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Chronic nonmelanoma skin cancers and health-related impairment: A case-control study

To the Editor: Nonmelanoma skin cancer (NMSC) has become an epidemic. The annual incidence of NMSC is estimated to be 5 million, and we spend more than $4.8 billion annually on treatment.[1,2] Our group has proposed that NMSC be considered a chronic disease in a subset of patients, with the goal of developing chronic disease management strategies that focus on prevention.[3] By definition, an illness meets the criteria for a chronic disease if it lasts longer than 1 year, requires ongoing medical care, and/or limits activities of daily living.[4] The purpose of this study was to determine whether patients with 5 or more NMSCs meet the criteria for having a chronic disease.

A 2:1 matched case control study was designed to compare patients with 5 or more NMSCs (excluding genetic cancer syndromes) with patients who have had 1 to 4 NMSCs in their lifetime. A power analysis based on sample variance from the pilot data revealed that 20 patients were needed to detect a significant difference of 15 points in their 20-Item Short Form Health Survey scores.

The cutoff of 5 or more NMSCs was selected on the basis of the clinical experience of our dermatologic surgeon, according to which patients meeting this threshold often continue to develop NMSCs and use our system more extensively, as measured by clinic visits and procedures required to manage their NMSCs. Patients were recruited sequentially from the dermatologic surgery clinics at Keck Medicine of the University of Southern California. Approximately 3% of patients seen for Mohs micrographic surgery in our clinic had 5 or more NMSCs in their lifetime.

In all, 73 patients agreed to participate in the study (survey response rate, 96%); 4 patients had incomplete surveys and could not be used in the analysis. The mean age of the analytic cohort was 69 years, 71% were male, and 96% identified as white (Table I). There were no statistically significant differences in age, sex, or ethnicity. Of the patients with 1 to 4 NMSCs, 27% were immunosuppressed; in contrast, 50% of those with 5 or more NMSCs were immunosuppressed ($P = .08$).

Table I. Patient characteristics (N = 69)

Variable	1-4 skin cancers (n = 26)	≥5 skin cancers (n = 43)	*P* value
Age, y, range*	68.6 (37-87)	69.7 (31-96)	.75
Sex, n (%)			1.00
Male	19 (73.1%)	30 (69.8%)	
Female	7 (26.9%)	13 (30.2%)	
Ethnicity, n (%)			.07
Hispanic	3 (11.5%)	0	
Non-Hispanic	23 (88.5%)	37 (100.0%)	
Race*			.62
White	25 (96.2%)	41 (97.6%)	
Asian	1 (3.9%)	0	
African American	0	1 (2.4%)	
Time since diagnosis of first skin cancer, y†	8.8	27.0	<.001
Total skin cancers, n (%)†			
In the past 1 y	1.2	5.0	<.001
In the past 5 y	1.7	14.7	.004
In lifetime	1.9	30.0	.004
Total skin cancers, n (%)†			
In the past 1 y	1.2	5.0	<.001
In the past 5 y	1.7	14.7	.004
In lifetime	1.9	30.0	.004
Family history of skin cancer, n (%)	8 (33.3%)	23 (53.5%)	.13
Dermatology visits, n (%)			
In the past month			<.001
0-1	18 (75.0%)	10 (24.4%)	
2-3	6 (25.0%)	23 (56.1%)	
4-5	0	5 (12.2%)	
≥6	0	3 (7.3%)	
In the past year			.001
0-3	17 (70.8%)	10 (23.3%)	
4-5	4 (16.7%)	14 (32.6%)	
6-10	3 (12.5%)	11 (25.6%)	
≥11	0	8 (18.6%)	

P values comparing the groups were obtained by using a *t* test or analysis of variance for continuous variables and the Fisher exact test for discrete variables. Percentages reflect the percentage of patients within each cancer cohort.
*Data represent the mean.
†One patient did not identify race.

Notable differences were found between the groups in time since diagnosis of first NMSC (27.0 years in the group with 5 or more NMSCs vs 8.8 years in the group with 1-4 NMSCs), number of required dermatology visits, and impact on quality of life. Specifically, 71% of patients with 1 to 4 skin cancers had 3 or fewer visits over the past year, whereas 77% of patients with 5 or more NMSCs required more than 3 visits.

Patients with 5 or more NMSCs had statistically lower scores on the physical ($P < .04$) and role subscales of the 20-Item Short Form Health Survey ($P < .02$), representing a greater impact on quality of life in these domains (Table II). Importantly, there was no difference between the groups in score on the Lawton IADL scale, which evaluates functional status. The cohort of patients with 5 or more skin cancers had greater bother in all subscales of the Skindex-16.

Reconceptualization of NMSC as a chronic disease in patients with 5 or more skin cancers will further validate NMSC as a condition that requires strategies for chronic disease management in such patients. Our data show that individuals with 5 or more skin cancers diagnosed over a period longer than 1 year meet the criteria for having a chronic disease. This reconceptualization will promote the development of coordinated prevention, education, and treatment strategies that aim to improve the health and outcomes of patients.

Future prospective analysis is needed to further characterize this cohort and determine which

Table II. Quality of life measures by skin cancer group

Scale	1-4 skin cancers (n = 26)	≥5+ skin cancers (n = 43)	*P* value
SF-20			
Physical	81.1	62.0	.04
Role	92.3	72.7	.02
Social	89.2	80.0	.11
Mental health	76.0	79.1	.54
Current health	69.6	63.7	.38
Pain	76.2	67.4	.17
Skindex-16			
Symptoms	16.5	30.0	.03
Emotional	23.9	42.1	.01
Functional	7.9	21.3	.02
Lawton IADL scale	6.9	6.6	.16

Results are presented as means.
IADL, Instrumental Activities of Daily Living; *SF-20*, 20-Item Short Form Health Survey.

strategies improve outcomes. First, however, we must have criteria to define NMSC as a chronic disease, and our data suggest that 5 or more skin cancers can be used to operationalize this distinction.

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Sirolimus for treatment of verrucous venous malformation: A retrospective cohort study

To the Editor: Verrucous venous malformation (VVM) is a rare, congenital vascular malformation.[1] The treatment for VVM is particularly difficult.[2] Couto et al[3] found a somatic MAP3K3 mutation in patients with VVM. MAP3K3 is an upstream molecule of the mammalian target of rapamycin signaling pathway, and sirolimus is an inhibitor of the mammalian target of rapamycin.

We retrospectively analyzed a cohort of 10 patients with VVM who were treated with sirolimus. Patients who presented with VVM were consecutively enrolled in a study at the Dermatology and Venereology Department of the Capital Institute of Pediatrics in Beijing, China, between 2015 and 2017. Individuals with comorbidities including malignancy, pneumonia combined with serious sepsis, or encephalitis were to be excluded; however, no patients had these comorbidities. Informed consent forms were obtained from all subjects or their family members. According to the International Society for the Study of Vascular Anomalies classification of vascular anomalies and the 10th edition

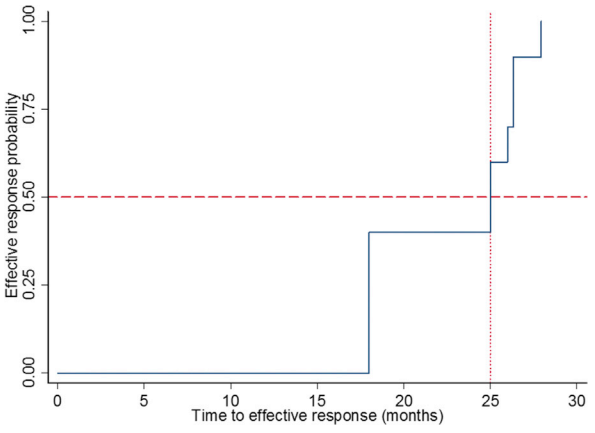

Fig 1. Effective treatment response rate curve for sirolimus in the treatment of verrucous venous malformation.