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Efficacy of combined approaches of periocular reconstruction and dermatologic treatment in the management of invasive cutaneous malignant neoplasm: a systematic review of functional and cosmetic outcomes

Eficacia de los enfoques combinados de reconstrucción periocular y tratamiento dermatológico en el manejo de la neoplasia maligna cutánea invasiva: una revisión sistemática de los resultados funcionales y cosméticos

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ABSTRACT

Background: The periocular region is a high-risk site for cutaneous malignancies, particularly basal and squamous cell carcinomas. Because of its role in protecting the eye and supporting tear film dynamics, even small defects in this area can disrupt function and lead to notice able cosmetic changes. Managing tumors here requires a careful balance between complete cancer removal and preserving eyelid function and appearance. Objective: To evaluate the functional and cosmetic outcomes of combining periocular reconstruction with dematologicand systemic treatments in patients with invasive periocular skin cancers. Methods: We conducted a systematic review of 57 studies involving patients with invasive cutaneous malignancies of the periocular region. Included treatments spanned Mohs micrographic surgery (MMS), conventional excision with frozen-section control, radiotherapy, and systemic therapies such as vismodegib and cemiplimab. We examined outcomes related to eyelid function, visual protection, tear drainage, and patient-reported cosmetic satisfaction. Results: MMS consistently offered high cure rates and minimal tissue loss, resulting in favorable functional and cosmetic out comes when paired with oculoplastic reconstruction. Flap techniques such as the Hughes and Mustardé flaps showed high success rates in restoring eyelid structure and function. In advanced cases, neoadjuvant therapies reduced the need for orbital exenteration and preserved visual function in 40–60% of patients. Radiation therapy was effective but often resulted in chronic ocular surface problems. Patients undergoing exenteration reported lower satisfaction despite acceptable prosthetic rehabilitation. Conclusion: A combined approach to periocular skin cancer—integrating precise excision, functional reconstruction, and selective use of systemic therapy—yields better outcomes than single-modality treatment. Multidisciplinary planning is essential to preserve both form and function. Future studies should standardize outcome reporting and inclu

Keywords: Periocular reconstruction, Dermatologic treatment, Invasive cutaneous malignant neoplasm.

RESUMEN

Antecedentes: La región periocular es una zona de alto riesgo para neoplasias cutáneas malignas, en particular carcinomas bas ocelulares y escamocelulares. Debido a su función en la protección ocular y el mantenimiento de la dinámica de la película lagrimal, incluso pequeños defectos en esta zona pueden alterar su función y provocar cambios estéticos notables. El manejo de los tumores en esta zona requiere un cuidadoso equilibrio entre la extirpación completa del cáncer y la preservación de la función y la apariencia del párpado. Objetivo: Evaluar los resultados funcionales y estéticos de la combinación de la reconstrucción periocular con tratamientos dermatológicos y sistémicos en pacientes con cánceres de piel perioculares inva sivos. Métodos: Realizamos una revisión sistemática de 57 estudios en pacientes con neoplasias cutáneas invasivas de la región periocular. Los tratamientos incluidos incluyeron cirugía micrográfica de Mohs (MMS), escisión convencional con control por congelación, radioterapia y terapias sistémicas como vismod egib y cemiplimab. Examinamos los resultados relacionados con la función palpebral, la protección visual, el drenaje lagrimal y la satisfacción estética reportada por los pacientes. Resultados: La MMS ofreció consistentemente altas tasas de curación y mínima pérdida de tejido, lo que resultó en resultados funcionales y estéticos favorables al combinarse con la reconstrucción oculoplástica. Las técnicas de colgajo, como los colgajos de Hughes y Mustardé, mostraron altas tasas de éxito en la restauración de la estructura y la función palpebral. En casos avanzados, las terapias neoadyuvantes red ujeron la necesidad de exenteración orbitaria y preservaron la función visual en el 40-60% de los pacientes. La radioterapia fue eficaz, pero a menudo provocó problemas crónicos de la superficie ocular. Los pacientes sometidos a exenteración reportaron menor satisfacción a pesar de una rehabilitación protésica aceptable. Conclusion: A combined approach to periocular skin cancer—integrating precise excision, functional reconstruction, and selective use of systemic therapy—yields better outcomes than single-modality treatment. Multidisciplinary planning is essential to preserve both form and function. Future studies should standar dize outcome reporting and include long-term patient-centered data to guide best practices.

Palabras clave: Reconstrucción periocular, Tratamiento dermatológico, Neoplasia maligna cutánea invasiva.

INTRODUCTION

Cutaneous malignant neoplasms include basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and malignant melanoma. BCC is the most common, accounting for roughly 80% of cases, followed by SCC at 16%, and melanoma at around 4% (Lomas et al., 2012). These cancers frequently appear in sun-exposed areas, particularly the head and neck. The periocular region is a high-risk site, where about 10% of skin cancers arise (Cook & Bartley, 2001). Among these, BCC predominates, with up to 90% of periocular cases (Lang & Ma, 2009). These are the lesions grow slowly but can be locally invasive, often eroding tissue planes and affecting deeper structures. The periocular region is not just visually prominent; it also supports critical functions. The eyelids protect the globe, support tear film distribution, and help maintain corneal health. Any defect or distortion in this area can disrupt tear drainage, blink reflex, and visual function (Patipa, 2000). From a cos metic standpoint, asymmetry or scarring here is immediately noticeable. Small deformities can have a disproportionate psychological and social impact, particularly in older adults who are most affected by these cancers (Klingenstein et al., 2016). Therefore, treatment here is more than tumor removal-it is about preserving both function and appearance. Mohs micrographic surgery is the preferred method for periocular BCC and SCC, as it maximizes tissue conservation while ensuring margin control (Smeets et al., 2004). Radiotherapy is a second-line option, often for patients unfit for surgery, but risks include skin atrophy and poor wound healing. Topical agents like imiguimod and 5-fluorouracil are limited to superficial lesions and lack long-term efficacy in invasive disease (Spencer et al., 2009). Reconstruction ranges from primary closure to complex flaps and grafts, depending on defect size and location. However, no technique fits all cases. Each reconstructive decision affects eyelid mechanics and appearance. The risk is not simply cosmetic--it includes exposure keratopathy and chronic tearing or dryness (Murchison et al., 2004). Yet, many studies fail to report these outcomes systematically. A single treatment often cannot meet the dual goals of local tumor control and functional restoration. Integrated care-combining dermatologic treatment with immediate or staged reconstruction-offers a path to better outcomes. Despite case reports and small series suggesting benefits, comparative data remain sparse. There is no unified framework to guide clinicians, and outcomes such as patient satisfaction and evelid function are inconsistently measured or reported.

Objective of the Review: this review critically assesses the functional and cosmetic outcomes of combined dermatologic and reconstructive approaches in managing invasive periocular skin cancers. The goal is to clarify what works, what doesn't, and where evidence is lacking.

METHODOLOGY

This systematic review assessed the efficacy of combined periocular reconstruction and dermatologic treatment in managing invasive periocular cutaneous malignancies. The primary outcomes were functional (eyelid closure, tear drainage, vision preservation) and cosmetic (symmetry, scarring, patient-reported satisfaction).

Search Strategy

Databases searched included PubMed, Scopus, and Cochrane Library from January 1980 to December 2023. Search terms were: periocular skin cancer, eyelid reconstruction, Mohs surgery, neoadjuvant therapy, functional outcomes, and cosmetic outcomes.

Eligibility Criteria

Included studies reported outcomes in patients with periocular basal cell carcinoma (BCC), squamous cell carcinoma (SCC), or other invasive malignancies, with a minimum follow-up of 6 months. Case reports with fewer than five patients, non-invasive lesions, and studies lacking outcome data were excluded. Screening was independently performed by two reviewers; a third reviewer resolved conflicts.

Data Extraction and Synthesis

Data collected included demographics, tumor type, treatment modality (surgical excision, adjuvant therapy), and reconstruction method (flaps, grafts, prosthetics). Functional and cosmetic outcomes were systematically extracted. Treatments were stratified into:

• Surgical excision (Mohs vs. frozen section)

- Reconstruction techniques (local flaps, free grafts, prosthetic integration)
- Adjuvant therapies (radiotherapy, systemic agents)

Statistical Analysis

Fixed-effects or random-effects models were applied depending on heterogeneity. Continuous variables (e.g., satisfaction scores) were pooled using weighted mean differences.

Quality Assessment

The Newcastle-Ottawa Scale and Cochrane Risk of Bias Tool were applied. Studies at high risk of bias were excluded.

Term	MeSH Equivalent
Periocular skin cancer	Skin Neoplasms / Eyelid Neoplasms
Eyelid reconstruction	Reconstructive Surgical Procedures
Mohs surgery	Mohs Surgery
Neoadjuvant therapy	Neoadjuvant Therapy
Functional outcomes	Treatment Outcome / Visual Acuity
Cosmetic outcomes	Esthetics / Cicatrix / Patient Satisfaction

Table 1. Key Terms Mesh Table

Source: the authors.



Figure 1. Prisma Flow Diagram of Included Papers

RESULTS AND DISCUSSION

This systematic review synthesizes findings from 57 studies examining the efficacy of combined surgical, dermatologic, and systemic approaches for managing invasive periocular skin cancers. Across all tumor types, evidence supports a multidisciplinary paradigm prioritizing oncologic control while aiming to preserve visual function and facial cosmesis (Trotier et al., 2024).

Table 2. Main Findings

Author(s), Year	Key Findings on Periocular Reconstruction
Moran & Phelps, 2020	Periocular skin cancers require careful management due to proximity to vital structures; reconstruction must balance oncologic
	control with functional and cosmetic outcomes.
Essers et al., 2007	Facial aesthetics significantly impact patient quality of life post-reconstruction, emphasizing the need for cosmetically sensitive
	approaches.
NCCN Guidelines,	Mohs micrographic surgery or PDEMA techniques are preferred for periocular BCC and SCC due to high-risk location. Surgical
2023	margins must be carefully assessed.
Gulleth et al., 2010	Meta-analysis shows 3-mm surgical margins for small BCC yield a 95% cure rate, but periocular cases often require tissue-sparing
	techniques.
Karcioglu & Caldwell,	Frozen-section control is crucial for margin assessment in periocular malignancies to ensure complete excision.
1984	
Mohs, 1986	Mohs surgery for eyelid BCC achieves a recurrence rate of 0.6%, preserving maximal normal tissue.
Arlette et al., 1998	Periocular BCC often requires multidisciplinary management due to anatomic complexity.
Rajak et al., 2019	The "over-the-top" modified Cutler-Beard procedure is effective for upper eyelid reconstruction.
Czyz et al., 2011	Medial canthus and lacrimal system involvement complicates reconstruction; options include tarsal strips and flaps.
Martel et al., 2021	Orbital exenteration is indicated for orbital invasion but carries significant morbidity; alternatives like neoadjuvant thera py are
	emerging.
Bartley et al., 1989	Orbital exenteration outcomes vary; reconstruction techniques include grafts, flaps, or prostheses.
Tyers, 2006	Orbital exenteration for invasive tumors requires careful planning to address functional and aesthetic deficits.
Holliday et al., 2016	Proton therapy can spare orbital structures in epithelial tumors, with dose constraints to minimize toxicity (e.g., cornea < 35 Gy).
Hata et al., 2012	Noninvasive radiation therapy is curative for sebaceous carcinoma, avoiding extensive surgery.
Lee et al., 2019	Meta-analysis shows Mohs surgery has lower recurrence rates (0.2%) than radiotherapy (1.8%) for skin cancers.
Avril et al., 1997	Randomized trial favoring surgery over radiotherapy for facial BCC due to lower recurrence rates (0.7% vs. 7.5%).
Rodriguez & Deutsch,	Radiotherapy for periocular BCC achieves high local control (100% in studied cases).
1992	
Bertrand et al., 2021	Neoadjuvant vismodegib for facial BCC reduces tumor size by 66%, enabling less invasive surgery.
Kahana et al., 2021	VISORB trial: Neoadjuvant vismodegib preserves visual function in periocular BCC, with 56% achieving complete response.
Unsworth et al., 2022	Residual "micro-tumors" post-vismodegib highlight the need for surgical excision to prevent recurrence.
Gross et al., 2022	Neoadjuvant cemiplimab for SCC achieves 51% pathologic complete response, sparing orbital exenteration in some cases.
Steren et al., 2022	Cemiplimab for orbital SCC avoids exenteration in 82% of cases, with durable responses.
Tiosano et al., 2023	Primary cemiplimab for orbital SCC reduces the need for exenteration, improving quality of life.

Source: the authors.

Functional and Cosmetic Outcomes of Surgical Management

Mohs Micrographic Surgery (MMS) was the most commonly employed primary treatment modality, particularly for basal and squamous cell carcinomas. Studies consistently report high local control rates (up to 99.4%) and low recurrence rates (0.6%) in periocular BCC when MMS is used, with minimal cosmetic disruption due to tissue-sparing capabilities. The precision of MMS enables maximal preservation of eyelid structure, facilitating direct closure or minor flap reconstruction in 40–70% of cases. Cosmetic outcomes were rated good to excellent in over 80% of reported cases, especially when combined with oculoplastic reconstruction techniques.

Frozen-section margin control, while utilized in centers without access to MMS, showed higher margin uncertainty and increased defect size. This translated into more extensive reconstructions and slightly worse cosmetic scores. The lack of intraoperative precision led to a 5–10% increase in secondary surgeries for margin clearance in comparison to MMS.

Orbital exenteration, required in cases of orbital invasion (notably in sebaceous gland carcinoma and SCC), resulted in the most significant functional and cosmetic loss. While exenteration achieved local control in 90% of cases, the impact on quality of life was substantial, with loss of the globe and associated structures. Functional loss included binocular vision disruption and impaired lacrimal function. Cosmetic rehabilitation via prosthesis was described as "acceptable" by patients in 60–70% of studies, though lower satisfaction rates were noted compared to globe-sparing surgeries (Trotier et al., 2024).

Reconstructive Approaches and Their Impact

Eyelid reconstruction techniques varied by defect size and location. For small- to medium-sized defects, primary closure and skin grafting were sufficient, offering excellent functional restoration. For larger defects, local flaps such as the Hughes flap for lower lid and Mustardé cheek rotation for lateral canthus were frequently employed. These provided stable lid support, good contour, and functional blink restoration. Functional success rates were reported between 85–95%, with most patients achieving satisfactory lid closure and protection of the cornea.

Cosmetically, flaps yielded better results than grafts in terms of color match and contour. However, staged flaps occasionally led to temporary disfigurement and patient dissatisfaction during the healing phase. Objective assessments noted that 70% of patients reported their postoperative appearance as "close to preoperative baseline" within 6 months.

Lacrimal system involvement was encountered in 20–35% of cases, particularly with medial canthus tumors. Reconstructive strategies ranged from silicone intubation to conjunctivodacryocystorhinostomy (CDCR) for irreparable duct involvement. While epiphora was reduced in 60–75% of cases with these techniques, complete functional lacrimal restoration was rare. Cosmetically, the presence of visible tubes or rhinostomy scars reduced patient satisfaction in 15–20% of cases (Trotier et al., 2024).

Role and Outcomes of Radiation Therapy

Radiotherapy was employed either as definitive treatment for inoperable lesions or as adjuvant therapy post-surgery for close/positive margins. In adjuvant settings, radiation doses ranging from 50–66 Gy led to local control rates above 85%, particularly when combined with MMS. Radiation-related complications, including dry eye (23%), keratopathy (10%), and eyelash loss (35%), affected both function and appearance.

Superficial modalities (electrons, orthovoltage) preserved eyelid function in early tumors, while IMRT and proton therapy enabled conformal delivery for deeper lesions. Despite ocular dose-sparing techniques, lacrimal gland toxicity and dry eye symptoms were common, reported in 20–30% of patients, affecting quality of life and cosmesis (Trotier et al., 2024).

Systemic and Neoadjuvant Therapies: Shaping Surgical and Functional Outcomes

In select cases, neoadjuvant therapy allowed surgical de-escalation and globe preservation.

• Hedgehog Inhibitors (HHIs), especially vismodegib and sonidegib, were used in advanced BCC. In the VISORB trial and similar cohorts, tumor reduction enabled conversion of 82% of orbital-involving BCC cases to globe-sparing surgeries. Functional preservation of the orbit and lid structure was achieved in the majority, and cosmetic outcomes were judged superior to exenteration-based strategies. Complete response (CR) rates ranged from 43–56%. Side effects (muscle cramps, alopecia, dysgeusia) impacted quality of life in 30–40% of patients but were reversible.

• Immunotherapy, particularly anti-PD-1 agents (cemiplimab, pembrolizumab), showed promise in SCC. In a prospective cohort, neoadjuvant cemiplimab led to a 51% pathologic CR, and avoided orbital exenteration in nearly half of the cases initially deemed unresectable. Functional preservation of vision and ocular mobility was maintained in 70% of these patients. However, cosmetic deformity from partial orbital debulking still occurred in a minority.

• For melanoma, combination neoadjuvant immunotherapy (nivolumab/ipilimumab) resulted in pathologic CRs up to 57%, with some globe-sparing successes. However, high toxicity (grade \geq 3 adverse events in 73%) limited wider application. Targeted therapies (BRAF/MEK inhibitors) achieved fast tumor shrinkage (49% CR) but with 57% relapse at one year, posing risks for delayed reconstruction and more aggressive salvage procedures.

• Merkel Cell Carcinoma (MCC) patients receiving neoadjuvant nivolumab reported 46% CRs. Case reports documented favorable cosmetic results when exenteration was avoided, although data were sparse.

• Sebaceous Gland Carcinoma (SGC) remains the least responsive to systemic therapy. Anecdotal reports of success with pembrolizumab in mismatch-repair deficient tumors exist, but no large-scale evidence guides therapy. Chemotherapy occasionally reduced tumor burden enough for lid-sparing resection, but with limited cosmetic predictability (Trotier et al., 2024).

Composite Findings Across Modalities

Across all approaches, combination therapy yielded superior outcomes over single modalities. MMS combined with appropriate flap reconstruction and adjuvant radiotherapy yielded the best balance of local control, functional preservation

(blinking, tear film protection), and cosmetic outcomes. Neoadjuvant systemic therapy reduced tumor volume in nearly half of advanced cases, with some avoiding extensive surgeries. This translated into improved patient satisfaction and quality of life scores. However, systemic toxicities and long-term functional follow-up data were variably reported, limiting definitive conclusions.Cosmetic satisfaction was highest in patients undergoing MMS with primary or local flap closure, followed by those receiving neoadjuvant therapies enabling lid-sparing surgeries. The lowest satisfaction was noted in exenteration patients and those requiring complex reconstructions post-radiation.

Managing invasive periocular skin cancers involves more than removing a tumor. The eyelids protect the eye, help spread tears, and support vision. Because of these roles, treatment must preserve both function and appearance. This makes the periocular region one of the most complex areas for cancer management.

Mohs Micrographic Surgery (MMS) remains the primary treatment for basal and squamous cell carcinoma in this area. It offers precise margin control while sparing healthy tissue. This method results in high cure rates and allows for better cosmetic outcomes. Several studies report recurrence rates as low as 0.6% in periocular BCC treated with MMS (Mohs, 1986; Lee et al., 2019). When paired with oculoplastic reconstruction, more than 80% of patients rate their cosmetic outcomes as good to excellent (Trotier et al., 2024).

In settings where MMS is not available, surgeons often rely on frozen-section margin control. This technique lacks the same precision, leading to wider tissue removal and larger surgical defects. As a result, patients are more likely to need secondary surgeries to clear margins (Gulleth et al., 2010). Larger defects also require more complex reconstructions, which can reduce satisfaction in both functional and cosmetic outcomes (Essers et al., 2007). For advanced cases, especially those with orbital invasion as seen in sebaceous carcinoma or squamous cell carcinoma, orbital exenteration may be required. This procedure removes the eye and surrounding structures. While it can achieve local control in about 90% of cases (Bartley et al., 1989; Tyers, 2006), it causes significant functional loss. Patients lose binocular vision and often require prosthetic rehabilitation. Even when the prosthesis is well-fitted, only 60–70% of patients report that the result meets their expectations (Trotier et al., 2024).

Reconstruction strategies must match the defect's size and location. For smaller defects, direct closure or grafts may be sufficient. For larger or more complex cases, local flaps are often preferred. Techniques like the Hughes flap for the lower eyelid and the Mustardé flap for lateral defects are widely used. These methods support the eyelid, restore contour, and allow for normal blinking (Rajak et al., 2019; Czyz et al., 2011). Flaps tend to produce better cosmetic outcomes than grafts, particularly in terms of skin color match and contour. Functional success rates of 85–95% have been reported. However, some flaps require staged procedures, and patients may experience dissatisfaction during the healing phase due to temporary changes in appearance (Martel et al., 2021). Tumors involving the medial canthus often affect the tear drainage system. In these cases, reconstructive efforts must also address the lacrimal pathway. Silicone stents or procedures like conjunctivodacryocystorhinostomy (CDCR) can help restore drainage. While these methods reduce tearing in many patients, full functional recovery is rare, and visible tubes or scars may lower cosmetic satisfaction (Czyz et al., 2011).

Neoadjuvant therapies are becoming more common, especially in advanced or borderline resectable tumors. These include targeted agents like vismodegib for basal cell carcinoma and immune checkpoint inhibitors like cemiplimab for squamous cell carcinoma. Studies report that these treatments can shrink tumors in 50–60% of patients, making surgery less invasive or avoiding exenteration altogether (Bertrand et al., 2021; Kahana et al., 2021; Steren et al., 2022). These approaches help preserve vision and eyelid function. However, some patients still have residual tumor after therapy, which must be confirmed and managed surgically (Unsworth et al., 2022). Overall, the evidence supports an integrated, multidisciplinary approach. Combining dermatologic control with reconstructive planning leads to better outcomes than single-modality treatment. Long-term studies focusing on patient-centered outcomes—such as vision, comfort, appearance, and quality of life—are still needed to guide future practice.

CONCLUSION

This review shows that combining dermatologic care with focused periocular reconstruction improves both function and appearance in patients with invasive skin cancers near the eye. Mohs surgery remains the preferred method for removing tumors because it spares healthy tissue while ensuring full removal. When this is followed by reconstruction using proven techniques like the Hughes or Mustardé flaps, most patients regain both function and appearance. In more advanced cases, drugs like vismodegib or cemiplimab can shrink tumors before surgery, helping to avoid disfiguring procedures like orbital exenteration. While radiation can be useful when surgery isn't an option, it often leads to poorer cosmetic results over time. Successful reconstruction depends on matching the technique to the size and location of the defect, especially when the tear drainage system is involved. Patients care most about seeing well and looking like themselves again. Future studies should use consistent ways to measure both of these outcomes.

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