CLINICAL, HISTOPATHOLOGICAL, AND BIOLOGICAL PREDICTORS OF THE NEED FOR COMPLEX SURGERY IN CERVICO-FACIAL SKIN CANCERS – A NARRATIVE REVIEW

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Summary

Cervico-facial skin cancers currently represent a major therapeutic challenge due to the functional and aesthetic impact associated with the affected anatomical region. Although surgical excision remains the standard treatment, a subset of patients requires complex reconstructive procedures and/or associated oncological management. Early identification of these cases is essential for optimizing therapeutic strategies.

A narrative review of the literature was conducted using the PubMed and Google Scholar databases, analyzing studies evaluating predictive factors associated with tumor aggressiveness and the need for complex surgery.

Clinical factors such as tumor size and localization in high-risk anatomical areas (nose, eyelids, lips) are frequently associated with extensive surgical interventions. Histopathological characteristics, including perineural invasion, poor differentiation, and positive surgical margins, significantly influence treatment complexity. Systemic inflammatory biomarkers, including the neutrophil-to-lymphocyte ratio and C-reactive protein, may play an emerging role in the assessment of tumor severity.

The integration of these factors may contribute to the development of predictive models useful for multi-disciplinary decision-making and optimization of patient management.

Received: 6.04.2026 *Accepted: 12.05.2026*

Introduction

Skin cancers are currently the most common forms of neoplasia worldwide, with basal cell carcinoma and squamous cell carcinoma being predominant, particularly in the cervico-facial region [1]. Ultraviolet radiation represents the principal etiological factor, and the incidence of these tumors continues to increase globally [2].

The cervico-facial region presents complex anatomical and functional characteristics, including essential structures such as the eyes, nose, and oral cavity [3]. Consequently, surgical treatment aims not only at complete tumor excision but also at preserving both functional and aesthetic integrity.

The majority of lesions can be treated through simple excision; however, certain cases require extensive surgical procedures and complex reconstructions, including the use of local or free flaps [3,4]. Currently, no standardized model exists for the early identification of such patients.

The aim of this review is to analyze and synthesize the existing evidence regarding the clinical, histopathological, and biological factors

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involved in predicting the need for complex surgery in cervico-facial skin cancers.

Materials and Methods

A narrative review of the literature was performed with the objective of identifying clinical, histopathological, and biological factors associated with the need for complex surgery in cervico-facial skin cancers.

The literature search was conducted using the PubMed and Google Scholar databases, employing combined terms and relevant keywords such as: "facial skin cancer," "cutaneous carcinoma," "reconstruction," "predictors," "perineural invasion," "NLR," and "CRP."

Original articles (prospective and retrospective clinical studies), observational studies, and review articles published between 2000 and 2025 were included if they evaluated the relationship between tumor characteristics and surgical treatment complexity or the need for advanced reconstruction.

Inclusion criteria comprised studies reporting data regarding oncological prognostic factors, including tumor size, localization, histological differentiation grade, perineural invasion, and resection margin status, as well as systemic inflammatory biomarkers.

Studies lacking direct relevance to the objective of the review, isolated case reports, and articles without full-text access or insufficient data for analysis were excluded.

Study selection was performed through title and abstract screening, followed by full-text evaluation of eligible publications. Extracted data were qualitatively analyzed and synthesized according to the category of evaluated factors.

Results

Clinical Factors

Tumor size represents one of the most important predictors of surgical complexity in cervico-facial skin cancers [5]. Large tumors are frequently associated with more extensive local invasion, consequently requiring wider excisions and resulting in significantly larger postoperative defects [5,6]. Such situations often necessitate advanced reconstructive techniques, including local or free flaps, in order to restore tissue continuity and regional functionality [6].

Tumor localization constitutes another essential clinical factor in assessing surgical treatment complexity [7]. High-risk anatomical regions, such as the nose, eyelids, and lips, present specific anatomical and functional features that substantially limit reconstructive options [7]. In these regions, the therapeutic objective extends beyond complete lesion excision and includes preservation of essential functions (respiration, vision, oral competence) as well as achievement of an acceptable aesthetic outcome, thereby significantly increasing surgical difficulty [7,8].

Tumor recurrence and advanced disease stage are clinical factors associated with a significantly increased degree of therapeutic aggressiveness [9]. Recurrent tumors frequently exhibit tissue alterations secondary to previous interventions, complicating resection margin delineation and increasing the risk of incomplete excision [9]. Similarly, advanced stages are correlated with local or regional disease extension, requiring more radical surgical interventions and often a multimodal therapeutic approach that may include radiotherapy or combined adjuvant treatment modalities [9,10].

Histopathological Factors

Histopathological characteristics of cutaneous tumors represent essential elements in oncological risk assessment and therapeutic planning [11]. These parameters provide important information regarding tumor biological behavior and the likelihood of local extension or recurrence.

Perineural invasion is considered one of the most important negative prognostic factors, being associated with an increased tendency for tumor spread along neural pathways [12]. Its presence is frequently correlated with more aggressive forms of disease, increased risk of local recurrence, and the need for extensive

surgical excisions, sometimes associated with adjuvant treatment [12].

Tumor differentiation grade represents another important histopathological predictor [11]. Poorly differentiated tumors generally exhibit a more aggressive biological behavior, characterized by increased proliferative activity and enhanced local invasive potential [11,13]. These characteristics necessitate a more radical surgical approach and stricter postoperative surveillance [13].

Furthermore, positive resection margins and deep tumor invasion are factors associated with a significantly increased risk of recurrence [11]. In such cases, reintervention is frequently required to achieve local disease control, while in certain situations adjuvant oncological treatment becomes necessary depending on lesion extension and aggressiveness [11,13].

Biological Factors

In recent years, systemic inflammatory biomarkers have been extensively investigated as potential indicators of tumor aggressiveness and oncological prognosis [14]. These biomarkers reflect a complex interaction between the host immune response and tumor biological behavior, providing supplementary information beyond classical clinical and histopathological parameters [14].

The neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) are among the most frequently evaluated inflammatory markers, being associated in multiple studies with unfavorable prognosis across various malignancies [15,16]. Elevated levels of these markers suggest the presence of persistent systemic inflammation, which may promote tumor proliferation, angiogenesis, and disease progression [15].

From a clinical perspective, these biomarkers may indirectly reflect tumor aggressiveness and neoplastic process extension [15]. Although their exact role in predicting the need for complex surgical intervention in cervico-facial skin cancers has not yet been fully standardized, existing literature suggests potential utility in preoperative risk stratification and support of multidisciplinary decision-making [16].

Nevertheless, the use of these markers currently remains complementary to clinical and histopathological evaluation, and additional studies are required to validate their role as independent predictive tools within surgical decision-making algorithms [14,16].

Discussions

The findings of this review highlight that the need for complex surgery in cervico-facial skin cancers is determined by the interaction of multiple clinical, histopathological, and biological factors.

Tumor size and localization within anatomically critical regions represent the principal clinical determinants of surgical complexity [1,3]. These variables directly influence the extent of the anticipated postoperative defect and, consequently, the choice of reconstructive strategy, with significant impact on technical difficulty and functional and aesthetic outcomes [2,3].

From a histopathological perspective, the analyzed factors provide essential information regarding tumor biological behavior [7]. Perineural invasion and tumor differentiation grade are frequently associated with a more aggressive tumor phenotype, increased risk of local extension and recurrence, thereby influencing therapeutic decision-making and the extent of surgical resection [7,8].

Moreover, the integration of systemic inflammatory biomarkers into preoperative assessment represents an emerging research direction [14]. Although existing evidence suggests a possible correlation between these markers and tumor aggressiveness, their clinical applicability remains limited and insufficiently standardized, requiring further prospective studies to validate their role in decision-making algorithms [14–16].

Overall, these observations support the need for the development of integrated predictive models combining clinical, histopathological, and biological factors in order to optimize patient selection and support therapeutic decision-making within multidisciplinary teams [7,14].

Conclusions

Cervico-facial skin cancers require a complex therapeutic approach, and early identification of cases at risk of requiring extensive surgical inter-

ventions is essential for optimizing therapeutic management.

The clinical, histopathological, and biological factors analyzed in this review appear to play an important role in predicting surgical treatment complexity. Tumor size, localization in anatomically critical regions, histopathological features such as perineural invasion and differentiation grade, as well as systemic inflammatory biomarkers, may contribute to more accurate risk stratification [7,14].

The integration of these parameters into a multidimensional predictive model represents a promising future direction, with the potential to support therapeutic decision-making and improve patient management within multidisciplinary teams [7,14].

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Conflict of interest
NONE DECLARED

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