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Itch and Pain in Nonmelanoma Skin Cancer: Pain as an Important Feature of Cutaneous Squamous Cell Carcinoma

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Pain is a common feature of cancer with an estimated prevalence rate between 52% and 77%.[1] Itch is the most common dermatologic symptom and is also a common feature of lymphoma.[2] However, no studies have been performed examining the prevalence rates of pain and itch in common skin cancers. Squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are the 2 most common types of nonmelanoma skin cancer (NMSC). They have a rapidly increasing incidence in the United States, with nearly 4 million new cases of NMSC diagnosed each year.[3] The purpose of the present study was to assess the prevalence and intensity of pain and itch among the 2 most common skin cancers.

Methods

Data for this institutional review board–approved study were prospectively collected on a total of 576 biopsy-proven NMSCs from 478 patients with either BCC or SCC seen in the dermatologic surgery department at Wake Forest University Baptist Medical Center from July 2010 to March 2011. Patients rated their pain and itch intensity on a visual analog scale from 0 (least intense) to 10 (most intense). A multiple logistic regression model was fit to examine the relationship of pain and itch with BCC and SCC using age, sex, chronic pain- or itch-related conditions, tumor size, and depth of invasion as covariates. A subanalysis was also performed to compare SCC in situ vs invasive SCC.

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Author Contributions: Dr Mills, Mr Kwatra, and Drs D'Agostino and Yosipovitch had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Mills, Pearce, D'Agostino, and Yosipovitch. *Acquisition of data:* Mills, Kwatra, Feneran, Pearce, Williford, and Yosipovitch. *Analysis and interpretation of data:* Mills, Kwatra, Feneran, D'Agostino, and Yosipovitch. *Drafting of the manuscript:* Mills, Kwatra, Feneran, D'Agostino, and Yosipovitch. Critical revision of the manuscript for important intellectual content: Mills, Kwatra, Pearce, Williford, D'Agostino, and Yosipovitch. *Statistical analysis:* D'Agostino. *Administrative, technical, and material support:* Kwatra, Pearce, Williford, and Yosipovitch. *Study supervision:* Mills, Pearce, and Yosipovitch.
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Results

Of the 505 patients approached, 478 completed the study. The mean (SD) age was 68.8 (12.7) years (age range, 27-94 years), and most patients were male (304 men, 174 women). There were 353 biopsy-proven SCCs and 223 BCCs.

Itch was the most common symptom reported in both skin cancers (43.5% of SCCs and 33.4% of BCCs). This difference was not statistically significant.

The prevalence of pain was 39.8% (95% CI, 35.4%-44.2%) in SCC and 17.7% (95% CI, 13.4%-21.9%) in BCC. A patient's pain score was a highly significant predictor of having an SCC as opposed to a BCC ($P<.001$). For each point increase on the VAS in pain, there was a 30% increase in the odds of having an SCC compared with having a BCC (**Figure**, A). Further analysis revealed that patients presenting with a pain score higher than 2 had a nearly 4-fold increase in the likelihood of having an SCC compared with a BCC (odds ratio [OR], 3.94 [95% CI, 2.49-6.23) ($P<.001$).

To account for potential intraindividual differences in patients with multiple skin cancers, data were stratified into 2 groups, patients with 1 skin cancer vs those with 2 or more skin cancers. Analyses were repeated in each group, and comparable results were obtained, suggesting no difference between these groups. Interestingly, pain did not significantly differ in patients with SCC in situ compared with invasive types of SCC ($P=.47$).

Comment

Our findings reveal that pain and itch are common symptoms of NMSC. A previous study reported tenderness in SCC,[4] but to our knowledge, ours is the first study to assess the prevalence of pain and itch and their intensities in NMSC. Specifically, we have shown the intensity of pain to be a unique factor to help in differentiating SCC from BCC. This finding is of significant clinical utility in the diagnosis and treatment of NMSCs. With an increasingly aging population, patients often present with numerous BCCs and SCCs, and it is often difficult for the clinician to prioritize lesion biopsy and removal. Thus, there is a need for better clinical tools to aid the physician in selecting lesions most likely to be SCCs, which have the greatest potential for metastasis. The results of this study suggest that a simple assessment of pain intensity will aid in the clinical diagnosis of SCC and lead to earlier appropriately aggressive treatment of these lesions.

Our subanalysis of the histologic features of these cancers revealed a correlation with perineural invasion and pain. Perineural invasion was identified in 3 cases (2 cases of SCC and 1 case of BCC). While all cases with perineural invasion were painful, the small sample size limits the generalizability of this finding.

References

1. van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, Schouten HC, van Kleef M, Patijn J. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. Ann Oncol. 2007; 18(9):1437–1449. [PubMed: 17355955]
2. Yosipovitch G. Chronic pruritus: a paraneoplastic sign. Dermatol Ther. 2010; 23(6):590–596. [PubMed: 21054705]
3. Rogers HW, Weinstock MA, Harris AR, et al. Incidence estimate of nonmelanoma skin cancer in the United States, 2006. Arch Dermatol. 2010; 146(3):283–287. [PubMed: 20231499]
4. Askari SK, Schram SE, Wenner RA, et al. Evaluation of prospectively collected presenting signs/symptoms of biopsy-proven melanoma, basal cell carcinoma, squamous cell carcinoma, and

seborrheic keratosis in an elderly male population. J Am Acad Dermatol. 2007; 56(5):739–747. [PubMed: 17258839]

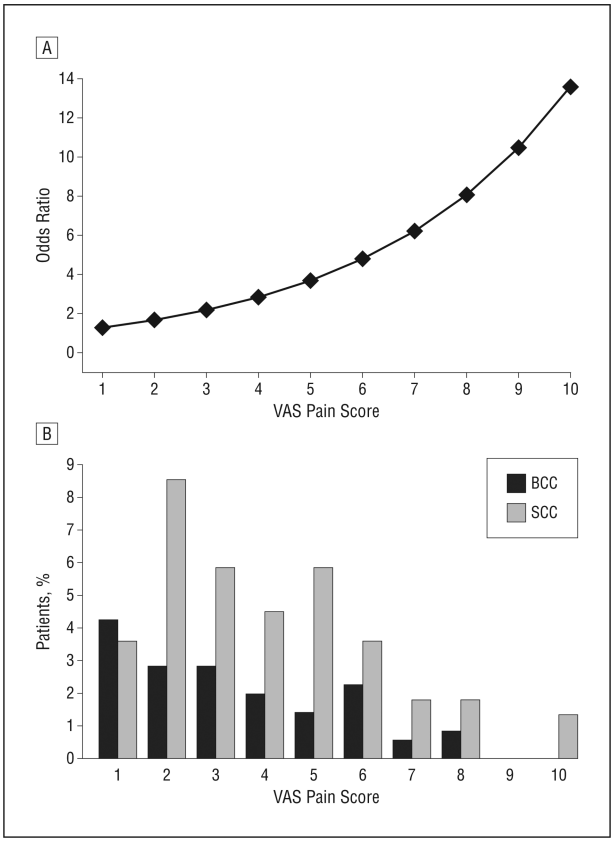

Figure.
Comparisons of squamous cell carcinoma (SCC) with basal cell carcinoma (BCC). A, Odds ratios for having SCC vs BCC for each additional point on the visual analog scale (VAS) for pain. B, Distribution of VAS pain scores in BCC and SCC.