Clinical Accuracy of Skin Cancer Diagnosis: Investigation of Keratinocyte Carcinoma Mismatch Rates

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PRACTICE **POINTS**

- Malignant lesions may be misdiagnosed when assessments are guided by clinical features that align with typical presentations of other lesion types, potentially leading to diagnostic errors among experienced clinicians.
- Although dermoscopy is a beneficial tool in examining potential skin cancers, clinical observations should not bypass the gold standard of histopathologic examination.

To the Editor:

The incidence of nonmelanoma skin cancer (NMSC) is rapidly increasing worldwide. Due to its highly curable nature when treated early, accurate diagnosis is the cornerstone to good patient outcomes.[1] Accurate diagnosis of skin cancer and subsequent treatment decisions rely heavily on the congruence between clinical observations and histopathologic assessments. Clinical misdiagnosis of a malignant lesion can lead to delayed and suboptimal treatment, which may contribute to serious complications such as metastasis or even mortality. In this study, data from clinically diagnosed basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs) were compared to their identified histopathologic subtype classifications. The accuracy of the clinical diagnosis of these NMSCs was assessed by determining the rate of misdiagnosis and the respective positive predictive value (PPV).

A retrospective review of medical records from a private dermatology practice in Lubbock, Texas, was conducted to identify patients diagnosed with NMSC from January 1, 2017, through December 31, 2021. A total of 11,229 NMSCs were diagnosed and treated in 5877 patients. Of the NMSCs diagnosed, 11,145 were identified as keratinocyte carcinomas and were classified as BCCs or SCCs. The accuracy of the clinical diagnoses was determined by comparison to the histologic subtype identified via biopsy of the lesion. Although the use of a dermatoscope during the clinical encounter was not formally recorded, reports from the examining dermatologists indicated it was not used in the majority of cases.

If a lesion was clinically diagnosed as a BCC but was identified as a subtype of SCC on histology (or vice versa), the lesion was considered to be mismatched. The number of mismatched lesions and the mismatch rate for each lesion type/subtype is recorded in the Table. Of the total 11,145 keratinocyte carcinomas included in our study, there was an overall 10.63% mismatch rate, with 1185 of the malignancies having a differing clinical diagnosis (eg, BCC vs SCC) from the histologic findings. The clinical mismatch rate was notably higher for SCC compared to BCC (15.83% vs 7.03%, respectively).

The Table provides a breakdown of the BCC subtypes identified by histology with their computed mismatch rate and PPV. It is worth clarifying that lesions classified as more than one BCC subtype per the histologic findings were diagnosed as mixed BCC; these were further classified as mixed-aggressive BCC (if at least one aggressive BCC subtype was present) and mixed nonaggressive

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The authors have no relevant financial disclosures to report.

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Cutis. 2024 May;115(5):162-164. doi:10.12788/cutis.1204

BCC (if no aggressive BCC subtype was present). Overall, BCCs were less likely to be misdiagnosed, with an average PPV of 92.97% compared to 84.17% for SCCs. Basosquamous BCC was the BCC subtype with the highest mismatch rate (25.48%), while sclerosing BCC has the lowest overall mismatch rate (1.33%). The most common malignancy was BCC, with nodular BCC being the most common subtype.

The Table also breaks down the SCC subtypes, reporting the most commonly misdiagnosed of any BCC or SCC subtype to be poorly differentiated SCC (mismatch rate, 38.46%). The lowest mismatch rate of the SCC subtypes was 5.97% for well-differentiated SCC.

There was an overall PPV of 89.37% in clinically evaluated malignancies and their respective histologic subtypes. Basal cell carcinoma had a lower overall mismatch rate of 7.03% compared to 15.83% in SCC. The most common misdiagnosis was attributed to poorly differentiated SCC (mismatch rate, 38.46%), while the least common misdiagnosed malignancy was sclerosing BCC (1.33%). The high mismatch rate of poorly differentiated SCC may be due to its diverging presentation from a typical SCC as a flat lesion with the absence of scaling, keratin, or bleeding, leading to the misdiagnosis of BCC.[2]

Accurate clinical diagnosis of NMSCs is the basis for further evaluation and treatment that should ensue in a timely manner; however, accurately identifying BCCs vs SCCs solely based on clinical examination can be challenging due to variable manifestations and overlapping features. Basal cell carcinoma commonly presents as a shiny pink/flesh-colored nodule, macule, or patch with surface telangiectasia, sometimes appearing with ulceration or crusting.[3] Alternatively, SCC typically appears as a firm, sharply demarcated, red nodule with a thick overlying scale.[4] Definitive diagnoses can be difficult upon clinical examination since these features can be shared

TABLE. Clinical Diagnosis Mismatch Rates

Lesion type/subtype	No. of total lesions	No. of mismatched lesions	Mismatch rate, %	PPV, %
KC	11,145	1185	10.63	89.37
BCC	6585	463	7.03	92.97
Basosquamous BCC	157	40	25.48	74.52
Unspecified BCC	1429	127	8.89	91.11
Infiltrative BCC	982	73	7.43	92.57
Nodular BCC	3088	183	5.93	94.07
Nonaggressive mixed BCC	294	17	5.78	94.22
Mixed BCC	966	55	5.69	94.31
Aggressive mixed BCC	672	38	5.65	94.35
Superficial BCC	559	31	5.55	94.45
Micronodular BCC	295	8	2.71	97.29
Sclerosing BCC	75	1	1.33	98.67
SCC	4560	722	15.83	84.17
Poorly differentiated SCC	13	5	38.46	61.54
In situ SCC	249	56	22.49	77.51
Moderately differentiated SCC	1231	261	21.20	78.80
Superficial SCC	842	165	19.60	80.40
Acantholytic SCC	7	1	14.29	85.71
Well-differentiated SCC	972	58	5.97	94.03

Abbreviations: BCC, basal cell carcinoma; KC, keratinocyte carcinoma; PPV, positive predictive value; SCC, squamous cell carcinoma.

between the 2 subtypes. To aid in these uncertainties, a growing number of clinicians are implementing the use of dermoscopy in their everyday practice.

Dermoscopy is an extremely useful tool in improving the diagnostic accuracy of skin cancers compared to examination with the naked eye, as it provides detailed visualization of specific structures and patterns in skin cancer lesions.[5] The dermoscopic appearance of BCC is characterized by pearly blue-gray or translucent globules with arborizing vessels, spoke-wheel structures, and leaf-like areas.[5,6] Conversely, dermoscopic features of SCC may include a milky-red globule with a scaly, sharply demarcated, crusted lesion with polymorphous vasculature, sometimes resembling a persistent sore or nonhealing wound.[4,5] Though the use of dermoscopy can aid in diagnosis upon initial examination, certain factors such as trauma, ulceration, and previous treatments that distorted the lesion's architecture may lead to misdiagnosis. Furthermore, the distinct vascular patterns found in BCC and SCC may be mistaken for each other and therefore lead to misdiagnosis upon examination.[7] Other variables that may complicate diagnosis include the location of the lesion, its size, and the presence of other skin conditions or nearby lesions.

The primary limitation of the current study was the limited scope of the data, as they were derived from patients seen at one private dermatology practice, preventing the generalizability of our findings. However, our results show trends similar to those observed in other studies analyzing the clinical accuracy of skin cancer diagnoses, with higher PPVs for BCC compared to SCC. A study by Ahnlide and Bjellerup[8] was based in a hospital dermatology department and demonstrated a PPV of 85.5% for BCC compared to 92.97% in our study; for SCC, the PPV was 67.3% compared to 84.17% in our study. In another study by Heal et al,[9] data were collected from an Australian registry that included records of all histologically confirmed skin cancers from December 1996 to October 1999 from 202 general practitioners and 42 specialists, including 1 dermatologist. The PPVs for BCC and SCC were 72.7% and 49.4%, respectively. Although our results indicated higher PPVs compared to these 2 studies, some of the discrepancies can be accounted for by the differences in clinical setting as well as the lack of expertise of nondermatologist physicians in identifying skin malignancies in the study by Heal et al.[9]

The current study was further limited by the lack of data quantifying the number of lesions clinically suspected to be malignant but found to be histologically benign. It is typical for clinicians to have a low threshold to biopsy a suspicious lesion with atypical features (eg, rapid evolution and growth, bleeding, crusting). Furthermore, the identification of risk factors in the patient's medical and family history (eg, exposure to radiation, personal or family history of skin cancers) can heavily influence a clinician's decision to biopsy a lesion with an atypical appearance.[10] Many benign lesions are biopsied to avoid missing a diagnosis of malignancy. Consequently, our results suggest a high degree of clinical misdiagnosis of BCCs and SCCs. Obtaining data on the number of lesions suspected to be BCC or SCC that were found to be histologically benign would be a valuable addition to our study, as it would provide a measurable insight into the sensitivity of clinicians' decision-making to identify a lesion as suspicious and warranting biopsy.

While clinical diagnosis plays a vital role in identifying suspected NMSCs such as BCC and SCC, its accuracy can be limited even with the use of dermoscopy. Overall, our data have shown a high rate of diagnostic accuracy upon suspicion of malignancy, but the different variables that affect clinical presentation promote histologic diagnosis to prevail as the gold standard.

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