Influence of sex, neutering, breed, age, and geographic origin on malignant tumor development in cats: a multicenter retrospective study

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Supplementary materials

Supplementary Table 1. Behavioral classification (benign or malignant) of feline tumors coded uncertain whether benign or malignant [/1] or in situ [/2] in the Vet-ICD-O-Canine1 coding system.

Tumor Code and Type	Classification
8006.1/1 Round cell tumor, NOS	excluded[A]
8010/2 Carcinoma in situ, NOS	Malignant[B]
8070/2 Squamous cell carcinoma in situ[C]	Malignant[B]
8410.1/1 Meibomian gland epithelioma	benign[D] [1]
8410/1 Sebaceous epithelioma	benign[D] [1]
8590/1 Sex cord-gonadal stromal tumor, NOS	excluded[A]
8594/1 Mixed germ cell-sex cord-stromal tumor	excluded[A]
8640/1 Sertoli cell tumor, NOS	benign[E] [1]
8650/1 Interstitial cell tumor, NOS	benign[E] [1]
8815.1/1 Canine perivascular wall tumor, NOS	excluded[A,F] [1,4]

Tumor Code and Type	Classification
9310.2/1 Acanthomatous ameloblastoma	benign[D] [1]
9391/1 Cellular ependymoma	excluded[F]
9530.0/1 Meningioma, NOS	excluded[A]
9563/1 Nerve sheath tumor, NOS	malignant[G] [3]
9734/1 Plasmacytoma, extramedullary (digestive tract)	benign[E] [1]
9734/1 Plasmacytoma, NOS**	benign[E] [1]
9740/1 Visceral/Intestinal mast cell tumor	malignant[G] [3]
9740/1 Cutaneous mast cell tumor without malignancy description	benign[E] [1,3,5]
9740.2/1 Cutaneous mast cell tumor with malignancy description	malignant[H] [5]

[A] Uncertain diagnosis regarding behavioral and prognostic classification of tumor;
[B] In situ [/2] was assigned to neoplasms indicating their potential of malignant progression, exception: in situ mammary carcinoma in which standardized criteria to differentiate it from epitheliosis are lacking [2]; [C] Diagnoses of actinic keratosis were included and analyzed in analogy to Squamous cell carcinoma in situ [8070/2], with the de-novo code [8070.1/2]; [D] Rare (<10%) occurrence of metastasis observed; [E] Described as (frequently/usually) benign; [F] Small numbers of tumor type; [G] Described as malignant; [H] Frequent occurrence of metastasis is observed; NOS: not otherwise specified.

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Supplementary Table 2. Distribution of the 5,289 feline tumor cases (sample size and percentage out of the total) grouped by topography and morphology in the Pisa and Lazio Animal Cancer Registries.

Variables	Groups	Vet-ICD-O-canine1 codes	Pisa		Lazio		Total	
			n°	%	n°	%	n°	%
Topography	Skin	C44	966	27.5%	577	32.6%	1543	29.2%
	Soft tissue	C49	955	27.1%	432	24.4%	1387	26.2%
	Mammary gland	C50	491	14.0%	274	15.5%	765	14.5%
	Lip, oral cavity, pharynx	C00-14	285	8.1%	122	6.9%	407	7.7%
	Digestive organs	C15-26	260	7.4%	130	7.3%	390	7.4%
	Bones	C40-41	80	2.3%	31	1.8%	111	2.1%
	Nose, ear, sinuses, larynx	C30-32	87	2.5%	18	1.0%	105	2.0%
	Lymph nodes	C77	74	2.1%	24	1.4%	98	1.9%
	Eye and adnexa	C69	53	1.5%	32	1.8%	85	1.6%
	Urinary organs	C64-68	45	1.3%	30	1.7%	75	1.4%
	Hematopioetic system	C42	53	1.5%	14	0.8%	67	1.3%
	Respiratory system	C33-34	39	1.1%	23	1.3%	62	1.2%
	Unknown	C80	17	0.5%	29	1.6%	46	0.9%
	Nervous system	C47,70-72	35	1.0%	3	0.2%	38	0.7%
	Female genital organs	C51-56	19	0.5%	12	0.7%	31	0.6%
	Peritoneum and retroperitoneum	C48	24	0.7%	4	0.2%	28	0.5%
	Endocrine glands	C73-75	20	0.6%	5	0.3%	25	0.5%
	Ill defined	C76,80	8	0.2%	5	0.3%	13	0.2%
	Intrathoracic organs (excl. lung)	C37-38	3	0.1%	5	0.3%	8	0.2%
	Male genital organs	C60-63	4	0.1%	1	0.1%	5	0.1%
Total			3518	100.0%	1771	100.0%	5289	100.0%
Morphology	Adenomas and adenocarcinomas	814-838	598	17.0%	258	14.6%	856	16.2%
	Squamous cell neoplasms	805-808	470	13.4%	286	16.1%	756	14.3%
	Soft tissue tumors and sarcomas, NOS	880	464	13.2%	100	5.6%	564	10.7%
	Fibromatous neoplasms	881-883	309	8.8%	251	14.2%	560	10.6%
	Malignant lymphomas, NOS or diffuse	959-972	332	9.4%	167	9.4%	499	9.4%
	Basal cell neoplasms	809-811	202	5.7%	111	6.3%	313	5.9%
	Mast cell neoplasms	974	193	5.5%	108	6.1%	301	5.7%
	Adnexal and skin appendage neoplasms	839-842	164	4.7%	113	6.4%	277	5.2%
	Lipomatous neoplasms	885-888	140	4.0%	34	1.9%	174	3.3%
	Ductal and lobular neoplasms	850-854	91	2.6%	78	4.4%	169	3.2%
	Osseous and chondromatous neoplasms	918-924	80	2.3%	43	2.4%	123	2.3%
	Blood vessel tumors	912-916	89	2.5%	33	1.9%	122	2.3%
	Melanocytoma and Melanomas	872-879	63	1.8%	34	1.9%	97	1.8%
	Epithelial neoplasms, NOS	801-804	38	1.1%	33	1.9%	71	1.3%
	Nerve sheath tumors	954-957	33	0.9%	27	1.5%	60	1.1%
	Neoplasms of histiocytes and accessory lymphoid cells	975	18	0.5%	27	1.5%	45	0.9%
	Myxomatous neoplasms	884	41	1.2%	2	0.1%	43	0.8%
	Myomatous neoplasms	889-892	34	1.0%	7	0.4%	41	0.8%
	Cystic, mucinous and serous neoplasms	844-849	30	0.9%	4	0.2%	34	0.6%
	Odontogenic tumors	927-934	24	0.7%	8	0.5%	32	0.6%
	Transitional cell papillomas and carcinomas	812-813	18	0.5%	11	0.6%	29	0.5%
	Complex epithelial neoplasms	856-857	27	0.8%	1	0.1%	28	0.5%
	Plasma cell neoplasms	973	9	0.3%	7	0.4%	16	0.3%
	Complex mixed and stromal neoplasms	893-899	5	0.1%	6	0.3%	11	0.2%
	Lymphatic vessel tumors	917	7	0.2%	3	0.2%	10	0.2%
	Specialized gonadal neoplasms	859-867	6	0.2%	3	0.2%	9	0.2%
	Thymic epithelial neoplasms	858	6	0.2%	1	0.1%	7	0.1%
	Mature T- and NK-cell lymphomas	970-971	5	0.1%	1	0.1%	6	0.1%
	Neoplasms, NOS	800	1	0.0%	4	0.2%	5	0.1%
	Lymphoid leukemias	981-983	5	0.1%		0.0%	5	0.1%
	Meningiomas	953	1	0.0%	3	0.2%	4	0.1%
	Acinar cell neoplasms	855	2	0.1%	2	0.1%	4	0.1%
	Myeloid leukemias	904	3	0.1%		0.0%	3	0.1%
	Synovial-like neoplasms	900-903	2	0.1%	1	0.1%	3	0.1%
	Fibroepithelial neoplasms	984-993	3	0.1%		0.0%	3	0.1%
	Mucoepidermoid neoplasms	843		0.0%	3	0.2%	3	0.1%
	Mesothelial neoplasms	905	1	0.0%	1	0.1%	2	0.0%
	Mature B-cell lymphomas	967-972	2	0.1%		0.0%	2	0.0%
	Gliomas	906-909	1	0.0%		0.0%	1	0.0%
	Germ cell neoplasms	938-948	1	0.0%		0.0%	1	0.0%
Total			3518	100.0%	1771	100.0%	5289	100.0%

Supplementary Table 3. Distribution of the 5,289 feline tumor cases (sample size and percentage out of the total) for each of the 21 individual breeds included in the data set and sorted by the Pisa and Lazio Animal Cancer Registries (ACRs).

Breed	FIFe code	Pisa		Lazio		Total	
		n°	%	n°	%	n°	%
House Cat Shorthair/Longhair	HCS/HCL	3029	86.1%	1533	86.6%	4562	86.3%
unknown	NA	220	6.3%	129	7.3%	349	6.6%
Persian	PER	121	3.4%	43	2.4%	164	3.1%
Siamese	SIA	41	1.2%	13	0.7%	54	1.0%
Maine Coon	MCO	29	0.8%	6	0.3%	35	0.7%
Chartreux	CHA	17	0.5%	14	0.8%	31	0.6%
Norwegian Forest Cat	NFO	17	0.5%	4	0.2%	21	0.4%
Siberian	SIB	10	0.3%	3	0.2%	13	0.2%
Exotic	EXO	8	0.2%	2	0.1%	10	0.2%
Ragdoll	RAG	9	0.3%		0.0%	9	0.2%
Abyssinian	ABY		0.0%	7	0.4%	7	0.1%
Sacred Birman	SBI	1	0.0%	6	0.3%	7	0.1%
British	BRI	2	0.1%	5	0.3%	7	0.1%
Devon Rex	DRX	4	0.1%	1	0.1%	5	0.1%
Thai	THA	2	0.1%	1	0.1%	3	0.1%
Turkish Angora	TUA	3	0.1%		0.0%	3	0.1%
Scottish Fold	SFS (n.d.)	2	0.1%	1	0.1%	3	0.1%
Russian Blue	RUS	2	0.1%		0.0%	2	0.0%
Oriental Shorthair	OSH		0.0%	1	0.1%	1	0.0%
RagaMuffin	RGM (n.d.)	1	0.0%		0.0%	1	0.0%
California Spangled	CLS (n/d)		0.0%	1	0.1%	1	0.0%
Sphynx	SPH		0.0%	1	0.1%	1	0.0%
Total		3518	100.0%	1771	100.0%	5289	100.0%

Supplementary Table 4. Results of Pearson's Chi-square test with Yates' continuity correction assessing differences in the malignancy proportion by sex, neuter status, district, and breed.

Variable	Categories	% Malignant Tumors	χ^2 (df)	p-value
Sex			27.47 (1)	<0.001
	Male	77.0%		
	Female	83.1%		
Neuter status			0.25 (1)	0.614
	Intact	81.0%		
	Neutered	80.4%		
District			7.45 (2)	0.024
	Tuscany	80.1%		
	Lazio	80.0%		
	Liguria	84.3%		
Breed			23.78 (1)	<0.001
	Mixed-breed	81.5%		
	Purebred	71.1%		

Supplementary Table 5. Results of the logistic regression models for overall malignancy and for the 4 most common malignant tumor groups showing the odds ratios (ORs), the 95% confidence intervals, and measures of goodness of fit for each model in cats. OR: Odds ratio; Std. Error: standard error; 95%CI: 95% confidence interval; LL: lower limit; AIC: Akaike information criterion.

Malignancy logistic regression model								
(Intercept)		0.52	1.68	0.12	4.02	< 0.001	1.31	2.17
Age	< 1	-	-	-	-	-	-	-
	1-25	0.07	1.08	0.01	7.49	< 0.001	1.06	1.10
Sex	Male	-	-	-	-	-	-	-
	Female	0.33	1.39	0.08	4.18	< 0.001	1.19	1.62
Neuter status	Intact	-	-	-	-	-	-	-
	Neutered	-0.05	0.95	0.09	-0.62	0.537	0.80	1.12
Breed	Mixed-breed	-	-	-	-	-	-	-
	Purebred	-0.63	0.53	0.13	-5.01	< 0.001	0.42	0.68
District	Tuscany	-	-	-	-	-	-	-
	Lazio	0.05	1.06	0.09	0.63	0.526	0.89	1.25
	Liguria	0.34	1.40	0.13	2.55	0.011	1.09	1.82
	Other districts	0.34	1.40	0.20	1.66	0.097	0.95	2.12
(Dispersion parameter for binomial family taken to be 1) Null deviance: 4312.4 on 4377 degrees of freedom Residual deviance: 4202.9 on 4370 degrees of freedom AIC: 4218.9 Number of Fisher Scoring iterations: 4								

Fibrosarcoma logistic regression model								
Variable	Value	Estimate	OR	Std. Error	z value	p value	95%CI LL	95%CI UL
(Intercept)		-1.69	0.18	0.14	-11.73	< 0.001	0.14	0.24
Age	< 1	-	-	-	-	-	-	-
	1-25	0.05	1.05	0.01	4.43	< 0.001	1.03	1.07
Sex	Male	-	-	-	-	-	-	-
	Female	-0.53	0.59	0.08	-6.55	< 0.001	0.50	0.69
Neuter status	Intact	-	-	-	-	-	-	-
	Neutered	-0.10	0.90	0.09	-1.19	0.234	0.76	1.07
Breed	Mixed-breed	-	-	-	-	-	-	-
	Purebred	-0.39	0.67	0.16	-2.42	0.016	0.48	0.92
District	Tuscany	-	-	-	-	-	-	-
	Lazio	-0.02	0.98	0.09	-0.18	0.859	0.82	1.18
	Liguria	0.31	1.37	0.12	2.59	0.010	1.08	1.73
	Other districts	0.04	1.04	0.19	0.19	0.852	0.70	1.50
(Dispersion parameter for binomial family taken to be 1) Null deviance: 4066.1 on 4377 degrees of freedom Residual deviance: 3994.1 on 4370 degrees of freedom AIC: 4010.1 Number of Fisher Scoring iterations: 4								

Adenocarcinoma logistic regression model								
Variable	Value	Estimate	OR	Std. Error	z value	p value	95%CI LL	95%CI UL
(Intercept)		-3.37	0.03	0.18	-18.33	< 0.001	0.02	0.05
Age	< 1	-	-	-	-	-	-	-
	1-25	0.04	1.04	0.01	3.65	< 0.001	1.02	1.07
Sex	Male	-	-	-	-	-	-	-
	Female	1.92	6.85	0.13	15.27	< 0.001	5.39	8.83
Neuter status	Intact	-	-	-	-	-	-	-
	Neutered	-0.24	0.79	0.09	-2.60	0.009	0.66	0.94
Breed	Mixed-breed	-	-	-	-	-	-	-
	Purebred	0.38	1.47	0.15	2.58	0.010	1.09	1.95
District	Tuscany	-	-	-	-	-	-	-
	Lazio	-0.14	0.87	0.10	-1.48	0.140	0.71	1.05
	Liguria	0.03	1.03	0.14	0.21	0.833	0.78	1.34
	Other districts	-0.01	0.99	0.22	-0.06	0.949	0.63	1.50
(Dispersion parameter for binomial family taken to be 1) Null deviance: 3804.7 on 4377 degrees of freedom Residual deviance: 3420.3 on 4370 degrees of freedom AIC: 3436.3 Number of Fisher Scoring iterations: 5								

Squamous cell carcinoma logistic regression model								
Variable	Value	Estimate	OR	Std. Error	z value	p value	95%CI LL	95%CI UL
(Intercept)		-2.35	0.10	0.16	-14.34	< 0.001	0.07	0.13
Age	< 1	-	-	-	-	-	-	-
	1-25	0.05	1.05	0.01	4.02	< 0.001	1.02	1.07
Sex	Male	-	-	-	-	-	-	-
	Female	-0.08	0.93	0.09	-0.85	0.397	0.78	1.11

Neuter status	Intact	-	-	-	-	-	-	-
	Neutered	0.03	1.03	0.10	0.27	0.789	0.85	1.25
Breed	Mixed-breed	-	-	-	-	-	-	-
	Purebred	-0.24	0.79	0.18	-1.33	0.183	0.55	1.10
District	Tuscany	-	-	-	-	-	-	-
	Lazio	0.19	1.21	0.10	1.95	0.051	1.00	1.46
	Liguria	-0.22	0.80	0.15	-1.45	0.147	0.58	1.07
	Other districts	-0.23	0.80	0.24	-0.96	0.337	0.49	1.24
(Dispersion parameter for binomial family taken to be 1) Null deviance: 3469.1 on 4377 degrees of freedom Residual deviance: 3441.7 on 4370 degrees of freedom AIC: 3457.7 Number of Fisher Scoring iterations: 4								

Lymphoma logistic regression model								
Variable	Value	Estimate	OR	Std. Error	z value	p value	95%CI LL	95%CI UL
(Intercept)		-1.03	0.36	0.16	-6.27	< 0.001	0.26	0.49
Age	< 1	-	-	-	-	-	-	-
	1-25	-0.10	0.90	0.01	-7.94	< 0.001	0.88	0.93
Sex	Male	-	-	-	-	-	-	-
	Female	-0.45	0.64	0.10	-4.27	< 0.001	0.52	0.79
Neuter status	Intact	-	-	-	-	-	-	-
	Neutered	-0.02	0.98	0.11	-0.20	0.841	0.78	1.23
Breed	Mixed-breed	-	-	-	-	-	-	-
	Purebred	-0.36	0.70	0.22	-1.66	0.098	0.45	1.05
District	Tuscany	-	-	-	-	-	-	-
	Lazio	0.04	1.04	0.12	0.30	0.767	0.82	1.31
	Liguria	0.32	1.38	0.16	2.03	0.042	1.00	1.87
	Other districts	0.48	1.61	0.22	2.15	0.032	1.02	2.45
(Dispersion parameter for binomial family taken to be 1) Null deviance: 2776.4 on 4377 degrees of freedom Residual deviance: 2676.7 on 4370 degrees of freedom AIC: 2692.7 Number of Fisher Scoring iterations: 5								