

Statin use may be a predictor of larger and more aggressive tumor characteristics in squamous cell carcinoma

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INTRODUCTION

- Cutaneous squamous cell carcinoma is the second most common malignancy worldwide, with more recent data suggesting its incidence is increasing disproportionately compared to basal cell carcinoma
- Despite overall low rates of metastasis, mortality rates in some regions approach that of melanoma
- Given these factors, it is imperative to characterize patient- and tumor specific risk factors for high-risk tumors
- Current staging guidelines such as the AJCC and BWH alternative criteria have formalized tumor-specific risk factors
- However, person-specific and environmental factors have not been as well elucidated

Patient characteristics	No. (%)
Gender	
M	129 (64.5)
F	71 (35.5)
Age	
<40	3 (1.5)
≥40, <75	101 (50.5)
≥75	96 (48.0)
Former/Current smoker	
Yes	114 (57.0)
No	86 (43.0)
Hypothyroidism	
Yes	26 (13.0)
No	174 (87.0)
Hyperlipidemia	
Yes	124 (62.0)
No	76 (38.0)
Statin use	
Yes	109 (54.5)
No	91 (45.5)
Tumor characteristics	No. (%)
Size (cm)	
<2	163 (81.5)
≥2	37 (18.5)
Location	
Head and neck	112 (61.0)
Trunk	9 (4.5)
UE	53 (26.5)
LE	13 (6.5)
Genitalia	3 (1.5)

Table 1. Demographics

METHODS

This retrospective chart study was approved by the University of Nebraska Medical Center Institutional Review Board.

CoPath was used to retrieve all cases of specimens of skin with “squamous cell carcinoma” in the final diagnosis from 2010-2018. This search yielded a total of 707 unique patients and 1080 tumors. Each patient record was subsequently reviewed to verify the diagnosis of SCC. Patient-specific information was gathered from the chart, including demographics, smoking history, medical history, immune status, and statin use. Tumor-specific information needed to stage by BWH and AJCC criteria was also gathered, including tumor diameter, differentiation on histology, perineural invasion, and tumor invasion depth. If information from the patient chart was not adequate to stage patients by BWH criteria, the slides were reviewed by a board-certified, dermatology-trained dermatopathologist. Patients were excluded if they had history of immunosuppression, multiple SCCs, recurrent SCCs, or nodal metastases.

The remaining cohort of patients was stratified by statin use, size of tumor (<2 cm or ≥2 cm), and high (BWH stage T2b-T3) or low (T1-T2a) risk. A statistical analysis was performed using chi-square test to evaluate for any differences between tumor size and stage and statin use.

Characteristics	SCC patients		P-value
	with statin use, No. (%)	without statin use, No. (%)	
Age at diagnosis			
<40	0	3(5.9)	.04
≥40, <75	34(43.6)	27(52.9)	
≥75	44(56.4)	21(41.2)	
Former/Current smoker			
Yes	51(65.4)	30(58.8)	.45
No	27(34.6)	21(41.2)	
Hypothyroidism			
Yes	7(9)	3(5.9)	.52
No	71(91)	48(94.1)	
Tumor size			
<2	57(73.1)	45(88.2)	.04
≥2	21(26.9)	6(11.8)	
BWH staging			
T1-T2a	59(75.6)	46(90.2)	.04
T2b-T3	19(24.4)	5(9.8)	
Location			
Head and neck	51(65.4)	38(74.5)	.27
Trunk	1(1.3)	2(3.9)	
UE	24(30.8)	8(15.7)	
LE	1(1.3)	1(2.0)	
Genitalia	1(1.3)	2(3.9)	

Table 2. Patients and tumor characteristics in male SCC patients with and without statin use

RESULTS

- Our cohort consisted of a total of 200 patients, of which approximately two-thirds was male
- Just over half of patients had history of current or prior statin use
- Among male patients, the age distribution of SCC patients with history of statin use was significantly older compared to the age of patients without history of statin use
- Across the entire cohort, there was no significant difference in tumor size or BWH risk (high or low) between patients with history of statin use compared to those without
- However, when separated by gender, we found that a greater proportion of male patients with statin history had tumor size of 2 centimeters or greater compared to those without statin history
- Further, 24.4% of male patients with statin history presented with high risk tumors (BWH stage T2b-T3) compared to those without (9.8%, p=0.038).
- There was no significant difference in tumor size or tumor stage in female patients.

CONCLUSIONS

- The role of statins in the incidence and prognosis of cutaneous squamous cell carcinoma is unclear
- A previous systematic review and meta-analysis by Kuoppala, et al found that statins may confer slight increased risk of melanoma and non-melanoma skin cancer
- Another study also demonstrated a higher risk of basal cell carcinoma with longer duration of statin use in men
- Conversely, several studies have reported statin use to be associated with better outcomes in head and neck squamous cell carcinoma
- Potential mechanisms by which statin use may increase risk of cSCC include immunomodulatory effects on regulatory T cells or inhibition of the ras signaling pathway.
- However, further research is necessary to determine the definitive role of statins on development of cSCC and whether particular statins pose more risk compared to others

REFERENCES

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