Table I. Demographic comparisons across study domains

Study domains, Likert scale	Median (IQR)		Median (IQR)	*P* value*	Adjusted difference in median	*P* value†
Communication						
Less education‡	1.4 (1.0-1.8)	More education§	1.4 (1.1-1.8)	.41	0.13	.39
Age ≤65 y	1.4 (1.0-1.8)	Age >65 y	1.4 (1.1-1.8)	.64	−0.13	.36
Women	1.1 (1.0-1.5)	Men	1.4 (1.1-1.8)	.09	0.25	.08
Excellent/very good‖	1.2 (1.0-1.5)	Good/fair/poor‖	1.6 (1.1-1.9)	.01	0.25	.08
Complications						
Less education	1.8 (1.3-2.0)	More education	2.0 (1.5-2.2)	.19	0.25	.10
Age ≤65 y	2.0 (1.5-2.5)	Age >65 y	1.8 (1.5-2.0)	**.03**	−0.38	**.01**
Women	1.8 (1.5-2.2)	Men	1.8 (1.5-2.2)	.99	0.13	.40
Excellent/very good	1.8 (1.5-2.2)	Good/fair/poor	1.8 (1.5-2.4)	.71	0.13	.39
Facility						
Less education	1.4 (1.0-1.8)	More education	1.6 (1.4-2.0)	.30	0.2	.07
Age ≤65 y	1.6 (1.4-1.8)	Age >65 y	1.4 (1.0-1.8)	.20	−0.2	.052
Women	1.6 (1.2-1.8)	Men	1.6 (1.2-1.8)	.99	0	.99
Excellent/very good	1.4 (1.2-1.6)	Good/fair/poor	1.8 (1.4-2.0)	**.01**	0.4	<**.01**
Courtesy						
Less education	1.2 (1.0-1.8)	More education	1.4 (1.0-2.0)	.32	0	.99
Age ≤65 y	1.6 (1.2-1.8)	Age >65 y	1.2 (1.0-1.8)	.04	−0.4	**.01**
Women	1.2 (1.0-1.6)	Men	1.6 (1.0-1.8)	.26	0.2	.18
Excellent/very good	1.2 (1.0-1.8)	Good/fair/poor	1.6 (1.2-2.0)	.05	0.2	.17

IQR, Interquartile range.
*Wilcoxon rank sum tests were used to compare median IQR.
†Quantile regression models were used to obtain the adjusted differences in median scores comparing more education with less education, older patients with younger patients, men with women, and good/fair/poor overall health with excellent/very good overall health. Significant *P* values confirmed in the adjusted analysis are shown in bold.
‡Less education (high school, some college, or a 2-year degree).
§More education (a 4-year graduate degree or more than 4 years).
‖Refers to self-reported assessment of overall health.

REFERENCES

1. *Rewarding Provider Performance: Aligning Incentives in Medicare*. Washington, DC: Institute of Medicine; 2007.
2. Anhang Price R, Elliott MN, Zaslavsky AM, et al. Examining the role of patient experience surveys in measuring health care quality. *Med Care Res Rev*. 2014;71(5):522-554.
3. Kantor J. Primary surgical closure versus second intention healing after Mohs micrographic surgery: patient satisfaction and clinical implications. *J Am Acad Dermatol*. 2016;75(1):e35.
4. Asgari MM, Bertenthal D, Sen S, Sahay A, Chren MM. Patient satisfaction after treatment of nonmelanoma skin cancer. *Dermatol Surg*. 2009;35(7):1041-1049.
5. CMS.gov. US Centers for Medicare and Medicaid Services. Outpatient and Ambulatory Surgery CAHPS (OAS CAHPS). Available at: https://www.cms.gov/Research-Statistics-Data-and-Systems/Research/CAHPS/OAS-CAHPS.html; 2016. Accessed December 9, 2017.
6. Golda N, Beeson S, Kohli N, Merrill B. Recommendations for improving the patient experience in specialty encounters. *J Am Acad Dermatol*. 2018;78(4):653-659.

https://doi.org/10.1016/j.jaad.2018.10.011

Morphea and systemic sclerosis are associated with an increased risk for melanoma and nonmelanoma skin cancer

To the Editor: It is well-known that systemic autoimmune diseases confer an increased risk for cancer.[1] In recent years, studies have described an increased risk for epithelial malignancies in patients with systemic sclerosis—most commonly lung carcinoma.[2-4] There are no current studies in the literature evaluating the prevalence of epithelial skin cancers in patients with the localized form of scleroderma, morphea. Using the Slicer Dicer feature of the electronic medical record system EPIC, we retrospectively collected anonymous, aggregate-level data on patients ≥18 years of age seen at Johns Hopkins Hospital (JHH) over a 6-year period (March 9, 2012-March 9, 2018). The prevalences of melanoma, squamous cell carcinoma of

Table I. Patients >18 years with morphea or systemic sclerosis and concomitant diagnosis of melanoma, squamous cell carcinoma, or basal cell carcinoma compared with the general Johns Hopkins Hospital patient population, by race, March 9, 2012-March 9, 2018

Race	Cancer	Morphea, n (%)	General population, n (%)	OR (95% CI)	*P* value	Systemic sclerosis, n (%)	OR (95% CI)	*P* value
All								
Morphea, n = 1445	Melanoma	16 (1.1)	7936 (0.2)	6.6 (4.1-10.9)	<.0001	16 (0.6)	3.4 (2.1-5.5)	<.0001
Systemic sclerosis, n = 2822	SCC	28 (1.9)	7269 (0.2)	12.8 (8.8-18.6)	<.0001	31 (1.1)	7.2 (5.0-10.3)	<.0001
General population, n = 4,713,781	BCC	45 (3.1)	11,546 (0.2)	13.1 (9.7-17.5)	<.0001	28 (1.0)	4.1 (2.8-5.9)	<.0001
White								
Morphea, n = 1105	Melanoma	13 (1.2)	7455 (0.3)	4.1 (2.4-7.1)	<.0001	15 (0.8)	2.8 (1.7-4.6)	.0001
Systemic sclerosis	SCC	27 (2.4)	6476 (0.3)	9.9 (6.7-14.6)	<.0001	29 (1.5)	6.2 (4.3-9.0)	<.0001
General population, n = 2,574,911	BCC	45 (4.1)	11,255 (0.4)	9.7 (7.2-13.0)	<.0001	27 (1.4)	3.3 (2.3-4.9)	<.0001
Black								
Morphea, n = 217	Melanoma	1 (0.5)	163 (0)	25.7 (3.5-184.3)	.001	0 (0)	NA	NA
Systemic sclerosis, n = 520	SCC	1 (0.5)	500 (0.1)	8.4 (1.2-59.8)	.03	2 (0.4)	7.0 (1.7-28.1)	.006
General population, n = 904,608	BCC	0 (0)	67 (0)	NA	NA	0 (0)	NA	NA

In all cases, morphea and systemic scleroderma were associated with a statistically significantly increased risk of both melanoma and non-melanoma skin cancer. Our findings suggest that a diagnosis of morphea or systemic sclerosis is associated with an additional increased risk of developing skin cancer that is unrelated to race.

BCC, Basal cell carcinoma; *CI*, confidence interval; *NA*, not applicable; *OR*, odds ratio; *SCC*, squamous cell carcinoma.

Table II. Sex and race of patients with morphea, systemic sclerosis, morphea or systemic sclerosis with concomitant skin cancer, and general population at Johns Hopkins Hospital

	Sex		Race		
Patient population	Female, n (%)	Male, n (%)	White, n (%)	Black, n (%)	Unknown/other, n (%)
General population	2,579,606 (54.4)	2,160,855 (45.6)	2,574,911 (54.2)	904,608 (19.0)	1,274,821 (26.8)
All with morphea	1294 (89.4)	154 (10.6)	1105 (76.3)	217 (15.0)	126 (8.7)
Morphea and melanoma	16 (100)	0 (0)	13 (81.3)	1 (6.3)	1 (6.3)
Morphea and SCC	25 (86.2)	3 (10.7)	27 (96.4)	1 (3.6)	0 (0)
Morphea and BCC	40 (88.9)	5 (11.1)	45 (100)	0 (0)	0 (0)
All with systemic sclerosis	2347 (83.1)	479 (16.9)	1877 (66.4)	520 (18.4)	429 (15.2)
Systemic sclerosis and melanoma	14 (87.5)	2 (12.5)	15 (93.8)	0 (0)	1 (6.3)
Systemic sclerosis and SCC	18 (58.1)	13 (41.9)	29 (93.5)	2 (6.5)	0 (0)
Systemic sclerosis and BCC	25 (89.3)	3 (10.7)	27 (96.4)	0 (0)	1 (3.6)

The majority of patients with either morphea or systemic sclerosis and skin cancer were white females. This distribution is likely reflective of the tendency for autoimmune diseases to predominantly affect females and for skin cancer to predominantly affect white patients.

Female patients with morphea were not significantly more likely to have melanoma or nonmelanoma skin cancer than male patients with morphea (OR 1.2, 95% CI 0.6-2.6; $P = .6$). Likewise, female patients with systemic sclerosis were not significantly more likely than male patients with systemic sclerosis to receive a melanoma or nonmelanoma skin cancer diagnosis (OR 0.6, 95% CI 0.3-1.1; $P = .1$). Thus, this increased risk for skin cancer appears to be unrelated to sex.

In all of our cohorts, most patients were between 50-75 years of age (66.3% of morphea patients, 68.8% of systemic sclerosis patients, 68.5% of melanoma patients, 77.1% of SCC patients, 81.5% of BCC patients).

BCC, Basal cell carcinoma; *CI*, confidence interval; *OR*, odds ratio; *SCC*, squamous cell carcinoma.

the skin, and basal cell carcinoma were collected for patients with concomitant diagnosis of morphea or systemic sclerosis. As a control, we compared these values with those of the general JHH patient population and then calculated the odds ratios (ORs) and *P* values for each comparison using a 95% confidence interval (CI) (Table I). We found that, compared with the general population of patients at JHH, patients with morphea were 6.6 times more likely to have melanoma (OR 6.6, 95% CI 4.1-10.9; $P < .0001$), 12.8 times more likely to have squamous cell carcinoma of the skin (OR 12.8, 95% CI 8.8-18.6; $P < .0001$), and 13.1 times more likely to have basal cell carcinoma (OR 13.1, 95% CI 9.7-17.5; $P < .0001$). The prevalence of these skin cancers was also significantly elevated in patients with systemic sclerosis compared with the general population, although not to the same degree. This increased risk for skin cancer in patients with morphea and systemic sclerosis was still present after stratifying by race (Table I). In both our morphea and systemic sclerosis cohorts, most patients with concomitant skin cancer were white females (Table II).

This is the first report describing an increased risk for both melanoma and nonmelanoma skin cancer in patients with morphea. There are several explanations for this association. One is that the treatment of morphea—either with immunosuppressive agents or ultraviolet light therapy—increases the risk for epithelial malignant transformation. Chronic inflammation and elevated levels of the cytokine transforming growth factor β in patients with morphea might contribute to malignant transformation of epithelial tissue as well.[5] Another explanation is that the anticancer immune response to epithelial malignancy leads to attack of normal host tissue, resulting in autoimmunity. Patients with a genetic predisposition for autoimmune disease might also be predisposed to the development of cancer, and it is possible that the inciting exposure for both outcomes is the same.

Limitations of this study include an inability to determine a temporal relationship between the diagnosis of skin cancer and morphea. Further, patients with morphea or systemic sclerosis are more likely to be seen by either a rheumatologist or dermatologist, who are skilled at diagnosing skin cancer. The characteristics of morphea or treatments associated with a greater risk for epithelial malignancy should be evaluated in future studies to determine which patients might benefit from an increased frequency of skin cancer screening.

Emily Boozalis, BA,[a] Ami A. Shah, MD, MHS,[b] Fredrick Wigley, MD,[b] Sewon Kang, MD,[a] and Shawn G. Kwatra, MD[a,c]

From the Department of Dermatology,[a] and Scleroderma Center,[b] Johns Hopkins University School of Medicine, Baltimore, Maryland and Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland[c]

Funding sources: None.

Conflicts of interest: Dr Kwatra is an advisory board member for Menlo and Trevi Therapeutics. All other authors have no conflicts of interest to disclose.

Reprints not available from the authors.

Correspondence to: Shawn G. Kwatra, MD, Cancer Research Building II, Johns Hopkins University School of Medicine, Ste 206, 1550 Orleans St, Baltimore, MD 21231

E-mail: skwatra1@jhmi.edu

REFERENCES

1. Joseph CG, Darrah E, Shah AA, et al. Association of the autoimmune disease scleroderma with an immunologic response to cancer. *Science*. 2014;343(6167):152-157.
2. Onishi A, Sugiyama D, Kumagai S, Morinobu A. Cancer incidence in systemic sclerosis: meta-analysis of population-based cohort studies. *Arthritis Rheum*. 2013;65(7):1913-1921.
3. Shah AA, Rosen A, Hummers L, Wigley F, Casciola-Rosen L. Close temporal relationship between onset of cancer and scleroderma in patients with RNA polymerase I/III antibodies. *Arthritis Rheum*. 2010;62(9):2787-2795.
4. Shah AA, Casciola-Rosen L. Cancer and scleroderma: a paraneoplastic disease with implications for malignancy screening. *Curr Opin Rheumatol*. 2015;27(6):563-570.
5. Takahashi M, Akamatsu H, Yagami A, et al. Epithelial–mesenchymal transition of the eccrine glands is involved in skin fibrosis in morphea. *J Dermatol*. 2013;40(9):720-725.

https://doi.org/10.1016/j.jaad.2018.10.022

A retrospective study: Application site pain with the use of crisaborole, a topical phosphodiesterase 4 inhibitor

To the Editor: Topical corticosteroids are among the cornerstone treatments of atopic dermatitis (AD); however, prolonged use is associated with skin atrophy, hypopigmentation, and telangiectasia.[1] Nonsteroidal alternatives include topical calcineurin inhibitors such as pimecrolimus and tacrolimus and the phosphodiesterase 4 inhibitor crisaborole, which have application site pain as a side effect. The