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Concordance Test Between Dermoscopic and Histopathological Parameteres in Basal Cell Carcinoma

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ABSTRACT

Background: Basal cell carcinoma (BCC) is the most common skin cancer and can cause local tissue damage. BCC can occur in all populations, regardless of skin color. Dermoscopy has compatibility with histopathology in determining the benign or malignant nature of a lesion. Dermoscopy can improve the diagnostic accuracy of BCC by >90%, with 7 parameters that can be found: arborizing vessels, blue-gray ovoid nests, blue-gray dots/globules, maple leaf-like areas, spoke-wheel areas, ulceration, and hiny white areas. **Purpose:** To assess the compatibility of each dermoscopy parameter with its corresponding histopathological parameters. **Methods:** Observational analytic study with a cross-sectional approach was performed. Dermoscopy parameters were obtained by reassessing all photographs, while histopathological parameters were obtained from pre-existing slide reviews. Cohen's Kappa test was performed to analyze both variables. **Result:** A Total of 26 samples met the inclusion criteria. Most BCCs were found in female sex (65.4%), age >50 years (80.8%), and facial location (88.5%). Cohen's Kappa test was significant in 2 out of 7 dermoscopy parameters: "blue-gray ovoid nests" ($p = 0.0019$; $r = 0.458$) and "spoke wheel areas" ($p = 0.037$; $r = 0.371$). The “shiny white areas” parameter could not be analyzed because there was no negative variation in the examination. The possibility of false positives and negatives could not be ruled out. **Conclusion:** Significance between the two variables is found in 28.6% of the 7 parameters analyzed. Improved methods and studies are needed to prove that dermoscopy can be used as the sole examination for BCC to increase patients’ life expectancies.

Keywords: basal cell carcinoma, cancer, dermoscopy, histopathology, life expectancy.

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BACKGROUND

Basal cell carcinoma (BCC) is most commonly found on the skin as a result of sun exposure, and it seldom emerges on mucous membranes or the palms and soles. BCC is often a slow-growing tumor that seldom spreads. Although BCC is seldom lethal, it can cause local tissue damage if therapy is insufficient or delayed. BCC is a complicated illness since the possibility of getting it is determined by the interplay of hereditary and environmental risk factors.[1] Over the next two decades, the World Health Organization (WHO) expects a 70% increase in skin cancer diagnoses, including BCC, with the majority happening in low- and middle-income nations.[2] Arisanty et al. discovered 896 cases of BCC at Cipto Mangunkusumo Hospital in Jakarta over a 20-year period (2010-2019) that were dominated by the age range of 65-70 years and were female.[3] The higher photoprotection effect in people of color is due to the dispersion of melanosomes inside keratinocytes, and it is estimated that the stratum corneum of people of color has an SPF of 13.4, whereas pale skin has an SPF of 3.3. According to Gupta et al., the link between skin

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pigmentation and photoprotection is significantly more complicated than previously understood. Skin cancer may develop in any community, regardless of skin tone, according to recent research. The high death rate in the colored population is related to the fact that most skin malignancies are not clearly visible, causing diagnostic delays. Because of rising demographics, morbidity, mortality, and a lack of clinical data, people of color must be educated about early diagnosis of skin malignancies and photopreventive strategies to improve their quality of life.[2]

One of the most significant obstacles to diagnosing BCC in Indonesia is that not all health providers have access to histological testing, particularly in rural regions where health facilities are few. Because biopsy testing is invasive and time-consuming, physicians are increasingly employing dermoscopy to diagnose BCC. The dermoscopy examination is very essential in helping to raise the accuracy of the diagnosis of BCC to more than 90%.[4] Dermoscopy parameters in the diagnostic approach to pigmented BCC are grouped into a 7-point checklist, namely large blue-gray ovoid nests, multiple blue-gray globules, maple leaf-like areas, spoke-wheel areas, shiny white areas, ulceration (non-trauma-related), and arborizing telangiectasias.[5] This study builds on the findings of Bintanjoyo et al. and Huda et al. in 2022. Bintanjoyo et al. found in their study that dermoscopy had substantial compatibility with histology in detecting the malignant or benign nature of a skin tumor.[6] Huda et al. found a remarkable correlation between dermoscopy and histological investigation in the diagnosis of BCC without assessing the appropriateness of each dermoscopy parameter with its histology.[7] With the findings of the previous two studies in hand, this study was carried out to assess the applicability of the diagnostic parameters of dermoscopy and histopathology in patients diagnosed clinically with BCC so that it may be used as a reference in establishing a more comprehensive early diagnosis of BCC.

METHODS

This is an analytical observational study with a cross-sectional design. Dermatological parameter data were gathered from the reassessment of dermoscopy images of BCC patients by three dermatologists, whereas histopathological parameter data were derived from original data gained from previously recorded review slide examinations of BCC patients. With regard to preset inclusion and exclusion criteria, the sample strategy employed a purposive sampling method. This study's inclusion criteria were as follows: 1) patients with BCC; 2) dermoscopy examination findings in the form of a picture; and 3) histological evaluation before (through a hole biopsy) and/or after the BCC excision. Exclusion criteria include: 1) inadequate data; 2) hazy or unusable dermoscopy pictures; and 3) a lack of full histopathology slides. The dermoscopy parameters sought in this study include the following: 1) arborizing vessels (associated with “dilation of the blood vessels of the dermis” on histopathology); 2) blue-gray ovoid nests (associated with "aggregation of tumor nests in the papillary dermis with pigmentation"); 3) blue-gray dots/globules (associated with “small tumors nest in the papillary and/or reticular dermis or small tumor aggregates in the dermal-epidermal junction or superficial dermis”); 4) maple leaf-like areas (associated with “multifocal tumor nests containing pigment aggregates, connected to each other by lobular extensions localized in the epidermis and papillary dermis”); 5) spoke wheel areas (associated with “tumor nests connected to the epidermis are marked with finger-like projections and centrally located pigmentation”); 6) ulceration (associated with "loss of epidermis and part of dermis"); 7) and shiny white areas (associated with “stromal collagen and fibrosis in the dermis”).

A Cohen's kappa test using SPSS Statistics version 24.0 was used to analyze the concordance of each dermoscopy and histopathology parameter based on all of the data gathered. A P-value of less than 0.05 was considered statistically significant. This research has obtained ethical approval from the Ethics Committee of Dr. Soetomo General Academic Hospital Surabaya (1238/LOE/301.4.2/II/2023).

RESULT

This study collected a total of 26 samples. Dermoscopy and histological examinations were performed on all 26 samples at the same time. Table 1 displayed information on the demographic characteristics of the samples in this study. The total number of female patients was 17 (65.4%), while the number of male patients was 9 (34.6%). The ratio of the whole sample of patients aged >50 years to those aged 50 years is 4:1. The face was the most common site for lesions, accounting for 23 individuals (88.5%). The most prevalent area for facial lesions is the cheek, followed by the nose. Non-facial lesions were found in 3 patients (11.5%), where 1 patient came with a BCC lesion on the forearm in 2021 and 2 patients came with a location on the neck and chest in 2022.

Table 1. Demographic characteristics of the samples

	2019 n (%)	2020 n (%)	2021 n (%)	2022 n (%)
Sex				
Male	2 (50)	0 (0)	0 (0)	7 (53.8)
Female	2 (50)	3 (100)	6 (100)	6 (46.2)
Age				
<50 y.o	2 (50)	0 (0)	3 (50)	0 (0)
>50 y.o	2 (50)	3 (100)	3 (50)	13 (100)
BCC location				
Facial				
Nose	1 (25)	2 (66.7)	1 (16.7)	2 (15.4)
Cheek	2 (50)	1 (33.3)	3 (50)	5 (38.5)
Temple	0 (0)	0 (0)	1 (16.7)	2 (15.4)
Ear	1 (25)	0 (0)	0 (0)	0 (0)
Forehead	0 (0)	0 (0)	0 (0)	2 (15.4)
Non-facial				
Neck	0 (0)	0 (0)	0 (0)	1 (7.7)
Chest	0 (0)	0 (0)	0 (0)	1 (7.7)
Lower arm	0 (0)	0 (0)	1 (16.7)	0 (0)

BCC : basal cell carcinoma

Table 2. BCC clinical and histopathological subtypes of the samples

Clinical subtypes	n (%)	Histopathological subtypes	n (%)
Pigmented nodular	7 (26.9)	Nodular	17 (65.4)
Pigmented noduloulcerative	5 (19.2)	Pigmented nodular	4 (15.4)
Infiltrative	4 (15.4)	Nodular infiltrative	3 (11.6)
Pigmented	4 (15.4)	Morpheaform infiltrative	1 (3.8)
Pigmented infiltrative	2 (7.7)	Micronodular	1 (3.8)
Nodular	1 (3.8)		
Noduloulcerative	1 (3.8)		
Nodular infiltrative	1 (3.8)		
Pigmented micronodular	1 (3.8)		

BCC : basal cell carcinoma.

Table 2 depicted the clinical and histopathological subtype distribution in our study, while Table 3 showed the distribution of dermoscopy parameter findings with their corresponding histopathology parameters. Table 4 summarized all the results of the Cohen's Kappa test analysis between dermoscopy and histopathological parameters. There were a total of seven parameters that were measured and analyzed in this study. In this study, significant results were found in two parameter groups: 1) parameter 2 between dermoscopy "blue-gray ovoid nests" and histopathology "aggregation of tumor nests in the papillary dermis with pigmentation"; and 2) parameter 5 between dermoscopy "spoke wheel areas" and histopathology "tumor nests connected to the epidermis characterized by finger-like projections and pigmentation located in the center". There was one parameter group that could not be analyzed because there was no negative variation, namely parameter 7 between dermoscopy “shiny white areas” and histopathology “collagen stroma and fibrosis in the dermis”.

Table 3. Distribution findings of dermoscopy and histopathological parameters

Dermoscopy parameter	n (%)	Histopathological parameter	n (%)
Arborizing vessels	9 (34.6)	Dilation of the blood vessels of the dermis	9 (34.6)
Blue-gray ovoid nests	24 (92.3)	Aggregation of tumor nests in the papillary dermis with pigmentation	24 (92.3)
Blue-gray dots/globules	14 (53.8)	Small tumors nest in the papillary and/or reticular dermis, or small tumor aggregates in the DEJ junction or superficial dermis	6 (23.1)
Mapple leaf-like areas	8 (30.8)	Multifocal tumor nests containing pigment aggregates, connected to each other by lobular extensions localized in the epidermis and papillary dermis	15 (57.7)
Spoke wheel areas	4 (15.4)	Tumor nests connected to the epidermis are marked with finger-like projections and centrally located pigmentation	7 (30.8)
Ulceration	21 (80.8)	Loss of epidermis and part of dermis	15 (57.7)
Shiny white areas	26 (100)	Collagen stroma and fibrosis in the dermis	2 (7.7)

DEJ : dermal-epidermal junction

Table 4. Cohen's Kappa analysis between dermoscopy and histopathological parameters

	p	r
Parameter 1	0.443	0.150
Parameter 2	0.019*	0.458
Parameter 3	0.473	0.114
Parameter 4	0.741	0.056
Parameter 5	0.037*	0.371
Parameter 6	0.907	-0.020
Parameter 7	0.000	1.000

p : level of marginal significance (p-value < 0.05 : statistically signifiant)
r : correlation coefficient (r-value 0.01-0,20 : very weak; 0.21-2.40 : weak; 0.41-0.60 : rather weak; 0.61-0.80 : rather; 0.81-0.99 : strong; 1.00 : very strong)

DISCUSSION

All 26 study samples that met the inclusion criteria went through the same two stages of data collection, the first of which was dermoscopy photo analysis to look for the seven dermoscopy parameters, followed by the second stage of histopathological slide review analysis to look for the seven histopathological parameters. The drop-out value in this study was 0%.

Our study samples were dominated by women (17 patients, 65.4%) compared to men (9 patients, 35.6%). This finding is in accordance with research conducted by Wibawa et al., who analyzed 263 cases of skin cancer patients, where the dominance of skin cancer was found by women in their study.[8] The age group >50 years comprised 21 patients (80.8%), whereas the age group 50 years had 5 patients (19.2%). This is consistent with Moore et al.'s study between the asian group and the Caucasian control group. Their study indicated that the average age among Asians suffering from BCC was 68.9 years, which was close to the average age in this study, which was 67.6 years.[9]

In this study, the cheeks and nose are the first and second most prevalent regions that dominate the facial preference in BCC patients, respectively. This is consistent with the findings of a study by Wibawa et al., who discovered that of the 263 skin cancer samples they collected, the most sites were also on the nose and cheeks.[8] We discovered three samples with a proclivity for BCC lesions in non-facial regions, especially the neck, chest, and arms. According to a 13-year retrospective study published in 2016 by Rivers et al., the most prevalent cause of BCC emerging in areas not exposed to sunlight is intermittent and intense exposure to ultraviolet (UV) radiation throughout childhood and adolescence.[10] This theory is consistent with findings from an analytical cohort study conducted by Hidayati et al. in 2015 and 2018, which compared outdoor to indoor workers as a control group and discovered that direct exposure to UV light for 8 weeks can affect the

increase in HSP72 (heat shock protein-72) levels, B-cell lymphoma protein 2-associated X / B-cell lymphoma protein 2 (BAX/BCL-2) ratio, and IL-10 levels in peripheral blood.[11-13] Because HSP72 has cytoprotective qualities against cellular stress, the BAX/BCL-2 ratio is associated with cell death, and IL-10 is an immune-suppressing cytokine, we might anticipate that UV exposure for years in the infancy period can cause future BCC development, even in places not ordinarily exposed to the sun.

This study discovered that the most dermoscopy characteristics detected in the research samples (found in 100% of the samples) were shining white patches. Shiny white patches can only be observed using polarized dermoscopy, and even then, the operator must spin the dermoscope over the lesion (depending on the angle) to notice them.[14] The shiny white area parameter was found in 100% of the sample, even though the sample in this study did not consist entirely of non-pigmented BCC, making the possibility of a false positive undeniable, even though the readings had been carried out by three expert staffs. Arborizing vessels as a vascular structure from the dermoscopy parameters of BCC is in fifth place of the 7 dermoscopy parameters that we analyzed. This is slightly different from what was revealed by Popadic in their research, where they found that arborizing vessels ranked top in nodular and superficial subtype BCCs.[15] Dermoscopy is indeed a subjective examination. In addition, direct dermoscopy readings also have higher accuracy compared to photographs, which certainly cannot capture the entire field of view of a lesion.

Histopathological parameters in this study were mostly dominated by aggregation of tumor nests in the papillary dermis with pigmentation, which represented dermoscopy of blue-gray ovoid nests. This is in line with what we found in the pattern of dermoscopy parameters, where blue-gray ovoid nests occupy the second highest number of parameters in this study sample. It is also in stark contrast to the finding where the parameters that should represent dermoscopy parameters of shiny white areas were only found in 2 patient samples (7.7%), while shiny white areas were found in 100% of dermoscopy readings. Histopathological examination in our study found that the predominant subtype was the nodular subtype and the rest were mixed subtypes, so it is possible that the parameter shiny white areas on dermoscopy readings that reached 100% could be confounded by false positives. This study found that there were only two parameters that correlated with each other out of the seven parameters analyzed. These parameters are dermoscopy of blue-gray ovoid nests with histopathology of aggregation of tumor nests in the papillary dermis with pigmentation and dermoscopy of spoke wheel areas with histopathology of tumor nests connected to the epidermis marked by finger-like projections and centrally located pigmentation. Both of these parameters are included in the pigment structure. According to Lallas et al.'s literature review, four parameters of pigment structure in dermoscopy (blue-gray ovoid nests, blue-gray dots/globules, maple leaf-like areas, and spoke wheel areas) are very important and specific components in the diagnosis of BCC, particularly in people with dark skin.[16] Because all of the samples in the current study were of Asian origin and had colored skin, it was only logical that the two dermoscopy criteria that showed a substantial agreement with histology were pigment structures.

Popadic's prospective observational study of variations in dermoscopy in 151 BCC samples revealed that certain dermoscopy parameters cannot be generalized to all BCC subtypes because the distribution of each of these parameters varies depending on the subtype. Maple leaf-like areas, for example, are the least common parameter in the nodular BCC subtype, whereas ulceration is the least common in the superficial BCC subtype.[15] Given the substantial subtype variation in this study, it is only logical that several parameters were not significant.

The concept of overlapping BCC subtypes and the numerous combinations of dermoscopy characteristics contained therein are confounding variables in this study. This might be the most major confounding factor causing false positives or negatives in both dermoscopy and histological interpretation, resulting in more parameters being determined to be insignificant in this study. Furthermore, when we analyze the conceptual framework and pathophysiology of BCC development, we can observe that the two pigment structure parameters have substantial value, suggesting that the majority of the BCC patients in our sample are in the continuation phase. This can be a prediction that people's awareness of BCC is still poor, since they tend to seek treatment when the lesion is advanced and often has an ulcerated look.

The limitations identified in this study are : dermoscopy assessment using photographs taken with different devices and lighting results in high bias readings; the use of histopathological slides that were not entirely from excision preparations (mixed with punch biopsy); the use of the double-blind method on histopathological operators; and collagen staining

using Masson's Trichrome has not been utilized in parameter 7.

In summary, this study found significance in two of the seven parameter groups, accounting for 28.6% of the total. Because the strength of the association established by the two is still in the weak and moderate range, the two parameters cannot be generalized to the general population. To improve early identification and quality of life for BCC patients, further studies with improved research protocols are needed to corroborate the pioneering findings in this study.

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