Our results demonstrate that the scalp is a "high-risk region" for metastasis of cSCC, similar to the lip and ear.

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Melanoma in situ and invasive melanoma of the vulva: An analysis of the National Cancer Database

To the Editor: Vulvar melanoma (VM) accounts for 6% to 10% of vulvar malignancies.[1] Current knowledge comes from smaller retrospective studies.[1,2] This study investigated the demographics and survival of VM in situ (MIS) and invasive VM (IVM) using the National Cancer Database (NCDB).

International Classification of Diseases for Oncology third edition histology codes for melanoma 8720 to 8774, combined with primary site codes for the vulva (C510-519), were used to identify patients with VM in NCDB between 2004 and 2016. The analysis included 394 patients with vulvar MIS and 1688 patients with IVM, with a median age at diagnosis of 63 and 66 years, respectively. The median Breslow thickness for IVM was 2.00 mm, and 56.8% of patients presented with ulceration. Regional lymph node metastasis was found in 22.8% of patients (Table I). The 5-year overall survival (OS) was 74.4% for vulvar MIS and 42.7% for IVM (Figs 1 and 2).

When adjusting for confounders, independent predictors of worse OS in IVM were age (hazard ratio [HR], 1.02; 95% confidence interval [CI], 1.01-1.03), Charlson-Deyo Comorbidity Index score of 1 (HR, 1.31; 95% CI, 1.06-1.63), and Charlson-Deyo Comorbidity Index score of ≥2 (HR, 2.181; 95% CI, 1.58-3.02), nodular melanoma histology (HR, 1.23; 95% CI, 1.00-1.52), Breslow thickness >4 mm (HR, 1.37; 95% CI, 1.07-1.74), stage II (HR, 1.94; 95% CI, 1.42-2.66), stage III (HR, 2.21; 95% CI, 1.45-3.38), stage IV (HR, 5.81; 95% CI, 3.77-8.93), positive regional lymph nodes (HR, 1.92; 95% CI, 1.33-2.79), and regional lymph nodes not examined (HR, 1.64; 95% CI, 1.31-2.04). Private insurance (HR, 0.49; 95% CI, 0.29-0.84) and government insurance (HR, 0.47; 95% CI, 0.33-0.98) were also independently associated with improved OS in IVM (Table II).

The 5-year OS for IVM (42.7%) is consistent with previous studies showing worse OS in IVM compared with cutaneous melanoma (52%-88% depending on the cutaneous melanoma subtype), even when accounting for stage.[1-3] These results underscore the importance of vulvar screening as part of full-body skin examinations and educating patients in self-examination in anatomically sensitive areas.

A survey of dermatologists showed that only 4% of dermatologists included the vulva as part of their full-body skin examinations.[4] Only 66% of dermatologists felt diagnosing VM was their role compared with 81% of gynecologists.[4] However, dermatologists play a key role in educating patients on features of VM and in bridging the gap with other specialties to ensure adequate screening.

Insurance coverage in our study for patients with IVM was independently associated with improved OS. Similarly, in patients with vulvar MIS, annual income >$63,000 was independently associated with improved OS. Low socioeconomic status has been previously linked with advanced disease at presentation and poor prognosis of melanoma, particularly in the elderly, which is especially relevant in VM given the median age of diagnosis.[5]

Table I. Baseline characteristics of invasive vulvar melanoma and vulvar melanoma in situ

	Vulvar melanoma in situ (n = 394)			Invasive vulvar melanoma (n = 1688)		
Demographics	**No.**	**%**	***P****	**No.**	**%**	***P****
Age, y			**.0001**			**.0001**
<70	272	69.0		945	56.0	
≥70	122	31.0		743	44.0	
Race			**.0001**			**.0001**
White	370	93.9		1560	92.4	
Black	7	1.8		64	3.8	
Other	15	3.8		45	2.7	
Missing	2	0.5		19	1.1	
Primary site			**.0001**			**.0001**
Labia major	41	10.4		143	8.5	
Labia minor	41	10.4		116	6.9	
Clitoris	11	2.8		56	3.3	
Overlapping lesion of vulva	10	2.5		55	3.3	
Vulva NOS	291	73.9		1318	78.1	
Surgical procedure			**.0001**			**.0001**
Local tumor excision	156	39.6		266	15.8	
Surgery NOS	1	0.3		25	1.5	
Simple/partial surgical removal	193	49.0		680	40.3	
Total surgical removal	32	8.1		284	16.8	
Radical surgery	12	3.0		336	19.9	
None	…	…		97	5.7	
Breslow thickness, mm						**.0001**
<1	…	…		503	29.8	
1-2	…	…		257	15.2	
2-4	…	…		254	15.0	
>4	…	…		513	30.4	
Missing	…	…		161	9.5	
Ulceration						**.0001**
No ulceration present	…	…		605	35.8	
Ulceration present	…	…		958	56.8	
Missing	…	…		125	7.4	
Facility type						**.0001**
Community program	147	37.3		604	35.8	
Academic/research program	155	39.3		731	43.3	
Integrated network cancer program	47	11.9		221	13.1	
Missing	45	11.4		132	7.8	
Charlson-Deyo Comorbidity Score			**.0001**			**.0001**
0	342	86.8		1359	80.5	
1	39	9.9		252	14.9	
≥2	13	3.3		77	4.6	
Stage						**.0001**
I	…	…		432	25.6	
II	…	…		554	32.8	
III	…	…		368	21.8	
IV	…	…		131	7.8	
Missing	…	…		203	12.0	
Chemotherapy			**.0001**			**.0001**
No	381	96.7		1551	91.9	
Yes	1	0.3		82	4.9	
Missing	12	3		55	3.3	
Radiotherapy			**.0001**			**.0001**
No	389	98.7		1507	89.3	
Yes	1	0.3		161	9.5	

Continued

Table I. Cont'd

Demographics	Vulvar melanoma in situ (n = 394)			Invasive vulvar melanoma (n = 1688)		
	No.	%	P*	No.	%	P*
Missing	4	1		20	1.2	
Immunotherapy			**.0001**			**.0001**
No	387	98.2		1492	88.4	
Yes	4	1		182	10.8	
Missing	3	0.8		14	0.8	
Income Status			**.0001**			**.0001**
<$38,000	47	11.9		242	14.3	
$38,000-$47,999	67	17		395	23.4	
$48,000-$62,999	113	28.7		476	28.2	
≥$63,000	167	42.4		566	33.5	
Missing	…	…		9	0.5	
Insurance status			**.0001**			**.0001**
Not insured	9	2.3		46	2.7	
Private/managed care	208	52.8		715	42.4	
Government insurance (Medicaid, Medicare, other government)	167	42.4		893	52.9	
Histology			**.0001**			**.0001**
Malignant melanoma NOS or other histologies	371	94.2		980	58.1	
Nodular melanoma	…	…		291	17.2	
Superficial spreading melanoma	22	5.6		356	21.1	
Mucosal lentiginous melanoma	1	0.3		61	3.6	
Regional lymph node status			**.0001**			**.0001**
Negative	…	…		678	40.2	
Positive	…	…		385	22.8	
Not Examined	…	…		604	35.8	
Missing	…	…		21	1.2	

No., Number; *NOS*, not otherwise specified.
*Bold values denote statistical significance ($P < .05$) on Pearson χ^2 analysis or Fisher exact test.

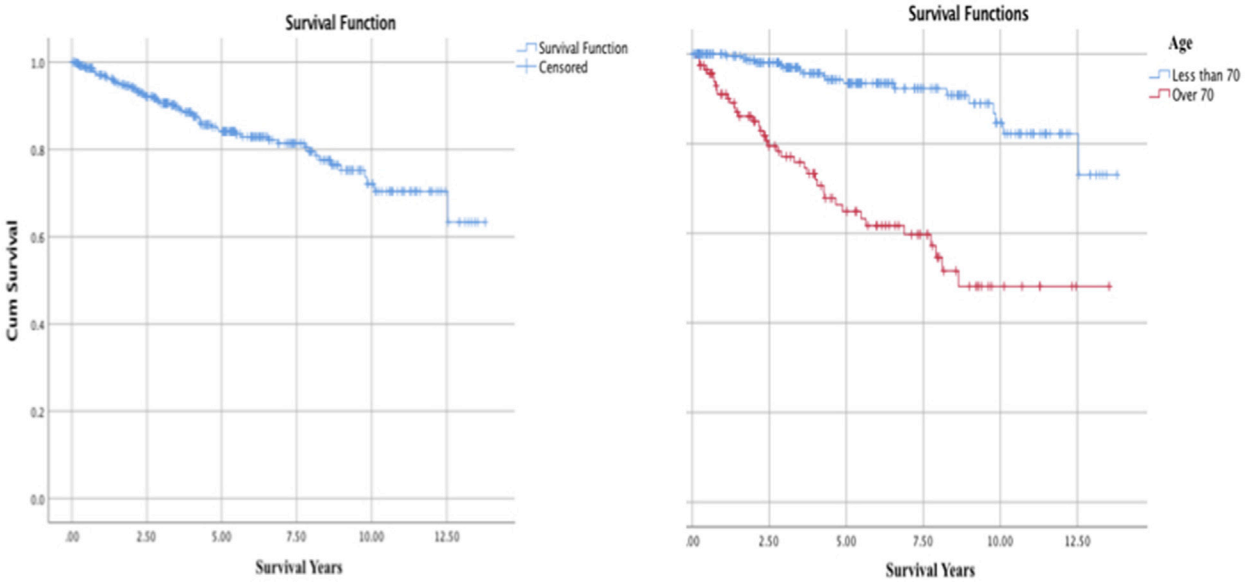

Fig 1. Kaplan-Meier overall survival for invasive vulvar melanoma and survival by age.

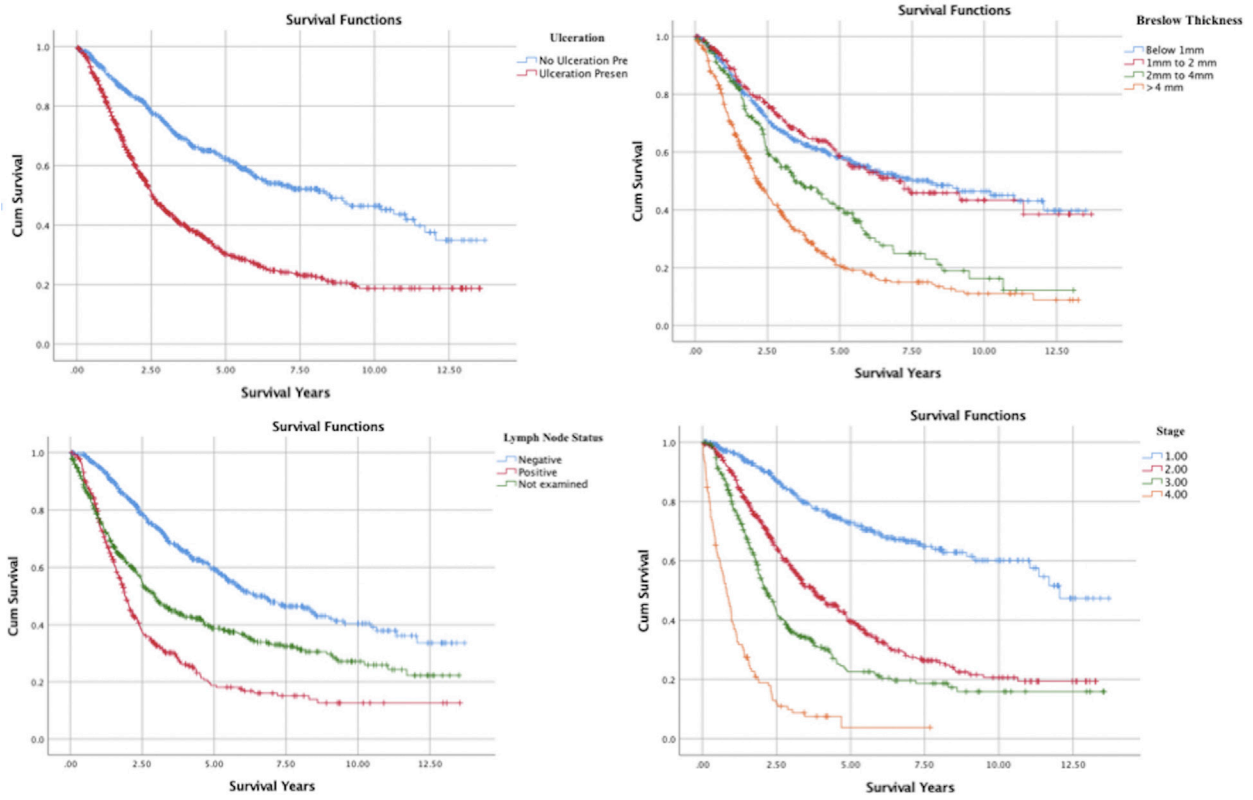

Fig 2. Kaplan-Meier overall survival curves in invasive vulvar melanoma by ulceration, Breslow thickness, regional lymph node status, and stage.

Table II. Multivariate Cox proportional hazards models of vulvar melanoma in situ and invasive vulvar melanoma

	Vulvar melanoma in situ[a,†]		Invasive vulvar melanoma[†,‡]	
Variable	**HR (95% CI)**	***P*[§]**	**HR (95% CI)**	***P*[§]**
Age	1.094 (1.051-1.139)	**.0001**	1.019 (1.009-1.028)	**.0001**
Race				
White	Ref	Ref	Ref	Ref
Black	0.858 (0.001-9.818)	.948	0.912 (0.582-1.429)	.686
Other	0.742 (0.001-9.528)	.920	0.602 (0.299-1.212)	.155
Primary site				
Labia major	Ref	Ref	Ref	Ref
Labia minor	0.991 (0.001-3.230)	.833	1.044 (0.667-1.635)	.849
Clitoris	1.408 (0.130-15.236)	.778	1.447 (0.858-2.439)	.166
Overlapping lesion of vulva	0.801 (0.0001-1.64)	.940	1.090 (0.632-1.880)	.757
Vulva NOS	1.899 (0.567-6.363)	.298	1.131 (0.810-1.580)	.469
Breslow thickness, mm				
<1	…	…	Ref	Ref
1-2	…	…	0.962 (0.718-1.289)	.797
2-4	…	…	1.066 (0.805-1.410)	.656
>4	…	…	1.368 (1.074-1.743)	**.011**
Ulceration				
No ulceration present	…	…	Ref	Ref
Ulceration present	…	…	1.184 (0.959-1.462)	.116
Facility type				
Community program	Ref	Ref	Ref	Ref
Academic/research program	0.524 (0.253-1.085)	.082	0.793 (0.657-0.957)	**.016**
Integrated network cancer program	0.631 (0.252-1.580)	.326	0.941 (0.736-1.202)	.626

Continued

Table II. Cont'd

Variable	Vulvar melanoma in situ*,†		Invasive vulvar melanoma†,‡	
	HR (95% CI)	P§	HR (95% CI)	P§
Charlson-Deyo Comorbidity Score				
0	Ref	Ref	Ref	Ref
1	1.715 (0.752-3.909)	.199	1.310 (1.055-1.626)	**.015**
≥2	2.822 (0.811-9.812)	.103	2.181 (1.576-3.019)	**.0001**
Stage				
I	…	…	Ref	Ref
II	…	…	1.942 (1.419-2.658)	**.0001**
III	…	…	2.215 (1.452-3.380)	**.0001**
IV	…	…	5.805 (3.744-8.929)	**.0001**
Chemotherapy				
No	…	…	Ref	Ref
Yes	…	…	0.967 (0.647-1.444)	.868
Radiotherapy				
No	…	…	Ref	Ref
Yes	…	…	1.074 (0.830-1.390)	.585
Immunotherapy				
No	…	…	Ref	Ref
Yes	…	…	1.057 (0.801-1.395)	.694
Income status				
<$38,000	Ref	Ref	Ref	Ref
$38,000-47,999	0.464 (0.179-1.204)	.114	1.182 (0.898-1.555)	.233
$48,000-$62,999	0.394 (0.152-1.019)	.055	1.005 (0.769-1.312)	.973
≥$63,000	0.416 (0.175-0.989)	**.047**	0.977 (0.747-1.279)	.868
Insurance status				
Not insured	Ref	Ref	Ref	Ref
Private/Managed Care	9.710 (0.0001-40.190)	.931	0.494 (0.290-0.840)	**.009**
Government Insurance (Medicaid, Medicare, Other Government)	9.415 (0.0001-41.800)	.981	0.569 (0.329-0.985)	**.044**
Histology				
Malignant melanoma NOS or other	Ref	Ref	Ref	Ref
Nodular melanoma	…	…	1.234 (1.002-1.521)	**.048**
Superficial spreading melanoma	1.207 (0.254-5.728)	.813	0.951 (0.761-1.189)	.66
Mucosal lentiginous melanoma‖	…	…	1.783 (0.903-3.519)	.096
Regional lymph node status				
Negative	…	…	Ref	Ref
Positive	…	…	1.925 (1.330-2.786)	**.001**
Not examined	…	…	1.639 (1.314-2.045)	**.0001**
Surgical procedure				
Local tumor excision			Ref	Ref
Surgery NOS	33.467 (0.887-300.898)	.985	1.654 (0.770-3.553)	.197
Simple/partial surgical removal	0.965 (0.490-1.898)	.917	1.059 (0.812-1.382)	.672
Total surgical removal	0.443 (0.057-3.458)	.438	1.161 (0.854-1.579)	.341
Radical surgery	0.979 (0.212-4.517)	.978	0.977 (0.728-1.312)	.879
None	…	…	2.490 (1.518-4.084)	**.0001**

CI, Confidence interval; *HR*, hazard ratio; *NOS*, not otherwise specified; *Ref*, reference.

*Multivariate HRs are presented. Variables controlled for and included in the model for vulvar melanoma in situ were age, race, primary site, facility type, Charlson-Deyo Comorbidity Score, income status, insurance status, histology, surgical procedure. HRs presented are adjusted HRs for the aforementioned variables.

†The variables did not violate the proportionality assumption. The proportionality assumption for each variable included was evaluated graphically using log-negative-log survival curves and statistically using interactions with time.

‡Multivariate HRs are presented. Variables controlled for and included in the model for invasive vulvar melanoma were age, race, primary site, Breslow thickness, ulceration, facility type, Charlson-Deyo Comorbidity Score, stage, chemotherapy, radiotherapy, immunotherapy, income status, insurance status, histology, regional lymph node status, and surgical procedure. HRs presented are adjusted HRs for the aforementioned variables.

§Bold values denote significance ($P < .05$) on Cox proportional hazards multivariate model.

‖All cases analyzed were censored.

Retrospective, registry-based studies have several limitations. NCDB is a clinician-reported database that relies on accurate record keeping and reporting by contributing institutions. NCDB does not report disease-specific survival, which may overestimate the mortality risk from VM.

Vulvar MIS and IVM show worse OS than cutaneous melanoma. Our results confirm that Breslow thickness, lymph node status, and stage are significant predictors of survival. Earlier diagnosis, better health care access, and treatment at academic facilities may help improve OS in patients with VM. Supplemental material is available via Mendeley at https://data.mendeley.com/datasets/s24y42424b/1.

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Human papillomavirus–induced lesions of the anogenital tract among women with vulvar high-grade squamous intraepithelial lesions

To the Editor: Human papillomavirus (HPV) lesions can be found at all sites of the anogenital tract, and their multifocal involvement has not been well studied in the published literature.[1-3] Although the link between anal and cervical HPV infection is well known, the link between vulvar high-grade squamous intraepithelial lesions (HSIL) and HPV-induced lesions in adjacent affected sites is not.

The aim of our study was to assess the concomitant presence of HPV-induced lesions of the cervix, vagina, and anus in cases of vulvar HSIL.

This retrospective study included all women with a diagnosis of vulvar HSIL (confirmed by a biopsy specimen) and treated in the dermatologic unit of Cochin Hospital and Hartmann Clinical colposcopy center (January 2004 through December 2015). Sociodemographic, clinical, and histopathologic data were collected from medical files. The number and location of other affected areas (cervix, vagina, and anus) as well as the type of intraepithelial lesion (low- or high-grade) was determined by one doctor

Table I. Patient characteristics and sites of squamous intraepithelial lesions

Average age, y (range)	38 (18-73)
Immunosuppressed women,* n (%)	20 (16)
Tobacco use, n (%)	56 (46)
No. of affected sites, n (%)	
1	62 (51)
2	50 (41)
3	9 (7.5)
HPV lesion on another site, n/N (%)	59/121 (49)
HSIL in another site, n/N (%)	42/121 (35)
Other affected sites, n (%)	
Vagina	25/121 (20)
Anus	22/121 (18)
Cervix	22/121 (18)

HPV, Human papillomavirus; *HSIL*, high-grade squamous intraepithelial lesion.
*Immunosuppressed women: HIV (n = 14), organ transplant (n = 2; 1 kidney, 1 heart transplant), non-Hodgkin lymphoma (n = 1), systemic lupus under immunosuppressive therapy (n = 2), and CD4 idiopathic lymphopenia (n = 1).