ORIGINAL ARTICLE

Risk factors for complicated Mohs surgery in the South Sweden Mohs Cohort

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Abstract

Background Mohs micrographic surgery (MMS) is a precise, tissue-sparing surgical technique that offers superior cure rates compared to traditional surgical excision. However, the degree of difficulty of MMS depends on many variables, and consequently, the number of surgical stages required for each case is quite unpredictable.

Objectives To identify risk factors for complicated MMS, defined as MMS requiring ≥3 stages.

Methods In a cohort study design, data were prospectively collected from 612 patients that underwent MMS for basal cell carcinoma (BCC) at the Department of Dermatology, Skåne University Hospital, Lund, between 2009 and 2020. Univariate and multivariate logistic regression were used to estimate the risk of MMS requiring ≥3 stages. Due to the risk of multicollinearity between recurrent or incompletely excised BCC and previous treatments, a partially and a fully adjusted multivariate logistic regression model were constructed.

Results In fully adjusted multivariate analyses, age (odds ratio (OR) 1.02; confidence interval (CI) 95% 1.00–1.04), previous cryotherapy (OR 2.3; CI 95% 1.1–4.8), and >1 previous surgery (OR 3.4; CI 95% 1.5–7.7) were significantly associated with risk of complicated MMS. Recurrent BCC was associated with the risk of complicated MMS in partially adjusted multivariate analyses, but not in the fully adjusted analyses. In this highly selected cohort, histopathological subtype, and tumour localization were not associated with the risk of complicated MMS.

Conclusions Older age and tumours previously treated with cryotherapy or multiple prior surgeries increased the risk of MMS requiring ≥3 stages. Whether recurrent BCC is an independent risk factor for complicated MMS needs further evaluation. Knowledge of these risk factors may ameliorate the planning of Mohs surgeries.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Introduction

Basal cell carcinoma (BCC) is the most common type of skin cancer, and the worldwide incidence is increasing.[1,2] In Sweden, the incidence of BCC has also increased and, in 2017, approximately 54 000 histopathologically verified BCCs were registered in the Swedish Basal Cell Cancer Registry.[3] Although BCC rarely causes death, the tumours may cause significant morbidity due to local tissue destruction.[1,4] Moreover, BCC poses an economic burden on society given its high incidence rates.[5]

Surgery is considered the gold standard treatment for BCC. Mohs micrographic surgery (MMS) is a precise, tissue-sparing surgical technique characterized by intraoperative microscopic examination of all margins of the excised specimen.[6,7] Through complete microscopic control of the margins, MMS offers superior cure rates compared to traditional surgical excision.[8]

On the downside, MMS is resource-intensive and adequate planning and scheduling are therefore desirable to maintain a high availability and manage costs. The degree of difficulty of MMS depends on many variables and, consequently, the number of surgical stages and the time required for the surgery are quite unpredictable.[9,10]

To facilitate and ameliorate the planning and scheduling of MMS surgeries we aimed to identify risk factors for complicated surgery. This is important to preserve the limited resources for MMS and to provide patients with accurate information about the expected procedure and surgical outcome.

Patients and methods

Cohort

This cohort study was conducted at the Department of Dermatology, Skåne University Hospital, Lund, Sweden. Regional ethical review board approval (2013–482) was acquired before the start of the study. Data were prospectively collected on all patients undergoing MMS between January 2009 and October 2020. Written informed consent was obtained. No patients declined to participate. Indications for MMS were morpheaform primary (including incompletely excised) BCC in the face, infiltrative primary BCC in the face with ill-defined margins or at critical locations, and morpheaform or infiltrative recurrent BCC in the face. Complicated Mohs surgery was defined as MMS requiring 3 or more stages, without attributing weight to the location of the tumour or the reconstructive technique.

Data were collected using questionnaires, including information on age, gender, date of surgery, histopathological subtype, location, previous treatments, type of BCC (primary, recurrent, or incompletely excised), length and width of the tumour and final defect, reconstructive technique, and number of surgical stages. In mixed-type tumours, the most aggressive histopathological subtype was registered.

Statistical methods

Analyses were performed using Stata version 16.1 (StataCorp LLC, College Station, TX, USA). The primary outcome was number of MMS stages. For the purpose of analysis, the number of MMS stages was categorized as 1–2 or ≥3 stages.

Multivariate logistic regression models were constructed, using all exposure variables that were significantly associated with the outcome in univariate analyses, or that have previously been shown to be associated with the outcome (histopathological subtype and tumour localization).[11–15] Due to the risk of multicollinearity between recurrent or incompletely excised BCC and previous treatments we used 2 different models. Both models were adjusted for age, histopathological subtype (nodular/superficial, infiltrative, and morpheaform), tumour localization (cheek, nose, periorbital/ear, forehead/chin, and other), and tumour diameter (<10, 10–20, and >20 mm). In the partially adjusted model, type of BCC (primary, recurrent, or incompletely excised), any (unspecified) previous treatment, and specified previous treatments (cryotherapy (yes/no), number of previous surgeries (0, 1, and >1)) were separately analysed. In the fully adjusted model, all exposure variables were analysed simultaneously. *P*-values <.05 were considered statistically significant.

Results

Patient and tumour characteristics

Patient demographics are outlined in Table 1. Between 2009 and 2020, MMS was performed on 612 patients. The mean age was 67 years (range 24–94), and the majority were women (63%). Out of 610 patients (two missing values), 297 (48.7%) had a primary BCC and 223 (36.6%) had a recurrent BCC. The remaining 90 (14.8%) tumours were incompletely excised BCC. The distribution of histopathological subtypes was: morpheaform 72.6%, infiltrative 24.8%, and nodular or superficial 2.6%. The most

Table 1 Demographic data and tumour characteristics in the Mohs micrographic surgery cohort at the Department of Dermatology, Skåne University Hospital

Characteristics	Count *n* = 612
Age, years, mean (range)	67 (24–94)
Gender, *n* (%)	
Men	229 (37.4)
Women	383 (62.6)
Type of BCC*	
Primary, *n* (%)	297 (48.7)
Recurrent, *n* (%)	223 (36.6)
Incompletely excised, *n* (%)	90 (14.8)
Histopathological subtype, *n* (%)†	
Morpheaform	444 (72.6)
Infiltrative	152 (24.8)
Nodular or superficial	16 (2.6)
Tumour localization, *n* (%)	
Nose	386 (63.1)
Cheek	65 (10.6)
Forehead	49 (8.0)
Periorbital	35 (5.7)
Ear	12 (2.0)
Chin	5 (0.8)
Other (temple, perioral, and scalp)	60 (9.8)
Number of surgical stages, *n* (%)	
1	136 (22.2)
2	316 (51.6)
3	125 (20.4)
4	24 (3.9)
5	10 (1.6)
6	1 (0.16)
Tumour diameter, mm, mean (range)	17.8 (3–75)
Final defect diameter, mm, mean (range)	26.7 (8–95)
Reconstructive technique, *n* (%)	
Full-thickness skin graft	219 (36.7)
Primary closure	97 (16.3)
Transposition flap	89 (14.9)
Advancement flap	66 (11.1)
Rotation flap	47 (7.9)
Combination	45 (7.6)
Healing by secondary intention	33 (5.5)
Missing information	16 (2.6)

BCC, basal cell carcinoma; MMS, Mohs micrographic surgery.
*Data on primary, recurrent, or incompletely excised BCC missing for 2 patients.
†In mixed-type tumours, the most aggressive histopathological subtype was registered.

Table 2 Multivariate logistic regression analyses assessing the risk of ≥3 Mohs micrographic surgery stages

Exposure variables	Number of surgical stages* Partially adjusted model† OR (95% CI)	Number of surgical stages* Fully adjusted model‡ OR (95% CI)
Age§	**1.02 (1.00–1.04)**	**1.02 (1.00–1.04)**
Histopathological subtype§		
Morpheaform	Reference	Reference
Infiltrative	1.0 (0.7–1.6)	1.0 (0.6–1.5)
Nodular or superficial	0.8 (0.2–2.9)	0.8 (0.2–3.2)
Tumour localization§		
Cheek	Reference	Reference
Nose	1.4 (0.7–2.7)	1.4 (0.7–2.7)
Periorbital or ear	0.9 (0.4–2.4)	0.8 (0.3–2.1)
Forehead or chin	0.7 (0.3–1.7)	0.6 (0.2–1.5)
Other (temple, perioral, and scalp)	0.9 (0.4–2.1)	0.8 (0.3–2.0)
Tumour diameter (mm) §		
<10	Reference	Reference
10–20	1.1 (0.6–1.9)	1.1 (0.6–1.9)
>20	1.8 (1.0–3.3)	1.6 (0.8–3.0)
Type of BCC		
Primary BCC	Reference	Reference
Recurrent BCC	**2.5 (1.6–4.0)**	1.1 (0.4–2.5)
Incompletely excised	**2.2 (1.2–4.0)**	1.1 (0.4–2.7)
Previously treated, unspecified	**2.3 (1.5–3.5)**	-
Specified previous treatments		
Cryotherapy	**2.2 (1.4–3.9)**	**2.3 (1.1–4.8)**
Number of previous surgeries		
0	Reference	Reference
1	1.5 (0.9–2.5)	1.5 (0.6–3.3)
>1	**3.5 (2.1–5.8)**	**3.4 (1.5–7.7)**

OR (95% CI) = odds ratio (95% confidence interval); BCC = basal cell carcinoma.
Note bold letters are used for statistically significant (p=<.05) results.
*Categorized as 1–2 (reference) or ≥3 surgical stages.
†Partially adjusted model due to risk of multicollinearity between recurrent or incompletely excised BCC and previous treatments. These results are adjusted for age, histopathologic subtype, tumour localization, and tumour diameter.
‡Including all variables in the table except for unspecified previous treatment that was omitted due to multicollinearity with specified previous treatments.
§Adjusted for the type of BCC.

common number of MMS stages required to clear the tumour was 2 (52%, n = 316), 26% (n = 160) required 3 or more stages while only 5.7% (n = 35) required 4 or more stages. The mean tumour and final defect diameter were 17.8 and 26.7 mm, respectively.

Number of MMS stages

The results of the multivariate logistic regression analyses are presented in Table 2. The risk of ≥3 MMS stages increased by 2% for every year of increased age. In the partially adjusted model, recurrent and incompletely excised BCC significantly increased the risk of complicated surgery compared to primary BCC (odds ratio (OR) 2.5 and 2.2, respectively). Having received any previous treatment or previous cryotherapy both increased the risk of undergoing MMS in ≥3 stages about 2 times (OR 2.3; confidence interval (CI) 95% 1.5–3.5 and OR 2.2; CI 95% 1.4–3.9) while having had >1 previous surgery increased the risk 3.5 times (CI 95% 2.1–5.8). In the fully adjusted model, only previous treatment with cryotherapy (OR 2.3; CI 95% 1.1–4.8) and >1 previous surgery (OR 3.4; CI 95% 1.5–7.7) remained significantly associated with the risk of MMS in ≥3 stages. There were no associations between the number of surgical stages and histopathological subtype or tumour localization.

Discussion

Our findings suggest that older age and previous treatment with cryotherapy or >1 previous surgery are risk factors for complicated Mohs surgery. Recurrent BCC may convey an increased risk of MMS in ≥3 stages. However, the importance of a recurrence might be subordinate to the association between specified previous treatments and the risk of complicated MMS. Histopathological subtype and tumour localization were not

found to be associated with complicated surgery in the Lund Mohs cohort.

In accordance with several previous studies, we defined complicated surgery as requiring ≥3 MMS stages, without attributing weight to the tumour location.[13–16] Complicated surgery was associated with older age in this study, which is supported by some previous studies. In a study from 2018, Camarero-Mulas *et al*. compared MMS in patients younger and older than 80 years.[16] They showed that the elderly more often required a higher number of MMS stages.[16] Accordingly, Hoorens *et al*. showed that age >80 years is a strong predictor of MMS in ≥2 stages, but did not find it a significant predictor of ≥3 MMS stages.[15] In 2002, Batra *et al*. found that the mean number of stages required tended to increase by age, but the trend was not significant.[14] However, a significantly decreased risk of ≥3 MMS stages in patients younger than 35 years was detected.[14] Part of the explanation for the association between older age and many MMS stages could be that younger individuals often present with smaller tumours compared to the elderly.[16,17] It has also been found that the time to diagnosis is delayed in patients over 65 years.[18] This could result in larger and more complex BCCs at the time of diagnosis. Moreover, photodamaged skin is more common in the older patient group.[17] Thus, it might be difficult to outline the macroscopically visible tumour, possibly leading to additional surgical stages.

Recurrent BCC increased the risk of complicated surgery about 2 times compared to primary BCC in the partially adjusted model, which is consistent with several previous studies.[12,13,15] A possible explanation is that recurrent tumours growing in fibrosis result in an unpredictable growth pattern.[19] Interestingly, the effect of recurrent BCC disappeared when the results were adjusted for specified previous treatments. There might be several explanations for this finding; firstly, the analyses might be affected by multicollinearity between recurrent BCC and having received previous treatment. Secondly, the local practise at our department during MMS is to remove all fibrotic tissue, even if there is no visible tumour (due to the possible tumour growth beneath the fibrosis in incompletely excised BCC) in the removed specimen.[20] This procedure might lead to an increased number of stages in the incompletely excised but not clinically recurrent BCC. However, the results might also indicate that previously received treatment is a more important risk factor for complicated surgery than having had a diagnosed recurrence. The impact of previous treatment modalities on the risk for complicated surgery has not been well studied previously, and future research should further investigate the association between different treatment modalities, recurrent BCC, and the risk of complicated Mohs surgery.

Intriguingly, we neither found histopathological subtype nor tumour localization to be significantly associated with the number of MMS stages. These results contrast with those of previous studies that have shown that aggressive histopathological subtype and tumour localization in the H-zone convey an increased risk of complicated surgery.[11–15] The contradictive result of our study could be explained by the strict recommendations for MMS in Sweden where MMS is only available at three university hospital centres. The Swedish indications for MMS are morpheaform primary BCC in the face, infiltrative primary BCC in the face with ill-defined margins or at critical locations, and morpheaform or infiltrative recurrent BCC in the face.[21] Consequently, very few BCCs with nodular or superficial histopathological subtype are treated with MMS (only 2.6% of the tumours in our cohort), of which the majority are expected to be of unusual complexity, such as multiple recurrences or previous unsuccessful treatments.

Strengths and limitations

The main strength of this study is the prospectively collected comprehensive data on all patients that have undergone MMS in South Sweden between 2009 and 2020. The main limitation is that this is a single-centre study with a limited number of observations affecting the statistical power to more closely explore risk factors. The low number of and highly selected non-aggressive BCC subtypes in this study are likely not representative of the common behaviour of these tumours, and the results might therefore not be generalizable.

Conclusion

Older age and previous treatments, or by further specification, treatment with cryotherapy and >1 previous surgery are risk factors for complicated Mohs surgery. The risk of ≥3 MMS stages with recurrent BCC and specified previous treatments should be further investigated to entangle the separate contributions of these intertwined risk factors. Knowledge of risk factors may be useful to facilitate and ameliorate the planning of MMS surgeries and help to provide patients with more precise information about the planned procedure.

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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