LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

TUMORREGISTER MÜNCHEN (TRM)
BAYERISCHES KREBSREGISTER (LGL) – REGIONALZENTRUM MÜNCHEN
INSTITUT FÜR MEDIZINISCHE INFORMATIONSVERARBEITUNG, BIOMETRIE UND EPIDEMIOLOGIE (IBE)
AM KLINIKUM GROSSHADERN, MÜNCHEN

Anal cancer – population-based data from the Munich Cancer Registry

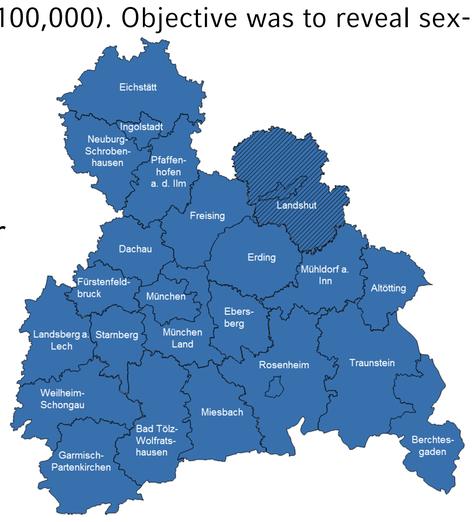
A. Schlesinger-Raab [1], C. Hörl [2], H. Schorer [3], C. Belka [4], S.E. Combs [5], R. Ruppert [6], J. Werner [7], H. Friess [8], J. Engel [1]

1 Munich Cancer Registry (MCR), Bavarian Cancer Registry - Regional Centre Munich (LGL) at the Institute for Medical Information Processing, Biometry, and Epidemiology (IBE), University Hospital LMU, Munich, Germany
2 Department of Radiotherapy and Radiation Oncology, Munich Hospital Schwabing, Munich, Germany
3 Department of Radiotherapy and Radiation Oncology, Munich Hospital Bogenhausen-Harlaching-Neuperlach, Munich, Germany
4 Department of Radiotherapy and Radiation Oncology, University Hospital LMU, Munich, Germany
5 Department of Radiation Oncology, Klinikum rechts der Isar, Technical University of Munich (TUM), Germany
6 Department of General, Visceral and Endocrine Surgery and Coloproctology, Munich Hospital Neuperlach, Munich, Germany
7 Department of General-, Visceral-, Vascular- and Transplant- Surgery, University Hospital LMU, Munich, Germany
8 Department of Surgery, Klinikum rechts der Isar, Technical University of Munich (TUM), Germany

Introduction

Anal cancer is rare and linked to HPV infections similar to cervical and some oropharyngeal cancers. In Germany, the incidence differs clearly between men and women (1.3/100,000 vs. 2.0/100,000). Objective was to reveal sex-related differences.

Figure 1. Catchment area of the Munich Cancer Registry



Methods

The number of anal cancer diagnoses (ICD10 C21) between 1998 and 2016 registered in the catchment area of the Munich Cancer Registry were analysed by sex, and prognostic factors. Cumulative incidence of tumour progression, and secondary tumours in consideration of competing risks as well as survival analyses by Kaplan-Meier method, relative survival and multivariate Cox regression analysis were conducted.

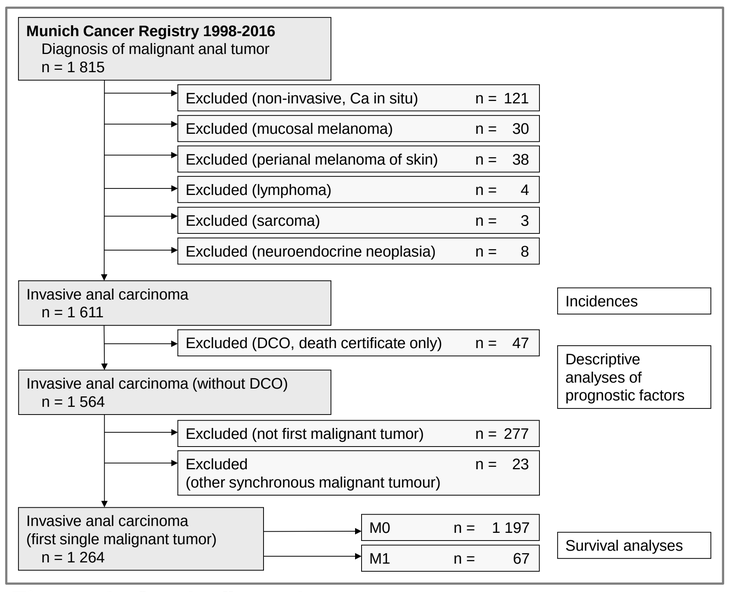


Figure 2. Study flow chart

Results

Incidence

A total of 1,815 malignant anal tumors were recorded. After exclusion of non-invasive cases, mucosal and skin melanomas, lymphomas, sarcomas, and neuroendocrine neoplasia the age-adjusted annual incidence (European Standard Population) was 1.2/100,000 in men and 2.0/100,000 in women without changes since 1998.

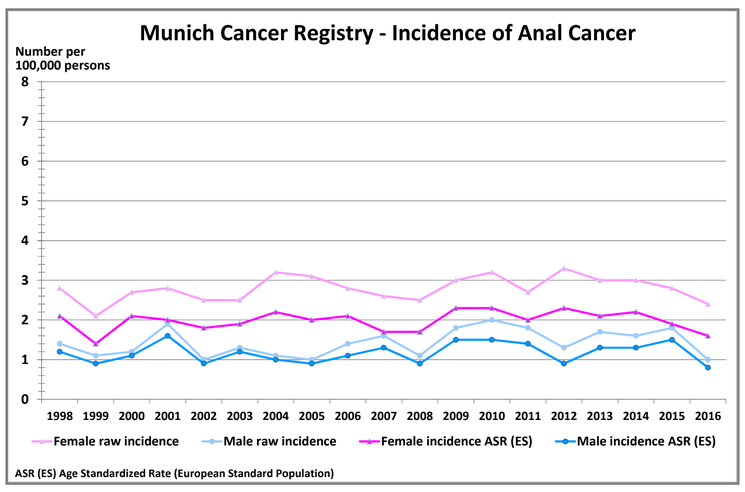


Figure 3. Incidence in men and women

Patient and tumour characteristics

1,564 invasive anal cancers were finally analysed after excluding death certificate only (DCO) cases. Median age at initial diagnosis accounted for 65.1 years and did not change essentially over 18 years (table 1).

Table 1. Patient and tumour characteristics by time of diagnosis

Period of initial diagnosis		1998-2007 n=649		2008-2012 n=511		2013-2016 n=404		Total n=1564		p-value
Prognostic factors		n	(%) [a]	n	(%) [a]	n	(%) [a]	n	(%) [a]	
Age	mean ± SD	64.7	± 14.0	65.6	± 13.6	65.2	± 12.7	65.1	± 13.5	0.5348 n.s.
Age in classes	< 40 yrs.	24	(3.7)	10	(2.0)	8	(2.0)	42	(2.7)	**0.0219**
	40-49 yrs.	84	(12.9)	57	(11.2)	35	(8.7)	176	(11.3)	
	50-59 yrs.	126	(19.4)	122	(23.9)	102	(25.3)	350	(22.4)	
	60-69 yrs.	182	(28.0)	129	(25.2)	108	(26.7)	419	(26.8)	
	70-79 yrs.	125	(19.3)	109	(21.3)	101	(25.0)	335	(21.4)	
	≥ 80 yrs.	108	(16.4)	84	(16.4)	50	(12.4)	242	(15.5)	
Sex	male	205	(31.6)	174	(34.1)	144	(35.6)	523	(33.4)	0.3738 n.s.
	female	444	(68.4)	337	(66.0)	260	(64.4)	1041	(66.6)	
c/p T-Category	T1	116	(23.2)	92	(22.6)	86	(25.4)	294	(23.6)	0.5630 n.s.
	T2	179	(35.8)	154	(37.8)	128	(37.8)	461	(37.0)	
	T3	142	(28.4)	109	(26.7)	75	(22.1)	326	(26.1)	
	T4	63	(12.6)	53	(13.0)	50	(14.8)	166	(13.3)	
	n.a.	*149*	*(22.9)*	*103*	*(20.2)*	*65*	*(16.1)*	*317*	*(20.3)*	
c/p N-Category	N0	227	(46.8)	171	(44.1)	129	(40.6)	527	(44.3)	**<0.0001**
	N+	133	(27.4)	145	(37.4)	141	(44.3)	419	(35.2)	
	NX	125	(25.8)	72	(18.6)	48	(15.1)	245	(20.6)	
	n.a.	*164*	*(25.3)*	*123*	*(24.1)*	*86*	*(21.3)*	*373*	*(23.8)*	
M-Category (primary)	M1	35	(5.4)	31	(6.1)	23	(5.7)	89	(5.7)	0.8861 n.s.
Histopathology	SCC	574	(90.7)	468	(92.5)	385	(95.8)	1427	(92.6)	**0.0043**
	Adenocarcinoma	32	(5.1)	26	(5.1)	15	(3.7)	73	(4.7)	
	Other carcinoma / n.a.	27	(4.3)	12	(2.4)	2	(0.5)	41	(2.7)	
	n.a.	*16*	*(2.5)*	*5*	*(1.0)*	*2*	*(0.5)*	*23*	*(1.5)*	
Grade	G1	62	(11.2)	52	(11.5)	26	(7.0)	140	(26.6)	**0.0013**
	G2	324	(58.5)	241	(53.3)	186	(50.1)	751	(54.5)	
	G3/4	168	(30.3)	159	(35.2)	159	(42.9)	486	(35.3)	
	n.a.	*95*	*(14.6)*	*59*	*(11.5)*	*33*	*(8.2)*	*187*	*(12.0)*	

SD: standard deviation n.s.: not significant as defined by a level α set at 0.05 n.a. not available
[a] Missing values were excluded from calculations of frequency distribution, column percentage can differ slightly from 100% due to rounding.

Men were 2 years younger than women (table 2). The male/female ratio of 1:2 did not change over the observed time. TNM-categories were similar frequent in men and women. Whereas G3 tumors were significantly more in women (39% vs. 28%) and adenocarcinomas were more in men (7.8% vs 3.2%).

Table 2. Patient and tumour characteristics by sex

Period of initial diagnosis		Male n=523		Female n=1041		Total n=1564		p-value
Prognostic factors		n	(%) [a]	n	(%) [a]	n	(%) [a]	
Age	mean ± SD	63.5	± 13.0	66.0	± 13.7	65.1	± 13.5	**0.0005**
Age in classes	< 40 yrs.	16	(3.1)	26	(2.5)	42	(2.7)	**0.0046**
	40-49 yrs.	61	(11.7)	115	(11.1)	176	(11.3)	
	50-59 yrs.	134	(25.6)	216	(20.8)	350	(22.4)	
	60-69 yrs.	145	(27.7)	274	(26.3)	419	(26.8)	
	70-79 yrs.	112	(21.4)	223	(21.4)	335	(21.4)	
	≥ 80 yrs.	55	(10.5)	187	(18.0)	242	(15.5)	
c/p T-Category	T1	95	(23.5)	199	(23.6)	294	(23.6)	0.4206 n.s.
	T2	160	(39.5)	301	(35.8)	461	(37.0)	
	T3	104	(25.7)	222	(26.4)	326	(26.1)	
	T4	46	(11.4)	120	(14.3)	166	(13.3)	
	n.a.	*118*	*(22.6)*	*199*	*(19.1)*	*317*	*(20.3)*	
c/p N-Category	N0	177	(44.9)	350	(43.9)	527	(44.3)	0.2241 n.s.
	N+	127	(32.2)	292	(36.6)	419	(35.2)	
	NX	90	(22.8)	155	(19.5)	245	(20.6)	
	n.a.	*129*	*(24.7)*	*244*	*(23.4)*	*373*	*(23.8)*	
M-Category (primary)	M1	32	(6.1)	57	(5.5)	89	(5.7)	0.6045 n.s.
Histopathology	SCC	464	(90.3)	963	(93.8)	1427	(92.6)	**0.0002**
	Adenocarcinoma	40	(7.8)	33	(3.2)	73	(4.7)	
	Other carcinoma / n.a.	10	(1.9)	31	(3.0)	41	(2.7)	
	n.a.	*9*	*(1.7)*	*14*	*(1.3)*	*23*	*(1.5)*	
Grade	G1	75	(16.2)	65	(7.1)	140	(26.6)	**<0.0001**
	G2	257	(55.5)	494	(54.1)	751	(54.5)	
	G3/4	131	(28.3)	355	(38.8)	486	(35.3)	
	n.a.	*60*	*(11.5)*	*127*	*(12.2)*	*187*	*(12.0)*	

SD: standard deviation n.s.: not significant as defined by a level α set at 0.05 n.a.:not available SCC: Squamous cell carcinoma
[a] Missing values were excluded from calculations of frequency distribution, column percentage can differ slightly from 100% due to rounding.

Treatment

The most frequent treatment was combined chemo-radiation (RCTX) in 42% of all cases. In other 25% this was done in addition to surgery. Over time the proportion of surgery + RCTX decreased slightly (table 3).

Table 3. Treatment by time of diagnosis

Period of initial diagnosis		1998-2007 n=649		2008-2012 n=511		2013-2016 n=404		Total n=1564		p-value
		n	(%) [a]	n	(%) [a]	n	(%) [a]	n	(%) [a]	
Treatment	Surgery	71	(10.9)	67	(13.1)	58	(14.4)	196	(12.5)	**0.0177**
	Radiation therapy	42	(6.5)	30	(5.9)	23	(5.7)	95	(6.1)	
	Combined Chemoradiation	263	(40.5)	216	(42.3)	177	(43.8)	656	(41.9)	
	Surgery + RTX	31	(4.8)	17	(3.3)	9	(2.2)	57	(3.6)	
	Surgery + RCTX	182	(28.0)	122	(23.9)	88	(21.8)	392	(25.1)	
	others / n.a.	60	(9.2)	59	(11.5)	49	(12.1)	168	(10.7)	

RTX: radiation therapy RCTX: combined chemoradiation [a] column percentage can differ slightly from 100% due to rounding.

Differences in treatment by sex were not statistically significant. But surgery was done slightly more often in men and combined chemoradiation was more frequent in women (table 4).

Table 4. Treatment by sex

Period of initial diagnosis		Male n=523		Female n=1041		Total n=1564		p-value
Prognostic factors		n	(%) [a]	n	(%) [a]	n	(%) [a]	
Treatment	Surgery	73	(14.0)	123	(11.8)	196	(12.5)	0.1600 n.s.
	Radiation therapy	37	(7.1)	58	(5.6)	95	(6.1)	
	Combined Chemoradiation	198	(37.9)	458	(44.0)	656	(41.9)	
	Surgery + RTX	24	(4.6)	33	(3.2)	57	(3.6)	
	Surgery + RCTX	136	(26.0)	256	(24.6)	392	(25.1)	
	others / n.a.	55	(10.5)	113	(10.9)	168	(10.7)	

RTX: radiation therapy RCTX: combined chemoradiation n.s.:not significant as defined by a level α set at 0.05
[a] column percentage can differ slightly from 100% due to rounding.

Survival, time to progression and post progression survival

Overall and relative survival of the single first malignant tumour cohort was 64.3% and 71,6% after 5 years and 51.0% and 62.8% after ten years. The 5-year and 10-year relative survival was better in women vs. men with 73.8% and 68.8% vs. 61.1% and 50.2% (figure 4).

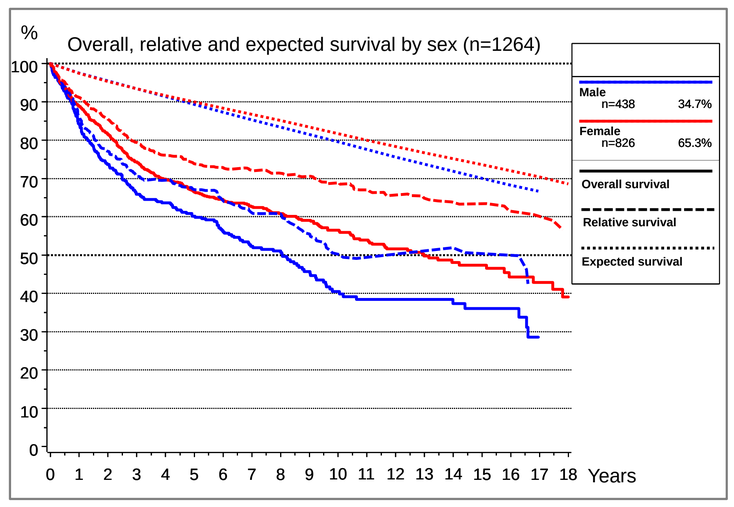


Figure 4. Survival by sex

The cumulative incidence (CI) of distant metastasis in primary M0 patients was similar in men and women after 10 years, 18.9% and 18.4% . In contrast the CI of local recurrence after 10 years was twice as much in men than in women: 19.2% vs. 9.6% (figure 5).

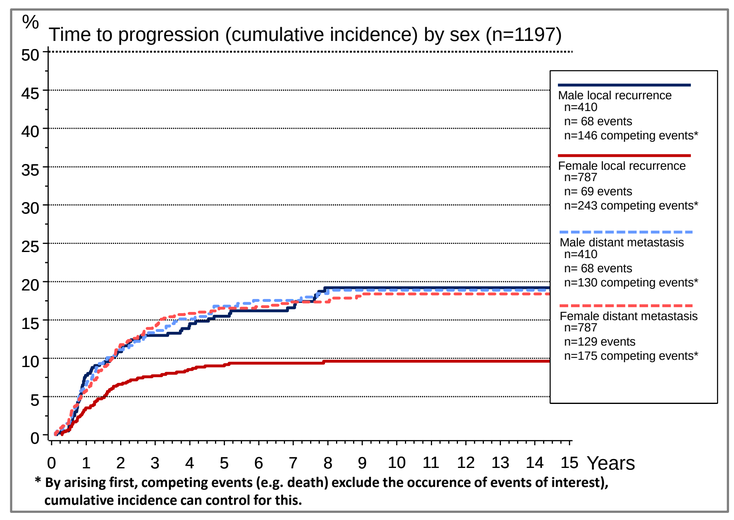


Figure 5. Time to progression by sex

Assessing relative survival by sex and type of progression reveals slight differences between men and women in subgroups of type of progression (beware: small groups). The main difference is seen in those without information about any recurrence. In men their 10-year relative survival is 70.4%, in female it is much better with 95.1% (figure 6) .

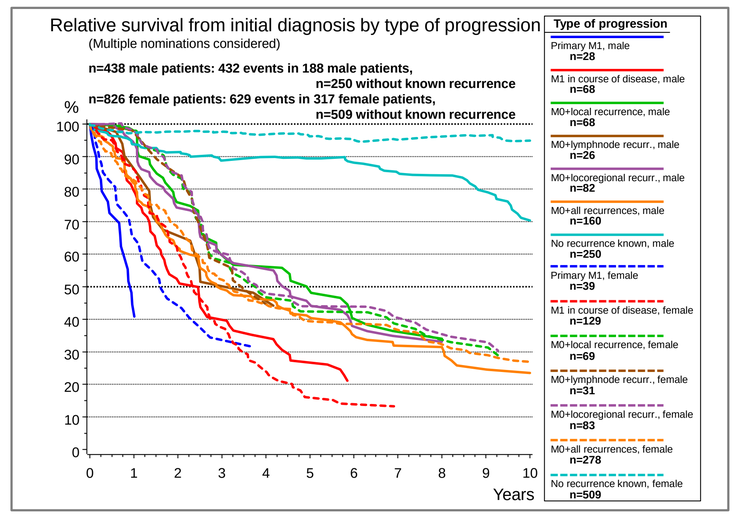


Figure 6. Relative survival by sex and type of progression

The better prognosis in female patients remained significant in multiple Cox regression when controlling for age, TNM, grade and time period with a male hazard ratio of 1.74 [CI $_{95\%}$ 1.45 -2.09].

Conclusions

Women have a better outcome in anal cancer, although no patient- or tumour-specific characteristics were attributed to this difference.

The authors have declared no conflicts of interest.

Contact: Dr. Anne Schlesinger-Raab: phone 089 - 4400-74485 fax 089 - 4400-74753 e-mail: schlesi@ibe.med.uni-muenchen.de