Recurrence of periocular basal cell carcinoma and squamous cell carcinoma after Mohs micrographic surgery: a retrospective cohort study

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Summary

Background Despite the widespread use of Mohs micrographic surgery (MMS) for periocular basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) – together called keratinocyte carcinoma (KC) – follow-up data regarding recurrences are limited.

Objectives To investigate the recurrence rate for periocular KCs after MMS and to describe our experience with interdisciplinary collaborations.

Methods Patients with periocular KCs treated with MMS between 2006 and 2016 in a tertiary MMS referral hospital were included in this retrospective cohort study. Descriptive statistics were used to describe the MMS procedure-related characteristics. Using follow-up data from the electronic patient records and linkage with the Dutch nationwide network and registry of histopathology and cytopathology on 30 June 2017, the recurrence rate was evaluated and calculated using a cumulative incidence curve.

Results In total, 683 (93·7%) periocular BCCs and 46 (6·3%) SCCs were treated with MMS. Three-quarters (n = 549) were primary tumours and the majority were located at the medial canthus or lower eyelid (n = 649, 89·0%). In 505 MMS procedures (69·3%) an oculoplastic surgeon participated, and in 63 patients (8·6%) a plastic surgeon performed the reconstruction. After a median follow-up of 46 months the recurrence rate was 3·0%, based on 22 recurrences (20 BCCs and two SCCs).

Conclusions MMS is an excellent treatment option for periocular KCs, with a low recurrence rate. Due to this specific anatomical location an interdisciplinary approach should pre-eminently be considered.

What's already known about this topic?

- Mohs micrographic surgery (MMS) is a widespread treatment for periocular basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) because of the expected high cure rate, while preserving healthy tissue.
- Follow-up data on the risk of recurrence after periocular MMS are limited.

What does this study add?

- This retrospective cohort study demonstrates that with a recurrence rate of 3·0% after almost 4 years, MMS has proven to be an excellent surgical treatment option for periocular BCC and SCC.
- We advise a low threshold for interdisciplinary collaborations, especially in case of recurrent BCCs, BCCs localized in the medial canthus and aggressive BCCs.

Keratinocyte carcinomas (KCs), representing both basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), are the most common forms of skin cancer in the periocular region. The large majority are BCCs (84–96%), while 3–9% are SCCs.[1–5] Morbidity of periocular KCs can be significant due to the close proximity and possible spread to functional (peri)ocular structures such as the eyelid, lacrimal duct or intraorbital structures. Additionally, compared with other locations, periocular BCCs may grow more rapidly.[6] Periocular KCs are usually treated surgically, but preferably with limited excision margins due to the sensitivity of this area. Such interventions also require specific knowledge of the different periocular structures and careful consideration of treatment and interdisciplinary care is needed.

Approximately one-quarter of periocular KCs are incompletely removed after standard excision, with histopathologically aggressive tumours and localization in the medial canthus having the highest risk.[7–10] Especially in the periocular region complete resections are important. It is estimated that 30–50% of incompletely excised KCs result in a recurrence.[11–13] A recurrent tumour may require larger resections, and if a tumour in this region invades the ocular muscles or postseptal space, exenteration is usually the only option to prevent the tumour from invading the sinuses and brain.[14,15]

To increase surgical completeness, thereby minimizing the chance of tumour recurrence, and to spare healthy skin in this high-risk and functionally important location, Mohs micrographic surgery (MMS) is suggested as the preferred treatment for periocular KCs.[2,7,15–20] However, despite the currently widespread use of MMS for periocular KC, follow-up data are often available only for a subgroup of patients or restricted by limited follow-up time,[17] which makes comparison of data difficult. Estimations of recurrence rates after MMS for periocular KC vary from 0·7% to 5·9% over 60–120 months.[16,18,21–24]

There is a need to describe the outcomes of periocular MMS for KCs in a well-defined population with complete and sufficiently long follow-up time. Furthermore, because of the functional and cosmetic sensitivity of the periocular region, dermatologists performing MMS for periocular KCs may also seek interdisciplinary collaborations with (oculo)plastic surgeons, but it is unclear which patients are selected. The primary aim of this study was therefore to determine the post-MMS recurrence rate of periocular KCs treated in a large tertiary MMS referral hospital. Secondly, we will describe our 10-year experience with MMS for periocular KCs, including the need for interdisciplinary care.

Patients and methods

Study population

This single-centre retrospective cohort study was performed at the department of dermatology of the Erasmus MC Cancer Institute, Rotterdam, the Netherlands. In this study, all patients who underwent MMS for periocular KC between 1 January 2006 and 31 December 2016 were included and anonymized.

Periocular KC was defined as tumours located on the upper or lower eyelid, or the medial or lateral canthus.

Patient and tumour characteristics

The following patient and tumour characteristics were extracted from the electronic patient records: age, sex, tumour localization, histopathological subtype, presence of perineural or perivascular invasion, and prior treatment. BCCs were categorized into infiltrative, micronodular, nodular or superficial. SCCs were categorized into well differentiated, moderately differentiated or poorly differentiated. If, on biopsy, a mixed-type tumour was found, or if during MMS a histological subtype was found other than that seen on biopsy, the tumour was categorized according to the most aggressive subtype. For statistical analyses, BCC subtypes were also dichotomized into aggressive (infiltrative and micronodular) or nonaggressive (nodular and superficial).

Recurrent keratinocyte carcinomas

Tumour recurrence was defined as a biopsy-proven BCC or SCC in or just next to (< 1 cm) a scar of a preceding MMS procedure.[25] Recurrence was evaluated by follow-up data from the electronic patient records and by linkage with 'the nationwide network and registry of histo- and cytopathology in the Netherlands' (Dutch acronym: PALGA; http://www.palga.nl), which is a comprehensive registry of all pathology reports in the Netherlands.[26] The follow-up time per patient was defined as the time from the MMS procedure until the end of the study (linkage to PALGA on 30 June 2017), the date of recurrence or the date of death, whichever came first. Information about dates of death during the study were obtained from the Dutch Municipal Population Register.

Possible recurrences (n = 62) were assessed by two Mohs surgeons independently (M.W. and R.R.vdB.). Cases were then categorized into 'very likely', 'possibly', 'cannot be determined' and 'unlikely'. In case of discrepancies in assessment, consensus was obtained by debate. For calculations of recurrence, the cases that were categorized into 'very likely' and 'possibly' were grouped and counted as recurrence. The category 'cannot be determined' consisted of cases in which patients had a subsequent BCC registered in PALGA, but without details about localization. Tumours for which complete excision could not be achieved by MMS and patients with a strong genetic predisposition for KCs (mainly basal cell naevus syndrome) were excluded from the recurrence analysis.

Mohs procedure and reconstruction

Patients with periocular KCs were preoperatively discussed and it was determined whether collaboration with an oculoplastic surgeon or plastic surgeon would be beneficial. All tumours were removed by standard MMS, performed by experienced Mohs surgeons (certified by the European Society of Micrographic Surgery) or by residents under supervision of

experienced Mohs surgeons. During an interdisciplinary MMS procedure, the Mohs surgeon defined the tumour borders and performed the subsequent MMS procedure, while the oculoplastic surgeon was involved in determining surgical completeness for difficult-to-treat areas. After MMS, surgical reconstruction followed, which was conducted by a Mohs surgeon, an oculoplastic surgeon or, in cases where a large reconstruction under general anaesthesia was expected, a plastic surgeon.

The following MMS characteristics were extracted from the electronic MMS records: total number of Mohs stages, final defect size, reconstruction method and who performed the reconstruction (Mohs surgeon, oculoplastic surgeon and/or plastic surgeon). Defect sizes (in cm^2) were calculated from diameters reported in the MMS files (formula: $\pi \times r \times r$). Reconstructions were classified according to the reconstructive ladder (Fig. 1), which adds a complexity hierarchy to the available reconstructive options.[27] When a combination was used, the most complex method was recorded.

Statistical analysis

Descriptive statistics were used to describe patient, tumour and MMS characteristics. Comparison of nominal data (e.g. sex) was done with the χ^2-test, while ordinal or non-normally distributed ratio and interval data were compared between groups by the Mann–Whitney U-test (e.g. age or final defect size). P-values < 0.05 (two sided) were considered statistically significant. To determine the risk of KC recurrence over time, taking into account the competing risk of death, we calculated a cumulative incidence curve.[28] Due to the small number of recurrences (n = 22), we analysed a

limited number of a priori selected potential independent risk factors for BCC recurrence, based on the available literature, using a univariable Cox proportional hazard regression. This analysis was not possible for SCC due to the limited number of patients. The proportional hazard assumption was met for each risk factor, as verified with a log-minus-log plot. Statistical analyses were performed with IBM SPSS Statistics 24·0·0·1 (IBM, Armonk, NY, U.S.A.) and R 3·3·3 (R Foundation, Vienna, Austria).

Ethical considerations

The institutional ethical committee of the Erasmus MC University Medical Centre Rotterdam reviewed and approved the study design. A written confirmation of this statement was given (MEC-2017-168).

Results

Patient and tumour characteristics

In total, 729 periocular KCs were treated with MMS. Of these, 683 (94%) were BCC and 46 (6%) were SCC (Table 1). The median age at MMS was slightly higher for patients with SCC (73 years) than for those with BCC (69 years, P = 0·007). Overall, 43% (315 of 729) were male, with sex showing a comparable distribution for BCC and SCC (P = 0·51).

Three-quarters were primary tumours, and the majority were located at the medial canthus and on the lower eyelid (649 of 729, 89%; Table 1). Regarding BCCs, 44% (299 of 683) were of aggressive histological subtypes. Of the SCCs, 23 (50%) were well to moderately differentiated, three (7%)
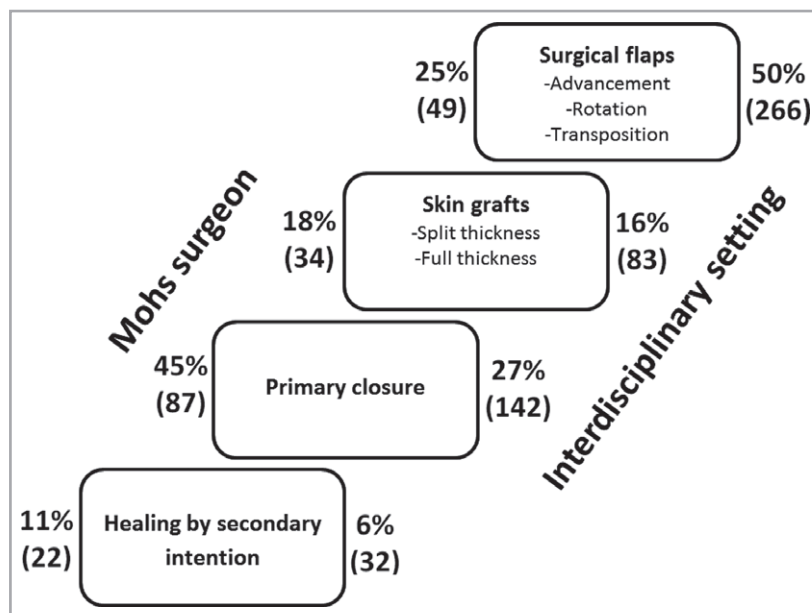

Fig 1. The reconstructive ladder.

Table 1 Baseline characteristics of patients treated with Mohs micrographic surgery (MMS) for periocular keratinocyte carcinoma

Tumours	Total (n = 729)	BCC (n = 683, 93·7%)	SCC (n = 46, 6·3%)
Age (years), median (IQR)	69 (59–78)	69 (58–77)	73 (66–81)
Sex male	315 (43·2)	293 (42·9)	22 (48)
Status prior to MMS			
Primary	549 (75·3)	513 (75·1)	36 (78)
Residue/recurrent	180 (24·7)	170 (24·9)	10 (22)
Localization[a]			
Medial canthus	325 (44·6)	310 (45·4)	15 (33)
Lower eyelid	324 (44·4)	301 (44·1)	23 (50)
Upper eyelid	54 (7·4)	50 (7·3)	4 (9)
Lateral canthus	26 (3·6)	22 (3·2)	4 (9)
Histopathology[b]			
Superficial BCC		14 (2·0)	
Nodular BCC		367 (53·7)	
Micronodular BCC		43 (6·3)	
Infiltrative BCC		256 (37·5)	
BCC of unknown differentiation		3 (0·4)	
Well-differentiated SCC			9 (20)
Moderately differentiated SCC			14 (30)
Poorly differentiated SCC			3 (7)
SCC of unknown differentiation			20 (43)
Perineural or perivascular invasion	11 (1·5)	8 (1·2)	3 (7)

Data are given as n (%) unless stated otherwise. BCC, basal cell carcinoma; SCC, squamous cell carcinoma; IQR, interquartile range. [a]When tumour was present in more than one location, the location covering the largest surface area was chosen. [b]Histopathological subtype (determined by biopsy and MMS) was subclassified according to the most aggressive subtype.

were poorly differentiated and in 20 SCCs (43%) histopathology was not specified. Perineural or perivascular invasion was seen in three SCCs (7%) and eight infiltrative BCCs (1·2%). Nineteen tumours were treated in patients with basal cell naevus syndrome (2·8%) and one patient was diagnosed with Schimmelpenning–Feuerstein–Mims syndrome.

Of the patients referred with incompletely treated or recurrent tumours (180 of 729, 25%), the majority were previously treated by standard excision (n = 167, 93%), five (3%) by MMS (elsewhere) and five (3%) by radiotherapy. Recurrent or previously incompletely treated BCCs more often had an aggressive histopathology than primary BCCs (55% vs. 40%). For SCCs, a dichotomization into aggressive and nonaggressive was not informative due to the low number of SCCs in this study and the incomplete registration of subtypes in the past.

Recurrent keratinocyte carcinoma after Mohs micrographic surgery

After excluding tumours from patients with a genetic predisposition for KC (n = 20) and tumours that could not be completely resected with MMS (n = 7), 702 of 729 (96%) KCs were available for survival analysis. There were 2929 person-years of follow-up, during which 22 KCs were classified as a 'very likely' (n = 21) or 'possible' (n = 1) recurrence (20 BCCs and two SCCs). At a median follow-up time of 46 months [interquartile range (IQR) 24–70] this resulted in a recurrence rate of 3·0%. At the maximum available follow-up time of 135 months the recurrence rate was 4·3% (Fig. 2). The median time to a recurrence was 19 months (IQR 13–40). Nearly 22% of recurrences occurred in the first year of follow-up, 73% within 3 years of follow-up and 91% within 5 years of follow-up. The two recurrent SCCs recurred after 6 and 11 months.

None of the a priori determined potential risk factors for BCC recurrence were associated with tumour recurrence in the univariable Cox proportional hazard analyses. These were localization at the medial canthus: crude hazard ratio (HR) 1·01, 95% confidence interval (CI) 0·43–2·39; need for more than two MMS stages: HR 1·75, 95% CI 0·64–4·79; incomplete treatment or recurrence before MMS: HR 1·70, 95% CI 0·70–4·10; and aggressive BCC subtype: HR 2·23, 95% CI 0·88–5·66.

Mohs procedure and reconstruction

Almost all tumours could be completely excised by MMS (722 of 729, 99%). For 580 BCCs (86%), surgical completeness was achieved within two MMS stages, while 96 (14%) needed three or more stages (with a maximum of seven stages) (Table 2). For 41 SCCs (89%) surgical completeness was achieved within two MMS stages, while (11%) needed three or four stages. The median final defect size was comparable between BCC and SCC: 1·21 cm^2 (IQR 0·59–2·26) and 1·26 cm^2 (IQR 0·67–2·65), respectively (P = 0·25). The median number of MMS stages for BCC was the same for the different histological subtypes, while the median final defect size for aggressive BCCs was 1·7 times larger than for nonaggressive BCCs (1·57 vs. 0·93 cm^2, P < 0·01).

In the majority of treatments (536 of 729, 74%), interdisciplinary collaboration occurred for either the MMS procedure, reconstruction or both. Regarding MMS procedures, 505 of 729 (69%) were performed in an interdisciplinary setting, consisting of Mohs surgeons and oculoplastic surgeons (Table 3). Interdisciplinary collaborations occurred even more frequently for previously incompletely excised and recurrent tumours (151 of 180, 84%) and aggressive BCCs (237 of 299, 79%). Regarding localization, particularly KCs on the lower eyelid (274 of 324, 85%) and lateral canthus (22 of 26, 85%) were selected for interdisciplinary treatment. There was no major difference between BCC and SCC (70% and 74%, respectively). The median final defect size for tumours
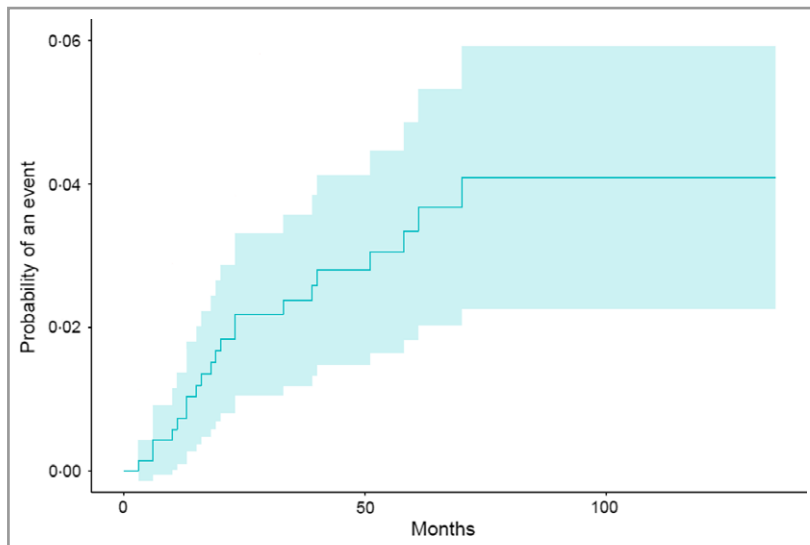
Fig 2. Recurrence rate after Mohs micrographic surgery for periocular keratinocyte carcinomas.

Table 2 Mohs micrographic surgery (MMS) characteristics of the patients

MMS characteristics[a]	Total (n = 722)	BCC (n = 676)	SCC (n = 46)
Mohs stages, mean ± SD[b]	1·8 ± 0·9	1·81 ± 0·9	1·67 ± 0·7
Mohs stages, n (%)			
1	299 (41·4)	278 (41·1)	21 (46)
2	322 (44·6)	302 (44·7)	20 (43)
≥ 3	101 (14·0)	96 (14·2)	5 (11)
Defect size[c] in cm² after final Mohs stage, median (IQR)	1·21 (0·61–2·32)	1·21 (0·59–2·26)	1·26 (0·67–2·65)
Nonaggressive BCC[d] (n = 380)		0·93 (0·49–1·77)	
Aggressive BCC[d] (n = 293)		1·57 (0·79–2·69)	

BCC, basal cell carcinoma; SCC, squamous cell carcinoma; IQR, interquartile range. [a]Excluding patients for whom surgical completeness with MMS could not be achieved. [b]No statistical difference for number of Mohs stages between BCC and SCC (P = 0·45). [c]No statistical difference for final defect size between BCC and SCC (P = 0·25). [d]Aggressive BCC: nodular and superficial. Nonaggressive BCC: infiltrative and micronodular. Excluding three patients without information on histopathology. Final defect size was statistically different between aggressive and nonaggressive BCC (P < 0·001).

treated in an interdisciplinary setting was larger than for tumours treated by the Mohs surgeon alone (1·30 vs. 0·91 cm², P = 0·008). Collaboration with plastic surgeons was sought in 63 cases (8·6%), especially when a surgical procedure required reconstruction of the entire upper or lower eyelid or eyelid pair. The Mohs surgeon most often used primary closure (n = 87, 45%), followed by a surgical flap (i.e. advancement, rotation or transposition flap), in 25% of cases (Fig. 1). When an (oculo)plastic surgeon was involved in reconstruction, a surgical flap (n = 266, 50%) was most often used, followed by primary closure (n = 142, 27%). Other types of reconstructions were comparable between groups.

For seven tumours (in seven patients, all BCCs) it was not possible to achieve a complete resection. Four were primary tumours and six were localized in the medial canthus. Almost all (n = 6) had an aggressive histological subtype and two of seven (29%) had perineural invasion, which is high compared with the 1·5% described in the remaining BCC group.

Subsequent treatment consisted of exenteration (n = 3), re-excision under general anaesthesia (n = 3) and staged excision (n = 1).

Discussion

In this retrospective cohort study, almost all tumours could be completely excised with MMS (99%) and the risk of KC recurrence was reasonably low (3·0%). This study further describes the high need for interdisciplinary collaboration in three-quarters of all periocular MMS procedures.

Although the recurrence rate was relatively low in our study, the risk reported in some other studies was even lower (0·7–2·0%).[16,18,21,22] However, it is rather difficult to compare the recurrence rate found in this study with others. The difference may be explained by incomplete or shorter follow-up time in other studies, a more high-risk KC population in our study and adjusting for the competing risk of death.

Table 3 Characteristics of Mohs micrographic surgery (MMS) treatments by Mohs surgeon only vs. interdisciplinary setting

	Mohs surgeon only (n = 193, 26·5%)	Interdisciplinary setting (n = 536, 73·5%)
Row percentages		
MMS procedure	224 (30·7)	505 (69·3)
Status prior to MMS, n (%)		
Primary	164 (29·9)	385 (70·1)
Residue/recurrent	29 (16·1)	137 (83·9)
Localization,[a] n (%)		
Lower eyelid	50 (15·4)	274 (84·6)
Medial canthus	116 (35·7)	209 (64·3)
Upper eyelid	23 (43)	31 (57)
Lateral canthus	4 (15)	22 (85)
Histopathology,[b] n (%)		
BCC	184 (26·9)	499 (73·1)
Aggressive	62 (20·7)	237 (79·3)
Nonaggressive	122 (30·0)	259 (70·0)
Unspecified	0 (0)	3 (100)
SCC	9 (20)	37 (80)
Defect size[c] in cm^2 after final Mohs stage, median (IQR)	0·91 (0·55–1·89)	1·30 (0·63–2·36)
Column percentages		
Reconstructions,[d] n (%)	Mohs surgeon (n = 193)	Interdisciplinary setting (n = 529)
Primary closure	87 (45·1)	142 (26·8)
Skin graft	34 (17·6)	83 (15·7)
Surgical flaps	49 (25·4)	266 (50·3)
Secondary intention	22 (11·4)	32 (6·0)
Not specified	1 (0·5)	6 (1·1)

Data are given as n (%) unless stated otherwise. BCC, basal cell carcinoma; SCC, squamous cell carcinoma; IQR, interquartile range. [a]When tumour was present in more than one location, the location covering the largest surface area was chosen. [b]Histopathological subtype (determined by biopsy and MMS) was subclassified according to the most aggressive subtype. [c]Statistically different between Mohs surgeon and multidisciplinary setting (P = 0·008). [d]Excluding seven patients for whom surgical completeness with MMS could not be achieved.

This current study has a relatively long follow-up time, which is available for all eligible patients due to data linkage. In prior studies the follow-up is often less clearly defined, incomplete due to loss of study patients or rather short (median varying from < 12 to 30 months).[16,18,21–24] Although most BCCs recur within 3 years after treatment, sufficient follow-up time is important because about one-third of recurrences (in our study 27%) occur after that time, with 18% even occurring after 5 years.[29]

Furthermore, compared with other periocular MMS studies, this cohort contains a relatively high proportion of high-risk KCs.[2,5,18,21,30] They were often located at the medial canthus (44%, vs. 24–36% in the literature), were previously incompletely excised or recurrent tumours (25%) and, in cases of BCC, were of aggressive histological subtypes (44%). This relatively high-risk population may also have affected the risk for

recurrence in this cohort. However, probably due to the small number of recurrences, we could not confirm the role of these potential risk factors by regression analyses.

Finally, death of patients during the study can be an issue in survival analysis, as it can be a competing risk to long-term outcomes, such as the risk for recurrence. In an elderly population, patients may die before they develop a recurrence. This issue can be prevented if patients are included in the analysis only as long as they are actually at risk of developing a recurrence. This is the first study on MMS for periocular KCs that includes the competing risk of death in recurrence analysis. Without this adjustment, in our study the risk of recurrence would otherwise be 2·6% (18 of 702) at a median follow-up time of 46 months.

A Mohs surgeon is proficient in defining tumour borders and performing the MMS procedure. However, when the tumour is located at difficult anatomical locations with important functional structures (e.g. the lacrimal duct) and when more complex reconstructions are required, interdisciplinary collaborations can offer extra possibilities for acquiring surgical completeness, sparing functional structures and reconstructions.[18] The high proportion of interdisciplinary care in this study (74%) confirms this hypothesis, as at our dermatology department with tertiary care, annually approximately only 10% of all 1400 MMS procedures require an interdisciplinary approach. Periocular KCs should therefore pre-eminently be considered for an interdisciplinary approach, especially in case of localization in anatomical units that are difficult to reconstruct, previously incompletely treated or recurrent KCs, aggressive BCCs, or when a large reconstruction under general anaesthesia is required.

The number of included periocular KCs is among the highest available in the literature. However, the absolute number of patients with SCC is relatively low, as is the total number of recurrences, which limits the possibilities to adjust for potential confounders. Furthermore, histopathological data for SCCs were not routinely registered prior to the update of the 2011 Dutch guideline for cutaneous SCC,[31] and therefore determining risk factors for recurrence based on histopathology was not possible.

Other strengths of this study are the long and well-defined follow-up, the absence of loss to follow-up, and correction for the competing risk of death. A limitation is that, while giving a more accurate view on recurrence rate, there are still cases in PALGA for which recurrence cannot be determined with high certainty, due to lack of information about localization of a BCC treated in another hospital. This might cause an underestimation of the actual recurrence rate of periocular MMS.

We conclude that MMS is an excellent treatment option for periocular KCs, although future research can further strengthen our findings and extend our knowledge by also looking at other outcomes such as the cost-effectiveness of periocular MMS. MMS for periocular KCs leads to high surgical completeness and low risk for recurrence, while it has the advantage of sparing healthy tissue. Due to the specialized

character of MMS for periocular KCs, we recommend to conduct these procedures in a centre of expertise where a multidisciplinary approach between Mohs surgeons and (oculo)plastic surgeons is available, especially in case of previously incompletely treated, recurrent or aggressive tumours. This collaboration leads to combining the best of both worlds, namely combining knowledge and skills and adding complex reconstructions to the aforementioned benefits of MMS.

Acknowledgments

References

1 Cook BE Jr, Bartley GB. Epidemiological characteristics and clinical course of patients with malignant eyelid tumours in an incidence cohort in Olmsted County. Minnesota. *Ophthalmology* 1999; **106**:746–50.

2 Carter KD, Nerad JA, Whitaker DC. Clinical factors influencing periocular surgical defects after Mohs micrographic surgery. *Ophthal Plast Reconstr Surg* 1999; **15**:83–91.

3 Lee SB, Saw SM, Au Eong KG *et al.* Incidence of eyelid cancers in Singapore from 1968 to 1995. *Br J Ophthalmol* 1999; **83**:595–7.

4 Yin VT, Merritt HA, Sniegowski M *et al.* Eyelid and ocular surface carcinoma: diagnosis and management. *Clin Dermatol* 2015; **33**:159–69.

5 Malhotra R, Huilgol SC, Huynh NT *et al.* The Australian Mohs database: periocular squamous cell carcinoma. *Ophthalmology* 2004; **111**:617–23.

6 Tan E, Lin FP, Sheck LH *et al.* Growth of periocular basal cell carcinomas. *Br J Dermatol* 2015; **172**:1002–7.

7 Nemet AY, Deckel Y, Martin PA *et al.* Management of periocular basal and squamous cell carcinoma: a series of 485 cases. *Am J Ophthalmol* 2006; **142**:293–7.

8 Breuninger H, Dietz K. Prediction of subclinical tumor infiltration in basal cell carcinoma. *J Dermatol Surg Oncol* 1991; **17**:574–8.

9 Wolf DJ, Zitelli JA. Surgical margins for basal cell carcinoma. *Arch Dermatol* 1987; **123**:340–4.

10 Kadyan A, Edmunds MR, Amissah-Arthur KN *et al.* High rate of incomplete resection after primary excision of eyelid BCC: multistaged resection rarely needs more than two procedures. *Orbit* 2011; **30**:275–9.

11 Miszczyk J, Charytonowicz M, Debski T *et al.* Incomplete excision of basal cell carcinoma (BCC) in the head and neck region: to wait, or not to wait? *Postepy Dermatol Alergol* 2017; **34**:607–11.

12 De Silva SP, Dellon AL. Recurrence rate of positive margin basal cell carcinoma: results of a five-year prospective study. *J Surg Oncol* 1985; **28**:72–4.

13 Richmond JD, Davie RM. The significance of incomplete excision in patients with basal cell carcinoma. *Br J Plast Surg* 1987; **40**:63–7.

14 Donaldson MJ, Sullivan TJ, Whitehead KJ *et al.* Squamous cell carcinoma of the eyelids. *Br J Ophthalmol* 2002; **86**:1161–5.

15 Slutsky JB, Jones EC. Periocular cutaneous malignancies: a review of the literature. *Dermatol Surg* 2012; **38**:552–69.

16 Mohs FE. Micrographic surgery for the microscopically controlled excision of eyelid cancers. *Arch Ophthalmol* 1986; **104**:901–9.

17 Narayanan K, Hadid OH, Barnes EA. Mohs micrographic surgery versus surgical excision for periocular basal cell carcinoma. *Cochrane Database Syst Rev* 2014; **12**:CD007041

18 O'Halloran L, Smith H, Vinciullo C. Periocular Mohs micrographic surgery in Western Australia 2009–2012: a single centre retrospective review and proposal for practice benchmarks. *Australas J Dermatol* 2017; **58**:106–10.

19 Oncoline. Behandeling van het Basaalcelcarcinoom (BCC). [Treatment of basal cell carcinoma]. Dutch national guideline, version 2.1, 2016. Available at: https://www.oncoline.nl/basaalcelcarcinoom (last accessed 8 January 2019).

20 Ad Hoc Task Force, Connolly SM, Baker DR *et al.* AAD/ACMS/ASDSA/ASMS 2012 appropriate use criteria for Mohs micrographic surgery: a report of the American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association, and the American Society for Mohs Surgery. *J Am Acad Dermatol* 2012; **2012**:531–50.

21 Sin CW, Barua A, Cook A. Recurrence rates of periocular basal cell carcinoma following Mohs micrographic surgery: a retrospective study. *Int J Dermatol* 2016; **55**:1044–7.

22 Malhotra R, Huilgol SC, Huynh NT *et al.* The Australian Mohs database, part II: periocular basal cell carcinoma outcome at 5-year follow-up. *Ophthalmology* 2004; **111**:631–6.

23 Litwin AS, Rytina E, Ha T *et al.* Management of periocular basal cell carcinoma by Mohs micrographic surgery. *J Dermatolog Treat* 2013; **24**:232–4.

24 Lindgren G, Lindblom B, Larko O. Mohs' micrographic surgery for basal cell carcinomas on the eyelids and medial canthal area. II. Reconstruction and follow-up. *Acta Ophthalmol Scand* 2000; **78**:430–6.

25 Mosterd K, Krekels GA, Nieman FH *et al.* Surgical excision versus Mohs' micrographic surgery for primary and recurrent basal-cell carcinoma of the face: a prospective randomised controlled trial with 5-years' follow-up. *Lancet Oncol* 2008; **9**:1149–56.

26 Casparie M, Tiebosch AT, Burger G *et al.* Pathology databanking and biobanking in the Netherlands, a central role for PALGA, the nationwide histopathology and cytopathology data network and archive. *Cell Oncol* 2007; **29**:19–24.

27 Ge NN, McGuire JF, Dyson S *et al.* Nonmelanoma skin cancer of the head and neck II: surgical treatment and reconstruction. *Am J Otolaryngol* 2009; **30**:181–92.

28 Putter H, Fiocco M, Geskus RB. Tutorial in biostatistics: competing risks and multi-state models. *Stat Med* 2007; **26**:2389–430.

29 Rowe DE, Carroll RJ, Day CL Jr. Long-term recurrence rates in previously untreated (primary) basal cell carcinoma: implications for patient follow-up. *J Dermatol Surg Oncol* 1989; **15**:315–28.

30 Malhotra R, Huilgol SC, Huynh NT *et al.* The Australian Mohs database, part I: periocular basal cell carcinoma experience over 7 years. *Ophthalmology* 2004; **111**:624–30.

31 Oncoline. Plaveiselcelcarcinoom van de huid. [Cutaneous squamous cell carcinoma]. Dutch national guideline, version 1.0, 2011. Available at: https://www.oncoline.nl/plaveiselcelcarcinoom-van-de-huid (last accessed 8 January 2019)