Original Article

Non-Melanoma Skin Cancer Treated with Mohs Micrographic Surgery in Thailand

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Background: Long-term follow-up, complications, and patient satisfaction are essential outcome measures regarding the benefits of Mohs micrographic surgery [MMS] for treating non-melanoma skin cancers [NMSCs].

Objective: To report risk factors, clinical findings, and follow-up outcomes of all NMSC patients treated with MMS.

Materials and Methods: The present retrospective study included all patients in the outpatient Dermatology Clinic of Siriraj Hospital, Bangkok, Thailand, with NMSC treated with MMS between 2008 and 2013. The outcomes measured were patient demographic data, duration of tumor, recurrence of tumor before MMS, number of lesions, risk factors for developing skin cancer, histological type and subtype, location of tumor, pre-operative and post-operative size, method of closure, operative time, 5-year recurrence rate after MMS, complications, and patient satisfaction.

Results: The present study included 108 patients (63% females and 37% males) with a mean age of 70±12 years (range 36 to 93 years). The mean duration of tumor was 37±60 months (range 0.5 to 480 months). Basal cell carcinoma [BCC] comprised 95.1% of cases, whereas squamous cell carcinoma [SCC] was 4.9%. The significant risk factor for both BCC and SCC was sun exposure. The most common locations for both BCC and SCC were the head and neck regions. The most common subtype for BCC was a non-aggressive subtype, 47%. The most commonly used method of closure was second intention, 28 cases (22.8%). The mean operative time was 116.13 minutes (range: 30 to 360 minutes). During the longest follow-up time (60 months), the recurrence rate was 0.81%. There were no major complications. The majority (96.4%) of patients gave a 75% to 100% satisfaction rate after surgery.

Conclusion: The present study demonstrates less than one percent recurrence rate in NMSCs treated with MMS and the necessity of margin control in high-risk tumors.

Keywords: Non-melanoma skin cancer, Mohs micrographic surgery

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Non-melanoma skin cancer [NMSC] has an incidence of around three million cases in the United States annually[1]. Basal cell carcinoma [BCC] accounts for the majority of NMSCs among white populations in the United States and Australia, whereas squamous cell carcinoma [SCC] accounts for the second most common NMSC[2]. In Thailand, BCC and SCC account for 23.4% to 60.0% and 20.0% to 61.4% of all skin cancers, respectively, in various skin cancer registries[3,4].

The significant identifiable risk factor for both BCC and SCC is sun-exposure, giving predilection sites on sun-exposure areas including the head and neck[5]. For BCC, a history of sunburn or intense sun-exposure rather than chronic sun-exposure signifies a risk factor. Most BCCs are indolent, with a slow-growing rate and low percentage of neural invasion and metastasis, but some subtypes with aggressive behavior exists[6]. In contrast to BCC, SCC is more aggressive, with a much higher rate of metastasis[7]. Both BCC and SCC require complete tumor removal and margin control along with conservation of function and cosmetic concerns[8].

There are several treatment modalities for treating BCCs and SCCs including surgical and non-surgical ones, all with their pros and cons. Mohs micrographic surgery [MMS] is a modality of treating skin cancers that give complete margin control with a clearance rate of 99% for primary tumors and 95% for recurrent NMSC[9,10]. The technique was based on constructing a tissue map followed by color coding of the excised tissue. Frozen sections of the entire outer margin in continuous layer were prepared, and the tissue was

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stained by hematoxylin and eosin. A trained Mohs technician performed all frozen-section preparation and all the slides were then reviewed by Mohs surgeon. Residual tumor, if any, was mapped, and serial levels were excised until the surgical margins were all free of tumors. There is also the advantage of conserving tissue from MMS when comparing to conventional surgical excision, resulting in an excellent outcome of function and cosmesis[11]. For BCCs, MMS is widely used for high-risk tumors, those located on the H-zone of the face, recurrent and incompletely excised tumors, BBC with aggressive histological characteristics, BCC with perineural invasion, and BCC with tumor size exceeding 2 centimeters. Indications for SCCs are similar to BCCs with additional locations on the penis and lesions occurring on chronic scars, which carry a higher risk for metastasis and local recurrence[12]. However, there have been no report on risk factors, clinical findings, and cure rates of NMSC treated with MMS in Thai population.

The objectives of the present study were to describe risk factors, clinical findings, and follow-up outcomes of all NMSC patients treated with MMS at Siriraj Hospital, Bangkok, Thailand.

Materials and Methods

The authors conducted a descriptive, retrospective, cross-sectional study on patients treated with MMS at the outpatient Skin Clinic, Department of Dermatology, Siriraj Hospital, Bangkok, Thailand, between 2008 and 2013. The inclusion criteria were all patients with histologically-confirmed NMSC including BCC and SCC treated with MMS. Data were collected from medical records. The information recorded were patient demographic data, duration of tumor, recurrence of tumor before MMS, number of lesions, risk factors for developing skin cancer, histological type and subtype, location of tumor, pre-operative and post-operative size, method of closure, operative time, 5-year recurrent rate after MMS, and complications. Additional information that had not been found in medical records, regarding the recurrent rate and patient satisfaction were obtained from the patients themselves, via phone call. The exclusion criteria were patients with insufficient data and/or those who refused to answer the questions via phone call.

All data were tabulated and analyzed by using SPSS statistical analysis software version 17. The categorical were summarized as simple frequencies and percentages. The numerical variables were described by mean and standard deviation.

The present study was approved by the Ethical Committee on Research Involving Human Subjects, Faculty of Medicine, Siriraj Hospital, Mahidol University, and conformed to the Guidelines of the 1975 Declaration of Helsinki. Written informed consents were obtained from all study subjects.

Results

The authors included 108 patients, with a total of 123 MMS performed for treating NMSC between September 2008 and August 2013. Twenty-three patients (21.3%) had more than one tumor. The mean age was 70±12 years (median 72 years, range 36 to 93 years). The mean duration of tumor before MMS was 37±60 months (median 24 months, range 0.5 to 480 months). Regarding other treatments before MMS, most patients (114, 92.7%) received none, whereas seven (5.7%) were treated with topical destructive remedies, laser, electro-surgery, or incomplete excisions.

The mean operative time was 116.13±68.6 minutes (median 105 minutes, range 30 to 360 minutes), with missing data in 45 patients. Most had no immediate or short-term complications (115, 93.5%), except for eight (6.5%) which had minor complications such as bleeding, wound infection, and bradycardia which was due to the patient taking beta-blockers.

For the follow-up part, the mean follow-up time after MMS was 20.86±15.75 months (median 15 months, range 1 to 60 months) with missing data in four patients. Most patients had no long-term symptoms (118, 95.9%), except for two patients, one patient (0.8%) with pain and one (0.8%) with itching. Only 0.81% of patients showed signs of recurrence upon follow-up, four patients with missing data. Most patients had no long-term complications (89, 72.4%), although 30 (24.3%) had minor long-term complications. Regarding patients' satisfaction, 24 (22.2%) had missing data, and those with valid data, 81 patients (96.4%) had 76% to 100% satisfaction and three patients (3.6%) had 51% to 75% satisfaction.

The other demographic data of patients and characteristic of tumors and procedures are demonstrated in Table 1.

Discussion

BCC is a common skin tumor, accounting for most of the NMSC with an increasing incidence worldwide. Although it is predominantly found on sun-exposed skin of white-skinned individuals, it can also occur in Asian populations[13]. The age on presentation of most BCC patients was between 50 to 80 years with male

Table 1. Demographic data of patients receiving MMS (n = 108)

Demographic data	Number (%)
Sex	
Male	40 (37.0)
Female	68 (63.0)
Tumor	
Primary	111 (91.7)
Recurrent	10 (8.3)
Risk factors*	
Significant sun exposure	67 (62.0)
Outdoor occupation	20 (18.5)
Heavy alcohol consumption	18 (16.6)
History of smoking and/or current smoker	17 (15.7)
Immunocompromised	4 (3.7)
Type of tumors	
BCC	117 (95.1)
- Non-aggressive subtype (micronodular, morpheaform)	55 (47.0)
- Aggressive subtype (superficial, nodular)	32 (27.4)
- Unidentified subtype	30 (25.6)
SCC	6 (4.9)
- Well-differentiated	1 (16.7)
- Moderately-differentiated	2 (33.3)
- Poorly-differentiated	3 (50.0)
Location	
Nose	50 (40.7)
Cheek	32 (26.0)
Forehead	12 (9.8)
Lips	8 (6.5)
Temples	7 (5.7)
Eyelids	5 (4.1)
Pinna	4 (3.3)
Zygomas	2 (1.6)
Chin	1 (0.8)
Scalp	1 (0.8)
Upper cutaneous lips	1 (0.8)
No. of stages	
1 stage	67 (54.5)
2 stages	49 (39.8)
≥3 stages	7 (5.7)
Closures	
Second intention	28 (22.8)
Complex linear closure	32 (26.0)
Graft	15 (12.2)
Flap	11 (8.9)
Biologic or synthetic skin substitutes	2 (1.6)
Mixed closures	7 (5.7)
Referred to plastic or ophthalmologic surgeon	13 (10.5)

BCC = basal cell carcinoma; MMS = Mohs micrographic surgery; SCC = squamous cell carcinoma

* Some patients may have more than 1 risk factor

predominance[14]. In our study, the mean age was 70±12 years (median 72 years, range 36 to 93 years) which is similar to previous reports. However, our study has a female predominance (63.0%), which differs from previous reports, maybe due to more concern among females[15].

Most lesions of BCCs arise on the head and neck regions. Scrivener et al[16] published a large retrospective study of 13,457 patients from a referral center in France, which found that 85% of lesions were located on the head or neck. Similar to a few other reports[17,18], all of the cases treated with MMS in our research had lesions on the head or neck region with the predominant site being on the nose (40.7%). The predilection site on the head and neck region may be due to more sun-exposure, which is the significant risk factor in tumor pathogenesis. However, in our cases, all lesions treated were on the head or neck possibly due to treatment bias, hence, mid-facial BCCs are more likely to be high-risk, with Mohs surgery the treatment of choice.

The histology of BCCs is composed of a tumor of basaloid cells with peripheral palisading from several histological subtypes. Aggressive subtypes are composed of morpheaform infiltration and baso-squamous, which are less common and account for only 18.5% of the cases in the literature[19]. In our study, the aggressive subtype was found in 32 lesions amounting to 27.4% of the total BCCs, which is higher than in previous reports. However, we found no statistically significant relationship between tumor aggressiveness, as defined by tumor subtype, and the previously mentioned risk factors, occupation with significant sun exposure, history of heavy alcohol consumption, history of smoking and/or being a current smoker, an underlying condition, and/or receiving drugs that make the patient immune-compromised.

In the large survey by Leibovitch et al[20], they found an overall 5-year recurrence rate of 2.6%, which was greater in the previously recurrent cases than in primary cases, 4% versus 1.4%, with two-thirds of tumors recurring in the first three years. In the other survey reported by Mohs[21], an overall 5-year recurrence rate of less than 1% was found. In our study, where the longest follow-up period was five years, we have found recurrent cases in only 0.81%, which may be due to the smaller number of cases and the mean follow-up time after MMS was only 20.86±15.75 months. Therefore, a longer follow-up period may be required.

In the present study, 84 patients (77.8%) answered our questionnaire about overall satisfaction of the procedure. We found that 81 of these patients (96.4%) had 76% to 100% satisfaction and three patients (3.6%) had 51% to 75% satisfaction.

In conclusion, the present research study found a zero percent recurrence rate in NMSCs treated with MMS, in both primary and recurrent tumors. This finding reinforces the necessity of margin control in

high-risk tumors, which agrees with the previous studies that recognized MMS as the gold standard in terms of cure rates for NMSC.

What is already known on this topic?

There are several treatment modalities for treating NMSC including surgical and non-surgical procedures. MMS is a modality of treating skin cancers that give complete margin control with a clearance rate of 99% for primary tumors and 95% for recurrent NMSC. There is also the advantage of conserving tissue from MMS when comparing to conventional surgical excision, resulting in an excellent outcome of function and cosmetics. However, there have been no report on risk factors, clinical findings, and cure rates of NMSC treated with MMS in Thai population.

What this study adds?

To the best of our knowledge, this is the first report of risk factors and clinical findings of NMSC patients treated with MMS in Thailand with the longest follow-up at 5 years. The present study demonstrates a zero percent recurrence rate in NMSCs treated with MMS and the necessity of margin control in high-risk tumors.

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Potential conflicts of interest

The authors declare no conflict of interest.

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