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Brief Report

Factors for Improving Diagnosis of Skin Tumors

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Abstract

***Background*:** Although several studies have investigated the accuracy of clinical diagnoses of skin tumors, specific ways to improve diagnostic accuracy have not been identified. This study investigated factors that influence the accuracy of clinical skin tumor diagnostic methods and discusses strategies to improve accuracy.

***Methods*:** Study 1 retrospectively analyzed 657 skin tumors excised at our hospital between March 2001 and March 2011. Data were extracted from surgical records to establish a diagnostic template for further research. Study 2 prospectively applied this template to aid clinical diagnosis at four facilities between April 2011 and March 2013. The clinical diagnoses were compared with the histological ones and the concordance was determined.

***Results*:** A total of 448 and 209 benign and malignant tumors, respectively, were included in Study 1. The overall diagnostic accuracy was 79.0%. In Study 2, 310 patients were clinically diagnosed using a standardized template, which did not affect the diagnostic accuracy. Age, sex, duration of disease, tumor size and location, skin tone, mobility, stiffness, and years of diagnostic experience did not significantly affect diagnostic accuracy. A high proportion of pathologically malignant tumors were clinically misdiagnosed as benign (16/22; 72%). Other clinical examinations were performed in only 35 cases.

***Conclusions*:** Auxiliary diagnostic tools such as dermoscopy and biopsies should be used to accurately diagnose malignant tumors.

Keywords
accuracy, skin tumor, misdiagnosis

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Introduction

The Japanese have the longest lifespans in the world, resulting in a greater incidence of skin malignancies. Several studies have reported skin tumor diagnostic rates, but not in Asian populations1[1-10)]. Misdiagnosis of malignant tumors as benign often leads to poorly planned excisions, which masks the tumor borders and makes complete excision difficult. Therefore, appropriate diagnosis of skin tumors is important.

The reported accuracy of skin tumor diagnoses by plastic surgeons and dermatologists is 61%-73%[1-4)]. Some studies have reported that dermatologists achieve more accurate skin tumor diagnoses than plastic surgeons[3,5)], while other studies demonstrated no significant differences between dermatologists and plastic surgeons[4)].

A series of studies were conducted to explore factors that could improve the diagnostic accuracy of skin and subcutaneous tumors.

Patients and Methods

This research consists of two studies. In Study 1, the data for patients with skin tumors excised by seven plastic surgeons, who had diagnosed >20 patients each, were extracted

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from the surgical records of our facility. After excluding ambiguous diagnoses, 657 skin tumors excised between March 2001 and March 2011 were included. The data extracted included age, sex, tumor site, clinical and pathological diagnoses, and surgeon experience. The accuracy of benign and malignant tumor diagnoses, and that for each tumor, was calculated. Accuracy was expressed as coincidence (n) divided by frequency (n). Coincidence was defined as the agreement between clinical and pathological diagnoses.

Accuracy (%) = Coincidence (n)/Frequency (n) × 100

In Study 2, a diagnostic template was created using FileMaker Pro 10® (Claris International Inc., Cupertino, CA, USA; Supplemental Figure 1). The template was used at our hospital and three other facilities to prospectively diagnose skin lesions based on medical examinations performed between April 2011 and March 2013. Patient data, such as age, sex, underlying diseases, duration of illness, and clinical findings at the initial presentation (site, size, color, skin and subcutaneous mobility, hardness, and various other characteristics; Supplemental Figure 1), were collected. Physician information, such as the initial and differential diagnoses during the first consultation, postoperative and histological diagnoses, and number of years of clinical experience, were also collected. In cases treated by multiple physicians, the physician at the first visit was recorded. Cases previously diagnosed by another physician, and those diagnosed by physicians who had experience of <10 patients, were excluded. The pathological diagnoses were made by two or more pathologists at each institution and compared with the clinical diagnoses.

Statistical analyses

The data were analyzed using Microsoft Excel software (Microsoft Corp., Redmond, WA, USA). Cross-tabulations, Chi-square tests, and multiple comparison tests ("population ratio difference" and Tukey's multiple comparison tests) were performed. *P* values of <0.05 were considered statistically significant.

Results

In Study 1, 657 cases (291 males and 366 females) were included (**Table 1**). The average patient age was 47.8 years (47.8 and 47.6 years for males and females, respectively). The diagnostic accuracy was 79.0% and there was no significant difference between males and females (80.4% and 77.8%, respectively).

A total of 448 and 209 cases were pathologically diagnosed as benign and malignant, respectively. Among the 448 benign tumors, 357 were consistent with the clinical diagnosis and the accuracy rate was 79.7%. Among the 209 malignant tumors, 162 were consistent with the clinical diagnosis and the accuracy rate was 77.5%. There was no statistically significant difference in accuracy between benign and malignant tumors (p = 0.5237). Tukey's multiple comparison test showed no significant differences in diagnostic rates according to age or site (data not shown). There was no significant difference in the diagnosis rate for the various age groups according to the number of years of surgeon experience (data not shown).

Table 1. Accuracy of Skin Tumor Diagnoses (Study 1).

	Frequency (n)	Coincidence (n)	Accuracy (%)
Total	657	519	79.0
Male	291	234	80.4
Female	366	285	77.8
Benign	448	357	79.7
Malignant	209	162	77.5

*) Coincidence (n) means that the clinical diagnosis agrees with the pathological diagnosis. Accuracy (%) = [Coincidence (n) /Frequency (n)] × 100. Analyzed by multiple comparison test

Table 2. Breakdown and Accuracy of Malignant Skin Tumor (Study 1).

	Frequency (n)	Coincidence (n)	Accuracy (%)
Basal cell carcinoma	60	51	85.0
Malignant melanoma	46	30	65.2
Squamous cell carcinoma	37	25	67.6
Actinic keratosis	21	17	81.0
Bowen's disease	16	14	87.5
Paget's disease	14	13	92.9
Dermatofibrosarcoma protuberance	4	4	100
Malignant lymphoma	3	3	100
Apocrine grand cell carcinoma	1	1	100
Merkel cell carcinoma	2	1	50.0
Others	5	3	60.0
Total	209	162	77.5

*) Coincidence (n) means that the clinical diagnosis agrees with the pathological diagnosis. Accuracy (%) = [Coincidence (n) /Frequency (n)] × 100

The malignant skin tumors in Study 1 included basal cell carcinomas (BCCs; n = 60), malignant melanomas (MMs; n = 46), squamous cell carcinomas (SCCs; n = 37), actinic keratosis (AK; n = 21), Bowen's disease (BD; n = 16), Paget's disease (PD; n = 14), dermatofibrosarcoma protuberans (DFSP; n = 4), and malignant lymphoma (MLs; n = 3). The diagnostic accuracy was 100% for DFSP and MLs; > 80% for BCCs, PD, BD, and AK; and about 60% for MMs and SCCs (**Table 2**).

Clinically benign tumors in Study 1 included nevocellular nevi (n = 116), epidermal cysts (n = 56), venous/lymphatic malformations (n = 51), lipomas (n = 23), seborrheic keratosis (n = 19), sebaceous nevi (n = 15), neurofibromas (n = 14), ganglions (n = 14), granulomas (n = 12), calcifying epitheliomas (n = 12), verruca vulgaris (n = 8), and scars/keloids (n = 10), among others. The average accuracy for granuloma (41.7%), verruca vulgaris (62.5%), keratoacanthomas (20%), foreign body granulomas (60%), neurilemmomas (50%), and dermatofibromas (33.3%) was ≤ 79.7%

(**Table 3**).

Study 2 included 310 cases from 4 facilities (A, n = 106; B, n = 61; C, n = 43; D, n = 100); there were 159 males, 149 females, and 2 patients of unknown gender (**Table 4**). The average patient age was 54.8 years. The mean accuracy was 70.6% (A, 72.6%; B, 72.1%; C, 48.8%; D, 77.0%; 71.1% and 69.8% for males and females, respectively). On final histology, 231 and 79 tumors were benign and malignant, with total accuracy rates of 66.8% and 78.1%, respectively.

Twelve plastic surgeons with an average of 14.3 years of experience (range, 4-33 years) were included (data not shown). In Study 2, there were no significant differences in accuracy according to age, sex, underlying disease, illness duration, tumor site, tumor diameter, tumor color, skin mobility, subcutaneous mobility, hardness, or surgeon experience (Supplemental Table 1).

The pathological and clinical diagnoses were different in 92 cases, including 70 cases of pathologically benign tumors and 10 of clinically malignant tumors. Meanwhile, among the 22 cases pathologically diagnosed as malignant, 16 were judged to be clinically benign (Supplemental Table 2). Other clinical examinations, such as biopsies (4.8%), magnetic resonance imaging (MRI; 4.2%), computed tomography (CT; 0.8%), dermoscopy (0.5%), and ultrasonography (0.3%), were performed in 35 cases (Supplemental Table 3). Among the 79 pathologically malignant tumors, biopsies were performed in 13 cases (Supplemental Table 4). Among the 66 cases without biopsies, 52 (79%) were clinically diagnosed as malignant, while malignancy was considered in the differential diagnosis in 58 (87%) cases.

Table 3. Breakdown and Accuracy of Benign Skin Tumor (Study 1).

	Frequency (n)	Coincidence (n)	Accuracy (%)
Nevocellular nevus	116	105	90.5
Epidermal cyst	56	46	82.1
Venous/lymphatic malformation	51	44	86.3
Lipoma	23	23	100
Seborrheic keratosis	19	16	84.2
Nevus sebaceous	15	14	93.3
Neurofibroma	14	13	92.9
Ganglion	14	14	100
Granuloma	12	5	41.7
Calcifying epithelioma	12	9	75
Verruca vulgaris	8	5	62.5
Scar/keloid	10	9	100
Preauricular sinus/ accessory ear	9	9	100
Pyogenic granuloma	6	5	83.3
Osteoma	5	5	100
Keratoacanthoma	5	1	20
Foreign body granuloma	5	3	60
Calcinosis cutis	3	3	100
Dermatofibroma	3	1	33.3
Neurilemmoma	2	1	50
Blue nevus	1	1	100
Eccrine poroma	1	1	100
Not tumor	58	24	41.4
Total	448	357	79.7

*) Coincidence (n) means that the clinical diagnosis agrees with the pathological diagnosis. Accuracy (%) = [Coincidence (n) /Frequency (n)] × 100

Discussion

Study 1 retrospectively examined the diagnostic accuracy at our institution over the past 10 years. The overall diagnostic accuracy rate was 79.0%, similar to previous reports[2-4,10,11]. Among malignant tumors, the accuracy for MMs and SCCs was relatively low and they were commonly misdiagnosed as pigmented nevi and ulcerative lesions, respectively. These entities cannot be easily discriminated based on gross observation alone. Among benign tumors, ganglions, calcified epitheliomas, and verruca vulgaris had >10 cases each, and their diagnostic accuracy rate was below the average of 79%. It is also difficult to differentiate between sub-

Table 4. Breakdown of Cases at Each Facility (Study 2).

	Facilities				Total
	A	B	C	D	
Frequency (n)	106	61	43	100	310
Coincidence (n)	77	44	21	77	219
Accuracy (%)	72.6	72.1	48.8	77.0	70.6
Male	56 (76.8%)	30 (80.0%)	22 (45.5%)	51 (70.6%)	159 (71.1%)
Female	50 (68.0%)	29 (62.1%)	21 (52.4%)	49 (83.7%)	149 (69.8%)
Unknown		2			2
Benign (Accuracy (%))	73 (62.0%)	46 (64.8%)	23 (48.1%)	89 (76.8%)	231 (66.8%)
Malignant (Accuracy (%))	33 (93.3%)	15 (80%)	20 (52.4%)	11 (60.0%)	79 (78.1%)

*) Coincidence (n) means that the clinical diagnosis agrees with the pathological diagnosis. Accuracy (%) = [Coincidence (n) /Frequency (n)] × 100. Analyzed by multiple comparison test

cutaneous tumors, and common warts can be easily mistaken for seborrheic keratosis.

Study 2 was designed to prospectively elucidate the factors that influence diagnostic accuracy. A multicenter study involving four facilities was conducted to increase the number of cases, and the template devised in Study 1 was used to standardize the diagnostic process. Due to the small number of cases and the fact that pathological diagnoses were made by pathologists at each facility, the diagnostic rates could not be accurately compared among the facilities. The results of Study 2 were not significantly different from those of Study 1. The collection of robust clinical data using a standardized template did not affect the diagnostic accuracy.

Study 2 examined the influence of clinical findings on diagnostic accuracy in greater detail. There were no statistically significant effects of age, sex, disease duration, location, tumor size, skin tone, mobility, stiffness, or years of diagnostic experience (**Table 2**, Supplemental Table 1). Among the 70 cases pathologically diagnosed as benign, 10 (14.2%) were clinically misdiagnosed as malignant. Meanwhile, there was a high rate of misdiagnosis of pathologically malignant tumors as benign (n = 16/22; 72%). In other words, malignant tumors were often unrecognized and overlooked during the first examination. Adjunctive diagnostic systems may be useful if clinical findings are likely to be missed. However, in this study, only 11.3% of the cases underwent imaging or biopsies. Among the 79 tumors pathologically diagnosed as malignant, 66 were not biopsied; this was despite clinical suspicion of malignancy in 52 cases.

Based on these results, active use of assistive medical equipment and biopsies is necessary. Imaging, such as CT, MRI, and ultrasonography, are useful for subcutaneous tumors, and MRI was used more often than CT in this study. Dermoscopy has also been reported to be useful for skin tumors[12-16]. In recent years, dermoscopy has been applied not only to pigmented diseases but also to vascular lesions, among other lesion types[16]. Diagnostic programs based on deep learning are also being developed and plastic surgeons should learn how to apply them as standard procedures[17,18].

Conclusions

Diagnostic accuracy was not improved using a simple template in this study. However, the accuracy of skin tumor diagnosis may be improved by diagnostic training programs, dermoscopy workshops, and novel imaging modalities, including artificial intelligence diagnostic programs.

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Ao, Miyauchi, and Tsuji carried out Study 2.
Murakami and Fujisawa provided advice regarding the histopathology of skin tumors.
Tozawa, Mori, and Nakaoka conceived and designed the study.
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