

Risk Factors and Rate of Recurrence after Mohs Surgery in Basal Cell and Squamous Cell Carcinomas: A Nationwide Prospective Cohort (REGESMOHS, Spanish Registry of Mohs Surgery)

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Randomized studies to assess the efficacy of Mohs micrographic surgery in basal cell and squamous cell carcinomas are limited by methodological and ethical issues and a lack of long follow-up periods. This study presents the “real-life” results of a nationwide 7-years cohort on basal cell carcinoma and squamous cell carcinoma treated with Mohs micrographic surgery. A prospective cohort was conducted in 22 Spanish centres (from July 2013 to February 2020) and a multivariate analysis, including characteristics of patients, tumours, surgeries and follow-up, was performed. A total of 4,402 patients followed up for 12,111 patient-years for basal cell carcinoma, and 371 patients with 915 patient-years of follow-up for squamous cell carcinoma were recruited. Risk factors for recurrence included age, non-primary tumours and more stages or unfinished surgeries for both tumours, and immunosuppression for squamous cell carcinoma. Incidence rates of recurrence were 1.3 per 100 person-years for basal cell carcinoma (95% confidence interval 1.1–1.5) and 4.5 for squamous cell carcinoma (95% confidence interval 3.3–6.1), being constant over time (0–5 years). In conclusion, follow-up strategies should be equally intense for at least the first 5 years, with special attention paid to squamous cell carcinoma (especially in immunosuppressed patients), elderly patients, non-primary tumours, and those procedures requiring more stages, or unfinished surgeries.

Key words: basal cell carcinoma; squamous cell carcinoma; Mohs surgery; recurrence; risk factors.

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SIGNIFICANCE

Mohs micrographic surgery is the treatment of choice for high-risk basal cell carcinoma and squamous cell carcinoma. Its efficacy and recurrence risk factors should be studied in large prospective cohorts. This paper presents the results of the first European nationwide 7-years cohort on basal cell carcinomas and squamous cell carcinomas treated with Mohs micrographic surgery. The results show that recurrences are low, but do occur. In conclusion, follow-up should be equally intense for at least the first 5 years, and more intense in patients with squamous cell carcinoma (especially immunosuppressed patients), elderly patients, recurrent and persistent tumours, and in those patients who have had procedures requiring more stages or unfinished surgeries.

Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common skin malignancies (1, 2). The incidence of both tumours is increasing (3–5). Mohs micrographic surgery (MMS) combines a high cure rate with complete margin examination and healthy tissue conservation (6). MMS is the first-line therapy in high-risk BCC and SCC (such as those which are recurrent or incompletely excised, mid-facial located, or which show aggressive histological features or perineural invasion) (7–10).

Randomized clinical trials have demonstrated the greater efficacy of MMS compared with standard surgery for recurrent BCC (11–13) and tissue-sparing with MMS (14).

Some factors have been reported to be associated with recurrence, such as treating recurrent tumours, multiple stages of MMS excision or Breslow depth (8, 15, 16).

However, risk factors have not been consistent between studies.

Previous observational studies describing the effectiveness of MMS to treat BCC and SCC in real-life are subject to important caveats, in that they are mainly single-centre studies or retrospective in nature, with uncertain or large numbers of losses to follow-up, and different follow-up periods (17). The need for a prospective study with comprehensive data capture and standardized follow-up for SCC has been highlighted recently (18).

We report here the results of the first European nationwide 7-year prospective cohort on MMS, REGESMOHS (Spanish registry of Mohs Surgery). The aim of this study is to describe the risk factors for recurrence after MMS for BCC and SCC, the effectiveness in terms of rates for recurrence, and the change in recurrence rates over time.

MATERIALS AND METHODS

A detailed description of the *Registro Español de Cirugía de Mohs* (REGESMOHS) prospective cohort has been published previously (19, 20). All consecutive patients considered for MMS from 22 participating Spanish hospitals were included in the registry. The sample represented a large percentage of all dermatology clinics performing MMS (more than 1 intervention per week) in Spain (21).

The registry was established in July 2013 to collect information on the characteristics of patients, tumours, and surgeries performed. Histological markers of aggressive tumours and level of invasion were registered. The location of the tumour was classified according to risk areas (H-M-L; 7). Patient follow-up was performed, according to usual practice. Data had to be updated in the registry within 1 month after surgery and at least once a year. If patients missed appointments, they were contacted by telephone. Recurrences were diagnosed clinically (tumour reappearance within the scar) and confirmed histologically in most cases. All researchers received training on the study methods before joining the registry. The information was collected online, and its quality was systematically checked through monthly online monitoring. On-site monitoring was performed periodically.

The duration of the study was based on pre-planned sample size calculation. As the recruitment was slower than expected, the duration of the study was increased by 1 year.

Statistical analysis

This report included only those patients who underwent surgery for BCC or SCC. A descriptive analysis was performed using onset of a first recurrence as the main outcome. Continuous variables were expressed as means with standard deviations for symmetrical distributions, or medians and interquartile ranges for asymmetrical variables. Categorical variables were expressed as total numbers with percentages. Descriptive data were compared individually between analysis groups and recurrence using the Mann–Whitney *U* test (or the Student's *t*-test, when necessary) and Pearson's χ^2 test (or Fisher's exact test when necessary) depending on the distribution of the variables.

Incidence rates of recurrences with 95% confidence intervals (95% CI) were calculated by dividing the number of recurrences by the patient-years of follow-up. Risk factors associated with recurrences were estimated using a mixed-effect Poisson regression model considering the hospital as a random effect and the year of surgery as a fixed effect. Forward selection models were

constructed using those variables with *p*-values <0.2 in the crude models. Final models were chosen using the likelihood-ratio test.

Cumulative incidence curves were used to represent survival time from surgery to recurrence of tumour, under a competing risk survival scenario. Death was considered the main competing factor for recurrence. Data were analysed using Stata 16.1 (StataCorp, College Station, TX, USA) and *p*-values less than 0.05 were considered statistically significant. REGESMOHS was approved by the Clinical Research Ethics Committee in Navarra (EO11/2013).

RESULTS

Characteristics of patients, tumours and surgeries

From July 2013 to February 2020, 5,226 patients were included in the REGESMOHS registry. A total of 453 patients had diagnoses other than BCC and SCC and were excluded from the study, leaving 4,402 patients with BCC and 371 with SCC. Their demographic characteristics are described in **Table I**.

Most procedures were performed under local anaesthesia, but sedation or general anaesthesia were used in some patients (10%) (**Table II**).

The fresh-tissue technique was performed in 93% of cases and slow Mohs in 7% of cases. Free margins were achieved in 57% of the surgeries with 1 stage, 11% required 3 or more stages and 2% did not achieve complete excision (unfinished surgeries). Dermatologists participated in the interpretation of histology (71%), commonly with a pathologist (87%), and reconstructed the defect (97%) in most cases.

Risk factors for recurrence after Mohs surgery

For BCC, univariate analysis showed an association between recurrence and being elderly, tumours of longer duration, recurrent or persistent tumours, previous therapeutic attempts (both surgical and non-surgical), asymmetry, and markers of complex surgery (longer surgery, higher number of stages, depth of the defect, hospitalization, and surgical morbidity) (**Tables I–III**). Since many of the variables measure similar domains, multivariate analysis reduced the number of variables associated with recurrence. After adjustment, for every 10 years of increasing age, the risk of recurrence increased by 24%. Persistent and recurrent tumours, as well as those requiring a higher number of surgical stages had a nearly 2-fold risk of recurrence. Unfinished surgery was the variable showing the strongest association with recurrence (IRR [incidence rate ratio] 4.49 (95% CI 2.33–8.66)).

Regarding SCC, univariate analysis showed an increased risk of recurrence for immunosuppressed patients, recurrent or persistent and asymmetrical tumours, and patients who required longer interventions, with deeper extent of the tumour and more surgical stages. Multivariate analysis showed that the main risk factors for recurrence were immunosuppression (IRR 2.87

Table I. Description of the study population and univariate risk factors for recurrence: characteristics of patients and tumours

Characteristics	Study population* n = 4,773	Recurrence in BCC			Recurrence in SCC		
		No n = 4,248 (%)	Yes n = 154 (%)	p-value	No n = 330 (%)	Yes n = 41 (%)	p-value
Patients							
Sex (male), n (%)	2,458 (52)	2,121 (50)	79 (51)	0.7385	225 (68)	33 (80)	0.1064
Age, years, median (IQR)	70.8 (59.3-79.5)	70.6 (59.4-79.5)	74.5 (66.5-80.7)	0.0029	76.9 (65.8-83.1)	75 (69.5-81.9)	0.8286
Immunosuppression, n (%)	149 (3)	109 (3)	8 (5)	0.0658	22 (7)	10 (24)	0.0010
Diabetes mellitus, n (%)	562 (12)	478 (11)	20 (14)	0.4034	57 (18)	7 (17)	0.9139
Multiple tumour syndromes, n (%)	113 (2)	100 (2)	3 (2)	1.0000	10 (3)	0 (0)	0.6100
Tumours							
Time since appearance, months, median (IQR)	14.3 (6.8-34.2)	14.3 (6.7-33.4)	19.3 (8.4-37)	0.0283	9.2 (5-19.5)	9.3 (4.1-28.1)	0.8384
Size, mm, n (%)				0.3299			0.1679
< 10	1,929 (41)	1,765 (42)	58 (38)	NA	98 (31)	8 (20)	NA
≥ 10	2,746 (59)	2,398 (58)	93 (62)	NA	223 (69)	32 (80)	NA
Type, n (%)				0.0000			0.0295
Primary	3,008 (63)	2,720 (64)	70 (45)	NA	201 (61)	17 (41)	NA
Recurrent	979 (21)	857 (20)	47 (31)	NA	61 (18)	14 (34)	NA
Persistent	786 (16)	671 (16)	37 (24)	NA	68 (21)	10 (24)	NA
Zone, n (%)				0.0482			0.4111
H-Area	3,813 (80)	3,441 (82)	114 (74)	NA	232 (71)	26 (63)	NA
M-Area	901 (19)	756 (18)	39 (25)	NA	91 (28)	15 (37)	NA
L-Area	26 (1)	20 (0)	1 (1)	NA	5 (2)	0 (0)	NA
Histologically aggressive, n (%)	3,402 (71)	3,028 (71)	104 (68)	0.3132	239 (72)	31 (76)	0.6656
Previous surgical treatments, n (%)	856 (18)	719 (17)	48 (31)	0.0000	77 (23)	12 (29)	0.4074
Previous non-surgical treatments, n (%)	232 (5)	190 (4)	14 (9)	0.0058	22 (7)	6 (15)	0.1065

*Some proportions cannot be calculated from the table due to few missing data on the variable.

BCC: basal cell carcinoma; SCC: squamous cell carcinoma; NA: non-applicable; IQR: interquartile range. Bold indicates statistically significant results.

Table II. Univariate risk factors for recurrence: characteristics of surgery

Surgery characteristics	Recurrence in BCC			Recurrence in SCC		
	No n = 4,248 (%)	Yes n = 154 (%)	p-value	No n = 330 (%)	Yes n = 41 (%)	p-value
Time from pre-surgical consultation to surgery, months, median (IQR)	1.5 (0.9-2.6)	1.6 (1-2.6)	0.5187	1.1 (0.5-2.2)	0.7 (0.4-1.7)	0.1934
Time in operating room, min*, median (IQR)	75 (60-100)	90 (60-120)	0.0212	80 (55-110)	90 (60-122)	0.0324
Defect difference (major axis - minor axis in mm), median (IQR)	4 (1-8)	5 (2-10)	0.0179	5 (0-10)	10 (5-20)	0.0030
Hospitalization, n (%)	689 (17)	39 (27)	0.0017	94 (30)	15 (44)	0.1035
Mohs surgery types, n (%)			0.5458			0.079
Fresh-tissue technique	4,025 (95)	143 (93)	NA	237 (72)	24 (59)	NA
Slow Mohs	220 (5)	10 (7)	NA	93 (28)	17 (41)	NA
Number of stages, n (%)			0.0002			0.0002
1	2,407 (57)	62 (41)	NA	204 (62)	15 (37)	NA
2	1,360 (32)	63 (41)	NA	104 (32)	17 (41)	NA
3 or more	458 (11)	27 (18)	NA	20 (6)	9 (22)	NA
Number of blocks, n (%)			0.3206			0.2745
1	391 (10)	8 (6)	NA	35 (11)	2 (5)	NA
2	1,115 (28)	34 (27)	NA	62 (20)	5 (14)	NA
3 or more	2,464 (62)	86 (67)	NA	211 (69)	30 (81)	NA
Unfinished surgery	56 (1)	11 (7)	0.0000	11 (3)	7 (17)	0.0001
Extent level, n (%)			0.0128			0.0048
Epidermis	26 (1)	4 (3)	NA	10 (3)	2 (5)	NA
Dermis	2,049 (50)	63 (43)	NA	106 (33)	9 (22)	NA
Hypodermis	1,678 (41)	61 (41)	NA	138 (44)	11 (27)	NA
Fascia	108 (3)	6 (4)	NA	15 (5)	6 (15)	NA
Muscle	242 (6)	11 (7)	NA	39 (12)	11 (27)	NA
Bone	27 (1)	3 (2)	NA	9 (3)	2 (5)	NA
Specialist who repaired, n (%)			0.8831			0.7324
Dermatologist	4,149 (98)	148 (98)		316 (96)	41 (100)	
Plastic surgeon	36 (1)	1 (1)		3 (1)	0 (0)	
Other	45 (1)	2 (1)		11 (3)	0 (0)	
Reconstruction technique, n (%)			0.0294			0.1140
Healing by secondary intention	484 (11)	17 (11)	NA	68 (21)	10 (24)	NA
Direct closure	1,128 (27)	42 (27)	NA	87 (26)	10 (24)	NA
Flap	1,993 (47)	58 (38)	NA	103 (31)	10 (24)	NA
Graft	498 (12)	31 (20)	NA	62 (19)	6 (15)	NA
Complete closure	142 (3)	5 (3)	NA	10 (3)	5 (12)	NA
Dermatologist participates in the interpretation, n (%)	3,129 (74)	91 (59)	0.0001	202 (61)	21 (51)	0.2091
Pathologist participates in the interpretation, n (%)	3,221 (76)	140 (92)	0.0000	296 (90)	38 (93)	0.5804
Intra or post-surgical morbidity, n (%)	277 (7)	16 (11)	0.0478	26 (8)	6 (15)	0.1535

*Time waiting outside operating room was excluded.

BCC: basal cell carcinoma; SCC: squamous cell carcinoma; NA: non-applicable; IQR: interquartile range. Bold p-values indicate statistically significant results.

Table III. Multivariate analysis: risk factors for recurrence

Characteristics	Incidence rate ratio 95% CI	p-value
BCC		
Age, in years	1.02 (1–1.03)	0.0099
Type		
Primary	Reference	
Recurrent	1.78 (1.20–2.63)	0.0040
Persistent	1.89 (1.25–2.86)	0.0025
Number of stages		
1	Reference	
2	1.62 (1.11–2.35)	0.0116
3 or more	1.93 (1.17–3.17)	0.0098
Unfinished surgery	4.49 (2.33–8.66)	0.0000
Pathologist participates in the interpretation Technique	2.42 (1.01–5.78)	0.0469
Healing by secondary intention	Reference	
Direct closure	1.65 (0.89–3.05)	0.1096
Flap	0.97 (0.53–1.78)	0.9319
Graft	1.76 (0.93–3.32)	0.0822
Complete closure	0.72 (0.25–2.03)	0.5303
SCC		
Immunosuppression	2.87 (1.28–6.45)	0.0106
Number of stages		
1	Reference	
2	3.83 (1.69–8.71)	0.0014
3 or more	4.15 (1.41–12.26)	0.0100
Unfinished surgery	6.71 (2.74–16.42)	0.0000
Defect diff. (mm)	1.03 (1.01–1.05)	0.0060

95% CI: 95% confidence interval; BCC: basal cell carcinoma; SCC: squamous cell carcinoma; NA: non-applicable; Defect diff.: difference between major and minor axis, mm: a marker of asymmetrical growth. Bold p-values indicate statistically significant results.

(95% CI 1.28–6.45)), a larger number of stages, and unfinished surgery, which increased the risk of recurrence by nearly 7 times (Table III).

In the overall population, the adjusted IRR of recurrence was 2.53 (95% CI 1.74–3.69) times higher for SCC than for BCC.

Incidence of recurrence after Mohs surgery, diagnosis, and therapeutic approach

Patients were followed-up for a mean \pm standard deviation of 2.7 ± 1.6 years, reaching 12,111 patient-years for the

Table IV. Incidence of recurrence, diagnosis, and approach

	BCC 4,402 (84.2)	SCC 371 (7.1)
Patient-years follow-up, n (%)	12,111	915
Average follow-up time, years, mean (SD)	2.8 (1.6)	2.5 (1.6)
Patients lost to follow-up prior to recurrence, n (%)	688 (15.6)	45 (12.1)
Deaths, n (%)	155 (3.5)	47 (12.7)
Recurrences, n (%)	154 (3.5)	41 (11.1)
All tumours ^a	1.3 (1.1–1.5)	4.5 (3.3–6.1)
Primary tumours ^a	0.9 (0.7–1.2)	3.2 (2.0–5.1)
Recurrent tumours ^a	1.8 (1.4–2.4)	7.7 (4.6–13.1)
Persistent tumours ^a	2.0 (1.4–2.7)	5.1 (2.7–9.4)
Number of recurrences		
1	136 (88)	33 (80)
2	13 (8)	7 (17)
3 or more	5 (2)	1 (2)
Diagnosis		
Clinical	21 (25)	8 (36)
Histological	63 (75)	14 (64)
Treatment		
Re-intervention	116 (75)	24 (59)
Radiotherapy	10 (6)	10 (24)
Chemotherapy	1 (0.7)	NA
Hedgehog inhibitors	6 (4)	NA
Tyrosine kinase inhibitors	2 (1.3)	NA
Other options	17 (11)	5 (12)
Palliative care	2 (1.3)	2 (5)

^aIncidence per 100 person-years 95% confidence interval. BCC: basal cell carcinoma; SCC: squamous cell carcinoma; NA: non-applicable.

BCC group and 915 patient-years for the SCC group. During follow-up, 3.5% of patients with BCC and 12.7% of SCC patients died (4.2% mortality) and 788 patients (15%) were lost to follow-up prior to any recurrence. Recurrence was histologically confirmed in most cases (75% of BCCs and 64% of SCCs).

For patients with BCC, 3.5% experienced recurrences ($n=154$), with an incidence of 1.3 cases per 100 person-years (95% CI 1.1–1.5). SCC patients presented a higher recurrence rate ($n=41$; 11%; 4.5 cases per 100 person-years; 95% CI 3.3–6.1) (Table IV). The cumulative incidences of recurrence for both BCC and SCC are shown in Fig. 1, which shows that the rate of recurrence

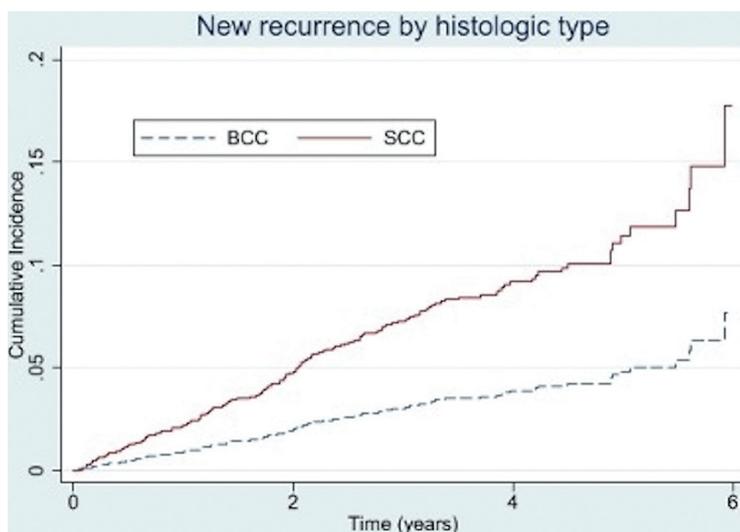


Fig. 1. Cumulative incidence curves of recurrence in basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) patients treated with Mohs micrographic surgery (MMS). Each line represents the probability of cumulative recurrence over time considering death as a competing risk factor. The linear pattern implies a constant rate.

increases consistently over time for BCC and SCC, but is approximately 2-fold higher in SCC groups in the period from 0 to 5 years.

Among recurrent cases, 10% of BCCs and 19% of SCCs experienced 2 or more recurrences. The most frequent treatment for recurrence was a repeat operation (75% in BCC and 59% in SCC), with radiotherapy also being a common option for SCC (24%) (Table IV).

DISCUSSION

We report here the results from REGESMOHS, which is, to our knowledge, the first European nationwide prospective cohort on MMS. Several risk factors for recurrence are described, including patient characteristics and tumour and surgical variables, which can help identify patients requiring closer monitoring. Overall, the study reports low recurrence rates for BCC and SCC treated with MMS, supporting the efficacy of this treatment modality.

This study has several strengths. It is prospective, multicentre, and representative of MMS in Spain (21). It reproduces previous research in a different setting and has been performed under strict quality standards, including pre-training of participants, and continuous monthly on-line monitoring. Nevertheless, some limitations of this study should be noted. Firstly, losses to follow-up represent an important limitation in long-term cohorts. However, losses of 15%, as in the current study, are commonly considered acceptable in long-term studies. Secondly, as it was a nationwide study, a certain degree of heterogeneity is possible in the patients and surgical methods described. To mitigate this effect, a multilevel analysis approach was taken, considering the centre as a random effect. This weakness is balanced with increased external validity. Two considerations should be taken into account when comparing results with other countries. Most hospitals participating in the study belong to the Spanish public health system, which presents, in certain locations, waiting lists of months. Another difference is that, in Spain, pathologists frequently participate in MMS interpretation, which differs from other countries, such as the USA, where dermatologists perform the histological analysis. Both facts could have influenced results, and thus they were described in the results.

Risk factors for recurrence

The main risk factors for recurrence of BCC, in order of decreasing importance, were unfinished surgery, recurrent or persistent tumours, and the need for more than 2 stages (as a measure of tumour infiltration). Other tumour characteristics classically associated with poor prognosis, such as aggressive histology or size, become less important when performing MMS and were not relevant in our models. These results agree with previous studies, such as the Australian nationwide series (8, 15,

22). The fact that participation of a pathologist in the interpretation was also associated in the current study with an increased risk of recurrence was probably due to this factor acting as a proxy for more difficult diagnosis or increased tumour depth, without implying causality.

The main risk factors for recurrence of SCC were unfinished surgery, the number of stages needed, immunosuppression and asymmetrical growth. SCC diagnosis is also a risk factor for recurrence, as these lesions are twice as likely to recur than are BCC lesions. Previous studies have included the number of stages as a predictor of recurrence (23). Marrazzo et al (24) reported that, in high-risk cutaneous SCCs, invasion beyond the subcutaneous fat and poor histological differentiation were positively associated with local recurrence, nodal metastasis and disease-specific death. Tschetter et al. (16) have also recently found Breslow depth to be statistically associated with those 3 outcomes, while they found no association between recurrence and perineural invasion. The presence of immunosuppression is a known risk factor for death in SCC (25).

Rates of recurrence

Rates of recurrence for both tumours were 1.3 (95% CI 1.1–1.5) recurrences per 100 person-years for BCC and 4.5 (95% CI 3.3–6.1) for SCC. The rates of recurrence were constant over the follow-up period. In terms of risk, there was a 3.5% risk of recurrence for BCC after a mean follow-up of 2.8 years, and 11.1% for SCC after a mean follow-up of 2.5 years.

Although the risk of recurrence can be affected by the population studied, there are no large differences between the current study and those previously published in the USA or Australia (20).

Few prospective studies have previously estimated the recurrence risks for BCC and SCC after MMS.

The most quoted study, by Leibovitch et al. (15), reported an overall recurrence risk of 2.6% in 3,370 Australian patients with BCC followed for 5 years. This is equivalent to a rate of 0.5 recurrences per 100 person-years. However, the 3,370 patients included in their paper represent only 30% of the recruited population. The percentage lost to follow-up in this study was not reported, and it is likely to represent an important threat to its validity. Other authors have reported recurrence risks of between 0.7% and 6.7% for BCC at different time-periods (22, 26–31), but these data come from retrospective studies (26–31), from single centres (26–30), report results in limited areas of the body (30, 31), have few events, leading to imprecise results (26), include no description of losses to follow-up and other uncertain methods (27–29), describe risks instead of rates (26–31), or have highly variable lengths of follow-up (30).

The same Australian group reported an overall 5-year recurrence risk of 3.9% in 381 SCC patients who com-

pleted a 5-year follow-up (8, 32). This is equivalent to a rate of recurrence of 0.7 per 100 person-years. Again, these data were calculated on the 30% of the recruited patients who completed 5 years of follow-up. The results in the remaining 70% were not reported, nor were the losses to follow-up; hence these estimates have a very low validity. Recently, Tschetter et al. (16) presented a prospective, multicentre analysis of 637 patients from the USA who were undergoing MMS for invasive SCC, with a risk of recurrence of 2.3% after a mean follow-up of 4 years, with 8% of losses to follow-up and 22% of deaths in the study period. Other results of recurrence describe values between 1.2% and 8% for SCC (23, 27, 31, 33, 34). Unfortunately, many of these are retrospective studies (23, 27, 31, 33, 34), have variable follow-up periods, and report risks at different times that are difficult to compare (23, 31, 34). Furthermore, they do not clearly describe their methods and losses to follow-up (23, 27, 31, 33, 34), or represent outcomes of 1 or a small group of dermatologists (23, 33, 34) or a certain area of the body (31, 33), leading to poor internal or external validity.

It is interesting to note that the rates of recurrence, although low, remained constant over the study period, implying the need for the same intensity of follow-up at least during the first 5 years after surgery. Previous reports have also highlighted the need to follow patients for longer than 5 years (22).

We believe that the improved methods of the multicentre prospective cohort in the current study explain the higher, and more realistic, rates of recurrence. The external validity of the current study is also increased, as the study was carried out nationwide, in a country with a long experience of MMS and a case-mix similar to that reported in other countries (20, 21).

We describe here the “real-life” results of MMS for BCC and SCC, which are more likely to be valid than previous findings. The recurrence rate was low for BCC (1.3 recurrences per 100 person-years) and higher for SCC (4.5 per 100 person-years). Risk factors for recurrence include: age, non-primary tumours, procedures requiring more stages of surgery, or unfinished surgery for both tumours, and immunosuppression for SCC. The rate of recurrence was constant over the study period. These results should be taken into consideration when informing patients of the prognosis, planning follow-up, and might be useful when making decisions about additional systemic therapy. They also highlight the difficulty of performing randomized clinical trials in these patients due to the low recurrence rates.

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