resection (histological verification of tumor-free margins after surgery)
Percentage of reoperation within 30 days of main surgery
Percentage of grade ≥ 3 late toxicities (> 3 months after radiotherapy)
Percentage of patients receiving intensity-modulated radiotherapy versus % receiving 3D conformal radiotherapy
Percentage of patients receiving stage-appropriate surgery (e.g., minimally invasive and reconstructive surgery). Quality of pathology reports after surgery

Percentage of pathology reports after surgery with a complete set of core data elements recorded. According to the Royal College of Pathologists: site and laterality of carcinoma, maximum tumor diameter, maximum depth of invasion, histological type of carcinoma, degree of differentiation (grade), pattern of invasion, margin status, lymph node involvement.
Availability of formalized multidisciplinary decision making (with expert members in head and neck cancers).
Participation in clinical and translational research.

Adapted from Trama A, Botta L, Foschi R, et al. Quality of Care Indicators for Head and Neck Cancers: The Experience of the European Project RARECAREnet. *Front Oncol*. 2019;9:837

The importance of these indicators lies in the fact that there are studies that ensure that compliance with certain quality indicators would improve outcomes in this group of patients, resulting in a better health care in this group, possibly because it is carried out by a more coordinated multidisciplinary team with greater adherence to clinical guidelines or scientific evidence in its management[7]. That is why, we sought to evaluate the current quality indicators and its outcomes in oropharyngeal squamous cell carcinoma.

Materials and Methods

Systematic literature search

A systematic review of the literature about quality indicators in oropharyngeal carcinoma was carried out. The literature search was carried out in the following databases: Scielo, PubMed, EMBASE and LILACS, incorporating articles in Spanish and English that evaluated quality indicators in oropharyngeal cancer. This search was carried out with the keywords shown in Table 4 until May 27th, 2025.

Table 4: Search Strategy

Database	Search Strategy	Number of articles
PubMed	("oropharynx cancer"[Title/Abstract] OR "oropharyngeal carcinoma"[Title/Abstract] OR "oropharyngeal cancer"[Title/Abstract] OR "oropharynx carcinoma"[Title/Abstract] OR "Oropharyngeal Neoplasms"[MeSH Terms]) AND ("quality indicators, health care"[MeSH Terms] OR ("quality indicator"[Title/Abstract] OR "quality criteria"[Title/Abstract] OR "care quality"[Title/Abstract]))	8
EMBASE	(('oropharyngeal cancer':ti,ab,kw OR 'oropharynx carcinoma':ti,ab,kw OR 'oropharyngeal carcinoma':ti,ab,kw))AND (('quality indicator':ti,ab,kw OR 'quality criteria':ti,ab,kw OR 'healthcare indicator':ti,ab,kw))	0
Scielo	(indicadores de calidad [Todos los indices] or criterios de calidad [Todos los indices]) and (cancer de orofaringe [Todos los indices] or carcinoma orofaringe)	0
LILACS	((oropharyngeal cancer [Words] or oropharyngeal carcinoma [Words])) and ((quality indicators [Words] or indicators [Words] or quality criteria [Words]))	0

Both the literature search, selection, and data extraction were carried out by the authors of the article (S.C and F.C.), independently, with no conflicts in the incorporation of articles. No funding was necessary for the development of this article.

Inclusion and exclusion criteria

The inclusion criteria were those studies that evaluate quality indicators in oropharyngeal cancer. Those studies that evaluated cancer in the head and neck in general or that evaluate other sites of the head and neck were excluded.

Analysis of the results

A descriptive analysis of the literature was carried out. Given the small number of articles in addition to the heterogeneity of the data, it was not possible to carry out quantitative analysis or meta-analysis.

Risk of bias assessment

In order to evaluate the risk of bias of each article, the ROBINS-E tool was used, because the selected articles were non-randomized retrospective observational studies. This tool includes 7 domains to evaluate: Domain 1 (Risk of bias due to confounding variables); Domain 2 (Risk of bias derived from exposure measurement); Domain 3 (Risk of bias arising from the selection of study participants); Domain 4 (Risk of bias derived from post-exposure interventions); Domain 5 (Risk of bias derived from missing data); Domain 6 (Risk of bias derived from measurement of results) and Domain 7 (Risk of bias derived from selection of reported results). Finally, according to their algorithm, each article is classified into 4 categories: Low risk of bias; Some concerns; High risk of bias; Very high risk of bias[11].

The risk of bias assessment was carried out independently by the 2 authors of this article (S.C. and F.C.).

Review of the Literature

A total of 8 articles were found in the literature search, of which, after reviewing their titles and abstracts, only 1 was selected. However, 3 additional studies were added after reviewing references, as shown in the PRISMA flow diagram (Figure 1). All articles were retrospective cohort studies. These articles will be described below.

Figure 1: PRISMA flow diagram
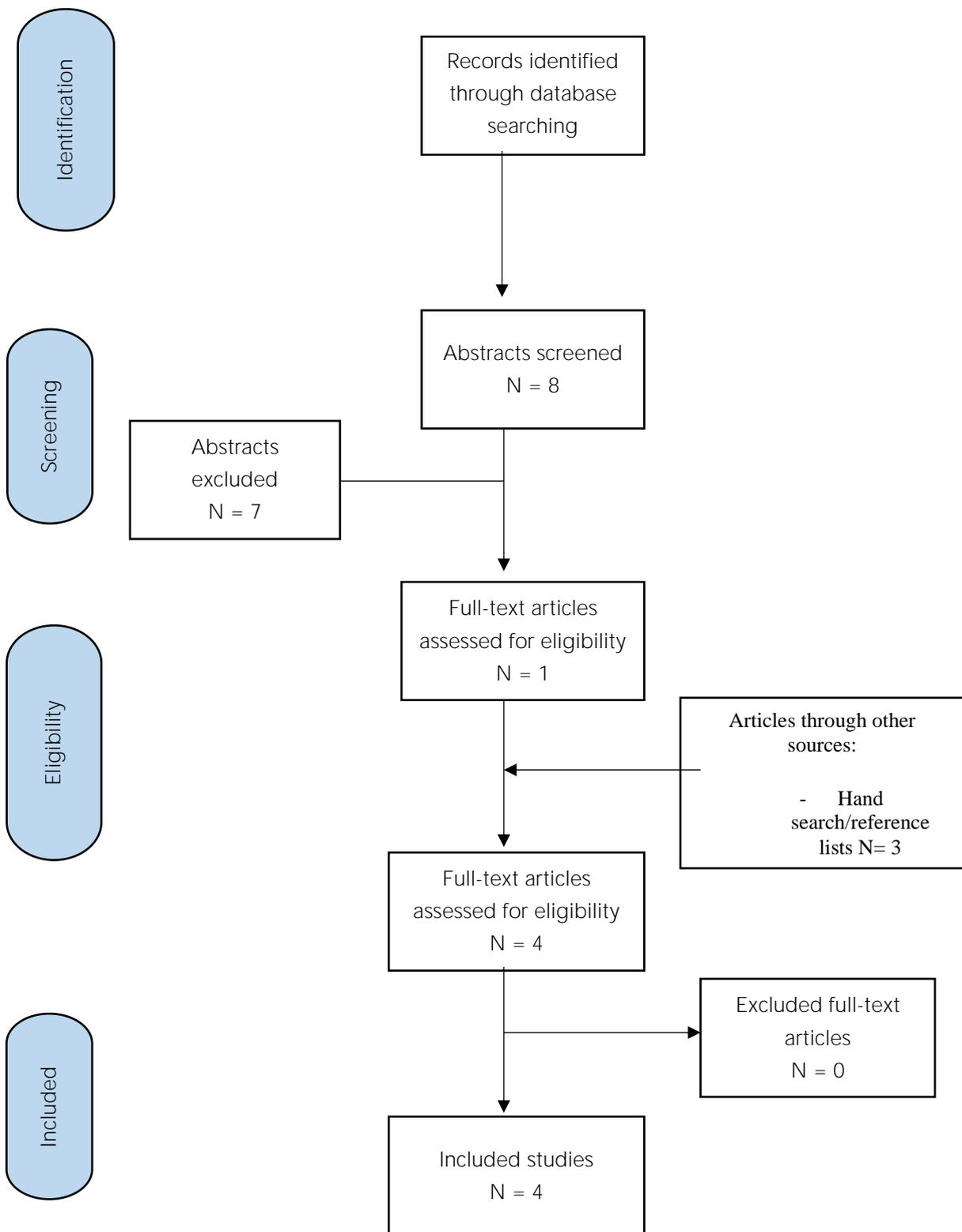
Descriptive analysis

The first 2 studies evaluate high-quality care in oropharyngeal cancer. Although there is no agreement on the basic indicators, these studies used recommendations based on the clinical guidelines of the National Comprehensive Cancer Network (NCCN), where we highlight the following indicators according to the study stage: 1) Diagnosis: Histological confirmation of the disease; pre-treatment imaging study; staging; dental evaluation prior to radiotherapy. 2) Initial treatment: Appropriate surgery; appropriate radiotherapy; appropriate chemoradiotherapy; initiation of adjuvant radiotherapy less than or equal to 6 weeks after surgery. 3) Follow-up: 1st year: 4 visits; 2nd year: 2 visits; 3rd-5th year: at least 1 visit[12].

Gourin et al evaluated adherence to these quality indicators extracted from the NCCN, in 666 patients diagnosed with oropharyngeal cancer extracted from the SEER database in the United States. They observed that high-quality care, defined as compliance with more than 50% of the previous indicators, had greater overall survival (HR = 0.53 [0.39 – 0.71]), as did surgery of High-quality salvage was associated with an increase in survival (HR = 0.16 [0.04 – 0.54])[12].

This same group of authors evaluated the association between high-quality care and risk of death in the same cohort of patients. It was observed that high-quality care was associated with a lower risk of death in patients with dysphagia (HR = 0.44 [0.32-0.60]), weight loss (HR = 0.42 [0.28-0.60]), 0.62]), gastrostomy (HR = 0.47 [0.33-0.68]), airway obstruction (HR = 0.41 [0.27-0.62]), tracheostomy (HR = 0 .17 [0.05-0.67]), and pneumonia (HR = 0.53 [0.33-0.85])[13].

The remaining 2 studies evaluated another quality indicator: time between diagnosis and the start and end of treatment. The group of Morse et al. evaluated patients diagnosed with oropharyngeal cancer treated with primary radiotherapy or chemoradiotherapy, extracted from the National Cancer Data Base (NCDB) between 2010-2013,

with 4089 patients. It was observed that the average duration between diagnosis – initiation of treatment, duration of radiotherapy and diagnosis – end of treatment were 35, 50 and 87 days, respectively. Furthermore, they observed that delays in the duration of radiotherapy and the time between diagnosis and completion of treatment, defined as those patients who were in the fourth quartile of duration, were negatively associated with overall survival (HR = 1.23 (1.03-1.47), p = 0.024 and 1.24 (1.04-1.48), p = 0.017, respectively)[14]. In this sense, it was established that, taking all the patients analyzed, a duration greater than 48 days from diagnosis and end of treatment presented a worse prognosis[14].

The same group evaluated a cohort of patients diagnosed with oropharyngeal cancer treated surgically, using the NCDB database in the same period (2010-2013). They found a total of 3708 patients, where the average duration of time between diagnosis – initiation of treatment, surgery – radiotherapy, duration of radiotherapy, total treatment time and diagnosis – end of treatment were 27, 42, 47, 90 and 106 days, respectively. It was observed that the delay in the total treatment time and the diagnosis time - treatment end was associated with a decrease in overall survival (HR = 1.81 [1.29-2.54], p = 0.001 and HR = 1 .97 [1.39-2.78], p /.001, respectively), which was maintained after stratification by HPV. Delay in time between surgery and radiotherapy was associated with a decrease in overall survival in HPV-negative patients, but not in positive ones (HR = 2.05 [1.19-3.52], P = .010 and HR = 1.15 [0.74-1.80], P = .535, respectively). Delay in the time between diagnosis and initiation of treatment and duration of radiotherapy were not associated with a worse prognosis (HR = 1.21 [0.86-1.72], P = .280 and HR = 1.40 [0.99- 1.99], P = .061, respectively). Finally, it was established that the delay threshold in total treatment time was 73 days and the diagnosis time – treatment end was 78 days, that means that a delay greater than those thresholds is associated with worse overall survival [15].

Bias Assessment

As noted above, the ROBINS-E tool was used to assess risk of bias in the articles described above.

The summary of the risk assessment is seen in table 5.

Table 5: Risk of bias (ROBINS-E tool)

	Gourin 2017	Gourin 2018	Morse 2018	Morse 2018 (2nd Article)
Overall Risk of Bias	Some Concerns	Some Concerns	Some Concerns	Some Concerns

Response Summary	Gourin 2017	Gourin 2018	Morse 2018	Morse 2018 (2nd Article)
Domain 1 (Variant A) Response:	Some Concerns	Some Concerns	Some Concerns	Some Concerns
Domain 2 (Variant A) Response:	Some Concerns	Some Concerns	Low Risk of Bias	Low Risk of Bias
Domain 3 Response:	Some Concerns	Some Concerns	Some Concerns	Some Concerns
Domain 4 Response:	Low Risk of Bias	Low Risk of Bias	Low Risk of Bias	Low Risk of Bias
Domain 5 Response:	Some Concerns	Some Concerns	Some Concerns	Some Concerns
Domain 6 Response:	Low Risk of Bias	Low Risk of Bias	Low Risk of Bias	Low Risk of Bias
Domain 7 Response:	Some Concerns	Some Concerns	Some Concerns	Some Concerns

It is observed that all the selected articles present a moderate risk of bias. This is due to 3 main domains: 1) patient selection: being retrospective studies, where patients are extracted from databases, even when reliable, implies a risk of selection bias from institutions that are incorporated into these databases. 2) confounding variables: The studies analyzed do not incorporate exposure variables that influence the prognosis of these patients, especially tobacco consumption, which in oropharyngeal carcinoma has been shown to be a prognostic factor [16]. 3) variable results: Given the small amount of clinical information obtained, there is also no analysis of recurrences in any of the studies, nor of complications associated with the primary treatment, all of which influences the final treatment of the patients (both in the duration of treatment and in adherence to quality criteria). Therefore, the results of the studies analyzed should be taken with caution.

Discussion

Currently there are no quality indicators in oropharyngeal cancer that are universally accepted, but the closest ones are the recommendations from clinical guidelines, especially the NCCN already mentioned. Despite the above and the limitations of the studies mentioned, it is observed that high-quality care presents a better oncological outcome, being associated with less morbidity in the long term [12,13]. However, more studies with better quality are necessary to confirm these results.

On the other hand, the negative effect of an increase in waiting times between diagnosis and completion of treatment in terms of overall survival stands out in the literature, where the longer the time, the worse the oncological outcome, establishing in the analyzed articles a threshold of 48 days and 78 days for the time between diagnosis and end of treatment in patients with oropharyngeal squamous cell carcinoma treated with chemo-radiotherapy and surgery, respectively [14,15].

In head and neck cancer, the time threshold is not well defined, where some indicate that 100 days should be the maximum total time between

surgery and the end of radiotherapy [17], while other authors indicate less than 14 weeks for the total treatment time [18]. It is important to consider that the times depend on the population studied, and local studies must be carried out to determine these and thus implement public policies that allow them to be achieved, generating expeditious referral mechanisms to achieve the best oncological outcome.

It is necessary to establish minimum quality indicators not only to improve oncological outcomes but also to improve the efficiency of the health system, considering the costs associated with the treatment of these patients with long-term functional morbidities. This is relevant because one of the goals of the health system, in general, is to achieve value-based healthcare (VBHC). This concept was proposed by Porter, who stated that "achieving a high value for patients must become the overarching goal of healthcare delivery, with value defined as the health outcomes achieved per dollar spent. This goal is what matters for patients and unites the interests of all actors in the system" [19]. Therefore, to define value, it is important to define relevant outcomes (including toxicity/complications) on one hand and costs (including waste and unnecessary expenses). In that sense, we believe that defining quality criteria for head and neck cancers in general would lead to improved health outcomes while reducing the costs associated with healthcare delivery.

However, as mentioned before, defining certain quality criteria could improve oncological outcomes and long-term morbidities associated with definitive treatment. This is important from the point of view of the costs afforded by the health system as well as from the patient perspective. There is an increasing body of literature on financial toxicity in cancer patients, especially in the head and neck, associated with esthetic and functional disabilities[20,21]. One of our hypotheses is that the adoption of quality criteria could lead to better functional and aesthetic outcomes and reduce financial toxicity, but there is no literature evaluating this idea.

Currently, there is no evidence of different quality criteria between HPV-positive and HPV-negative OPC, despite the different oncological outcomes between the two. Considering the de-escalation strategies for HPV-positive OPC under investigation along with well-adopted treatment modalities, such as transoral robotic surgery in the context of early-stage HPV-positive OPC[22], we believe that, in the future, it is important to establish different quality criteria between these two entities depending on the treatment modality differences between them.

Finally, this systematic review has numerous limitations. First, the lack of evidence on this topic makes it difficult to draw definitive conclusions. Second, the included studies are retrospective, with its associated biases, and no randomized controlled trials were found in the literature. Third, due to the lack of and heterogeneity of the results, a quantitative analysis was not possible.

Despite the above, this is the first systematic review regarding quality criteria in oropharyngeal carcinoma. The relevance of the quality criteria for management in OPC cancer cannot be overemphasized. Nonetheless, the adoption of these indicators should be supported by future studies so that decision-making institutions in oncology take them into consideration to standardize the management and care of patients with OPC cancer.

Conclusion

Interdisciplinary quality indicators are an excellent method to homogenize the management of this rare disease, establishing minimum standards for the quality of health care both in the referral, diagnostic process, and medical management and surgery to ensure the best outcome of care and optimize oncological outcomes for patients.

Currently, studies on this disease are scarce, and in some cases, lack methodological relevance.

However, high-quality care with a shorter time between diagnosis and the end of treatment is associated with better overall survival. Further studies are required to evaluate this issue.

It is important to conduct studies to determine the minimum quality indicators that must be evaluated for possible future adoption. The adoption of quality indicators can contribute to improving the care of patients with head and neck cancers.

Conflict of Interest:

The authors have no conflicts of interest to declare.

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