

Clinical Misdiagnosis of Cutaneous Malignant Tumors as Melanocytic Nevi or Seborrheic Keratosis: A Retrospective Analysis of a Chinese Population

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Purpose: The rising incidence and mortality associated with cutaneous malignant tumours highlight the importance of early diagnosis of these tumors. In clinical practice, these tumors are often misdiagnosed as benign skin lesions such as melanocytic nevi (MN) and seborrheic keratosis (SK) because of their similar morphologic features. The incidence and clinicopathological subtypes of cutaneous malignancies in East Asia populations significantly differ from those in fair-skinned groups. However, studies on misdiagnoses in Eastern countries are lacking. Therefore, this study focused on the clinical and pathological features of cutaneous malignant tumors misdiagnosed as MN or SK in a Chinese population.

Patients and Methods: A total of 4592 samples clinically diagnosed as MN (n = 3503) or SK (n = 1089) from July 2014 to June 2022 were collected and evaluated retrospectively. The clinical and pathological data were analyzed to identify associated factors.

Results: Pathological assessments showed that 2.5% (86/3503) of the specimens clinically diagnosed as MN were malignancies, predominantly basal cell carcinoma (BCC, 84.9%, 73/86), followed by malignant melanoma (MM, 8.1%, 7/86) and squamous cell carcinoma (SCC, 7.0%, 6/86). Similarly, 5.7% (62/1089) of the specimens clinically diagnosed as SK were malignant tumors, of which BCC (50.0%, 31/62) was the most common, followed by SCC (41.9%, 26/62) and MM (8.1%, 5/62). In both types of specimens, advanced age and facial lesions were risk factors for malignancy misdiagnosis. The malignancy rate, mean age, and proportion of SCC in the specimens clinically diagnosed as SK were higher than those in the specimens clinically diagnosed as MN. Dermoscopy significantly reduced the rate of misdiagnosis of these tumors as MN or SK.

Conclusion: In China, cutaneous malignant tumors misdiagnosed as MN or SK are not uncommon in clinical practice, and active introduction of noninvasive diagnostic techniques is essential to distinguish them.

Keywords: malignant melanoma, squamous cell carcinoma, basal cell carcinoma, skin benign neoplasms, dermoscopy, China

Introduction

The growing prevalence of skin tumors, especially cutaneous malignant tumors, poses a prominent public health challenge worldwide, and has attracted attention from clinicians and researchers.^{1,2} Early diagnosis is fundamental to reduce the complications and mortality associated with malignant tumors.³ However, cutaneous malignant tumors are frequently misdiagnosed as melanocytic nevi (MN) or seborrheic keratosis (SK), and the misdiagnosis rate is not low.⁴⁻⁸ In particular, special attention should be given to malignant melanoma (MM), the most lethal type of skin cancer, which is often misdiagnosed as MN or SK.^{4-6,9} MN and SK are the two most prevalent benign neoplasms in dermatology.¹⁰⁻¹² In China, many patients with MN or SK visit dermatologists because of concerns regarding malignancy or cosmetic needs,⁴ and clinicians in primary hospitals and even some tertiary hospitals habitually use minimally invasive methods such as laser treatment or cryotherapy to treat those conditions, which may result in misdiagnosis and inappropriate

treatment of malignant tumors. The prevalence and clinicopathologic features of skin cancer vary markedly across different races or skin types.^{1,13} Previous studies on the misdiagnosis of skin cancer were mainly conducted in Western countries, with a notable gap in research from East Asia.¹³ This study aimed to identify the risk factors for misdiagnosis of cutaneous malignant tumors as MN or SK in the Chinese population by using data obtained from a tertiary teaching hospital in China from July 2014 to June 2022, to guide clinical practices and reduce misdiagnoses in similar demographic groups.

Materials and Methods

Patients and Methods

This retrospective study examined all surgical and biopsy specimens initially diagnosed as MN or SK at the Department of Dermatology in the Affiliated Hospital of Guizhou Medical University (Guizhou Province, China) from July 2014 to June 2022. The specimens were subjected to pathological examination. If a specimen had multiple suspected diagnoses, it was included in the analysis on basis of the first diagnosis. Congenital MN, halo nevi, and specimens with unclear histopathological diagnosis were excluded. Out of 4986 MN and SK specimens, 4592 were analyzed, which included 3503 MN and 1089 SK specimens. To ensure accuracy of pathological diagnosis, two dermatopathologists (Wang and Cai) reviewed and diagnosed all hematoxylin and eosin (HE)-stained sections independently. In case of disagreement between the assessments by the two dermatopathologists, a third pathologist (Feng) was consulted to reach the final diagnosis after discussion. This study adhered to the diagnostic criteria outlined in the Third Edition of Dermatology edited by Bologna JL et al.¹⁰ General information of the patients, such as sex, age, lesion location, and the date of visit, was collected from the histopathology submission forms. This study was approved by the Ethics Committee of the Affiliated Hospital of Guizhou Medical University. No identifiable patient data were included in this study.

Statistical Analysis

A descriptive analysis was performed to evaluate the clinical and histopathological data, including sex, age, lesion location, and characteristics of the misdiagnosed tumors, in patients with clinically diagnosed MN and SK. Normally distributed data such as age were presented as mean \pm standard deviation (95% confidence interval [CI]) and further analyzed using *t* test, while non-normally distributed data were presented as median (first quartile-third quartile, Q1-Q3) and compared using nonparametric tests. The differences in cutaneous malignant tumor frequencies were assessed using chi-square test and, for comparisons with a small sample size, using Fisher's exact test. A two-tailed *P* value less than 0.05 was considered statistically significant. All statistical analyses in this study were performed using the SPSS22.0 software package (IBM, Armonk, NY, USA).

Results

Patient Information Collected from the Histopathology Submission Forms

A total of 4592 specimens from 3942 patients (median age, 38 years; Q1-Q3, 26–55 years; age range, 1–94 years), including 1363 male and 2579 female patients, were analyzed in this study. A substantial proportion of the specimens was obtained from patients aged 21–40 years (40.7%) and 41–60 years (27.1%), followed by those aged >60 years (17.5%) and \leq 20 years (14.6%) (Figure 1). The most common site for specimen collection was the face (44.8%), followed by the trunk (20.7%), limbs (17.8%), scalp and neck (13.2%), and buttocks and perineum (3.4%) (Figure 2).

Among the specimens submitted for histopathological assessments, 3503 (76.3%) were initially diagnosed as MN, while 1089 (23.7%) were initially diagnosed as SK. A sex-based disparity was observed, with a higher prevalence of female patients in the MN group ($P < 0.001$, Table 1). In terms of age, the MN group predominantly consisted of individuals aged 21–40 years, and the mean age in the MN group was significantly lower than that in the SK group, which mostly consisted of patients aged >60 years old (all $P < 0.001$, Table 1). Additionally, a notable difference was found in the distribution of tumor locations between the two groups, with MN primarily located on the face and SK more commonly found on both the face and trunk ($P < 0.001$, Table 1).

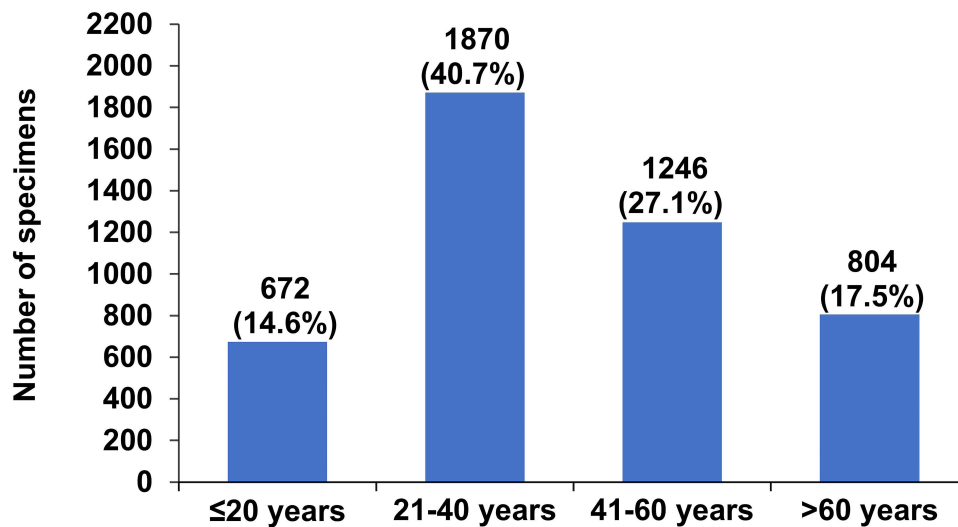


Figure 1 Age distribution of the patients whose specimens were submitted.
Note: The values are presented as number (%).

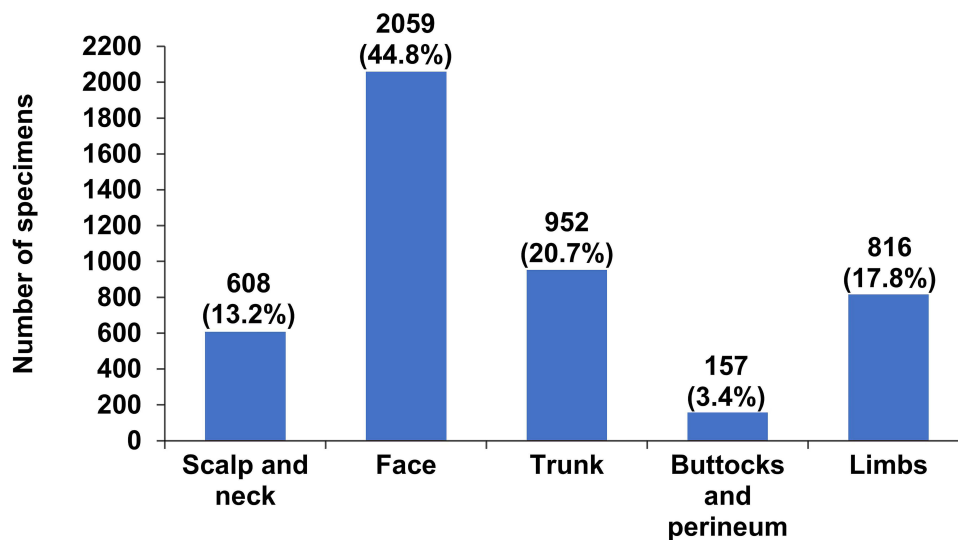


Figure 2 Location distribution of the submitted specimens.
Note: The values are presented as number (%).

Cutaneous Malignant Tumors Misdiagnosed as MN

Histopathological review of the specimens clinically diagnosed as MN indicated diseases other than MN in 590 (16.8%) specimens. Notably, 86 (2.5%) specimens showed pathological findings for cutaneous malignant tumors, including BCC, SCC, and MM. Among the diseases misdiagnosed, SK was predominant, accounting for 61.2% (361/590) of the specimens. The next most frequently misdiagnosed diseases were cutaneous malignant tumors, which accounted for 14.6% (86/590) of the specimens. Demographic analysis showed a higher probability of misdiagnosis in male patients ($P < 0.001$, Table 2), while sex was not significantly associated with the occurrence of cutaneous malignant tumors ($P = 0.147$, Table 2). Age was linked to the rate of misdiagnosis as MN, with misdiagnosed patients being significantly older than those who were correctly diagnosed (median age, 50 years [Q1-Q3, 40–62 years] vs median age, 30 years [Q1-Q3, 22–38 years]; $P < 0.001$). Similarly, among the cases misdiagnosed as MN, the age of patients with cutaneous malignant tumors (median age, 58 years [Q1-Q3, 48–66 years]) was obviously higher than that of patients without cutaneous malignant tumors (median age, 49 years [Q1-Q3, 38–60 years]). Age-group analysis showed that both the

Table 1 Characteristics of the Patients Whose Specimens Were Submitted (Cases, %)

| Characteristic | MN (3503) | SK (1089) | P value |
|---|-------------|------------|---------|
| Sex | | | < 0.001 |
| Male | 1055 (30.1) | 493 (45.3) | |
| Female | 2448 (69.9) | 596 (54.7) | |
| Age (years) | | | |
| Median (Q ₁ – Q ₃) | 32 (23–43) | 62 (51–71) | < 0.001 |
| Age group | | | < 0.001 |
| ≤20 years | 668 (19.1) | 4 (0.4) | |
| 21–40 years | 1777 (50.7) | 93 (8.5) | |
| 41–60 years | 816 (23.3) | 430 (39.5) | |
| >60 years | 242 (6.9) | 562 (51.6) | |
| Location | | | < 0.001 |
| Scalp and neck | 476 (13.6) | 132 (12.1) | |
| Face | 1626 (46.4) | 433 (39.8) | |
| Trunk | 622 (17.8) | 330 (30.3) | |
| Buttocks and perineum | 96 (2.7) | 61 (5.6) | |
| Limbs | 683 (19.5) | 133 (12.2) | |

Abbreviations: MN, melanocytic nevi; SK, seborrheic keratosis; Q₁–Q₃, first quartile to third quartile.

incidence of overall misdiagnosis and the rate of cutaneous malignant tumors increased with age, with significant distribution differences (all $P < 0.05$, Table 2). The lesion location on the body was also correlated with the overall misdiagnosis and incidence of cutaneous malignant tumors. Our findings revealed that overall misdiagnosis occurred more frequently in the specimens from the buttocks, perineum, and trunk (lesion locations, $P < 0.001$, Table 2) in comparison with specimens from other body areas. Cutaneous malignancies were found more frequently on the face ($P < 0.001$, Table 2), as was BCC ($P < 0.001$, Table 2). However, the incidence of SCC and MM did not significantly differ in terms of location (Table 2).

Cutaneous Malignant Tumors Misdiagnosed as SK

On the basis of the pathological diagnosis criteria, 238 (21.9%) specimens clinically diagnosed as SK were found to be misdiagnosed. Among these, 62 cases of skin cancer, including BCC, cutaneous SCC, and MM, had been clinically diagnosed as SK, representing 5.7% of the SK specimens. Viral warts constituted the majority of the misdiagnosed diseases, accounting for 22.7% (54/238) of the specimens misdiagnosed as SK, while skin cancers constituted 26.1% (62/238) of these specimens. Statistical analysis suggested that sex was associated with the incidence of misdiagnosis, with female patients being more prone to misdiagnosis than males ($P = 0.02$, Table 3), although no significant sex-related difference was observed in the misdiagnosis of cutaneous malignancies ($P = 0.063$, Table 3). The overall age of the misdiagnosed patients (median age, 63 years [Q₁–Q₃, 50–73 years]) was not significantly higher than that of the accurately diagnosed patients (median age, 61 years [Q₁–Q₃, 51–70 years], $P = 0.161$). In the misdiagnosed subgroup, patients with cutaneous malignant tumors were considerably older (median age, 71 years [Q₁–Q₃, 58–77 years]) than those without malignancies (median age, 60 years [Q₁–Q₃, 48–70 years], $P < 0.001$). Although the incidence of skin malignancies misdiagnosed as SK increased with age, significant differences in age distribution were only noted for

Table 2 Patient Characteristics in Cases of Malignant Tumors That Were Clinically Diagnosed as Melanocytic Nevi (Cases, %)

| Characteristics | | Overall Misdiagnosis | P value ^a | Malignant Tumor | P value ^a | BCC | P value ^a | SCC | P value ^a | MM | P value ^a |
|-----------------------|------|----------------------|----------------------|-----------------|----------------------|-----------|----------------------|---------|----------------------|---------|----------------------|
| Number | 3503 | 590 (16.8) | | 86 (2.5) | | 73 (2.1) | | 6 (0.2) | | 7 (0.2) | |
| Sex | | | < 0.001 | | 0.147 | | 0.196 | | 0.374 | | 1.0 |
| Male | 1055 | 241 (22.8) | | 32 (3.0) | | 27 (2.6) | | 3 (0.3) | | 2 (0.2) | |
| Female | 2448 | 349 (14.3) | | 54 (2.2) | | 46 (1.9) | | 3 (0.1) | | 5 (0.2) | |
| Age group | | | < 0.001 | | < 0.001 | | < 0.001 | | < 0.001 | | 0.003 |
| ≤20 years | 668 | 18 (2.7) | | 0 (0.0) | | 0 (0.0) | | 0 (0.0) | | 0 (0.0) | |
| 21–40 years | 1777 | 135 (7.6) | | 9 (0.5) | | 8 (0.5) | | 0 (0.0) | | 1 (0.1) | |
| 41–60 years | 816 | 280 (34.3) | | 43 (5.3) | | 37 (4.5) | | 3 (0.4) | | 3 (0.4) | |
| >60 years | 242 | 157 (64.9) | | 34 (14.0) | | 28 (11.6) | | 3 (1.2) | | 3 (1.2) | |
| Location | | | < 0.001 | | < 0.001 | | < 0.001 | | 0.333 | | 0.075 |
| Scalp and neck | 476 | 89 (18.7) | | 6 (1.3) | | 4 (0.8) | | 2 (0.4) | | 0 (0.0) | |
| Face | 1626 | 204 (12.5) | | 68 (4.2) | | 63 (3.9) | | 4 (0.2) | | 1 (0.1) | |
| Trunk | 622 | 158 (25.4) | | 5 (0.8) | | 3 (0.5) | | 0 (0.0) | | 2 (0.3) | |
| Buttocks and perineum | 96 | 35 (36.5) | | 0 (0.0) | | 0 (0.0) | | 0 (0.0) | | 0 (0.0) | |
| Limbs | 683 | 104 (15.2) | | 7 (1.0) | | 3 (0.4) | | 0 (0.0) | | 4 (0.6) | |

Note: ^aComparison of the incidence.

Abbreviations: BCC, basal cell carcinoma; SCC, squamous cell carcinoma; MM, malignant melanoma.

Table 3 Patient Characteristics in Cases of Malignant Tumors That Were Clinically Diagnosed as Seborrheic Keratosis (Case, %)

| Characteristics | | Overall Misdiagnosis | P value ^a | Malignant Tumor | P value ^a | BCC | P value ^a | SCC | P value ^a | MM | P value ^a |
|-----------------------|------|----------------------|----------------------|-----------------|----------------------|----------|----------------------|----------|----------------------|---------|----------------------|
| Number | 1089 | 238 (21.9) | | 62 (5.7) | | 31 (2.8) | | 26 (2.4) | | 5 (0.5) | |
| Sex | | | 0.020 | | 0.063 | | 0.457 | | 0.269 | | 0.068 |
| Male | 493 | 92 (18.7) | | 21 (4.3) | | 12 (2.4) | | 9 (1.8) | | 0 (0.0) | |
| Female | 596 | 146 (24.5) | | 41 (6.9) | | 19 (3.2) | | 17 (2.9) | | 5 (0.8) | |
| Age group | | | 0.128 | | 0.037 | | 0.689 | | 0.007 | | 1.000 |
| ≤20 years | 4 | 2 (50.0) | | 0 (0.0) | | 0 (0.0) | | 0 (0.0) | | 0 (0.0) | |
| 21–40 years | 93 | 24 (25.8) | | 2 (2.2) | | 1 (1.1) | | 1 (1.1) | | 0 (0.0) | |
| 41–60 years | 430 | 82 (19.1) | | 17 (4.0) | | 12 (2.8) | | 3 (0.7) | | 2 (0.5) | |
| >60 years | 562 | 130 (23.1) | | 43 (7.7) | | 18 (3.2) | | 22 (3.9) | | 3 (0.5) | |
| Location | | | < 0.001 | | < 0.001 | | 0.009 | | 0.249 | | 0.216 |
| Scalp and neck | 132 | 14 (10.6) | | 6 (4.5) | | 3 (2.3) | | 3 (2.3) | | 0 (0.0) | |
| Face | 433 | 132 (30.5) | | 41 (9.5) | | 22 (5.1) | | 16 (3.7) | | 3 (0.7) | |
| Trunk | 330 | 44 (13.3) | | 7 (2.1) | | 3 (0.9) | | 4 (1.2) | | 0 (0.0) | |
| Buttocks and perineum | 61 | 13 (21.3) | | 2 (3.3) | | 1 (1.6) | | 1 (1.6) | | 0 (0.0) | |
| Limbs | 133 | 35 (26.3) | | 6 (4.5) | | 2 (1.5) | | 2 (1.5) | | 2 (1.5) | |

Note: ^aComparison of the incidence.**Abbreviations:** BCC, basal cell carcinoma; SCC, squamous cell carcinoma; MM, malignant melanoma.

cutaneous SCC ($P = 0.007$, Table 3). Significant differences related to lesion locations were observed in the specimens misdiagnosed as SK ($P < 0.001$, Table 3), with the face being the most common site of such specimens. Likewise, skin cancer occurred more frequently on the face than on other areas ($P < 0.001$, Table 3). Among all skin cancer types, the location distribution of BCC was similar to the overall distribution of skin cancers ($P = 0.009$). In addition, the location distribution of SCC did not significantly differ from that of MM (Table 3).

Among the specimens clinically diagnosed as SK, 35 (3.2%, 35/1089) were identified as actinic keratosis, a common precancerous skin lesion. These cases showed significant differences in sex, age, and lesion location distributions ($P = 0.007$, $P = 0.005$, and $P < 0.001$, respectively).

Occurrence of Cutaneous Malignant Tumors in the Submitted Specimens

In this study, 828 (18%) specimens were misdiagnosed, of which 148 (17.9%) were cutaneous malignant tumors; these included 104 cases of BCC (70.3%), 32 cases of SCC (21.6%), and 12 cases of MM (8.1%). The specimens clinically diagnosed as SK had a significantly higher overall misdiagnosis rate than those clinically diagnosed as MN ($P < 0.001$, Table 4) and showed a higher incidence of misdiagnosed cutaneous malignancies ($P < 0.001$, Table 4). While BCC was predominant among the specimens misdiagnosed as MN (84.9%), the proportions of BCC (50.0%) and SCC (41.9%)

Table 4 Patient Characteristics in Cases of Malignant Tumors That Were Clinically Diagnosed as Melanocytic Nevi and Seborrheic Keratosis (Cases, %)

| Characteristics | MN (3503) | SK (1089) | P value |
|---|-------------|-------------|---------|
| Overall misdiagnosis | | | < 0.001 |
| Yes | 590 (16.8) | 238 (21.9) | |
| No | 2913 (83.2) | 851 (78.1) | |
| CMTs | | | < 0.001 |
| Yes | 86 (2.5) | 62 (5.7) | |
| No | 3417 (97.5) | 1027 (94.3) | |
| CMTs group | | | < 0.001 |
| BCC | 73 (84.9) | 31 (50.0) | |
| SCC | 6 (7.0) | 26 (41.9) | |
| MM | 7 (8.1) | 5 (8.1) | |
| Clinical diagnosis included "need to rule out CMTs" | | | 0.258 |
| Yes | 22 (25.6) | 11 (17.7) | |
| No | 64 (74.4) | 51 (82.3) | |
| Age of patients with CMTs (years) | | | < 0.001 |
| M±SD | 57.3 ± 12.9 | 67.5 ± 14.2 | |
| 95% CI | 54.5–60.0 | 63.9–71.1 | |
| Age groups of patients with CMTs | | | 0.001 |
| ≤ 20 years | 0 (0.0) | 0 (0.0) | |
| 21–40 years | 9 (10.5) | 2 (3.2) | |
| 41–60 years | 43 (50.0) | 17 (27.4) | |

(Continued)

Table 4 (Continued).

| Characteristics | MN (3503) | SK (1089) | P value |
|---------------------------|-----------|-----------|---------|
| >60 years | 34 (39.5) | 43 (69.4) | |
| Sex of patients with CMTs | | | 0.676 |
| Male | 32 (37.2) | 21 (33.9) | |
| Female | 54 (62.8) | 41 (66.1) | |
| CMTs location | | | 0.251 |
| Scalp and neck | 6 (7.0) | 6 (9.7) | |
| Face | 68 (79.1) | 41 (66.1) | |
| Trunk | 5 (5.8) | 7 (11.3) | |
| Buttocks and perineum | 0 (0.0) | 2 (3.2) | |
| Limbs | 7 (8.1) | 6 (5.4) | |

Abbreviations: CMTs, cutaneous malignant tumors; MN, melanocytic nevi; SK, seborrheic keratosis; BCC, basal cell carcinoma; SCC, squamous cell carcinoma; MM, malignant melanoma; CI, confidence interval; M, mean; SD, standard deviation.

were closer among the specimens misdiagnosed as SK. The differences in the proportions of BCC and SCC were significant between the specimens misdiagnosed as MN and SK ($P < 0.001$, Table 4). Demographic analysis showed that age was associated with the prevalence of cutaneous malignant tumors in the specimens clinically diagnosed as MN and SK ($P < 0.001$, Table 4), with the average age of patients with skin cancers in the SK group being 67.5 years (95% CI, 63.7–71.1 years) and that in the MN group being 57.3 years (95% CI, 54.5–60.0 years). Subgroup analysis by age indicated that patients with cutaneous malignancies in the MN group were usually aged 41–60 age, while those with cutaneous malignancies in the SK group were typically aged >60 years (Table 4). However, the two groups showed no significant differences in the distribution of skin cancers in terms of sex or location ($P = 0.676$, $P = 0.251$, respectively). Additionally, while clinician identified the need for further evaluations to rule out cutaneous malignant tumors in a small number of the submitted MN and SK specimens, the proportion of such specimens was low and did not differ significantly between the two groups ($P = 0.258$, Table 4).

Before the desktop dermoscopy system became operational (July 2014 to June 2021), a total of 3646 specimens were categorized as MN or SK, of which 129 were identified as cutaneous malignant tumors in pathological assessments, indicating a misdiagnosis rate of 3.5%. After the system's implementation (July 2021 to June 2022), 946 specimens were categorized as MN or SK, of which 19 were diagnosed as cutaneous malignancies in histopathological assessments, reflecting a misdiagnosis rate of 2.0%. Overall, the incidence of misdiagnosis in the latter period was significantly lower than that in the former ($P = 0.018$).

Discussion

In both East Asia and the Western countries, MN and SK are the two most frequent skin neoplasms^{10–12} and are common reasons for consultations and surgery in dermatological practice.^{14,15} Previous studies have confirmed that MN mainly occurs in individuals aged of 20–30 years,^{10,16,17} and the incidence of SK increases with age,^{10,12,18} consistent with our findings.

Many researchers have expressed concern regarding MN since they are potential precursors and the main discriminators of MM. Previous studies from Western countries have reported that the rate of misdiagnosis as MN in clinical practice varies from 11.0% to 38.7%.^{8,19,20} In this study, the overall rate of misdiagnosis as MN was 16.8%, and SK was the most commonly misdiagnosed disease in cases that were clinically diagnosed as MN. These results were similar to a recent investigation conducted in Hunan Province,⁴ which, like Guizhou, is a southern province in China. However, another study carried out in Beijing, which is located in the north of China, reported a higher rate of 42.1%.¹⁴ This

discrepancy may stem from regional variations in Chinese dermatologists' perceptions of MN morphology and patients' consultation patterns. SK mostly occurs in middle-aged and older individuals, and presents with various clinical manifestations.¹⁸ The rate of misdiagnosis as SK is evidently heterogeneous in fair-skinned populations,^{8,21} and was lower in our study than that in recent reports from China and South Korea.^{7,14} Karadag et al suggested that this heterogeneity may be due to differences in patients' populations, insufficient initial diagnosis data, and other factors.²² Some reports have suggested that the overall rate of clinical misdiagnosis as SK was higher than that of clinical misdiagnosis as MN,^{8,14} although they did not perform statistical analyses. This suggestion was corroborated by our results.

Because of their destructive and lethal nature, cutaneous malignant tumors have become a major concern for dermatologists and patients with skin diseases. In clinical practice, misdiagnosis of these tumors as MN or SK is rather common.^{4-8,20,22} BCC and cutaneous SCC are the two most important types of cutaneous malignancies.¹ The clinical phenotypes of BCC and SCC differ slightly between people of color and fair-skinned individuals.¹³ However, studies from Asia, Europe, and America have indicated that BCC is more frequent in cases with clinically diagnosed MN,^{4-6,20} and SCC is more prevalent in cases with clinically diagnosed SK.⁵⁻⁷ In this study, BCC was the most frequent type of cutaneous malignant tumor among the specimens clinically diagnosed as MN, while SCC was not more prevalent than BCC in those clinically diagnosed as SK. Lim et al showed that skin cancers adjacent to or related to SK were mainly BCC.²³ Unfortunately, this study did not distinguish whether the malignancies in the submitted specimens were missed as a result of an actual misdiagnosis or because of co-occurrence with SK or the appearance of the malignant tumor neighboring SK, and we also did not analyze the reasons for the higher incidence of BCC in specimens clinically diagnosed as SK. Ultraviolet accumulation is a risk factor for BCC and SCC in both the Eastern and the Western countries.²⁴⁻²⁶ With the aging of China's population, the incidence of these cancers is expected to rise, underscoring the importance of identifying them using a variety of excellent tools.

MM is the most lethal tumor in dermatology,^{1,10} and is often misdiagnosed due to its similarities to other skin tumors.⁹ Given its low prevalence but increasing incidence and lower survival rate in China,^{1,2,26,27} early diagnosis of MM is the key to improving the recovery rate.²⁴ The findings of this study suggest that MM should not be overlooked when the skin lesions clinically diagnosed as MN or SK appear in Chinese females, older patients, or on extremities.

In addition, among the specimens clinically diagnosed as SK, the incidence of actinic keratosis was relatively high, especially in older and female patients and among facial lesions. As a precancerous lesion of SCC, actinic keratosis is easily confused with SK,^{7,28} and should also be handled with caution by the clinicians.

In general, 2.5% of the specimens clinically diagnosed as MN and 5.7% of those clinically diagnosed as SK were histopathologically diagnosed as cutaneous malignant tumors, with a higher incidence of misdiagnosis in specimens clinically diagnosed as SK. These findings were similar to the incidence rates and differences reported in studies from the Eastern and Western countries.^{4-7,19} Some researchers believe that the differences in the incidence of cutaneous malignancies misdiagnosed as MN and SK may be attributed to the greater number of SK patients undergoing treatments like laser therapy and cryotherapy without histopathological examination.⁵ Our study also showed that older age and facial lesions were associated with a higher incidence of skin cancers being misdiagnosed as MN or SK, reflecting the fact that cutaneous malignant tumors, especially BCC and SCC, often occur in older people and are associated with ultraviolet exposure.^{25,26} This also suggests that in clinical practice, for older patients with skin lesions at exposed locations, the possibility of cutaneous malignant tumors should be carefully ruled out, regardless of whether they are suspected to have MN or SK.

Previous studies have shown that dermoscopy, *in vivo* confocal microscopy, and optical coherence tomography can prominently improve the diagnostic accuracy of skin tumors.^{29,30} This study also highlighted the effectiveness of dermoscopy in reducing the rate of misdiagnosis of cutaneous malignancies as MN or SK. Our department uses a tabletop dermoscopy system, and only physicians who have mastered the dermoscopy technique can issue examination reports. The reduction in the misdiagnosis rate may be attributable to the reinforcement of clinicians' understanding of skin tumors such as MN and SK after receiving training for dermoscopy and obtaining feedback on dermoscopic assessments. Currently, dermoscopy is only performed in the dermatology departments of a few hospitals

in China. These results indicate the need for wider implementation of dermoscopy and training for this technique in dermatology clinics.

This study had some limitations, including the fact that it only involved a retrospective review of the specimens that underwent pathological examination from a tertiary hospital, and the lack of a detailed analysis to determine whether the misdiagnosed disease existed alone or in conjunction with the clinically diagnosed disease, which may have led to bias in the misdiagnosis rate and potentially inflated the misdiagnosis rate. In addition, we did not categorize or confirm the pathological subtypes of various diseases. More in-depth research is needed to substantiate our findings.

Conclusion

The data indicated that approximately 2.5% of specimens clinically diagnosed as MN and 5.7% of those clinically diagnosed as SK were histopathologically confirmed to be cutaneous malignant tumors. In particular, misdiagnosis as MN or SK was more likely in older patients with skin cancers located on the face. Notably, BCC tended to be ignored and frequently misdiagnosed as MN, while SCC was often mistakenly identified as SK. Clinicians should be highly vigilant about potentially malignant facial lesions in elderly patients to diagnose them accurately and promptly. Furthermore, the use of dermoscopy significantly reduced the misdiagnosis rate of cutaneous malignant tumors, indicating that it was a valuable tool for the diagnosis of these lesions.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval

This retrospective study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Ethics Committee of the Affiliated Hospital of Guizhou Medical University approved this study (2022-735).

Consent to Participate

All patients from the data source signed the informed consent agreement of “My medical records and samples can be used for medical research without revealing identifiable information” before the surgery or biopsy of the rash.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Jun Zhang, Yu Wang, Wei Zhang; Linglong Cai, Jianglong Feng, Yiwei Zhu and Hongguang Lu have no conflicts of interest that are directly relevant to the content of this article.

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