

Table SI. Cox regression analysis using Firth's penalized likelihood method for predicting disease-specific survival in 85 patients with extramammary Paget's disease

Characteristics	Univariate analysis		Multivariate analysis (NLR model)		Multivariate analysis (PLR model)		Multivariate analysis (LMR model)	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Sex (Male vs Female)	1.99 (0.33-12.0)	0.392	NA	NA	NA	NA	NA	NA
Age (years old) (≥ 70 vs <70)	19.6 (3.01-128)	<0.001*	21.1 (2.01-220)	0.001*	26.9 (1.68-431)	0.001*	20.8 (2.34-185)	0.001*
Primary tumor site (Perianal vs Non-perianal ^a)	1.64 (0.27-10.1)	0.598	NA	NA	NA	NA	NA	NA
Tumor size (cm ²) (≥ 52 vs <52)	1.61 (0.46-5.70)	0.433	NA	NA	NA	NA	NA	NA
Tumor nodule (Yes vs No)	6.30 (0.92-42.9)	0.098	7.19 (0.56-93.0)	0.127	5.94 (0.40-87.2)	0.156	4.01 (0.26-63.0)	0.271
Tumor ulceration (Yes vs No)	8.84 (1.63-47.2)	0.060	1.35 (0.13-14.4)	0.780	1.55 (0.13-18.1)	0.694	1.15 (0.09-13.9)	0.902
Lymphovascular invasion (Yes vs No)	4.82 (0.76-30.4)	0.141	NA	NA	NA	NA	NA	NA
Invasive level (Dermal vs Non-dermal)	5.76 (1.73-19.2)	0.004*	1.93 (0.30-12.3)	0.485	2.36 (0.50-11.1)	0.261	3.83 (0.67-21.8)	0.139
Metastasis (Yes vs No)	29.9 (4.98-180)	<0.001*	0.62 (0.04-9.13)	0.695	5.38 (0.28-103)	0.198	1.27 (0.09-18.3)	0.843
Treatment (Surgery + other treatments ^b vs Surgery only)	5.82 (1.61-21.1)	0.010*	8.92 (0.76-104)	0.084	1.04 (0.12-9.22)	0.967	2.86 (0.34-23.8)	0.329
NLR (≥ 2.54 vs <2.54)	17.5 (2.89-106)	<0.001*	15.5 (1.61-148)	0.002*	NA	NA	NA	NA
PLR (≥ 117 vs <117)	21.7 (1.08-436)	<0.001*	NA	NA	22.5 (0.63-806)	0.012*	NA	NA
LMR (≥ 3.69 vs <3.69)	0.11 (0.03-0.41)	<0.001*	NA	NA	NA	NA	0.16 (0.04-0.71)	0.010*
PNR (≥ 55.6 vs <55.6)	0.28 (0.06-1.22)	0.052	NA	NA	NA	NA	NA	NA

CI, Confidence interval; HR, hazard ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; PNR, platelet-to-neutrophil ratio; NA, not assessed.

* Statistically significant.

^aNon-perianal regions include genital, pubic, and axillary area.

^bOther treatments include topical medicine (imiquimod or fluorouracil), chemotherapy, or radiotherapy.

Table SII. Cox regression analysis for predicting overall survival in 85 patients with extramammary Paget's disease

Characteristics	Univariate analysis		Multivariate analysis (NLR model)		Multivariate analysis (PLR model)		Multivariate analysis (LMR model)	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Sex (Male vs Female)	4.77 (0.63-35.9)	0.129	NA	NA	NA	NA	NA	NA
Age (years old) (≥ 70 vs < 70)	13.9 (3.89-49.9)	$< 0.001^*$	13.5 (3.13-58.1)	$< 0.001^*$	16.0 (3.86-66.5)	$< 0.001^*$	16.3 (3.89-69.6)	$< 0.001^*$
Primary tumor site (Perianal vs Non-perianal ^a)	0.63 (0.08-4.78)	0.655	NA	NA	NA	NA	NA	NA
Tumor size (cm ²) (≥ 52 vs < 52)	1.25 (0.48-3.23)	0.652	NA	NA	NA	NA	NA	NA
Tumor nodule (Yes vs No)	2.95 (0.38-23.1)	0.302	NA	NA	NA	NA	NA	NA
Tumor ulceration (Yes vs No)	4.37 (0.53-36.0)	0.170	NA	NA	NA	NA	NA	NA
Lymphovascular invasion (Yes vs No)	4.66 (1.05-20.7)	0.043*	1.14 (0.20-6.59)	0.880	2.56 (0.44-15.0)	0.297	2.66 (0.44-16.3)	0.289
Invasive level (Dermal vs Non-dermal)	6.68 (2.61-17.1)	$< 0.001^*$	4.50 (1.35-15.0)	0.014*	5.31 (1.57-18.0)	0.007*	3.49 (1.02-11.9)	0.046*
Metastasis (Yes vs No)	41.4 (7.49-229)	$< 0.001^*$	3.18 (0.21-48.7)	0.406	12.3 (0.90-168)	0.060	9.35 (0.69-121)	0.092
Treatment (Surgery + other treatments ^b vs Surgery only)	3.80 (1.31-11.0)	0.014*	1.61 (0.18-14.8)	0.668	0.73 (0.09-6.09)	0.774	0.80 (0.10-6.67)	0.836
NLR (≥ 2.54 vs < 2.54)	6.52 (2.31-18.4)	$< 0.001^*$	3.74 (1.15-12.2)	0.028*	NA	NA	NA	NA
PLR (≥ 158 vs < 158)	3.41 (1.28-9.08)	0.014*	NA	NA	4.44 (1.48-13.3)	0.008*	NA	NA
LMR (≥ 2.76 vs < 2.76)	0.12 (0.04-0.35)	$< 0.001^*$	NA	NA	NA	NA	0.26 (0.07-0.98)	0.046*
PNR (≥ 48.9 vs < 48.9)	0.51 (0.20-1.32)	0.165	NA	NA	NA	NA	NA	NA

CI, Confidence interval; HR, hazard ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; PNR, platelet-to-neutrophil ratio; NA, not assessed.

* Statistically significant.

^aNon-perianal regions include genital, pubic, and axillary area.

^bOther treatments include topical medicine (imiquimod or fluorouracil), chemotherapy, or radiotherapy.

Table SIII. Associations between NLR, PLR, LMR (based on DSS-derived cutoff values) and clinicopathological features in patients with extramammary Paget's disease

Characteristics	Total	NLR			PLR			LMR		
		High NLR (≥2.54)	Low NLR (<2.54)	P value	High PLR (≥117)	Low PLR (<117)	P value	High LMR (≥3.69)	Low LMR (<3.69)	P value
Number of patients	85	27	58		49	36		62	23	
Age										
<70 y	50 (59%)	12 (44%)	38 (66%)	0.066	24 (49%)	26 (72%)	0.031*	41 (66%)	9 (39%)	0.025*
≥70 y	35 (41%)	15 (56%)	20 (34%)		25 (51%)	10 (28%)		21 (34%)	14 (61%)	
Sex										
Female	18 (21%)	4 (15%)	14 (24%)	0.327	12 (24%)	6 (17%)	0.383	12 (19%)	6 (26%)	0.555
Male	67 (79%)	23 (85%)	44 (76%)		37 (76%)	30 (83%)		50 (81%)	17 (74%)	
Primary tumor site										
Non-perianal ^a	76 (89%)	24 (89%)	52 (88%)	>0.999	41 (84%)	35 (97%)	0.072	59 (95%)	17 (74%)	0.010*
Perianal	9 (11%)	3 (11%)	6 (12%)		8 (16%)	1 (3%)		3 (5%)	6 (26%)	
Tumor size (cm²)										
<52	42 (49%)	11 (41%)	31 (53%)	0.275	22 (45%)	20 (56%)	0.332	33 (53%)	9 (39%)	0.248
≥52	43 (51%)	16 (59%)	27 (47%)		27 (55%)	16 (44%)		29 (47%)	14 (61%)	
Tumor nodule										
Absent	80 (94%)	24 (89%)	56 (97%)	0.321	45 (92%)	35 (97%)	0.390	59 (95%)	21 (91%)	0.609
Present	5 (6%)	3 (11%)	2 (3%)		4 (8%)	1 (3%)		3 (5%)	2 (9%)	
Tumor ulceration										
Absent	82 (96%)	24 (89%)	58 (100%)	0.030*	47 (96%)	35 (97%)	>0.999	61 (98%)	21 (91%)	0.177
Present	3 (4%)	3 (11%)	0 (0%)		2 (4%)	1 (3%)		1 (2%)	2 (9%)	
Lymphovascular invasion										
Absent	81 (95%)	23 (85%)	58 (100%)	0.009*	45 (92%)	36 (100%)	0.134	60 (97%)	21 (91%)	0.295
Present	4 (5%)	4 (15%)	0 (0%)		4 (8%)	0 (0%)		2 (3%)	2 (9%)	
Invasive level										
Non-dermal invasion	67 (79%)	18 (67%)	49 (84%)	0.061	37 (76%)	30 (83%)	0.383	50 (81%)	17 (74%)	0.555
Dermal invasion	18 (21%)	9 (33%)	9 (16%)		12 (24%)	6 (17%)		12 (19%)	6 (26%)	
Lymph node metastasis										
Absent	80 (94%)	23 (85%)	57 (98%)	0.033*	45 (92%)	35 (97%)	0.390	60 (97%)	20 (87%)	0.120
Present	5 (6%)	4 (15%)	1 (2%)		4 (8%)	1 (3%)		2 (3%)	3 (13%)	
Distant metastasis										
Absent	84 (99%)	26 (96%)	58 (100%)	0.318	48 (98%)	36 (100%)	>0.999	62 (100%)	22 (96%)	0.271
Present	1 (1%)	1 (4%)	0 (0%)		1 (2%)	0 (0%)		0 (0%)	1 (4%)	
Treatment										
Surgery only	71 (84%)	22 (81%)	49 (84%)	0.759	38 (78%)	33 (92%)	0.083	54 (87%)	17 (74%)	0.189
Surgery + other treatments ^b	14 (16%)	5 (19%)	9 (16%)		11 (22%)	3 (8%)		8 (13%)	6 (26%)	

NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio.

* Statistically significant.

^aNon-perianal regions include genital, pubic, and axillary area.

^bOther treatments include topical medicine (imiquimod or fluorouracil), chemotherapy, or radiotherapy.

Table SIV. Associations between NLR, PLR, LMR (based on OS-derived cutoff values) and clinicopathological features in patients with extramammary Paget's disease

Characteristics	Total	NLR			PLR			LMR		
		High NLR (≥2.54)	Low NLR (<2.54)	P value	High PLR (≥158)	Low PLR (<158)	P value	High LMR (≥2.76)	Low LMR (<2.76)	P value
Number of patients	85	27	58		18	67		79	6	
Age										
<70 y	50 (58%)	12 (44%)	38 (66%)	0.066	8 (44%)	42 (63%)	0.163	49 (62%)	1 (17%)	0.077
≥70 y	35 (42%)	15 (56%)	20 (34%)		10 (56%)	25 (37%)		30 (38%)	5 (83%)	
Sex										
Female	18 (21%)	4 (15%)	14 (24%)	0.327	5 (28%)	13 (19%)	0.518	18 (23%)	0 (0%)	0.334
Male	67 (79%)	23 (85%)	44 (76%)		13 (72%)	54 (81%)		61 (77%)	6 (100%)	
Primary tumor site										
Non-perianal ^a	76 (89%)	24 (89%)	52 (90%)	>0.999	16 (89%)	60 (90%)	>0.999	71 (90%)	5 (83%)	0.500
Perianal	9 (11%)	3 (11%)	6 (10%)		2 (11%)	7 (10%)		8 (10%)	1 (17%)	
Tumor size (cm²)										
<52	42 (49%)	11 (41%)	31 (53%)	0.275	8 (44%)	34 (51%)	0.635	41 (52%)	1 (17%)	0.202
≥52	43 (51%)	16 (59%)	27 (47%)		10 (56%)	33 (49%)		38 (48%)	5 (83%)	
Tumor nodule										
Absent	80 (94%)	24 (89%)	56 (97%)	0.321	17 (94%)	63 (94%)	>0.999	76 (96%)	4 (67%)	0.038
Present	5 (6%)	3 (11%)	2 (3%)		1 (6%)	4 (6%)		3 (4%)	2 (33%)	
Tumor ulceration										
Absent	82 (96%)	24 (89%)	58 (100%)	0.030	17 (94%)	65 (97%)	0.515	77 (97%)	5 (83%)	0.199
Present	3 (4%)	3 (11%)	0 (0%)		1 (6%)	2 (3%)		2 (3%)	1 (17%)	
Lymphovascular invasion										
Absent	81 (95%)	23 (85%)	58 (100%)	0.009	16 (89%)	65 (97%)	0.196	77 (97%)	4 (67%)	0.024
Present	4 (5%)	4 (15%)	0 (0%)		2 (11%)	2 (3%)		2 (3%)	2 (33%)	
Invasive level										
Non-dermal invasion	67 (79%)	18 (67%)	49 (84%)	0.061	13 (72%)	54 (81%)	0.518	66 (84%)	1 (17%)	0.001
Dermal invasion	18 (21%)	9 (33%)	9 (16%)		5 (28%)	13 (19%)		13 (16%)	5 (83%)	
Lymph node metastasis										
Absent	80 (94%)	23 (85%)	57 (98%)	0.033	17 (94%)	63 (94%)	>0.999	76 (96%)	4 (67%)	0.038
Present	5 (6%)	4 (15%)	1 (2%)		1 (6%)	4 (6%)		3 (4%)	2 (33%)	
Distant metastasis										
Absent	84 (99%)	26 (96%)	58 (100%)	0.318	18 (100%)	66 (100%)	>0.999	79 (100%)	5 (83%)	0.071
Present	1 (1%)	1 (4%)	0 (0%)		0 (0%)	1 (0%)		0 (0%)	1 (17%)	
Treatment										
Surgery only	71 (84%)	22 (81%)	49 (84%)	0.759	14 (78%)	57 (85%)	0.483	68 (86%)	3 (50%)	0.054
Surgery + others ^b	14 (16%)	5 (19%)	9 (16%)		4 (22%)	10 (15%)		11 (14%)	3 (50%)	

NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio.

* Statistically significant.

^aNon-perianal regions include genital, pubic, and axillary area.

^bOthers include topical medicine (imiquimod or fluorouracil), chemotherapy, or radiotherapy.