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Review Article

SENSITIVITY AND SPECIFICITY OF DERMOSCOPY IN MALIGNANT DIAGNOSIS AND PREMALIGNANT SKIN LESIONS

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ABSTRACT

Background and objectives: Dermoscopy is an effective non-invasive diagnostic method that allows the examination of morphological features not detectable by the eye. Dermoscopy has potentially improved the diagnostic accuracy for skin lesions. This study aims to assess the sensitivity and specificity of Dermoscopy in diagnosing malignant and premalignant skin lesions and determining their dermoscopic pattern. **Methods:** This prospective observational study was carried out at the Dermatology Clinic of Imam Khomeini Hospital in *Ahwaz* with the participation of a total of 240 patients, clinically diagnosed with pigmented and non-pigmented skin lesions. Participants were examined with dermoscopy and the results were compared with histopathologic findings as the gold standard for diagnose of skin lesions. At the same time, the major dermoscopic patterns of prevalent skin lesions were investigated. Collected data was analyzed by means of SPSS® software. **Results:** In this study, a total of 240 lesions were evaluated in patients from 10 to 91 years of age. Of this, 69 cases (28.8%) were benign, 75 cases (31.3%) were premalignant, and 96 cases (40.0%) were malignant. BCC (32.9%), SK (16.7%), nevus (6.3%), and SCC (5.0%) were, respectively, the most prevalent types of skin lesions. There was a 75.4% accordance between the dermoscopy and biopsy results. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and the accuracy of dermoscopy in the diagnosis of malignant skin lesions were 85.42%, 70.59%, 80.40%, 77.42%, and 79.27% respectively (P=0.0001). The most prevalent dermoscopic pattern for benign lesions consisted of collarette scale/keratin plaque (26.9%), for premalignant lesions consisted of sharp border (28.0%), and for malignant lesions consisted of blue-gray ovoid nest (41.67%), leaf-like structure (41.67%), and ulceration (39.58%). **Conclusion:** Dermoscopy has high sensitivity and specificity for diagnosis of skin lesions, making this non-invasive real-time method a suitable diagnostic technique for routine dermatologic practices. It can also prove useful in the accurate diagnosis of suspicious lesions prior to conducting biopsy. Therefore, with the aid of dermoscopy, unnecessary invasive biopsy (skin excisions) can be avoided. Nevertheless, conducting additional studies on larger sample volumes is a future necessity.

Keywords: Dermoscopy, Skin lesions, Histopathology, Diagnostic accuracy

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INTRODUCTION

Skin cancers are one of the most common malignant lesions in white Caucasian population, comprising a third of cancers affecting them (1). Melanoma is fatal, unless it is diagnosed in early stages. Meantime, incidence of non-melanoma skin cell (NMSC) malignancies, including basal cell carcinoma (BCC) and squamous cell carcinoma (CSS), is increasing worldwide (2). NMSC seldomly results in death, except in advance stages, where it is accompanied with local damage and metastasis (3). They have a high rate of cure in cases with early diagnosis and effective treatment. Therefore, early diagnosis and treatment is the best strategy for reducing skin cancer-related mortality and morbidity (4).

Although, visual examination is the initial screening method employed by doctors, it often falls short of distinguishing benign lesions from malignant ones. Skin biopsy and histopathologic examination is regarded as the gold standard test for diagnosis (2). This is essentially true when dealing with malignant lesions. Nonetheless, it is an invasive and painful procedure. Thorough sampling is normally impossible in patients with multiple suspicious lesions and NMSC lesions possess varied clinical manifestations. Additionally, biopsy is a time-consuming test and processing samples for diagnosis takes a mean average time of 72 hours (5).

Meanwhile, non-invasive techniques provide better information for a more accurate diagnosis, monitoring and effective treatment of NMSC lesions (2). Furthermore, their common occurrence in areas with aesthetic importance increases the need of developing non-invasive methods that are comparable to histopathologic examination. Today, dermoscopy has become a leading non-invasive evaluation technique(6). The development of this non-invasive diagnostic method not only allows in-vivo tissue inspection for accurate diagnosis, but also contributes to the patient and the health system by being both time and cost effective (4).

Dermoscopy is a simple low-cost non-invasive diagnostic method that helps doctors easily examine the morphological features of a skin lesion (in dermis and papillary dermis) not visible to naked eye. In other words, dermoscopy acts as a link between macroscopic clinical dermatology and microscopic dermatopathology (7-9). Dermoscopy can also serve useful for determining the vascular structures of lesions and details that are barely visible to naked eye (10, 11). In recent years, dermoscopy has also been used for evaluating non-pigmented skin lesions and inflammatory skin diseases and infections. Generally speaking, the main applications of this device reportedly includes the evaluation of pigmented and non-pigmented skin tumors, evaluation of infectious or inflammatory diseases, nail evaluation in autoimmune diseases, monitoring responses to treatments, and evaluating side-effects resulting from treatment (12).

To this day, numerous studies have been conducted to measure the diagnostic accuracy of dermoscopy. A recent meta-analysis research comprising of 9 individual studies suggests the diagnostic accuracy of dermoscopy to be 4 times greater than that of the naked eye (13). Hence, at present, dermoscopy is widely used in dermatology for evaluating skin lesions (14, 15). Dermoscopy has significantly reduced the need for biopsy of skin lesions (16, 17).

Skin biopsy has long served as the sole method for conclusive diagnosis of skin lesions. However, skin biopsy is an invasive measure

with numerous complications and side-effects (5). Meantime, the simple non-invasive dermoscopy technique has found wide application in many centers across the world and is transforming into an integral part of the dermatology curriculum. Nevertheless, in certain regions including Iran, because of being newly introduced (18), the comparison of its results with histopathological findings is less extensively studied. For this reason, the present study was designed to assess the sensitivity and specificity of dermoscopy in diagnosis of malignant and premalignant lesions as compared to pathological examinations.

METHODS

This descriptive cross-sectional research was conducted on patients with skin lesions referring to the Dermatology Clinic of Imam Khomeini Hospital in *Ahwaz* in 2019. Sample volume was determined with respect to the diversity of sensitivity and specificity, a confidence interval (CI) of 95% (P=0.5), and accuracy of 0.065 (d=0.065), yielding to a total of 240 individuals. Participants were selected by simple sampling technique.

Qualification requirements included the existence of pigmented and non-pigmented, malignant and premalignant or suspiciously malignant skin lesions as visible to the naked eye of the examining dermatologist. Based on this criterion, premalignant lesions included were seborrheic keratosis, bowen actinic keratosis, and atypical nevus, while, malignant lesions included were squamous

s cell carcinoma, basal cell carcinoma and melanoma. Individuals with infectious lesions, skin inflammation, and initial non-skin cancer involvement were excluded from the study.

In agreement with the research confidentiality principle, participants were briefed about the basics and objectives of the study, confidentiality of data, and anonymity of checklists. Participation was on voluntary basis and individuals had the right of declining participation.

The present study was approved by Research Council and Ethics Committee of *Ahwaz* Jondishapour University of Medical Sciences under license number IR.AJUMS.REC.1398.119.

To begin with, skin lesions were directly examined and observed. An iPhone X camera was used for macroscopic imaging. Once done, dermoscopy was conducted by a dermatologist using a Dermlite™ (USA) dermatoscope. Once again, the iPhone X camera was used to record images of the dermoscopy process. Images were assessed by 2 experienced dermatologists who were not involved in the process of research. At the same time, dermoscopic patterns of prevalent dermatoses were described.

Patients for whom dermoscopic observation and macroscopic imagery and detailing did not yield a conclusive clinical diagnosis, underwent lesion biopsy and collected samples were examined by a pathologist. Results of naked-eye observation, dermoscopy imaging, and pathology findings for different lesions were eventually compared. Obviously enough, only biopsied lesions were taken into account for assessing the sensitivity and specificity of dermoscopy.

Normality of distributions was tested with Kolmogorov–Smirnov *test* and, owing to the statistically significant nature of the study, Kruskal-Wallis and chi-square tests were applied. At the same time, the diagnostic potential of dermoscopy for skin lesions was measured by means of a receiver operating characteristic curve (ROC). The minimum level of statistical significance was set to a p-value of less than 0.0/5 ($p<0.05$) and analysis was wholly carried out in SPSS®-v21 environment.

RESULTS

The study, attended by 240 patients between the age of 10 and 91 and the mean (standard deviation) age of 57.90 (16.73), aimed at assessing the sensitivity and specificity of dermoscopy in diagnosing malignant and non-malignant skin lesions. Gender distribution ratio was 116 males (48/30%) to 124 (51/70%) females.

Results of successful dermoscopic diagnosis of lesions is presented in table 1. Based on these results, in 75.40% of cases, dermoscopy proved helpful in diagnosing the prevailing dermatoses and, in 24.58% of cases, it proved unhelpful. Meantime, dermoscopy proved more helpful for diagnosis of malignant lesions (85.42%).

In the course of the study, results of successful dermoscopic diagnosis of lesions was also evaluated based on biopsy findings (table 2). As illustrated by the table, for malignant lesions, dermoscopy proved specifically useful in diagnosing BCC lesions (92.40% success), totally successful in diagnosing melanoma, and non-useful for distinguishing lentigo maligna melanoma from lentigo maligna. As for premalignant class, dermoscopy proved more useful in diagnosing lentigo lesions (100% success), and non-useful for EV and actinic chielitis. In the benign group, dermoscopy proved specifically useful for melanonchiya lesions (100% success), sebaceous hyperplasia (100% success), and PG (80% success), while proving non-useful for freckle, eczema, wart, pseudo lymphoma, hidradenoma, and café au lait macules.

One other component of research was to study the diagnostic power of dermoscopy based on the location of lesions (graph 1). Findings reflect a meaningful difference between the diagnosis power of dermoscopy in different parts of the body (P=0.033). Dermoscopy proved most effective for diagnosis of nail (100% success), torso (84.60% success), and face lesions (79.02% success) and least effective for genital lesions (41.7% success).

The diagnostic accuracy of dermoscopy for benign, premalignant, and malignant lesions was also assessed based on the biopsy results serving as the gold standard (table 3 and fig 2). The ROC analysis results for diagnostic power of dermoscopy in premalignant and malignant groups is illustrated by graph 6-3. As shown, area under curve (AUC) is 0.583 (p-value=0.029; CI95%:656.0 – 511.0). The graph also indicates a true positive value of 133 (55.4%), a true negative value of 48 (20.0%), false positive value of 20 (8.3%), and false negative value of 39 (16.3%).

DISCUSSION

Based on the obtained results, the comparison of diagnostic accuracy of dermoscopy for skin lesions with the biopsy findings serving as the gold standard suggests the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and the accuracy of dermoscopy in diagnosing malignant skin lesions to be 85.42%, 70.59%, 80.40%, 77.42%, and 79.27% respectively. In *Ibrahim et al'*s study, the agreement of dermoscopy and direct observation (clinical diagnosis) methods is 72.83% and agreement of dermoscopy and histopathology techniques is 75.76%. The same report indicates the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of dermoscopy in distinguishing benign from malignant skin lesions to be 96.20%, 100%, 100%, and 87.5% respectively (5). In an alternative study carried out by *Rosendahl et al.* (2011), diagnostic sensitivity for melanocytic and non-melanocytic lesions examined with or without dermoscope is 82.6% and 70.5% respectively. Besides, diagnostic accuracy of cases with non-melanocytic lesions was higher than melanocytic (19). In a parallel study, *Lin et al.* (2014) specify a dermoscopic sensitivity and specificity of 79.1% and 78.3% respectively for diagnosis of seborrheic keratosis (SK) (20). By comparing the dermoscopic and histologic results obtained from examining 74 premalignant and malignant lesions, *Stocia et al.* find a total agreement between the dermoscopic and histologic diagnosis of malignant cases and a 94.1% agreement between the two for premalignant cases. They also discover dermoscopy to diagnose malignant lesions with a sensitivity of 100%, specificity of 100%, positive predictive value (PPV) of 100%, and a negative predictive value (NPV) of 94.12% (21). The contradiction of results obtained in the present study as compared to those of the above may be due to the difference in number of samples, type of lesions, and dermatologist's skill.

In the present study, there was a 100% agreement between dermoscopy and pathology in the diagnosis of malignant melanoma, premalignant lentigo, and benign melanonychia and sebaceous hyperplasia lesions. A high agreement of 92.40% was also found between the said methods in the diagnosis of BCC. The previous studies suggest a fair to excellent agreement between dermoscopy and

histopathology in diagnosis of BCC lesions (22). They also suggest the diagnostic accuracy of an experienced dermatologist for the clinical diagnosis of BCC not exceeding 70%, while indicating an 87%, 96%, and 92.72% value for dermoscopic sensitivity and specificity of diagnosing BCC (23). Meantime, in the case of *Stoica et al*. (21), all BCC lesions were diagnosed successfully by means of dermoscopy.

In the study conducted by *Lallas et al.* (2014), dermoscopy is reported with 81.90% sensitivity and 81.80% specificity in BCC diagnosis (24). At the same time, *Reiter et al.* (2019) investigated the diagnostic accuracy of dermoscopy for BCC in their meta-analysis. The results obtained from the 17 parallel studies demonstrate a 91.20% dermoscopic sensitivity and a 95% dermoscopic specificity. In their comparative studies, they discovered that dermoscopy increases the naked-eye sensitivity and specificity from 66.90% to 85% (p=0.0001) and 97.20% to 98.20% (p=0.006) respectively. Dermoscopic sensitivity and specificity for pigmented BCC lesions is also proved to exceed that of non-pigmented types. Henceforth, dermoscopy can be considered a technique with an effectively high sensitivity and specificity for BCC diagnosis, particularly those of pigmented nature (25). In their 2012 study in Spain, *Huerta et al.* report a 0.917 agreement between dermoscopy results and histopathology findings in diagnosing actinic keratosis lesions. Dermoscopic sensitivity and specificity for AK diagnosis was 98.70% and 95% respectively. Therefore, dermoscopy can serve as an effective non-invasive real-time diagnostic procedure for the management of patients with these lesions (26). Dermoscopy is also a widely used non-invasive technique for an effective and rapid diagnosis of invasive melanoma (27). Other studies similarly suggest that dermoscopy increases the diagnostic accuracy of melanoma lesions and stands out as a helpful tool for distinguishing melanoma from nevi. Dermoscopy is, hence, a suitable technique for evaluation of pigmented skin lesions due to being pain-free and providing valuable information to help doctors adequately manage these lesions (28). Nevertheless, it's important to bear in mind that the diagnostic accuracy of dermoscopy depends greatly on the skill and experience of dermatologists (29) and this is a factor that can influence the turnout of any study. Thus, no matter how useful dermoscopy proves to be in the successful diagnosis of skin lesions, it is the expert knowledge of the user that determines its diagnostic value in identifying and evaluating skin lesions (15, 30). An alternative study also demonstrates the sensitivity of dermoscopy for the diagnosis of melanoma to decrease by 10% when conducted by an untrained and unexperienced dermatologist (31).

The strengths of this study over other studies include investigating the high diversity of concomitant malignant and pre-malignant lesions concurrently, describing the common patterns in the lesions studied separately and their frequency, and comparing the diagnostic value of mucosal lesions in comparison with the diagnostic value. The limitations of this study include the exclusion of several types of lesions due to lack of accessibility and non-investigation of macroscopic characteristics of lesions, including size, color, shape, edges, bleeding history, recurrence, histologic nature (i.e. localized, nodular, pigmented, mixed), thickness, and skin type (based on Fitzpatrick scale).

CONCLUSION

The study recommends dermoscopy as a precious tool for distinguishing skin lesions and their unique dermoscopic patterns. Dermoscopy was also determined to be least helpful for diagnosis of mucosal lesions (i.e. genital and labial mucosa), despite of high agreement between dermoscopy and histopathology results. Hence, dermoscopy can be used as a routine diagnostic method in dermatologic examinations to provide information on suspicious lesions prior to conducting invasive skin biopsy. Additionally, with the aid of dermoscopy, it is possible to avoid unnecessary invasive biopsy practices and their related costs, while accelerating the diagnosis process to prevent lesion expansion. Nonetheless, additional research on larger volume of samples is necessary.

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Table 1- Evaluation of the correct diagnosis of the type of lesion by dermoscopy based on biopsy results

Type of lesion	Dermoscopy is useful (n=181)	Dermoscopy is inefficient (n=59)
Malignant (n=69)	49 (71.01)	20 (28.98)
Pre malignant (n=75)	50 (66.67)	25 (33.33)
Benign (n=96)	82 (85.42)	14 (14.58)

Table 2- Evaluation of the correct diagnosis of the type of lesion by dermoscopy based on biopsy results

Result of biopsy	Frequency (percentage)	Dermoscopy is useful (n=181)	Dermoscopy is inefficient (n=59)
BCC	79 (32.9)	73 (92.4)	6 (7.6)
SCC	12 (5)	5 (41.6)	7 (58.4)
SK	40 (16.7)	27 (67.5)	13 (32.5)
Frenkle	1 (0.4)	0	1 (100)
Sebaceous hyperplasia	4 (1.7)	4 (100)	0
Lichen planus (LP)	4 (1.7)	3 (75)	1 (25)
Actinic chielitis	1 (0.4)	0	1 (100)
Actinic keratosis	10 (4.2)	4 (40)	6 (60)
Nevus	15 (6.3)	10 (66.7)	5 (33.3)
Epidermal nevus	10 (4.2)	7 (70)	3 (30)
Dysplastic nevus	2 (0.8)	1 (50)	1 (50)
Wart	2 (0.8)	0	2 (100)
Genital wart	1 (0.4)	0	1 (100)
Bowen	5 (2.1)	4 (80)	1 (20)
Cafe Au Lait macules	1 (0.4)	0	1 (100)
DLE	1 (0.4)	1 (100)	0
Dermatofibroma	5 (2.1)	4 (80)	1 (20)
Angio keratoma	3 (1.3)	3 (100)	0
Eczema	1 (0.4)	0	1 (100)
Melanony chia	4 (1.7)	4 (100)	0
Lentigo	10 (4.2)	10 (100)	0
Lentigo maligna melanoma	1 (0.4)	1 (100)	0
EV	1 (0.4)	0	1 (100)
PG	10 (4.2)	8 (80)	2 (20)
Melanoma	3 (1.3)	3 (100)	0
Kerato acantoma	2 (0.8)	1 (50)	1 (50)
Kaposi sarcoma	3 (1.3)	1 (33.3)	2 (66.7)
Pseudo lymphoma	1 (0.4)	0	1 (100)
Hidradenoma	1 (0.4)	0	1 (100)
Ashy dermatosis	1 (0.4)	1 (100)	0
Lentigo maligna	1 (0.4)	1 (100)	0
ALHE	2 (0.8)	2 (100)	0
DFSP	1 (0.4)	1 (100)	0
Spider angioma	1 (0.4)	1 (100)	0

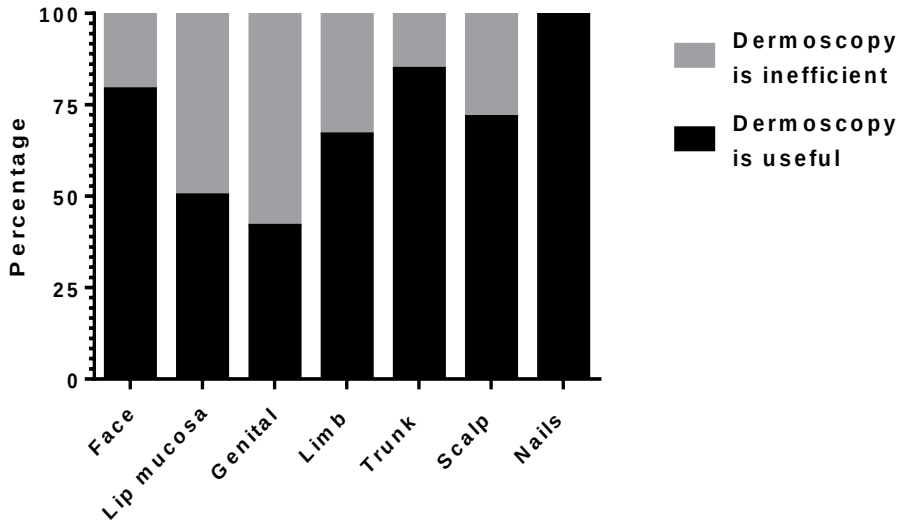

Figure 1- Evaluation of the correct diagnosis in the dermoscopy by location of the lesion

Table 3- Diagnostic accuracy of skin lesions by dermoscopy in percent

Type of skin lesion	Sensitivity	Property	Positive predictive value	Negative predictive value	Precision
Malignant	85.42	70.59	80.40	77.42	79.27
Pre malignant	66.67	70.59	71.43	65.75	68.54
Benign	100	70.58	47.61	100	71.01

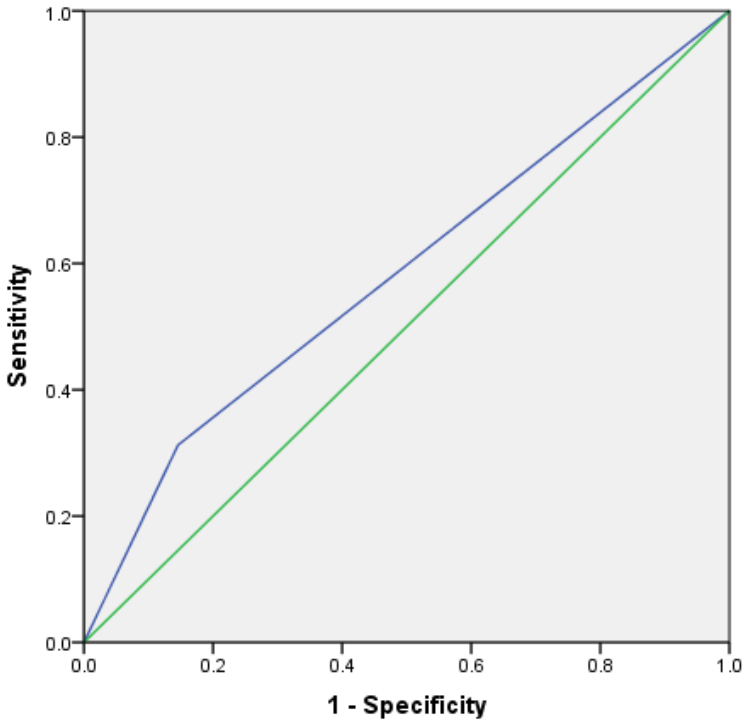

Figure 2- Diagnostic power of malignant and pre-malignant skin lesions by dermoscopy (AUC=0.583, CI: 0.511 – 0.656, p-value=0.029)