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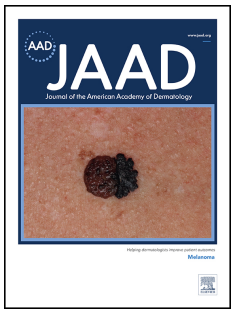

Dermoscopy of cutaneous squamous cell carcinoma by anatomical location and risk stratification: a retrospective cross-sectional study

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TITLE PAGE

Article type: ***Brief report***

Title: Dermoscopy of cutaneous squamous cell carcinoma by anatomical location and risk stratification: a retrospective cross-sectional study

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Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement: All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The patients in this manuscript have given written informed consent to publication of their case details. This study was approved by the Institutional Review Board of Azienda Unità Sanitaria Locale – IRCCS di Reggio Emilia, Italy (CE: CE: 875/2020/OSS/IRCCSRE).

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TEXT

Cutaneous squamous cell carcinoma (cSCC) is a common skin cancer; prognosis is usually favorable, yet a clinically relevant subset carries a risk of recurrence and metastasis.[1,2] With the 2022 NCCN update adding the "very-high risk" category, dermoscopic correlates across anatomical sites and risk categories warrant better characterization.[3] We evaluated dermoscopic features of invasive cSCC (iSCCs) by macro-anatomical location and NCCN risk category and explored dermoscopic predictors of very-high risk tumors defined by histopathological poor differentiation.

We retrospectively reviewed histopathologically confirmed iSCCs with dermoscopic images collected at an Italian Skin Cancer Center (2011-2021). Nail and genital tumors were excluded. Lesions were grouped into macro-areas (head/neck, trunk, upper/lower limbs, acral sites) and classified as low-, high-, or very-high risk according to NCCN criteria[3]. Two dermatologists assessed dermoscopic criteria while blinded to clinical data, risk group, and histopathology[4,5]. Group comparisons used univariate testing; logistic regression to identify predictors of poor differentiation was performed for head/neck only due to cohort distribution. No formal correction for multiple testing was applied, to avoid an excessive increase in type II error.

We analyzed 768 iSCCs; most occurred on the head/neck (79.9%) and most patients were male (76.8%). Differentiation grade was available for 668 tumors; poorly differentiated cSCCs were often located on lower limbs (71.4%) and acral sites (52.0%) ($p<0.001$). Dermoscopy showed site-related differences: small-caliber vessels predominated on upper limbs (73.8%) and acral sites (75.9%); diffuse (whole-lesion) vascularity was common on the trunk (70.4%) and lower limbs (62.5%), whereas a peripheral distribution prevailed on acral sites (73.4%) and head/neck (51.9%) ($p<0.001$). Dotted-glomerular vessels were frequent overall (65.6%, $p<0.001$); conversely, arborizing vessels were more common on trunk (38.6%) and head/neck (30.8%) ($p<0.001$). Ulceration occurred in 61.0%, particularly on head/neck and limbs ($p<0.001$). Pink structureless

areas were common (78.4%) without anatomical differences; white circles were uncommon but more frequent on head/neck (13.9%). Yellow crust was typical of acral sites, head/neck, and lower limbs (75.5%, 65.2%, and 63.5%, respectively; p=0.038).

By NCCN risk category, 8.5% were low-risk, 79.4% high-risk, and 12.2% very-high risk; age increased with risk severity (p<0.001) (**eTable**). Low-risk tumors often showed small-caliber, dotted-glomerular or hairpin vessels and white scale, whereas higher-risk tumors more often showed linear irregular or arborizing vessels and ulceration (p<0.001) (**Table 1**). On head/neck, independent predictors of poor differentiation were age (OR 1.03 per year; p=0.044), ulceration (OR 2.27; p=0.002), and yellow crust (OR 1.70; p=0.039) (**Table 2**, **eFigure**), while peripheral vessel distribution, dotted-glomerular vessels, and white circles were protective (**eFigure 2**).

In conclusion, dermoscopic patterns in iSCC vary by anatomical location and NCCN risk category. Acral lesions showed the most distinctive profile (small peripheral vessels and frequent central keratin or yellow crust, but rare ulceration). Poor differentiation (very high-risk tumor) was independently associated with older age, ulceration, and yellow crust. Notably, yellow crust may reflect purulent material/dried exudate from local contamination/secondary infection rather than keratinization (white scale), potentially contributing to higher prevalence in head/neck, lower-limb, and acral sites. Dermoscopy may support earlier risk upgrading while histology is pending, although the retrospective design warrant validation.

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1. Paganelli A, Zaffonato M, Donati B, et al. Molecular and Histopathological Characterization of Metastatic Cutaneous Squamous Cell Carcinomas: A Case-Control Study. *Cancers (Basel)*. 2024;16(12):2233. doi:10.3390/cancers16122233
2. Schmults CD, Karia PS, Carter JB, Han J, Qureshi AA. Factors predictive of recurrence and death from cutaneous squamous cell carcinoma: a 10-year, single-institution cohort study. *JAMA Dermatol*. 2013;149(5):541-547. doi:10.1001/jamadermatol.2013.2139
3. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology: Squamous Cell Skin Cancer*. Accessed January 3, 2026. https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf
4. Lallas A, Pyne J, Kyrgidis A, et al. The clinical and dermoscopic features of invasive cutaneous squamous cell carcinoma depend on the histopathological grade of differentiation. *Br J Dermatol*. 2015;172(5):1308-1315. doi:10.1111/bjd.13510
5. Rosendahl C, Cameron A, Argenziano G, Zalaudek I, Tschandl P, Kittler H. Dermoscopy of squamous cell carcinoma and keratoacanthoma. *Arch Dermatol*. 2012;148(12):1386-1392. doi:10.1001/archdermatol.2012.2974

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Table 1. Descriptive characteristics and comparisons among different risk groups

Variable	Total, n=1536	Low risk, n=130 (8.5)	High risk, n=1220 (79.4)	Very High Risk, n=186 (12.2)	p-value
Age*, mean ±SD (range)	80.4 ±10.0 (37-102)	76.3 ±12.1 (37-95)	80.6 ±9.8 (39-102)	81.9 ±8.9 (41-96)	**<0.001**
Sex (male)	1180 (76.8)	88 (67.7)	948 (77.7)	144 (77.4)	**0.036**
Caliber (vessels)					
small	708 (51.9)	82 (70.1)	553 (51.2)	73 (43.2)	**<0.001**
large	182 (13.3)	11 (9.4)	148 (13.7)	23 (13.6)	
both	475 (34.8)	24 (20.5)	378 (35.0)	73 (43.2)	
Distribution (vessels)					
whole lesions	612 (44.8)	64 (54.7)	453 (42.0)	95 (56.2)	**0.002**
center	36 (2.6)	1 (0.8)	31 (2.9)	4 (2.4)	
periphery	694 (50.8)	52 (44.4)	576 (53.4)	66 (39.0)	
cluster	23 (1.7)	0 (0.0)	19 (1.8)	4 (2.4)	
Dotted-glomerular	895 (65.6)	90 (76.9)	706 (65.4)	99 (58.6)	**0.006**
Arborizing vessels	384 (28.1)	15 (12.8)	315 (29.2)	54 (31.9)	**<0.001**
Hairpin vessels	368 (27.0)	34 (29.1)	305 (28.3)	29 (17.2)	**0.009**
Linear irregular vessels	1170 (85.7)	85 (72.6)	927 (85.9)	158 (93.5)	**<0.001**
Ulceration	936 (61.0)	56 (43.1)	744 (61.0)	136 (73.1)	**<0.001**
Pinkish structureless area	1204 (78.4)	91 (70.0)	982 (80.5)	131 (70.4)	**<0.001**
White halo	799 (52.1)	70 (53.8)	638 (52.3)	91 (49.2)	0.665
White circles	185 (112.0)	7 (5.4)	163 (13.4)	15 (8.1)	**0.006**
White scales	866 (56.5)	88 (67.7)	688 (56.5)	90 (48.4)	**0.003**
Central keratin distribution	661 (43.1)	53 (40.8)	539 (44.2)	69 (37.1)	0.162
Yellow scales	997 (64.9)	72 (55.4)	798 (65.5)	127 (58.3)	**0.043**

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Table 2 - Multivariate model for histopathology grading of differentiation in SCC of the head and neck (well-moderate vs poor differentiated/very high risk)

	Multivariate model		
	OR	**95%CI**	**P value**
Demographic criteria			
Age at diagnosis, *mean yrs ±SD(range)*	1.03	1.00-1.05	**.04**
Dermoscopy criteria			
Vessels distribution			
Whole lesion	ref.		
Center	0.30	0.6-1.49	.142
Periphery	0.38	0.23-0.62	**.000**
Cluster	1.55	0.22-9.18	0.79
Dotted-glomerular vessels	0.43	0.26-0.70	**.001**
Ulceration	2.27	1.33-3.84	**.002**
White circles	0.38	0.17-0.86	**.02**
Yellow crust	1.70	1.03-2.81	**.039**

Abbreviations: OR, odds ratio*; SD,* standard deviation; *CI*, confidence interva

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