Oncological and aesthetic outcome following surgical management of orbito-palpebral skin cancers: A retrospective study of 132 patients

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ABSTRACT

Background: The incidence of facial skin cancers continues to rise, with major studies on their impacts still lacking in the literature. This study reports on the oncological and aesthetic results following surgical management of an orbito-palpebral skin cancer.
Methods: This retrospective, monocentric study included patients treated for a non-melanoma skin cancer of the eyelid and orbit. Risk factors, location, histological type, invaded or insufficient margins, healing time, surgical management by excision and direct closure, skin graft or local flaps, self-evaluated aesthetics, and quality of life results were all compared.
Results: The study included 132 patients operated for basal cell carcinoma (71.9%), squamous cell carcinoma (22.9%), or for another type (5.2%) between November 2011 and January 2017. Average tumor size was 9.6 ± 6.3 mm. Surgical management resulted in excision and open healing (9.1%), excision and direct closure (3.9%), skin graft (31.1%), local flap (21.9%), or another type of reconstruction (3.0%). Significant links between invaded or insufficient margins and basal cell type (OR $= 3.37$, $p = 0.014$), tumor size over 7 mm (OR $= 2.7$, $p = 0.011$), double location (OR $= 8.44$, $p = 0.04$), flap-based reconstruction (OR $= 0.290$, $p = 0.02$), and female gender (OR $= 0.418$, $p = 0.034$) were reported throughout our multivariate analysis.
Conclusions: This study brings out consequential information on factors linked with invaded or insufficient excision margins. Larger cohorts should evaluate the aesthetic outcomes in such a population.

1. Introduction

With an ageing population, the incidence and impacts of facial skin cancers continue to increase, with a lack of major studies reporting on the long-term oncological and aesthetic results of the various surgical techniques employed in the affected population (ANAES, 2004; Bouhassira, 2013; INCa-HAS, 2009; Lasudry, 2011; Nseir, 2008; Silverman, 2017).

The eyelid represents one of the most fragile, complex, and aesthetic facial subunits; it is also the protecting envelope of the ocular globe. Therefore, eyelid cancer pathology raises aesthetic, functional, and sometimes vital issues, especially given the insidious evolution of these lesions, the difficulty in their detection in an

old population, and the consequently late management of some large tumors (ANAES, 2004; Bouhassira, 2013; INCa-HAS, 2009; Lasudry, 2011; Nseir, 2008; Silverman, 2017).

Large retrospective studies published by Ho et al. (Ho et al., 2013) and Nemet et al. (Nemet, 2006) reported the long-term management of such tumors, with important guidelines regarding their oncological results, follow-up, and surveillance, but did not focus on the specific results obtained with various surgical resection and reconstruction techniques, such as Mohs surgery (Lasudry, 2011; Harvey, 2013), full-thickness skin-graft, local flaps, or open healing. Some studies have focused on a particular histological type of tumor, and not reported results regarding the spectrum of eyelid skin cancers.

The new 8th TNM classification has revised it staging of periocular cancers, suggesting that previous versions were inaccurate with regard to eyelid lesions, and emphasizing the complex anatomy involved. Moreover, it remains unclear in the literature how

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the aesthetic sequelae have been reported and evaluated. This aspect of peri-ocular cancers should never be underestimated.

Many non-melanoma skin cancers remain easy to cure, with their prognosis is closely related to an early and efficient surgical treatment. However, early detection is increasingly difficult in an ageing population (ANAES, 2004; Bouhassira, 2013; INCa-HAS, 2009; Lasudry, 2011; Nseir, 2008; Silverman, 2017).

This study reports both aesthetic and oncological results, as well as the various techniques employed, in the surgical treatment of all non-melanoma orbit and eyelid tumors in a large cohort.

2. Materials and methods

We retrospectively reviewed all medical/oncological files on patients treated in our referral department for an orbito-palpebral, non-melanoma, skin cancer. For each patient, the following data were collected and processed:

- Epidemiological — age, gender, socio-economic status, profession, professional solar exposure, and other risk factors
- Clinical — medical or surgical past history, personal history of skin cancer or predisposing lesions, such as chronic wounds or ulcers, and immunosuppressive medications
- Complementary examinations — MRI, CT-scans, neck ultrasonography
- Oncological — TNM status (according the 8th TNM classification, reviewed by both AJCC and UICC) (Keohane et al., 2018), histological type, tumor location (external canthus, EC; internal canthus, IC; lower eyelid, LE; upper eyelid, UE)
- Ophthalmological — patent signs of ocular invasion, red eye, or recent vision loss
- Surgical — surgical technique used (deferred reconstruction (DR), excision and open healing (E-OH), excision and direct closure (E-DC), full-thickness skin graft (FTSG), local flap (LF), complex or free flap, mucosa graft), rate and type of postoperative complications, healing time, conventional or outpatient surgery, surgical resumption for insufficient or invaded margins
- Histological (final examination) — tumor size, margin situation (invaded or insufficient). Margins were considered insufficient when under 5 mm for a basal cell carcinoma and under 10 mm for a squamous cell carcinoma or a sclerodermal form of basal cell carcinoma, in accordance with the current recommendations (ANAES, Inca-HAS).
- Indication for adjuvant treatment — radiation therapy, chemotherapy, or other medical treatment
- Socio-economic — sick leave length, work resumption difficulties (self-evaluated on a scale ranging from 0 to 5), need for professional reclassification
- Aesthetic — Face-Q test results regarding global face and eyelid aspects (self-evaluated) (Lee, 2018)
- Functional — index of dermatological quality of life (IDQL) results, regarding surgical sequalae (Basra et al., 2008).

Data collection was performed from 2011 to 2017.

Inclusion criteria required each patient to have been managed within our department for an orbito-palpebral, non-melanoma, skin cancer.

Exclusion criteria were absence of file, or missing data regarding clinical examination, surgical technique, oncological result, histological type, final pathological analysis, and healing time.

Healing was considered to be complete when full epidermization was achieved, thus ending local nurse care. Patients who could not be reached by phone were excluded from our aesthetic and functional study.

The main analysed criterion was the rate of invaded and/or insufficient excision margins, bearing in mind that we did not make any distinction between invaded and insufficient margins in our multivariate analysis. Other analysed criteria were: full healing time, complication types and rates, aesthetic results according to the Face-Q test, and functional results according to the IDQL.

Univariate analyses were initially performed, using the Chi-squared test when applicable conditions were fulfilled; if not, the Fisher test for categorical variables was applied.

Average variables were compared using the Student t-test, and normal distributions of such variables with the Shapiro-Wilk test. All variable analysis results were considered significant if the p-value was <0.05.

Finally, a multivariate analysis using a logistic regression model was performed, and all results presented with the failure risk estimated using the odds-ratio (OR) and confidence ranges.

All statistical analyses were performed using the IBM SPSS statistics software.

In order to simplify our tests, we reinterpreted all quantitative variables using qualitative variables, using the median value as a cut-off regarding age (70.9 y), excision margin (5 mm), and histological tumor size (7 mm).

Thus, we aimed to evaluate the existence of significant links through odds-ratio calculations, in order to identify potential protective or risk factors regarding rate of invaded margins.

3. Results

3.1. Patient characteristics

Of the 135 patients whose medical files we reviewed, 132 had been operated; one patient died before surgery, one refused the proposed surgery, and another one was finally treated with vismodegib.

None of our patients had undergone a geriatric evaluation, while six of them underwent a specific ophthalmological evaluation to assess a potential globe invasion.

Lower eyelid (42.44%) and internal canthus (36.7%) were the most frequent locations.

Other characteristics are summarized in Table 1.

3.2. Surgical techniques

The surgical techniques employed are summarized in Table 2.

Direct closure and full thickness skin grafts were the most used surgical techniques (62% of our patients, regardless of tumor size or location) in our cohort (Fig. 1), while local flaps were the most likely to be used in lower eyelid locations (Fig. 2).

For tumor sizes under 20 mm, 17 lower eyelid locations were treated with local flaps, compared with two for external canthus locations and three for internal canthus locations. For tumor sizes over 20 mm, two out of three lower eyelid tumors were treated with local flaps, versus none for external or internal canthus locations.

3.3. Complications

Only 10 postoperative complications were observed over the entire cohort, comprising seven lower eyelid ectropiums after excision and direct closure and three lower eyelid entropiums after full thickness skin grafts for lesions under 20 mm. Four of the seven ectropiums were reoperated within 2 years (grade IIIb of the Clavien-Dindo classification) and none of the entropiums, which were managed with local nursing care. Evaluation criteria for both complications were: abnormal and frequent lacrimation,

Table 1
Main cohort characteristics.

Age, gender	
Gender: M/F (%)	61.48/38.51
Age (years); range	71.08; 26–97
Risk factors	
Solar exposure	22
Professional solar exposure	10
Genetics	4
Predisposing lesions	1
Personal history	42
Family history	2
Immunosuppressive medications	16
Histological type	
Basal cell carcinoma (%)	97 (71,85)
Squamous cell carcinoma	31
Rare type of cutaneous carcinoma	7
Tumor location	
Upper eyelid	7
Lower eyelid (%)	57 (42.44)
Internal canthus (%)	50 (36.70)
External canthus	21
Double location	9
Radiological examinations	
TDM	7
MRI	3
Ultrasonography	3
TNM status	
T1 (%)	96 (71.2)
T2	29
T3	6
T4	4
N1	1

Fig. 1. FTSG surgery for an internal canthal location (BCC): pre- and postoperative views.

Fig. 2. Local flap surgery for a lower eyelid location (SCC): pre-, peri-, and immediately postoperative views.

conjunctival erythema, and evaluation of standardized photographs in consultation.

None of our patients ever had corneal ulcerations, due to attentive local nursing with retentive strips, artificial tears, and vitamin A ointments pending surgery. Only one of them had an accidental lacrimal passage wound, which was managed by catheterizing the lacrimal passage (grade IIIb of the Clavien-Dindo classification).

3.4. Invaded and/or insufficient margins

Invaded or insufficient margins (IM) rate and long-term recurrence are summarized in Table 3.

The most notable result was a rate of invaded or insufficient margins (IM) of almost 40%, regardless of the tumor size or location. The rate of recurrence for truly invaded margins was 9.8%, and for insufficient margins 30.2%.

For a tumor size under 20 mm, IM occurred in 8/50 lower eyelid locations, 8/18 external canthus locations, and 11/38 internal canthus locations. For a tumor size above 20 mm, IM occurred in 1/3 lower eyelid locations and external canthus locations.

3.5. Histological features

Histological types and precise tumor sizes are summarized in Table 4.

3.6. Aesthetic and functional results

Aesthetic and quality-of-life results are summarized in Tables 5–7. Of our entire cohort, 66 patients (48.89%) were included

Table 2
Surgical techniques employed compared with tumor size and location.

Size	≤20 mm					>20 mm					Orbital invasion, >40 mm
Location	UE	LE	EC	IC	Double	UE	LE	EC	IC	Double	IC
Number	5	50	18	38	7	0	3	3	5	0	3
In-patient	5	36	11	15	7	0	3	2	4	0	3
Out-patient	0	14	7	23	0	0	0	1	1	0	0
DR	0	1	0	0	1	0	0	0	2	0	1
E-OH	0	4	0	3	1	0	0	0	1	0	1
E-DC	1	19	12	13	1	0	1	0	1	0	0
FTSG	2	9	4	19	3	0	0	3	1	0	0
LF	2	17	2	3	1	0	2	0	0	0	1
Healing time (days), ave (max−min)	10.2 (15−7, 4.38)	16.04 (60−7, 9.93)	13.3 (45−10, 10.2)	17.9 (45−7, 9.99)	22.62 (52−7, 13.79)	0	12.3 (15−7, 4.61)	20 (20−20, 0)	29.2 (48−7)	0	37.7 (23−63, 22,03)

Table 3
Rate of invaded margins compared with tumor size and location.

Size	≤20 mm					>20 mm					Orbital invasion, > 40 mm
Location	UE	LE	EC	IC	Double	UE	LE	EC	IC	Double	IC
DR	0	1	0	0	1	0	0	0	2	0	1
E-OH	0	4	0	3	1	0	0	0	1	0	1
E-DC	1	19	12	13	1	0	1	0	1	0	0
FTSG	2	9	4	19	3	0	0	3	1	0	0
LF	2	17	2	3	1	0	2	0	0	0	1
IM	0	8	8	11	3	0	1	1	0	0	2
Recurrence	0	2	0	3	0	0	2	1	0	0	1

Table 4
Oncological characteristics and tumor size within our cohort.

Size	≤20 mm	>20 mm	Orbital invasion
All mixed types	7.93 (19–2.5, SD: 3.82)	23.81 (40–20, SD: 5.79)	23 (27–22, SD: 3.6)
BCC	8.08 (19–2.5, SD: 3.82)	21.2 (26–20, SD: 2.68)	23 (27–22, SD: 3.6)
SCC	6.06 (15–3, SD: 3.01)	26.2 (40–21, SD: 7.79)	0
Others	8 (13–3, SD: 5)	22 (25–20, SD: 2.64)	0

Table 5
Global face FQTV results within our cohort.

Size	≤20 mm						>20 mm					Orbital invasion
Location	UE	LE	EC	IC	Double		UE	LE	EC	IC	Double	IC
Number	1	26	11	16	2		0	2	3	1	0	1
DR	0	0	0	0	0		0	0	0	18	0	0
E-OH	0	34.5	0	23	0		0	0	0	0	0	0
E-DC	0	31.9	32.12	34	0		0	31	0	0	0	0
FTSG	0	32.33	28	27.67	40		0	0	39	0	0	0
LF	23	29.9	24	35.67	35.67		0	37	30.5	0	0	14
Total	23	31.3	30.63	31.25	37.83		0	34	33.3	18	0	14
		(29.9–34.5, SD: 2.79)	(24–32.12, SD: 2.74)	(23–35.67, SD: 4.07)	(35.67–37.83, SD: 3.06)			(31–37, SD: 4.24)	(30.5–39, SD: 4.90)			

Table 6
Specific eyelid FQTV results within our cohort.

Size	≤20 mm						>20 mm					Orbital invasion
Location	UE	LE	EC	IC	Double		UE	LE	EC	IC	Double	IC
Number	1	26	11	16	2		0	2	3	1	0	1
DR	0	0	0	0	0		0	0	0	18	0	0
E-OH	0	34.5	0	23	0		0	0	0	0	0	0
E-DC	0	30.9	30.87	32.16	0		0	31	0	0	0	0
FTSG	0	32.33	28	31.67	40		0	0	40	0	0	0
LF	23	29.55	24	35.67	35.67		0	37	30	0	0	14
Total	1	30.77	29.72	32.06	37.83		0	34	33.3	18	0	14
		(29.55–34.5, SD: 1.43)	(24–30.87, SD: 4.43)	(23–35.67, SD: 2.85)	(35.67–37.83, SD: 3.06)			(31–37, SD: 4.24)	(30–40, SD: 5.73)			

Table 7
IDQL results within our cohort.

Size	≤20 mm						>20 mm					Orbital invasion
Location	UE	LE	EC	IC	Double		UE	LE	EC	IC	Double	IC
Number	1	26	11	16	2		0	2	3	1	0	1
DR	0	0	0	0	0		0	0	0	3 (1)	0	0
E-OH	0	0.5 (2)	0	3 (1)	0		0	0	0	0	0	0
E-DC	0	0.4 (10)	1 (8)	0.5 (6)	0		0	3 (1)	0	0	0	0
FTSG	0	0 (3)	4.5 (2)	3.16 (6)	0 (1)		0	0	0 (1)	0	0	0
LF	0	0.72 (11)	1 (1)	1 (3)	1 (1)		0	0 (1)	0.5 (2)	0	0	0 (1)
Total	0	0.5	1.63	1.74	0.5		0	1.5	0.33	3	0	0
		(0–0.72, SD: 0.23)	(1–4.5, SD: 1.41)	(0.5–3.16, SD: 1.27)	(0–1, SD: 0.71)			(0–3, SD: 2.12)	(0–0.5, SD: 0.28)			

in this analysis. Best results were obtained with direct closure (scores over 30, no matter the location) and worse results with open healing and T4 stage.

3.7. Multivariate analysis

Multivariate analysis revealed a significant link between a higher rate of invaded or insufficient margins and:

- a large tumor size (over 7 mm), OR = 2.7 (95% CI = 1.261–8.007; $p = 0.011$)
- a basal cell histological type, OR = 3.37 (95% CI = 1.284–8.829; $p = 0.014$)
- a double location, OR = 8.44 (95% CI = 1.101–64.702; $p = 0.04$)

On the other hand, we identified a significant link between a lower rate of invaded or insufficient margins and:

- a local flap-based reconstruction, OR = 0.290 (95% CI = 0.102–0.825; $p = 0.02$)
- female gender, OR = 0.418 (95% CI = 0.187–0.937; $p = 0.034$)

These results are summarized in Table 8.
Finally, there was significant link between a longer healing time and:

- immunosuppressive medications, OR = 2.981 (95% CI = 1.094–7.641; $p = 0.032$).

On the other hand, we identified a significant link between a shorter healing time and:

- the nodular clinical type for BCC, OR = 0.489 (95% CI = 0.246–0.973; $p = 0.041$)
- a direct closure, OR = 0.014 (95% CI = 0.01–0.268; $p = 0.05$)

These results are summarized in Table 9.
We were unable to identify any significant links between aesthetic results or quality of life and other factors.

Table 8
Significant results in a multivariate analysis (regarding invaded or insufficient margins rate).

Variable	OR	Multivariate	p-value
		95% CI	
Clinical			
Double location	8.44	1.101–64.7	0.04
Female	0.418	0.187–0.937	0.034
Histological			
BCC	3.37	1.284–8.829	0.014
Large	2.7	1.261–8.007	0.011
Surgical			
Local flap	0.29	0.102–0.825	0.02

Table 9
Significant results in a multivariate analysis (regarding healing time).

Variable	OR	Multivariate	p-value
		95% CI	
Clinical			
Immunosuppressive	2.981	1.094–7.641	0.032
Nodular form	0.489	0.246–0.973	0.041
Surgical			
Direct closure	0.014	0.01–0.268	0.05

4. Discussion

This study aimed to describe the long-term aesthetic and oncological outcomes after surgery in a large population of patients treated for a non-melanoma skin cancer of the eyelid and orbit.

While it has revealed some interesting results, including links between invaded margins rate, surgical technique, tumor location, and tumor size, it also presents some weaknesses. For example, regardless of the quality of the referral center, this is a monocentric, non-randomized, retrospective study. Nevertheless, it seems that our cohort matches the demographic distribution and clinical characteristics for such cancers, as presented by the literature, and it includes a large number of patients. While the largest cohorts published in the literature amount to 400–500 patients (485 patients for Nemet (2006) and 413 patients for Ho et al., 2013), they do not focus on the surgical results in terms of various techniques, or do not include all histological types of non-melanoma, orbito-palpebral tumor.

Our study raises some important points regarding the future management of such patients.

First, none of our patients had a geriatric examination, and only a few had a specific ophthalmological consultation. As a recommended quality criterion (ANAES, 2004; Bouhassira, 2013; INCa-HAS, 2009), a geriatric evaluation should be automatic for those over 75 years old, as should an ophthalmological examination.

There was a high prevalence in our cohort of the basal cell carcinoma histological type, which is in accordance with the literature (over 70%) (ANAES, 2004; Bouhassira, 2013; Lasudry, 2011; Nseir, 2008; Silverman, 2017; Ho et al., 2013; Nemet, 2006; Allen, 2017; Donaldson, 2002). The majority of locations were in the lower eyelid and internal canthus (42% and 37%, respectively), which was also the case for Ho et al. (2013) and Nemet (2006), and this raises an important issue regarding preservation of the lacrimal passage.

Both of the above factors were related to a high invaded margins rate, with multivariate analysis giving an OR > 3 ($p = 0.014$) for the basal cell histological type. An internal canthal location has been reported as a major risk factor several times in the literature, accounting for over 35% of invaded margins (Ho et al., 2013; Nemet, 2006).

There was also a significant link between a higher rate of invaded or insufficient margins and double location (OR = 8.44), and within those 'double location patients' there were six internal canthal locations. The main explanation for this may lie in the operator's desire to spare the lacrimal passage when excising badly located tumors, in order to avoid an accidental wound and a canthal dystopia, especially with an indolent basal cell tumor.

One of the most surprising results of this study was the high rate of invaded or insufficient margins, leading to a surgical resumption rate of over 40%. This is a higher rate than those usually described in large cohorts. For example, in their cohort Nemet et al. found a 25.4% invaded margins rate after first excision, reaching 35% for internal canthal locations) (ANAES, 2004; Bouhassira, 2013; Lasudry, 2011; Nseir, 2008; Silverman, 2017; Ho et al., 2013; Nemet, 2006; Allen, 2017; Donaldson, 2002; Holmström, 1975).This is almost certainly explained by the fact that most studies published do not equate an invaded margin (cancerous) to an insufficient margin. In addition, recommended margins vary from country to country (ANAES, 2004; Bouhassira, 2013; INCa-HAS, 2009; Keohane, 2018).

Another surprising result was a much lower rate of complications compared with those usually described (Ho et al., 2013; Nemet, 2006). Accordingly, the most employed surgical reconstruction techniques used in our study were FTSG and E-DC (applying to 62% of patients), which are safe and easily reproducible

techniques, but this does not explain the high rate of insufficient margins. Instead, this may be explained by the constant will of the operator to spare as much tissue as possible in a fragile population, with any oncological risk managed through further surgical resumptions.

Nevertheless, one-off surgery should remain the procedure of choice, because a second intervention, even under local anesthesia, can lead to severe complications, and will always increase the management costs, especially in an old population with various comorbidities. Further larger studies aiming to evaluate the healthcare costs related to such reinterventions should help us to confirm whether such an attitude is justified.

Another important result was the significant link between large tumors (over 7 mm), and a higher rate of invaded or insufficient margins (OR = 2.7), which seems logical and in accordance with the risk factors described in the literature.

In our opinion, the most important result in our study was the significant link between a lower rate of invaded or insufficient margins and a local flap-based reconstruction (OR = 0.29). This seems logical when compared with the other surgical techniques, because when the operator plans a local-flap based reconstruction, the excision area tends to be larger as it follows an aesthetic facial subunit, and not just the tumor with its margins.

An alternative explanation is that if the excision of the tumor and margins has to be performed regardless of any planned reconstruction, then the surgeon would realize that the best reconstruction to perform would be a local flap and therefore, unconsciously, the excision would be larger. Moreover, simple local flaps can often be performed under local anesthesia, with a healing time equal to a direct closure and with a better aesthetic result.

However, no direct conclusions can be drawn from this study because it is a retrospective study and not a prospective one, and so further prospective studies should be carried out to confirm the above.

In terms of healing time, the three factors picked out for multivariate analysis were direct closure, nodular forms, and the use of immunosuppressive medications. We proposed no hypotheses to explain such links, although some studies have reported on such risk factors (Perry, 2016).

Regarding aesthetic results, we were unable to establish any significant links through our multivariate analyses, even when we were able to identify T4 staging, margins over 5 mm, and a major healing time as factors contributing to a worsened aesthetic result, and direct closure as an obvious option for better results throughout univariate analysis. This was mostly due to the small number of patients in our cohort who completed our questionnaire (48.89%), suggesting the need for larger studies with incentives for patients to carry out self-evaluation.

Based on our results, we suggest the following:

- The 8th TNM classification should now be the standard staging system for such tumors.
- Ophthalmological and geriatric evaluations for the over 75-year-olds should be systematic, especially for stage T3 or T4 tumors.
- Surgeons should always keep in mind that excision has to be performed without any concerns regarding reconstruction, and that one-off surgery should always be performed when possible.

Systematic surgical planning with separate teams — one dealing with excision and the other one with reconstruction — should help.
- Canthopexy and cantholysis should be used for large tumors of the canthi or for large margins.
- Direct closure should be the first choice when presented with a tumor size under 20 mm and resection margins under 5 mm.

5. Conclusion

This study highlights the consequences of factors influencing the rate of invaded or insufficient margins rate in the surgical treatment of orbito-palpebral, non-melanoma skin cancers. Further prospective, multicentric studies should be undertaken to evaluate the protective and negative factors that influence oncological, functional, and aesthetic results.

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The authors have no conflicts of interest or any financial issues to declare.

Ethical approval

All patients have given informed and written consent for publication of this article and review.

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