Vulvar Cancer in Germany: Increase in Incidence and Change in Tumour Biological Characteristics from 1974-2013

Supplementary Table 1: Characteristics of patients with invasive vulvar cancer (ICD-9: 184.1-184.4, ICD-10: C51) from Saarland diagnosed

between 1989 and 2013 (analysis based on data with missing values).

	1989-1	1993	1994	-1998	1999-	-2003	2004-2	2008	2009-2	.013
	N	%	Ν	%	N	%	Ν	%	Ν	%
Overall	91		88		123		295		325	
Median age at diagnosis	72 yrs		76.5 yrs		75 yrs		70 yrs		69 yrs	
Lower and upper quartile	65.83		67.85		61.83		58.70		55.70	
of age at diagnosis	05, 85		07, 05		04, 05		50,79		55,79	
<= 54 years	10	11	3	9	12	10	63	21	76	23
55-74 years	41	45	8	34	48	39	121	41	134	41
>=75 years	40	44	30	57	63	51	111	38	115	35
Death certificate only notified	2	2	0	0	5	4	3	1	1	0
Tumour size available	50	55	57	65	87	71	244	83	259	80
T1 ¹	15	30	19	33	32	37	119	49	211	81
$T2^1$	22	44	27	47	47	54	112	46	37	14
T3/4 ¹	13	26	11	19	8	9	13	5	11	4
Clinical stage ³ available	40	44	30	34	53	43	111	38	139	43
Clinical stage I ^{1,3}	8	20	9	30	15	28	35	32	68	49
Clinical stageII ^{1,3}	2	5	3	10	14	26	21	19	6	4
Clinical stageIII ^{1,3}	15	38	9	30	13	25	35	32	38	27
Clinical stageIV ^{1,3}	15	38	9	30	11	21	20	18	27	19
Microscopically verified	89	98	85	97	117	95	289	98	322	99
Squamous cell carcinoma ^{1,2}	73	82	67	79	87	74	258	89	286	89

Adenocarcinoma ^{1,2}	1	1	2	2	1	1	2	1	2	1
Malignant melanoma ^{1,2}	2	2	3	4	5	4	4	1	7	2
Basal cell carcinoma ^{1,2}	6	7	1	1	13	11	16	6	13	4
Paget disease ^{1,2}	2	2	4	5	4	3	7	2	7	2
Other/unspecified tumors ^{1,2}	5	6	6	7	7	6	2	1	7	2
Histopathologic grade available	65	71	66	75	89	72	257	87	280	86
G1 ¹	10	15	19	29	9	10	16	6	16	6
$G2^1$	40	62	35	53	53	60	168	65	186	66
G3/4 ¹	15	23	12	18	27	30	73	28	78	28

¹Numbers of cases and percentages based on observations with available information. ²Squamous cell carcinoma (ICD-O-3 codes [first 3/4 digits]: 805-808), basal cell carcinoma (809-811), adenocarcinoma (814-838), Paget disease (8542), malignant melanoma (872-879), and other/unspecified (remaining codes). ³Clinical stage according to the International Federation of Gynecology and Obstetrics (FIGO) based on the sixth edition of the TNM [22].

Supplementary Table 2: Characteristics of patients with invasive vulvar cancer (ICD-9: 184.1-184.4, ICD-10: C51) from Saarland diagnosed

between 1989 and 2013 (analysis based on 15 multiply imputed datasets).

	1989-1	1989-1993		-1998	1999-	-2003	2004	-2008	2009-2	<i>P</i> value ¹	
	Ν	%	N	%	Ν	%	Ν	%	Ν	%	
Overall	91		88		123		295		325		
Median age at diagnosis	72 yrs		76.5 yrs		75 yrs		70 yrs		69 yrs		0.007
Lower and upper quartile	65.83		67.85		61.83		58.70		55.70		
of age at diagnosis	05, 85		07, 85		04,05		50,79		55,79		
<= 54 years	10	11	3	9	12	10	63	21	76	23	
55-74 years	41	45	8	34	48	39	121	41	134	41	< 0.001
>= 75 years	40	44	30	57	63	51	111	38	115	35	
T1 ²	31	34	33	38	52	42	146	49	257	79	
$T2^2$	40	44	38	43	55	44	127	43	46	14	< 0.001
T3/4 ²	20	22	17	20	17	14	22	8	22	7	
Clinical stage I ^{2,4}	28	31	28	32	49	40	113	38	170	52	
Clinical stage II ^{2,4}	7	8	16	18	24	20	52	18	17	5	0.001
Clinical stage III ^{2,4}	36	39	33	38	37	30	105	36	105	32	0.001
Clinical stage IV ^{2,4}	20	21	11	12	13	11	25	8	33	10	
Squamous cell carcinoma ^{2,3}	74	81	69	78	90	73	261	88	287	88	
Other invasive cancers ^{2,3}	17	19	19	22	33	27	34	12	38	12	
- Basal cell carcinoma ^{2,3}	6	7	1	1	13	11	17	6	13	4	
- Adenocarcinoma ^{2,3}	1	1	3	3	1	1	2	1	2	1	0.002
- Paget disease ^{2,3}	2	2	4	5	4	3	7	2	7	2	
- Malignant melanoma ^{2,3}	2	2	3	3	5	4	4	1	7	2	
- Other/unspecified tumors ^{2,3}	6	7	9	10	10	8	4	1	9	3	
G1 ²	15	16	27	31	10	8	24	8	24	7	
$G2^2$	56	61	39	44	63	51	183	62	215	66	< 0.001
G3/4 ²	20	22	22	25	49	40	88	30	87	27]

¹Mood's test (H0: no trend in median age at diagnosis over time) and chi-squared test (H0: no differences in the distribution of patient or tumour characteristics across different calendar periods; for testing whether the proportion of squamous cell carcinoma changed over time, all other invasive cancers were combined). ²Rounded numbers of cases and percentages based on 15 multiply imputed datasets. ³Squamous cell carcinoma (ICD-O-3 codes [first 3/4 digits]: 805-808), basal cell carcinoma (809-811), adenocarcinoma (814-838), Paget disease (8542), malignant melanoma (872-879), and other/unspecified (remaining codes). ⁴ Clinical stage according to the International Federation of Gynecology and Obstetrics (FIGO) based on the sixth edition of the TNM [22].

Supplementary Table 3: Truncated age-standardised incidence rates of invasive vulvar cancer (ICD-9: 184.1-184.4, ICD-10: C51) according to tumour size, clinical stage, tumour morphology and histopathologic grade in Saarland between 1989 and 2013 and distribution of tumour characteristics of patients diagnosed in 2009-13 across age groups

	Age <= 54 years									Age 5	5-74 yea	'S				P value ¹						
	1989-	1994-	1999-	2004-	2	2009-			1994-	1999-	2004-	2	.009-		1989-	1994-	1999-	2004-	2	2009-		
	1993	1998	2003	2008	2	2013 1		1993	1998	2003	2008	2	2013		1993	1998	2003	2008	2013			
	N	Ν	Ν	N	Ν			N	Ν	N	Ν	Ν			N	Ν	Ν	N	Ν			
Overall	10	8	12	63	76			41	30	48	121	134			40	50	63	111	115			
	TASR	TASR	TASR	TASR	TASR	Ν	%	TASR	TASR	TASR	TASR	TASR	Ν	%	TASR	TASR	TASR	TASR	TASR	Ν	%	
Overall	0.5	0.4	0.6	2.8	3.8			5.9	4.0	6.9	17.0	19.7			16.0	19.0	21.3	35.6	34.0			
Crude rate ²	0.5	0.4	0.7	3.7	4.8			6.3	4.3	7.3	18.5	20.1			15.7	19.6	21.6	35.7	34.5			
$T1^3$	0.5	0.1	0.3	2.0	3.6	70	92	1.8	1.4	3.3	9.6	16.3	109	82	3.3	8.0	7.3	11.1	23.0	78	68	0.008
$T2^3$	0.0	0.2	0.2	0.6	0.2	4	6	2.9	1.8	2.9	6.5	2.7	19	14	8.4	7.8	10.2	21.0	7.0	23	20	0.000
T3/4 ³	0.0	0.1	0.0	0.2	0.0	1	2	1.2	0.8	0.6	0.9	0.7	6	4	4.3	3.2	3.8	3.4	4.1	14	12	
Clinical stage I ³	0.4	0.1	0.3	1.4	2.6	50	66	1.8	1.3	3.2	7.5	10.6	70	52	3.2	6.6	7.0	8.8	14.9	50	44	
Clinical stage II ³	0.0	0.2	0.0	0.1	0.0	1	1	0.7	1.0	1.6	2.9	0.9	7	5	1.3	1.8	4.4	9.5	2.8	9	8	0.141
Clinical stage III ³	0.1	0.1	0.1	1.0	1.1	23	31	2.5	1.3	1.8	5.1	5.8	40	30	6.9	8.1	6.7	14.4	12.4	42	37	0.141
Clinical stage IV ³	0.0	0.1	0.1	0.2	0.1	2	3	1.0	0.4	0.3	1.6	2.3	17	13	4.6	2.6	3.2	2.9	4.0	13	12	
Squamous cell carcinoma ³	0.3	0.2	0.4	2.4	3.4	67	88	5.1	3.3	4.9	15.8	18.2	124	92	13.2	15.5	16.0	30.3	29.0	97	84	0 375
Other invasive cancers ³	0.2	0.2	0.1	0.3	0.5	9	12	0.7	0.7	1.9	1.1	1.4	10	8	2.8	3.6	5.3	5.2	5.0	18	16	0.575
- Basal cell carcinoma ³	0.0	0.0	0.0	0.2	0.1	2	3	0.4	0.0	1.0	0.2	0.6	4	3	1.1	0.4	2.0	3.1	1.9	7	6	
- Adenocarcinoma ³	0.0	0.0	0.0	0.0	0.0	0	0	0.1	0.0	0.0	0.2	0.0	0	0	0.0	0.9	0.3	0.0	0.5	2	2	
- Paget disease ³	0.1	0.0	0.0	0.0	0.1	2	3	0.0	0.2	0.1	0.4	0.5	3	2	0.0	0.7	1.0	1.2	0.6	2	2	
- Malignant melanoma ³	0.0	0.0	0.1	0.1	0.2	3	4	0.1	0.2	0.1	0.1	0.0	9	0	0.5	0.3	0.4	0.3	1.0	4	4	
- Other/unspecified ³	0.1	0.2	0.0	0.0	0.1	2	3	0.1	0.3	0.7	0.2	0.3	3	2	1.3	1.3	1.6	0.6	1.0	3	3	
G1 ³	0.0	0.1	0.1	0.3	0.2	4	5	1.4	1.2	0.4	0.9	1.2	8	6	2.4	6.7	1.9	3.2	3.4	12	10	
$G2^3$	0.4	0.2	0.2	1.7	2.7	52	68	2.9	2.2	3.3	10.7	14.0	93	69	10.5	7.4	12.2	21.5	20.7	70	61	1.000
$G3/4^{3}$	0.1	0.1	0.3	0.8	1.0	21	27	1.7	0.7	3.2	5.3	4.5	33	25	3.2	5.0	7.2	10.9	9.9	33	29	

TASR: truncated age-standardised rate. ¹Chi-squared test for homogeneity (H0: no differences in the distribution of tumour characteristics between patients aged ≤ 54 , 55-74, and ≥ 75 years in 2009-13; for testing whether the proportion of squamous cell carcinoma changed across age groups, all other invasive cancers were combined. ²No adjustment for age. ³TASRs, rounded numbers of cases, and percentages based on 15 multiply imputed datasets. ⁴Clinical stage according to the International Federation of Gynecology and Obstetrics (FIGO) based on the sixth edition of the TNM [22].