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Patient Concern as a Predictor of Cutaneous Malignancy

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To The Editor

History and physical examination remain the primary sources of information for the clinical decision of skin cancer diagnosis, even with in-vivo diagnostic aids.^{1,2} Marghoob and Scope³ identified six components for a decision to biopsy: five arise from visual examination, while the sixth relates to “history, e.g. patient concerns.” Patient concern has been suggested as a supporting factor for malignancy likelihood when clinical examination is inconclusive.^{4–6} The purpose of this study is to compare the statistical significance of patient “concern” with other historical features in assessing a potentially malignant lesion.

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We retrospectively analysed 3080 patient encounters for 3619 lesions in four US private-practice dermatology clinics (Rolla, Missouri; Columbia, Missouri; Plantation, Florida; Stamford, Connecticut) enrolled in a dermoscopy-aided melanoma diagnosis study (NIH-R44-CA101639-02A2).⁷ Phelps County Regional Medical Centre Institutional Review Board, Rolla Missouri, approved this study; consent was obtained for each subject. Lesions were included in the study if considered of interest to the dermatologist or patient. All invasive or in-situ melanoma (MM) lesions were confirmed with histopathology. Non-melanoma skin cancers (NMSCs) were similarly diagnosed, except for twelve diagnosed with dermoscopy and treated with cryotherapy.

Historical information was obtained for age, gender, lesion location, patient history of melanoma, 1st degree family history of melanoma, history of change, and concern. Concern was present if the patient or family member responded affirmatively to the question: “Is there any concern about this [lesion]?” Sensitivity, specificity, odds ratios (OR) and positive predictive values⁸ were computed using SAS (Statistical Analysis Software, version 9, SAS Institute Inc.). Age and lesion location were converted into categorical variables (Table 1). Lesions collected in this study (N=3,619) included 367 malignant melanomas (144 invasive, 223 *in situ*), 875 non-melanoma skin cancers (666 basal cell carcinomas, 209 squamous cell carcinomas), 734 dysplastic nevi, 308 seborrheic keratoses, 294 nevocellular nevi without atypia, 178 lentigines, 143 actinic keratoses, and 720 miscellaneous benign lesions.

Overall, 34.8% of malignancies (MM, NMSC) were associated with patient concern (39.5% MM, 33.0% NMSC, 28.1% benign). Table 1 shows highest OR for MM as: age 60y/o (OR=3.34), patient concern (OR=1.67), and gender (Male, OR=1.67). For both MM and NMSC, OR for concern (OR 1.67 for MM; 1.26 for NMSC) were higher versus change (OR 1.44 for MM, 0.87 for NMSC). While higher specificity for MM was seen with concern (73% vs. 59% for change), there is lower sensitivity (37% vs. 50% for change). The highest odds ratios for NMSC were age 60y/o (OR=4.12) and location head/neck (OR=3.67). A history of change was significant for MM (p=0.001), but not for NMSC (p=0.081). The most common benign diagnosis associated with patient concern was nevus (96 of 294 cases).

Patient concern was tabulated by age group for MM, NMSC, and benign lesions. Figure 1 shows that concern declines with age and loses diagnostic significance around 70 years of age. For the 71–80yo, 81–90yo, and 91yo age groups, there were no significant differences for concern between benign lesions and either MM or NMSC. (p>0.05 for all 3 age groups, t-test, unequal variances).

Lack of awareness in older persons could be related to diminishing visual acuity, general neurocognitive impairment,⁹ or a general indifference regarding the medical condition. Stone et al. noted that concern over health matters drops starting at 50 years of age and reaches the lowest adult levels starting at age 70.¹⁰ Age-related indifference to health matters, l’indifférence de la vieille,”— the indifference of aging, is common.

We believe that both change and concern are useful predictors of melanoma, as Bourne *et al.* denoted in their BLINCK algorithm, where ‘N’ denotes nervousness and ‘C’ denotes change.⁶ Patients have rated change as the most important feature in identifying

melanoma.¹¹ Our data show that change is correlated with concern: 825/1100 (77.5%) of patients with concern also noted change. Evidence suggests that patients may not be reliable at detecting change;^{11,12} our data supports this, as specificity for melanoma and NMSC were 72–73% for concern vs. 59% for change. When only change or concern were present, 9% of patients had melanoma; with both present, this increases to 14%. The clinical finding of concern adds useful clinical information that change alone does not provide.

Concern can encompass more than change, and includes things that a patient is not able to articulate. An “ugly duckling”, an atypical nevus that deviates from an individual’s nevus pattern,¹³ may be of concern, but may not be considered to show change. Perception of one’s own skin tends to be heightened or warped, and allows one to discern subtle ugly ducklings. It is possible that patients subconsciously perceive subtle changes that they are otherwise unable to communicate.⁴ Patients know more than they verbalize, and may summarize this by acknowledging concern, requesting a biopsy, or appearing nervous.⁶ In our study, 6 of 144 (4.2%) patients with invasive melanoma and 17 of 223 (7.6%) with in-situ melanoma exhibited concern when melanoma was not on the physician’s differential diagnosis. This proportion supports the 6.0% of patients with melanoma in a study by Gachon *et al.*, for whom seemingly benign lesions “were removed only to reassure the patient,” yet were histopathologically diagnosed as melanoma.⁴

One limitation of the study is the non-consecutive acquisition of cases in a private practice setting, implying that the images are collected subject to convenience; many cases, particularly epitheliomas, were biopsied and not entered into the study database. However, none of the authors were originally cognizant of the fact that “patient concern” was more significant than change. This was only revealed in *post hoc* data analysis, thereby reducing the risk of selection bias. Additionally, we did not attempt to measure any characteristics that led to patient concern, such as specific verbal features (i.e. “itch”, “feels funny”, etc). Future studies could accrue these characteristics to further elucidate the components leading to a feeling of concern.

In summary, patient concern held greater importance for malignancy than other historical factors, including a changing lesion appearance. Patient concern should be integrated with other information, such as dermoscopy evaluation, to improve the sensitivity of melanoma detection.

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Figure 1.

Concern by age group: malignant melanoma (MM), basal cell carcinoma and squamous cell carcinoma (BCC/SCC), and benign cutaneous lesions. Differences for concern between malignant and benign groups vanish after age 70 years.

Statistics for malignant melanoma (invasive and *in situ*) and for non-melanoma skin cancers (basal cell carcinoma and squamous cell carcinoma) from data obtained from patient interviews.

Table 1

STATISTICS: MALIGNANT MELANOMA						
HISTORICAL DATA	Odds Ratio ¹	95% CI	p-Value	Sensitivity(%)	Specificity (%)	Positive Predictive Value (%)
Age 60 y/o	3.34	2.64–4.22	<0.001	69	60	21
Male	1.67	1.34–2.09	<0.001	62	50	16
Concern	1.67	1.33–2.09	<0.001	39	73	18
Lesion on upper limbs ²	1.52	1.16–2.00	.0023	22	84	18
Change	1.44	1.16–1.80	.0011	50	59	16
Patient history of malignant melanoma	1.32	1.47–2.34	<0.001	36	77	19
Family history of malignant melanoma (1 st degree relative)	0.76	0.56–1.04	.0897	14	82	11
STATISTICS: NON-MELANOMA SKIN CANCER						
Age 60 y/o	4.12	3.47–4.89	<0.001	74	60	40
Lesion on head/neck ²	3.67	3.12–4.33	<.0001	52	77	46
Male	1.70	1.45–1.99	<.0001	62	51	32
Concern	1.26	1.06–1.49	0.0070	32	72	30
Change	0.868	0.74–1.02	0.0807	38	59	25
Patient history of malignant melanoma	0.701	.574-.855	.000432	18	77	22
Family history of malignant melanoma (1 st degree relative)	0.458	0.36–0.59	<.0001	9	82	16

¹ p-values for these odds ratios were computed from the Chi-square distribution using the Wald Chi-square value (Pearson uncorrected)

² Lesion locations were classified as head/neck, chest, back, abdomen, upper extremities, lower extremities, acral, and ano-genital. After calculation of odds ratio for malignant melanoma for each location vs. all other locations the highest odds ratio obtained (for location on upper extremities) is listed in the table. The same procedure was follow for non-melanoma skin cancer: the highest odds ratio obtained for NMSC was for head/neck region.