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Original Article

Impact of clinicopathological features of meibomian gland adenocarcinoma on the outcomes of surgical resection combined with eyelid reconstruction

Huiqin Zhan, Hanyan Mao, De Wu, Jilin Zhou

Department of Ophthalmology, The Third People's Hospital of Changzhou, Changzhou 213001, Jiangsu, China

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Abstract: This study aims to investigate the clinical and pathological characteristics of meibomian gland carcinoma (MGC) and their impact on the outcomes of surgical resection combined with eyelid defect reconstruction. A retrospective study was conducted on 128 patients diagnosed with MGC between December 2020 and January 2022. Demographic, clinical, pathological, surgical, and postoperative follow-up data were collected from the medical records. Patients were divided into two groups based on their total aesthetic outcome score: the satisfied group (score ≥27, n=87) and the dissatisfied group (score <27, n=41). Additionally, patients were categorized into recurrence (n=29) and non-recurrence groups (n=99) based on postoperative recurrence status. Results showed that age (OR=1.080, 95% CI: 1.015~1.149, P=0.015), tumor size (OR=1.625, 95% CI: 0.681~0.887, P<0.001), and tumor stage (OR1=0.007, 95% CI: 0.001~0.070; OR2=0.019, 95% CI: 0.003~0.145, P<0.001) significantly influenced aesthetic outcomes following surgical resection combined with eyelid defect reconstruction. Recurrence analysis indicated that tumor size (HR=1.224, 95% CI: 1.091~1.374, P<0.001) and stage (HR1=0.008, 95% CI: 0.001~0.084; HR2=0.051, 95% CI: 0.011~0.242, P<0.001) were significant factors affecting the recurrence. Receiver operating characteristic (ROC) curve analysis demonstrated that the combined prediction of clinical and pathological features had the highest efficacy in predicting aesthetic outcomes and tumor recurrence following surgical resection and reconstruction (aesthetic outcome: Z=5.544, 3.110, 4.527; recurrence: Z=3.319, 2.986; all P<0.05). The Kaplan-Meier survival curve revealed significant differences in disease-free survival rates across different stages of tumors (χ^2=29.275, P=0.005). In conclusion, the surgical treatment of MGC should consider clinical and pathological characteristics such as patient age, tumor size and stage, and individualized surgical and reconstruction plans should be developed accordingly. The combined prediction of aesthetic outcomes and recurrence risk can enhance surgical efifcacy and improve patient prognosis.

Keywords: Meibomian gland carcinoma, clinicopathological features, surgical resection, eyelid defect, reconstruction, outcome, recurrence

Introduction

Meibomian gland carcinoma (MGC), also known as meibomian carcinoma, is a malignant tumor originating from the meibomian or sebaceous glands of the eyelid. It ranks second in incidence among eyelid malignancies, following basal cell carcinoma (BCC), with higher prevalence in Asian regions such as India, China, and Japan, where its incidence is comparable to that of eyelid basal cell carcinoma and may even surpass it [1]. Statistics indicate that in China, MGC accounts for 31% to 50% of all eyelid malignancies, predominantly affecting middle-aged and elderly individuals [2, 3]. This tumor is highly malignant, with a tendency to invade surrounding tissues and metastasize to lymph nodes or distant sites, posing a serious threat to patients' lives.

Surgical resection, including wide excision and Mohs micrographic surgery (Mohs), remains the primary treatment for MGC [4]. However, surgical excision often results in eyelid defects, which can compromise the stability, appearance, and function of the eyelid, potentially leading to blindness or even life-threatening complications. Therefore, eyelid reconstruction is necessary to restore normal physiological functions and improve patients' quality of life

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after surgery [4, 5]. Currently, materials used for eyelid reconstruction include autologous tissues (e.g., conjunctival flaps, nasal septal cartilage, and auricular cartilage), allogeneic tissues (e.g., scleral grafts), and biological materials (e.g., labial mucosa or oral mucosa) [6, 7]. Repair techniques include autologous tarsal sliding/rotation flaps, scleral grafts, and nasal septal cartilage with mucosa [8]. Despite the application of various eyelid reconstruction methods in clinical practice, the quality of research evidence supporting clinical decision-making remains inconsistent, and results are often heterogeneous. Currently, no systematic review has summarized the efficacy and safety of surgical resection combined with eyelid defect reconstruction in MGC, particularly concerning the impact of clinicopathological features on reconstruction prognosis. This research gap limits the scientific basis for clinical decision-making and calls for further investigation.

The clinical and pathological features of MGC are complex and diverse. These factors not only affect the completeness of surgical resection but also significantly impact the outcomes of postoperative eyelid reconstruction. A comprehensive understanding of these characteristics and their impact on surgical resection combined with eyelid defect reconstruction is of great significance for formulating more scientific and rational treatment protocols. However, existing studies have primarily focused on recurrence prediction and analysis of clinical factors [9, 30], with limited attention to aesthetic and functional recovery following surgical resection and reconstruction. This gap fails to provide clinicians with adequate guidance when formulating treatment plans, especially when balancing the thoroughness of tumor resection with postoperative functional and aesthetic outcomes, which presents a particularly challenging dilemma. Given this, the present study aims to analyze the clinical and pathological features of MGC and their impact on surgical resection combined with eyelid defect reconstruction. The innovation of this study lies in its holistic approach, considering the relationship between clinical and pathological features and reconstruction outcomes, focusing not only on tumor recurrence but also on aesthetic and functional recovery, which are important concerns for patients. This research will contribute to the theoretical framework for MGC treatment and provide clinicians with a more comprehensive and evidence-based reference for formulating individualized treatment plans.

Materials and methods

Study population

Sample size calculation was based on multiple factor regression analysis, with the recommended sample size being 5-10 times the number of independent variables. In this study, 15 independent variables were considered, and considering a 20% dropout rate, the required sample size was calculated to be 102-180 cases. The final sample size of this study was 128 cases, satisfying the requirements.

This retrospective study included 128 patients with MGC treated at The Third People's Hospital of Changzhou from December 2020 to January 2022. Inclusion criteria: (1) patients diagnosed with sebaceous gland carcinoma of the eyelid through outpatient and pathology department assessment; (2) patients who underwent surgical treatment and histopathological examination; and (3) patients with complete medical records and pathological results. Exclusion criteria: (1) patients who had previously received medical therapy, chemotherapy, radiotherapy, or any other form of treatment; (2) patients with other malignancies or autoimmune diseases; and (3) pregnant or lactating women. This study was approved by the Ethics Committee of The Third People's Hospital of Changzhou.

Methods

(1) Preoperative Assessment: A comprehensive ocular evaluation was conducted. **Figure 1A** displays a large mass on the right eyelid, exhibiting an uneven surface with areas of ulceration and crusting, severely compromising both the appearance and function of the eyelid.

(2) Surgical Procedure: Local anesthesia was administered using a mixture of 2% lidocaine and 0.75% bupivacaine in an appropriate ratio, with a small amount of epinephrine added to achieve effective anesthesia and minimize intraoperative bleeding. Methylene blue was used to carefully mark a line 3-5 mm from the tumor edge within normal tissue to ensure

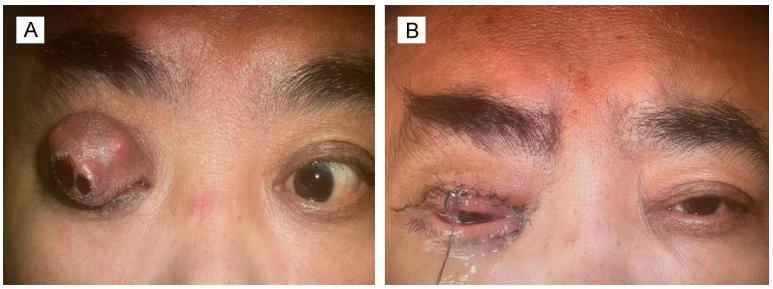

Figure 1. A patient with meibomian adenocarcinoma on the right eye. A: Preoperative photo; B: Intraoperative photo.

complete tumor excision while preserving as much normal tissue as possible. The excision was performed along the marked line, ensuring full-thickness removal of the tumor. A precise full-thickness incision, parallel to the eyelid margin, was made 3 mm from the lid margin, with the incision length corresponding to the lid defect. Subsequently, a full-thickness vertical incision was made at each end of the initial incision, extending to the lid margin, to create an appropriate eyelid tissue flap.

(3) Eyelid Reconstruction: The full-thickness eyelid tissue flap was carefully transposed through the bridge tissue of the lower (or upper) eyelid margin and gently pulled toward the eyelid defect. Meticulous layered suturing was performed, starting with the lower edge of the bridge tissue. Interrupted or continuous sutures were applied to the skin and conjunctival edges according to the specific situation to ensure wound stability and aesthetics. The cut edges of the bridge tissue, once exposed, were either allowed to heal spontaneously or sutured with 6-0 absorbable sutures (**Figure 1B**).

(4) Individualized Reconstruction: Reconstruction was based on the extent of the eyelid defect. For tumors with infiltration of the periocular or periorbital tissues, enucleation or orbital exenteration was performed. Additionally, lymph node dissection was carried out in cases of confirmed lymph node metastasis, with radiotherapy used as an adjuvant treatment. NOTE: the images used in this article were obtained with informed consent from the patient, following standard ethical procedures to protect their privacy and rights.

Data collection

Data collected included age, gender, preoperative diabetes, hypertension, disease duration, tumor location, tumor size and other relevant clinical information collected at admission. Surgical observations included pathological type, and protein expression (Ki67, TP53). Postoperative complications were documented one month after surgery, including eyelid deformity, entropion and trichiasis, ocular surface damage (e.g., dry eye, exposure keratitis, corneal leukoplakia). The recurrence rate was collected 2 years after surgery. Tumor staging followed the 8th edition of the American Joint Cancer Association (AJCC), with primary tumors classified as T1, T2, T3, or T4 [8].

The key focus of this study was to assess the impact of surgical resection combined with eyelid defect reconstruction on aesthetic outcomes and recurrence.

Aesthetic Outcomes: Aesthetic outcomes were evaluated one month after surgery by the attending physician, the patient's family, and the patient themselves, based on five criteria [10]. Symmetry: 3 points for bilateral symmetry, 2 points for mild asymmetry, and 1 point for severe asymmetry; Organ traction deformity: 3 points for no deformity, 2 points for mild deformity, and 1 point for obvious deformity; Local smoothness: 3 points for a smooth surface without protrusion or depression, 2 points for mild protrusion or depression, and 1 point for obvious protrusion or depression; Color matching: 3 points for complete color match, 2 points for partial difference, and 1 point for significant color mismatch; Texture: 3 points for soft texture, 2 points for moderate texture, and 1 point for hard texture. Based on the total aesthetic score, patients were divided into two groups: those with a total score ≥27 were classified as the satisfied group (n=87), and those with a score <27 were classified as the dissatisfied group (n=41).

Recurrence: Patients were followed up for 2 years after surgery using WeChat, email, and other means to monitor recurrence. Clinical data was collected during follow-up, and patients identified with recurrence underwent further examinations and treatment. Tumor recurrence was diagnosed by professional physicians through pathological and imaging exami-

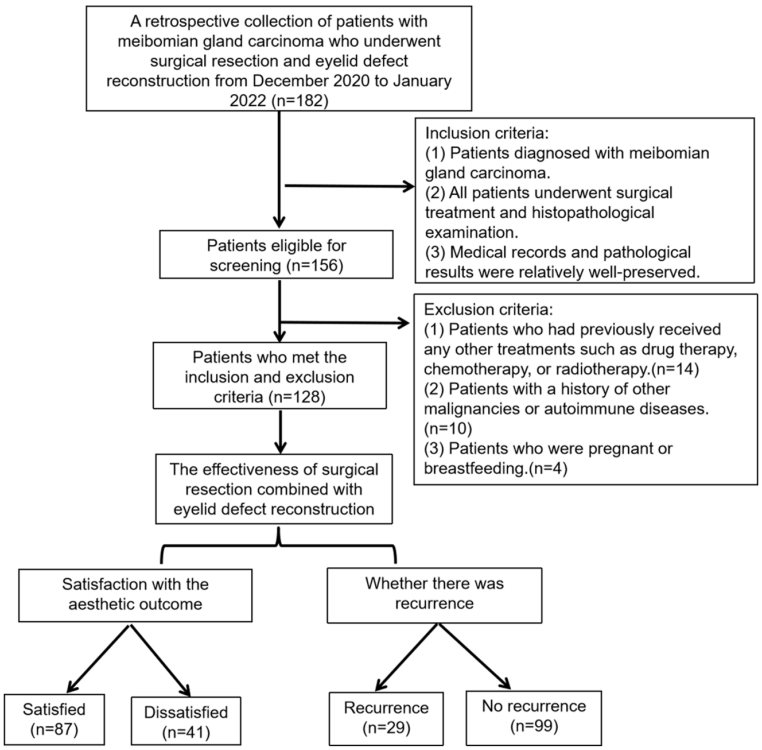

Figure 2. Study design flowchart.

nations. The study design flowchart is shown in **Figure 2**.

Outcome measures

(1) Clinical and pathological characteristics of patients with meibomian gland carcinoma; (2) Aesthetic outcomes and the influence of clinical and pathological characteristics on surgical resection and eyelid defect reconstruction outcomes; (3) Recurrence rates and the influence factors of clinical and pathological characteristics and recurrence. (4) Comparison of the predictive efficacy of influencing factors; (5) The recurrence of tumors over time analyzed using Kaplan-Meier survival curves.

Statistical analysis

Data analysis was performed using SPSS 26.0 statistical software, and GraphPad Prism 8.0 was used for statistical graphing. Qualitative data were described using frequencies and percentages [n (%)] and analyzed using the chi-square test. Quantitative data were presented as mean ± standard deviation ($\bar{X}\pm S$) or median (interquartile range), denoted as M [Q1, Q3], and analyzed using the independent samples t-test or Mann-Whitney U test (rank-sum test). Logistic regression analysis was employed to assess the impact of clinical and pathological features on the outcomes of surgical resection combined with lid defect reconstruction. Tumor recurrence at different stages was studied using Kaplan-Meier analysis, with factors related to recurrence assessed via Cox regression analysis. Predictive value analysis was performed using the receiver operating characteristic (ROC) curve, and the DeLong test was used to compare the area under the ROC curve (AUC) of each influencing factor. A p-value <0.05 was considered statistically significant.

Results

Clinical feature analysis

A total of 128 patients were included in this study, comprising 54 males (42.19%) and 74 females (57.81%). The age range was 35 to 81 years, with a mean age of 58 years. The majority of tumors were located in the upper eyelid. Detailed clinical characteristics are presented in **Table 1**.

Distribution of clinical and pathological features

Tumor differentiation: High differentiation was observed in 40 cases (31.25%), moderate differentiation in 28 cases (21.89%), and low differentiation in 50 cases (39.06%). Depth of invasion: Invasion not reaching the serosa was seen in 67 cases (52.34%), while invasion reaching the serosa was observed in 61 cases (47.66%) (**Figure 3**). Squamous cell carcinoma was observed in some patients, typically at the junction of the limbus, eyelid margin, and conjunctiva (**Figure 4**). These tumors often present as strawberry-like, papillary, or flat elevations that are fragile and prone to bleeding. Most have a gelatinous appearance.

Table 1. Baseline characteristics of patients

Item		Mean or M [Q1, Q3]	N	Proportion (%)
Age (year)		58.80±10.19		
Sex	Male		54	42.19
	Female		74	57.81
BMI (kg/m^2)		24.91±3.20		
Diabetes			21	16.41
Hypertension			40	31.25
Course of disease (month)		5.14 (2.40, 9.76)		
Tumor size (mm)		7.53 (2.87, 11.52)		
Affected eyes	Left eye		66	51.56
	Right eye		62	48.44
Tumor site	Upper eyelid		66	51.56
	Lower eyelid		44	34.38
	Upper and lower eyelids		9	7.03
	Superciliary arch		3	2.34
	inner canthus		6	4.69
Postoperative complication			22	17.19

Note: BMI: body mass index.

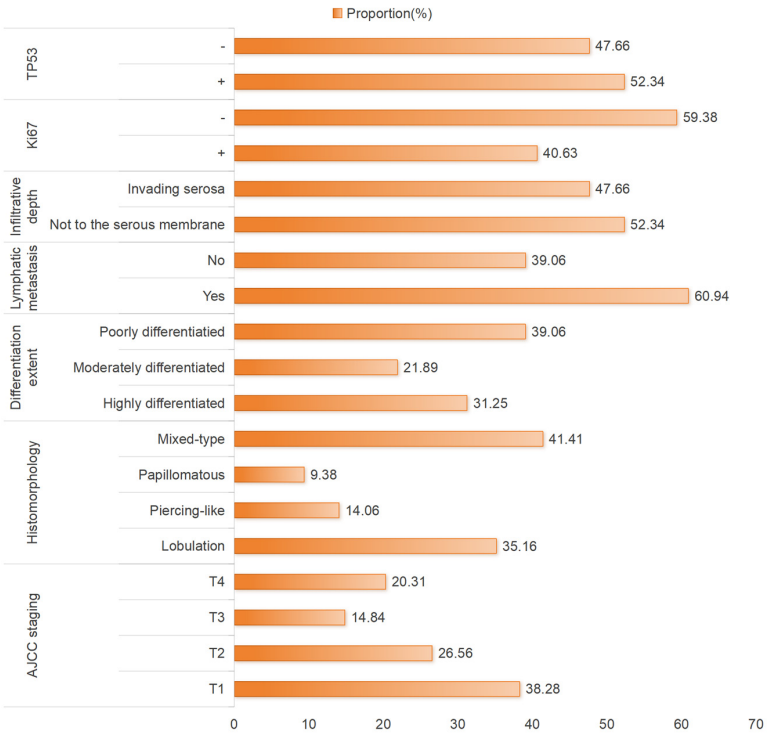

Figure 3. Distribution of clinical and pathological features. Note: AJCC: American Joint Committee on Cancer.

Most are well-differentiated, with surface keratinization. Immunohistochemistry results: P40 (+), P63 (+), HMB45 (-), S100 (-), EGFR (+), Ki67> 80%.

Univariate analysis of factors associated with aesthetic outcomes

One month after treatment, patients were divided into a satisfied group and a dissatisfied group based on their aesthetic outcomes. Statistically significant differences were observed between the two groups in terms of age, tumor size, and AJCC staging ($P<0.05$). However, no significant differences were observed in other indicators such as gender, BMI, and disease duration ($P>0.05$) (**Table 2**).

Cox regression analysis of factors independently affecting aesthetic outcomes

Logistic regression analysis, with aesthetic outcomes as the dependent variable (Satisfied=1, Not satisfied=0) and age, tumor size, and AJCC staging that showed statistical significance in univariate analysis as independent variables (**Table 3**), revealed that patients

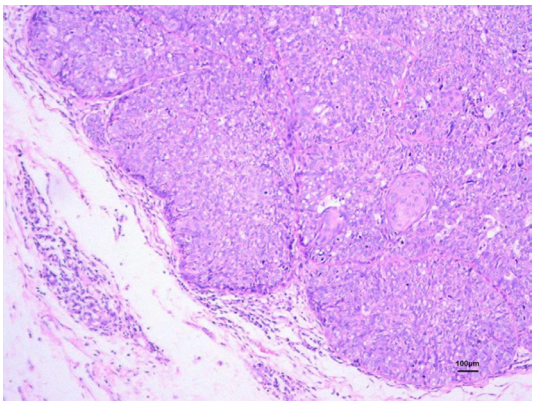

Figure 4. Immunohistochemical staining of squamous cell carcinoma. Scale bar: 100 μm.

with AJCC stage T4 had a higher risk of unsatisfactory aesthetic outcomes after surgery. Additionally, advanced age (OR=1.080) and larger tumor size (OR=1.625) were identified as risk factors for poor aesthetic outcomes following surgical resection combined with eyelid defect reconstruction (P<0.05). In contrast, AJCC stages T1 and T2 were protective factors for satisfactory aesthetic outcomes (P<0.05), as shown in **Table 4**. A nomogram was constructed to intuitively represent the impact of these variables on postoperative aesthetic outcomes (**Figure 5**).

Predictive value of age, tumor size, and AJCC stage for aesthetic outcomes

The ROC curve was used to evaluate the predictive performances of age, tumor size, AJCC stage and their combination for aesthetic outcomes. The results indicated that their combined prediction yielded an AUC of 0.941, with a sensitivity of 75.6% and a specificity of 96.6%. This triad of factors demonstrated the highest predictive efficacy (compared with individual factors, Z values were 5.544, 3.110, and 4.527, respectively; P<0.05) (**Table 5** and **Figure 6**).

Univariate analysis of factors associated with recurrence

The study found that the recurrence rate was not associated with patient gender, disease duration, or other characteristics (all P>0.05). However, tumor size and disease stage were significantly associated with recurrence rates (all P<0.05) (**Table 6**).

Cox regression analysis of factors independently affecting recurrence

Cox regression analysis, with post-treatment recurrence as dependent variable (recurrence=1, non recurrence=0), and tumor size and AJCC staging as independent variables, indicated that tumor size and AJCC staging were the factors independently affecting postoperative recurrence in patients with meibomian gland carcinoma (P<0.05) (**Table 7**).

Predictive value of tumor size and AJCC stage for recurrence

The ROC curve was used to evaluate the predictive value of tumor size, AJCC stage and their combination for recurrence. The results showed that their combined prediction had an AUC of 0.901, with a sensitivity of 75.6% and a specificity of 96.6%. This combination demonstrated the highest predictive efficacy (compared with the individual factors, Z values were 3.319 and 2.986, respectively; P<0.05) (**Table 8**; **Figure 7**).

Analysis of tumor recurrence rates in different AJCC phases

Among the 128 MGC patients, 29 patients experienced tumor recurrence. Recurrence was used as the endpoint, and the median disease-free survival from postoperative follow-up to the first tumor recurrence was 15 months. The Kaplan-Meier curve showed a statistically significant difference in disease-free survival rates (χ^2=29.275, P=0.005) across different AJCC stages (**Figure 8**).

Discussion

Meibomian gland carcinoma (MGC) was first reported by Thiersch in 1865. This tumor exhibits a distinct epidemiological difference between Eastern and Western populations. Compared to Western countries, MGC is more prevalent in Asia, predominantly affecting the elderly and female populations [11, 12]. In a cohort study by Yu S et al., the mean age of MGC patients in Tianjin was 60 years, with 65.52% being female [13]. In our study, 57.81% of patients were female, with a mean age of approximately 58 years, which is consistent with findings from other regions and reflects

Table 2. Univariate analysis of factors associated with aesthetic outcomes

Item		Unsatisfactory group (n=41)	Satisfactory group (n=87)	$t/\chi^2/Z$	*P*
Age ($\bar{X}$±S, years)		61.44±9.95	57.55±10.13	2.038	0.044
Sex [n (%)]	Male	15 (36.59)	39 (44.83)	0.776	0.378
	Female	26 (63.41)	48 (55.17)		
BMI ($\bar{X}$±S, kg/m^2)		24.88±3.37	24.92±3.14	0.060	0.952
Diabetes [n (%)]		9 (21.95)	12 (13.79)	1.352	0.245
Hypertension [n (%)]		14 (34.15)	26 (29.89)	0.236	0.627
Ki 67 (+) [n (%)]		18 (43.90)	34 (39.08)	0.269	0.604
TP53 (+) [n (%)]		21 (51.22)	46 (52.87)	0.031	0.861
Course of disease/M [Q1, Q3] (month)		4.94 (2.60, 9.30)	5.34 (2.37, 9.78)	0.115	0.734
Tumor size/M [Q1, Q3] (mm)		12.41 (8.43, 16.99)	4.55 (2.28, 9.32)	40.587	<0.001
Affected eyes [n (%)]	Left eye	24 (58.54)	42 (48.28)	1.175	0.278
	Right eye	17 (41.46)	45 (51.72)		
Tumor site [n (%)]	Upper eyelid	21 (51.22)	45 (51.72)	4.946	0.293
	Lower eyelid	11 (26.82)	33 (37.93)		
	Upper and lower eyelids	4 (9.76)	5 (5.75)		
	Superciliary arch	1 (2.44)	2 (2.30)		
	inner canthus	4 (9.76)	2 (2.30)		
AJCC staging [n (%)]	T1	7 (17.07)	42 (48.28)	22.318	<0.001
	T2	8 (19.51)	26 (29.89)		
	T3	10 (24.39)	9 (10.34)		
	T4	16 (39.02)	10 (11.49)		
Histomorphology [n (%)]	Lobulation	17 (41.46)	28 (32.18)	3.982	0.263
	Piercing-like	5 (12.20)	13 (14.94)		
	Papillomatous	6 (14.63)	6 (6.90)		
	Mixed type	13 (31.71)	40 (45.98)		
Differentiation [n (%)]	Highly differentiated	9 (21.95)	31 (35.63)	2.764	0.251
	Moderately differentiated	9 (21.95)	19 (21.84)		
	Poorly differentiated	23 (56.10)	37 (42.53)		
lymphatic metastasis [n (%)]	Yes	24 (58.54)	54 (62.07)	0.146	0.702
	No	17 (41.46)	33 (37.93)		
Infiltrative depth [n (%)]	Not to the serous membrane	18 (43.90)	49 (56.32)	1.723	0.189
	Invading serosa	23 (56.10)	38 (43.68)		
Postoperative complication [n (%)]	Yes	10 (24.39)	12 (13.79)	2.199	0.138
	No	31 (75.61)	75 (86.21)		

Note: AJCC: American Joint Committee on Cancer; BMI: body mass index.

Table 3. Coding table

Parameters	Assignment
Satisfied or not	Yes=1, No=0
Age	continuous variable
Tumor size	continuous variable
AJCC staging	T1=1, T2=2, T3=3, T4=4

Note: AJCC: American Joint Committee on Cancer.

the typical demographic characteristics of this tumor.

MGC can originate from the meibomian glands, Zeis glands, caruncle, or skin of the outer eyebrow, resulting in lesions that affect different areas of the periorbital skin [14, 15]. Primary tumors are commonly located in the upper eyelid, with an incidence rate ranging from 63% to 75% [16, 17]. In our study, 66 cases (51.56%) were located in the upper eyelid, 44 cases (34.38%) in the lower eyelid, and 9 cases (7.03%) involved both upper and lower eyelids. The dense distribution of meibomian glands in the upper eyelid may be the primary reason for the higher incidence of tumors in this area [18]. According to the 8th edition of the AJCC classification, most tumors in our study were categorized as T1 and T2 (64.84%).

Table 4. Logistic regression analysis of factors independently affecting aesthetic outcomes

Item	*β*	*SE*	*Wald/χ²*	*P*	*OR*	*95% CI*
Age	0.077	0.032	5.967	0.015	1.080	1.015-1.149
Tumor size	0.485	0.105	21.236	<0.001	1.625	0.681-0.887
AJCC staging T1	-4.972	1.177	17.850	<0.001	0.007	0.001-0.070
T2	-3.947	1.027	14.756	<0.001	0.019	0.003-0.145
T3	-1.546	0.884	3.058	0.080	0.213	0.038-1.205

Note: AJCC: American Joint Committee on Cancer.

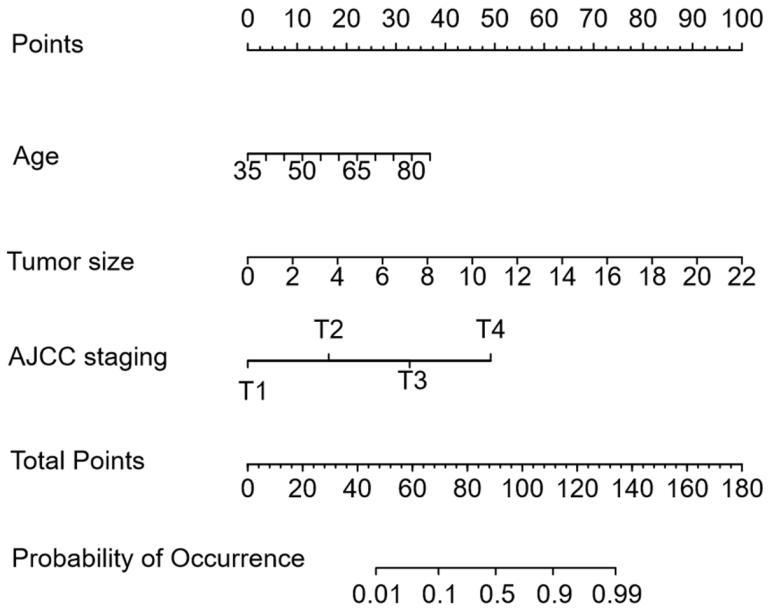

Figure 5. A nomogram for predicting aesthetic outcomes. Note: AJCC: American Joint Committee on Cancer.

Surgical resection is the preferred treatment for MGC. However, surgical removal compromises the integrity of the eyelid, resulting in eyelid defects that not only affect facial aesthetics but also potentially impair eyelid function [19, 20]. Therefore, timely repair is essential to restore eyelid closure function, prevent exposure of the eyeball, and avoid complications such as keratitis which can damage vision or even result in loss of the eyeball [21]. Moreover, with increasing awareness of eyelid defects and higher aesthetic demands, the treatment of MGC should not only focus on complete tumor removal and functional recovery but also strive to achieve optimal aesthetic outcomes [22, 23]. In this study, we retrospectively analyzed the clinical and pathological characteristics of MGC and the outcomes of surgical treatment, with a primary focus on aesthetic outcomes. Patients were divided into satisfied and dissatisfied groups based on the total aesthetic score after eyelid defect reconstruction. Our analysis revealed that AJCC stage T4, advanced age, and larger tumor size were risk factors for poor aesthetic outcomes following surgical resection combined with eyelid defect reconstruction.

As patients age, several physiological changes occur in the orbital regions, including degenerative changes in the orbital bones, varying degrees of bone resorption, and a shift in the attachment sites of the periosteum. These alterations reduce the supportive force of the orbital soft tissues, weaken muscle strength, diminish fat filling, and cause ligament laxity. These changes result in reduced elasticity and firmness of the eyelids, making it more challenging to restore eyelid shape after surgical resection and reconstruction [24, 25].

Additionally, slower metabolic rates in the elderly can contribute to a reduced postoperative recovery capacity, resulting in prolonged swelling and delayed resolution of postoperative edema. This can lead to poorer aesthetic outcomes compared to younger patients. Previous studies have also shown that older age is associated with worse postoperative recovery. For example, in a study on post-cesarean section scar healing, younger patients exhibited better scar recovery than older individuals [26].

Larger tumor size is associated with poorer aesthetic outcomes, highlighting the technical complexity and aesthetic challenges involved in

Table 5. Predictive value of age, tumor size, AJCC staging and their combination for aesthetic outcomes

Item	Best cutoff value	AUC	Sensitivity (%)	Specificity (%)	P	95% CI
Age	61 years old	0.637	61.0	69.0	0.011	0.547-0.720
Tumor size	7.51 mm	0.850	85.4	66.7	<0.001	0.776-0.907
AJCC staging	-	0.736	63.4	78.2	<0.001	0.650-0.810
Joint prediction	-	0.941	75.6	96.6	<0.001	0.886-0.957

Note: AJCC: American Joint Committee on Cancer.

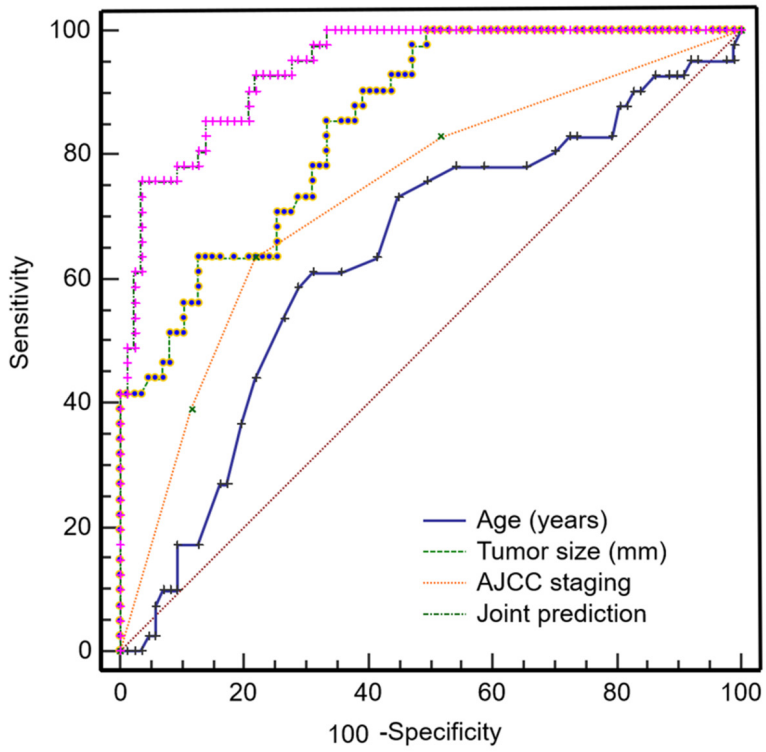

Figure 6. ROC curves for age, tumor size, AJCC staging and their combination for predicting aesthetic outcomes after eyelid defect reconstruction. Note: ROC: Receiver Operating Characteristic; AJCC: American Joint Committee on Cancer.

extensive resection. Tumors with a diameter exceeding 10 mm typically require more extensive tissue removal and thus necessitate more complex reconstruction techniques [27]. As the resection area increases, it becomes progressively difficult to achieve symmetrical and aesthetically pleasing results. Moreover, larger defects may preclude the use of simpler repair methods, such as direct suturing. In these cases, more advanced methods like skin grafts or complex flap techniques are required, which are, as previously mentioned, associated with higher rates of patient dissatisfaction [27, 28]. These findings underscore the importance of early detection and timely surgical intervention to limit tumor growth and make subsequent reconstruction more manageable.

Patients with MGC at AJCC stage T4 tend to have poorer aesthetic outcomes following surgical resection combined with eyelid defect reconstruction. The primary reasons are that T4 tumors typically exhibit higher invasiveness and larger tumor size. The extensive invasiveness of these tumors results in a broader surgical resection margin, which increases the complexity and difficulty of the surgery. Moreover, the higher recurrence risk associated with T4 tumors further impacts the long-term stability of postoperative aesthetic outcomes. Therefore, the surgical treatment for patients with stage T4 MGC requires not only more refined surgical techniques but also more complex reconstruction strategies to maximize postoperative aesthetic results.

In addition to aesthetic concerns, the risk of rumor recurrence after surgical resection of MGC remains high [29]. Our study observed a recurrence rate of 22.66%. However, in a study by Shields et al. in the United States [17] reported a recurrence rate of 18% (11/60), Ford et al. [30] reported a recurrence rate of 11% (7/65), and Choi et al. [31] in South Korea reported a recurrence rate of 5% (2/40). The recurrence rate in our study was higher than those in the aforementioned studies. This difference can

Table 6. Univariate analysis of factors associated with disease recurrence

Item		Recurrence (n=29)	non recurrence (n=99)	$t/\chi^2/Z$	*P*
Age ($\bar{X}$±S, year)		58.79±10.03	58.80±10.29	0.002	0.998
Sex [n (%)]	Male	11 (37.93)	43 (43.43)	0.279	0.598
	Female	18 (62.07)	56 (56.57)		
BMI ($\bar{X}$±S, kg/m^2)		24.31±3.52	25.08±3.10	1.135	0.259
Diabetes [n (%)]		6 (20.69)	15 (15.15)	0.502	0.479
Hypertension [n (%)]		10 (34.48)	30 (30.30)	0.182	0.669
Ki 67 (+) [n (%)]		15 (51.72)	38 (38.38)	0.910	0.340
TP53 (+) [n (%)]		19 (65.52)	48 (48.48)	2.608	0.106
Course of disease/M [Q1, Q3] (month)		6.54 (2.60, 9.30)	4.84 (2.37, 9.78)	0.436	0.509
Tumor size/M [Q1, Q3] (mm)		11.27 (7.72, 14.23)	5.77 (2.45, 10.89)	14.567	<0.001
Affected eyes [n (%)]	Left eye	17 (58.62)	49 (49.49)	0.748	0.387
	Right eye	12 (41.38)	50 (50.51)		
Tumor site [n (%)]	Upper eyelid	14 (48.28)	52 (52.53)	6.415	0.170
	Lower eyelid	7 (24.14)	37 (37.37)		
	Upper and lower eyelids	4 (13.79)	5 (5.05)		
	superciliary arch	1 (3.45)	2 (2.02)		
	inner canthus	3 (10.34)	3 (3.03)		
AJCC staging [n (%)]	T1	1 (3.45)	48 (48.48)	39.021	<0.001
	T2	4 (13.79)	30 (30.30)		
	T3	9 (31.03)	10 (10.10)		
	T4	15 (51.72)	11 (11.11)		
Histomorphology [n (%)]	Lobulation	10 (34.48)	35 (35.35)	3.723	0.293
	Piercing-like	5 (17.24)	13 (13.13)		
	Papillomatous	5 (17.24)	7 (7.07)		
	Mixed type	9 (31.03)	44 (44.44)		
Differentiation extent [n (%)]	Highly differentiated	7 (24.13)	33 (33.34)	1.182	0.554
	Moderately differentiated	8 (27.59)	20 (20.20)		
	Poorly differentiated	14 (48.28)	36 (36.36)		
Lymphatic metastasis [n (%)]	Yes	16 (55.17)	62 (62.63)	0.524	0.469
	No	13 (44.83)	37 (37.37)		
Infiltrative depth [n (%)]	Not to the serous membrane	12 (41.38)	55 (55.56)	1.807	0.179
	Invading serosa	17 (58.62)	44 (44.44)		
Postoperative complication [n (%)]	Yes	6 (20.69)	16 (16.16)	0.323	0.570
	No	23 (79.31)	83 (83.84)		

Note: AJCC: American Joint Committee on Cancer; BMI: body mass index.

Table 7. Cox regression analysis of factors independently affecting tumor recurrence

item	*β*	*S E*	*Wald/χ²*	*P*	*HR*	*95% CI*
Tumor size	0.101	0.032	10.194	0.001	1.106	1.040-1.177
AJCC staging T1	-3.388	1.034	10.741	0.001	0.034	0.004-0.256
T2	-1.686	0.565	8.914	0.003	0.185	0.061-0.560
T3	-0.768	0.436	3.103	0.078	0.464	0.197-1.177

Note: AJCC: American Joint Committee on Cancer.

likely be attributed to variations in sample size, surgical techniques, racial and environmental factors.

Clinical and pathological staging of tumors is crucial for reflecting the progression and severity of the disease, ultimately influencing the

Table 8. Predictive value of Tumor size, AJCC staging and their combination for tumor recurrence

Item	Best cutoff value	AUC	Sensitivity (%)	Specificity (%)	P	95% CI
Tumor size	4.55 mm	0.734	100.0	44.4	<0.001	0.648-0.808
AJCC staging	-	0.845	82.8	78.8	<0.001	0.770-0.903
Joint prediction	-	0.901	75.6	96.6	<0.001	0.835-0.946

Note: AJCC: American Joint Committee on Cancer.

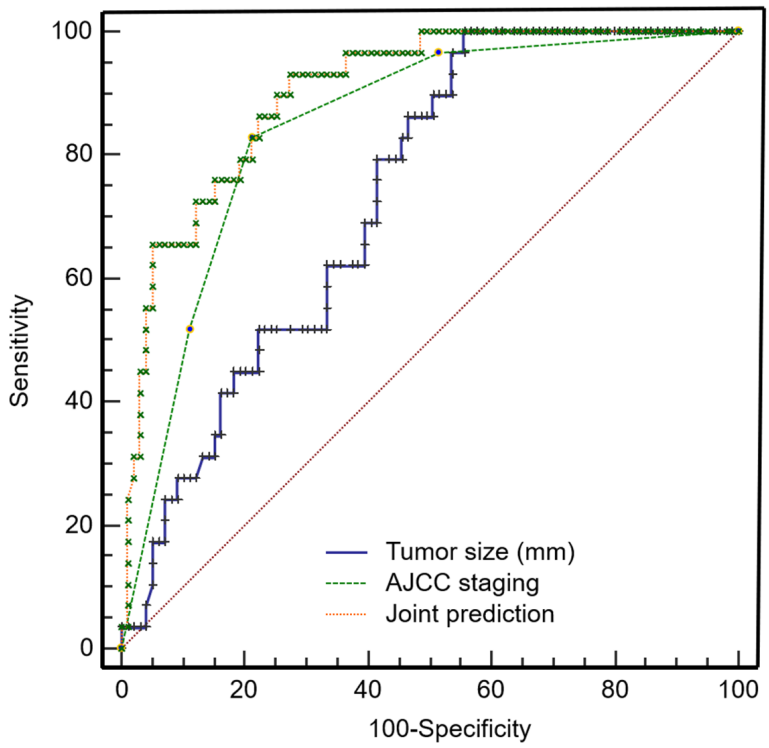

Figure 7. ROC curves for tumor size, AJCC staging and their combination in predicting tumor recurrence. Note: ROC: Receiver Operating Characteristic; AJCC: American Joint Committee on Cancer.

prognosis and survival of patients [32]. In our study, MGC was classified into three types based on the degree of cell differentiation: well-differentiated, moderately differentiated, and poorly differentiated. The classification boundaries for these categories were established based on the phenotypic similarity of MGC cells to sebaceous gland cells and the proportion of tumor cells showing sebaceous differentiation [33]. While literature reports indicate that prognosis in MGC is negatively correlated with the degree of differentiation, as moderately and poorly differentiated MGC have worse prognosis and higher recurrence rates compared to well-differentiated MGC [34]. However, our study did not show a statistically significant association between differentiation degree and clinical prognosis. This suggests that factors influencing MGC recurrence are multifaceted, involving not only cell differentiation status but also requiring systematic analysis in combination with different cell subtypes. Lam et al. [35] observed in Hong Kong patients that tumor stage was closely associated with lymph node metastasis, disease-free survival, and overall survival. In a Japanese study, Watanabe et al. [36] reported a strong association between T category and tumor recurrence. Similarly, Kaliki et al. [37] evaluated the clinical features and prognosis of sebaceous gland carcinoma (SGC) of the eyelid based on AJCC T staging (7th edition) and found that higher AJCC staging correlated with increased risk of systemic metastasis and death. In our study, tumor size is one of the important factors affecting recurrence. Larger tumors usually require more extensive resection, which increases the complexity of surgery and the difficulty of reconstruction, thus affecting the postoperative recurrence rate [38]. In addition, patients with higher tumor grades had a significantly higher recurrence risk, and AJCC staging was identified as a key factor influencing recurrence in eyelid sebaceous gland carcinoma. These findings suggest that clinical staging can provide valuable insights into the likelihood of recurrence post-surgery.

However, this study still has certain limitations. As a single-center retrospective study, all cases came from the same hospital, which may intro-

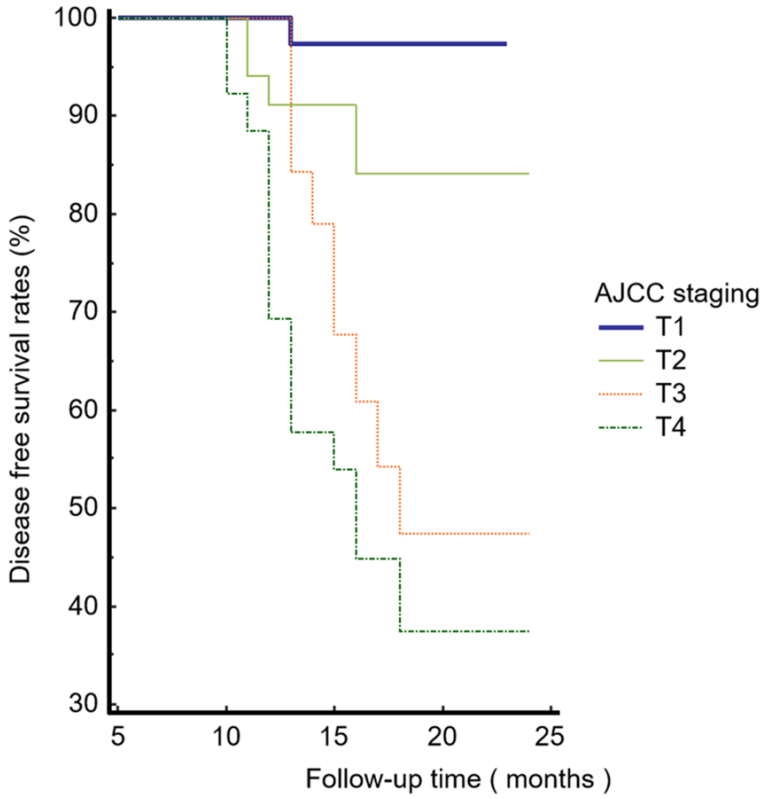

Figure 8. Tumor recurrence rates in different AJCC stages analyzed using Kaplan-Meier curves. Note: AJCC: American Joint Committee on Cancer.

duce selection bias and limit the generalizability of our results. Differences in race, genetic background, environmental factors, and healthcare standards across different regions or hospitals could all affect the epidemiological characteristics, clinical pathological features, and the effectiveness of surgical resection and eyelid defect reconstruction. Therefore, the conclusions drawn from this study must be validated through larger, multicenter studies with diverse patient populations to assess the broader applicability of these findings across different regions and medical settings.

Conclusion

The clinical and pathological characteristics of MGC, especially advanced age, tumor size, and AJCC staging, significantly influence the outcomes of surgical resection combined with eyelid defect reconstruction. These factors should be carefully considered when formulating treatment plans to optimize therapeutic outcomes and enhance patient satisfaction. Early surgical intervention is also essential for controlling tumor growth, minimizing the complexity of surgery, and improving both the quality of life and overall prognosis of patients.

Disclosure of conflict of interest

None.

Address correspondence to: Jilin Zhou, Department of Ophthalmology, The Third People's Hospital of Changzhou, No. 300, Lanling North Road, Changzhou 213001, Jiangsu, China. Tel: +86-0519-82008314; E-mail: czzhoujilin@163.com

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