

Salivary neoplasia in dogs and cats: 1996–2017

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Abstract

Objective: The objectives of this study were to report the contemporary demographical information, provide the incidence of and to assess sex and breed predisposition of salivary gland neoplasia in dogs and cats.

Materials and Methods: Information was collected from cats or dogs with salivary neoplasia (cases) and controls from the 26 university veterinary teaching hospitals within the Veterinary Medical Data Base. A total of 56 dogs and 24 cats were identified as having been diagnosed with salivary neoplasia.

Results: The incidence of salivary neoplasia in this population was calculated to be 15.3 per 100,000 dogs and 26.3 per 100,000 cats. The specific anatomic location of the salivary neoplasia was unable to be determined in 90.8% of cases in both dogs and cats. Results of the univariable conditional logistic regression models revealed no increased risk of salivary neoplasia in dogs or cats of any sex or neuter status (dogs: $p = .26$; cats: $p = .45$). There was no breed disposition within the feline species for salivary neoplasia. However, in the conditional logistic regression for dogs, poodles (toy and standard) trended towards significance ($p = .075$) with an odds ratio of 6.83 (95% CI: 1.16–40.10) compared to mixed breeds.

Conclusions and clinical relevance: The present study's results differ from previous conclusions made in regards to predisposed breeds and tumour location. Additional epidemiological studies should be performed to help in determining risk factors for salivary gland neoplasia.

KEYWORDS

canine, epidemiology, feline, oncology, salivary gland

1 | INTRODUCTION

Salivary gland disease is uncommon in dogs and cats, with a reported overall incidence of 0.17%. Tumours are equally uncommon in the salivary glands of dogs and cats, comprising less than 0.2% of all tumours detected in these species. However, this previously reported incidence has its limitations as it was based on histopathology reports from one institution (Carberry, Flaunders, & Harvey, 1988). Given the rarity of

this condition it is not surprising that there is minimal information on salivary gland neoplasia in the veterinary literature with much of the existing information being decades old (Carberry et al., 1988; Hammer, Getzy, & Ogilvie, 2001; Karbe & Schiefer, 1967; Koestner & Buerger, 1965; Sozmen, Brown, & Eveson, 1999; Spangler & Culbertson, 1991; Stebbins, Morse, & Goldschmidt, 1989). Additionally, much of the recent literature describing salivary neoplasia is limited to single case reports (Clark, Hanna, & Beraud, 2013; Fujiwara-Igarashi, Shimizu,

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& Michishita, 2017; Kishimoto, Yoshimura, & Saito, 2015; Nakahira, Michishita, & Kato, 2017).

Many different morphological diagnoses of primary neoplasia of the salivary gland have been reported in dogs and cats including adenocarcinoma, carcinoma, malignant mixed, adenoma/cystadenoma, anaplastic adenocarcinoma and malignant melanoma (Koestner & Buerger, 1965; Spangler & Culbertson, 1991). Additionally, salivary glands have been reported to be involved with other tumour types through direct extension and invasion including fibrosarcoma, lipoma, mast cell tumour and lymphoma (Carberry et al., 1988; Hammer et al., 2001; Koestner & Buerger, 1965; Spangler & Culbertson, 1991). Adenocarcinoma is reported as the most common tumour type in both dogs and cats (Hammer et al., 2001).

Breed disposition in dogs and cats with salivary neoplasia has been sparsely described. Spangler and Culbertson demonstrated that poodles were the most common breed to have salivary gland disease of any type (Spangler & Culbertson, 1991). Karbe & Schiefer (1967) reported a predisposition in spaniel breeds for salivary neoplasia in their study population, but these breeds were not overrepresented in a later report by Hammer et al. (2001). In cats, there have been reports of overrepresentation of the Siamese breed. Hammer *et al.* reported 30% (9/30) of cats with salivary neoplasia were Siamese or Siamese-cross and Sozmen et al. (1999) reported two out of five cats with salivary duct carcinoma were Siamese (Hammer et al., 2001). No sex predisposition has been determined in dogs through previous studies (Carberry et al., 1988; Hammer et al., 2001), however, Hammer et al. (2001) reported a 2:1 predilection ratio for male cats with salivary gland neoplasia.

The objectives of this study were to report the contemporary demographical information in cats and dogs with salivary gland neoplasia, provide the incidence of salivary gland neoplasia in cats and dogs and to assess for any sex or breed predisposition to salivary gland neoplasia by utilizing data from multiple institutions attained from the Veterinary Medical Database (VMDB).

2 | MATERIALS AND METHODS

Information was collected from cats or dogs with salivary neoplasia (cases) and controls from the Veterinary Medical Data Base (VMDB; <http://vmdb.org>, Accessed November 11, 2017; the VMDB does not make any implicit opinion on the subject of the article or study). This database includes patient medical records attained from 26 university veterinary teaching hospitals. As some of these hospitals provide primary care this study's population was comprised of both referral and primary care caseload. The VMDB stores abstracts of hospital records resulting in a compilation of all cases seen at these universities. For each patient visit the following information is recorded within the database: patient identification number, institution, discharge date, species, breed, sex, neuter status, age, body weight and diagnostic code. Therefore a VMDB search may be performed for any of these characteristics.

2.1 | Case selection

Eligible cases were retrieved from a computer search of the VMDB for dogs and cats presented during January 1, 1996 through December 31, 2017 that had the diagnostic code of any of the following: carcinoma of parotid gland, primary malignant neoplasm of parotid gland, sublingual gland, major salivary gland, salivary gland duct, malignant tumour of the submandibular gland, major salivary gland, salivary gland, sublingual gland, secondary malignant neoplasm of the major salivary gland and polymorphous low-grade adenocarcinoma of salivary gland. Duplicate cases/entries due to multiple visits by the same animal were eliminated.

2.2 | Control selection

For comparison, a reference population was created through a separate search of VMDB. Eligible controls were retrieved from a search for dogs and cats presented during January 1, 1996 through December 31, 2017 that had the diagnostic code: dental abscess. Each individual case of salivary neoplasia was then matched to two control subjects based on institution of admission, species and discharge date \pm 2 years. Additionally, the control subjects were matched to our case population of interest by an age constraint of being either the same age or older. In some rare instances, if a match could not be identified based on this age constraint, a constraint of up to 3 years younger was allowed. As multiple controls arose for each case the final selection of the controls for inclusion in the statistical analysis was performed through a random number list generator.¹ If no controls were identified for a case, the case was excluded from the study.

2.3 | Statistical analysis

Continuous data were assessed for normality using multiple methods including Shapiro Wilk tests, skewness and kurtosis. The mean and standard deviation were used for normally distributed data and the median and range were used for data that were non-normally distributed. Frequencies and percentages were used to describe any categorical data. Differences in demographics between the salivary neoplasia group and the control group in each species were assessed with Fisher's exact tests. Differences in age and weight between cases and controls were assessed using Kruskal Wallis tests. Conditional logistic regression was performed to assess for associations between sex, neuter status and breeds for risk of salivary neoplasia. A *p*-value of .05 was considered significant for these analyses. The analyses were performed using commercially available software.^{2,3}

3 | RESULTS

A total of 458,231 individual medical records were recorded in the VMDB between January 1, 1996 and December 31, 2017; 366,905

from dog patients and 91,326 from cat patients. Of those, a total of 227 dogs and cats were identified as having a diagnostic code matching the inclusion criteria (cases) and all cases were diagnosed at only six different veterinary university hospitals. Once duplicate cases due to multiple visits by the same animal were eliminated, a total of 56 dogs and 24 cats were identified as having been diagnosed with salivary neoplasia. The incidence of salivary neoplasia in this population was calculated to be 15.3 per 100,000 dogs and 26.3 per 100,000 cats. Four of the feline cases were eliminated due to the lack of availability of comparison (control) records. Therefore, a total of 56 dogs and 20 cats with salivary neoplasia were included in our statistical analysis and a total of 112 dogs and 40 cats were selected as controls.

The demographics of the salivary neoplasia and control populations for cats and dogs are described in Table 1. The median age of cats and dogs with salivary neoplasia was 13.4 years and 10.5 years, respectively. The median weight for cats and dogs affected with salivary neoplasia was 4.5 kg and 26.0 kg, respectively. There was no significant difference in sex and neuter status distribution between the salivary neoplasia and control groups in either species (dogs $p = .13$; cats $p = .73$). The anatomic location of salivary neoplasia lesions are described in Table 2. For the majority of tumours, the precise location was not able to be determined (90.8% of cases).

The majority of cats included in this study were either mixed or domestic shorthair ($n = 33$, 55%) and there was no apparent overrepresentation of any one breed among the cases (Table 3). The most prevalent dog breed in this study was mixed ($n = 62$, 55%) and similarly, there was no apparent overrepresentation of any one specific dog breed (Table 4). Results of the univariable conditional logistic regression models revealed no increased risk of salivary neoplasia in dogs or cats of any sex or neuter status (dogs: $p = .26$; cats: $p = .45$). There was no breed disposition within the feline species for salivary

neoplasia. However, in the conditional logistic regression for dogs, poodles (toy and standard) trended towards significance ($p = .075$) with an odds ratio of 6.83 (95% CI: 1.16–40.10) compared to mixed breed dogs (Table 5).

4 | DISCUSSION

To the authors' knowledge, this is the largest epidemiological study regarding salivary neoplasia in cats and dogs. The incidence of salivary neoplasia in our study for this specific population was calculated to be 15.3 per 100,000 dogs and 26.3 per 100,000 cats. To the authors' knowledge this is the first reported incidence of salivary neoplasia in veterinary medicine. In contrast to previous studies, no cat breeds in this population were determined to be at an increased risk for salivary neoplasia. However, poodles (toy and standard) may have a higher occurrence for salivary neoplasia than other breeds of dogs. A breed predisposition for salivary disease has been documented in poodles previously (Spangler & Culbertson, 1991).

TABLE 2 Distribution of salivary gland tumours in the dog and cat

Location	Total number of cases	Cat cases	Dog cases
Mandibular	3 (3.9%)	0 (0%)	3 (5.4%)
Parotid	4 (5.3%)	0 (0%)	4 (7.1%)
Sublingual	10 (13.2%)	4 (20%)	6 (10.7%)
Undefined location	69 (90.8%)	16 (80%)	53 (94.17%)
Total	76	20	56

TABLE 1 Age, weight, sex and location demographics for case and control populations

		Cats			Dogs		
		Salivary neoplasia (n = 20)	Control (n = 41)	p-value	Salivary neoplasia (n = 56)	Control (n = 112)	p-value
Age	Median (range)	13.4 (8.4–33.6)	14.6 (5.8–22.1)	.25	10.5 (1.0–16.0)	11.9 (2.0–17.6)	<.0001
Weight	Median (range)	4.5 (2.0–11.7)	4.1 (1.4–12.4)	.29	26.0 (1.5–106)	19.8 (1.4–62.3)	.08
Sex & neuter status	Female Intact	0 (0.0%)	1 (2.4%)	.73	2 (3.6%)	8 (7.1%)	.13
	Female Spayed	10 (50.0%)	17 (41.5%)		17 (30.4%)	51 (45.5%)	
	Male Castrated	10 (50.0%)	23 (56.1%)		34 (60.7%)	49 (43.4%)	
	Male Intact	0 (0.0%)	0 (0.0%)		3 (5.4%)	4 (3.5%)	
University	Purdue	3 (15%)	6 (14.6%)		8 (14.3%)	16 (14.2%)	
	KSU	4 (20%)	8 (19.5%)		7 (12.5%)	14 (12.5%)	
	OSU	4 (20%)	9 (21.9%)		12 (21.4%)	24 (21.4%)	
	Colorado	7 (35%)	14 (34.2%)		16 (28.6%)	32 (28.6%)	
	Michigan	2 (10%)	4 (9.8%)		4 (7.1%)	8 (7.1%)	
	Illinois	0 (0%)	0 (0%)		9 (16.1%)	18 (16.1%)	

Abbreviations: Colorado, Colorado State University; Illinois, Illinois State University; KSU, Kansas State University; Michigan, Michigan State University; OSU, Ohio State University; Purdue, Purdue University.

There was no significant difference in sex or neuter status distribution between the case and controls for either dogs or cats (dogs $p = .12$; cats $p = .72$). Additionally, no significant difference in sex status was appreciated in the conditional logistic regression. This is in contrast to the findings of a retrospective multi-institutional study of salivary neoplasia in 30 cats that found a 2:1 predilection ratio for male cats and no sex predilection for dogs (Hammer et al., 2001). In humans, salivary cancer is more common in males as compared to females (Kishimoto et al., 2015). Given this is a rare disease a larger cohort may be indicated to document a sex predilection in veterinary medicine. Additionally, there was no significant difference in weight between our feline and canine salivary neoplasia populations and their respective control populations. The median weight for dogs with salivary neoplasia (26.0kg) is within the range considered for a large breed dog. Therefore, salivary neoplasia may be less common in our small breed dogs, however, a larger cohort is indicated to confirm this claim.

Previously reported overall incidence of salivary gland disease was 0.17% (Carberry et al., 1988). This finding was specific to a population of biopsy samples submitted to the New York State College of Veterinary Medicine Pathology Department. An overall incidence of salivary neoplasia has not been reported in a companion animal population. The incidence of salivary neoplasia in our study was calculated to be 15.3 per 100,000 dogs and 26.3 per 100,000 cats. The higher incidence in this study may simply reflect that the VMDB collected data from tertiary referral hospitals. Furthermore, as this is an aggressive neoplastic process often needing more advanced imaging and/or surgery, as well as carrying a more positive prognosis than other types of cancer, these cases may be more likely to be referred providing us with an increased number of cases within our study population. As only six of the 26 hospitals with the VMDB database had salivary neoplasia cases it is possible that they are over represented at these centres for a multitude of reasons including more well-established oncology departments, larger case loads in general, or having a stronger referral base.

In 2009 the reported incidence of major salivary gland cancer in humans was 16 per 1,000,000 which is an increase from 1973 in which the incidence was 10.4 per 1,000,000 (Del Signore

TABLE 3 Distribution of cat breeds for cases with salivary neoplasia and controls

Reported Breed	Total	Case	Control
American shorthair	14	3 (21%)	11 (79%)
Domestic longhair	4	1 (25%)	3 (75%)
Domestic medium hair	2	1 (50%)	1 (50%)
Domestic shorthair	17	6 (35%)	11 (65%)
Manx	2	1 (50%)	1 (50%)
Mixed	15	7 (43.8%)	9 (56.3%)
Oriental	3	0 (0%)	3 (100%)
Persian	2	0 (0%)	2 (100%)
Russian blue	1	1 (100%)	0 (0%)
Total	60	20 (33%)	40 (67%)

& Megwalu, 2017). In humans the risk of salivary gland cancer increases with age (American Cancer Society 2017). In our study, the mean age of cats and dogs diagnosed with salivary neoplasia was 13.4 years (range, 8.4–33.6) and 10.5 years (range, 1–16 years), respectively, which is similar to previous studies in which the median age for affected cats was 12 years (range, 7 to 22 years) and for dogs it was 10 years (range 3 to 14 years) (Hammer et al., 2001). Similar to other types of cancer, salivary neoplasia may be a disease process more commonly seen in older patients, and as the average lifespan increases this may account for an increased disease incidence in both human or veterinary medicine.

In our cohort of cats, there was no breed disposition and there were no Siamese cats. In contrast, in a previous study, Siamese or Siamese cross cats represented 30% (9/30) of affected cats (Hammer et al., 2001) and in a case series of salivary duct carcinoma two out of five cats were Siamese (Sozmen et al., 1999). In dogs, a predisposition in Spaniels has been suggested (Karbe & Schiefer, 1967), but in our canine cohort, Spaniels were not over-represented and other studies have not found a spaniel breed predisposition (Hammer et al., 2001). There were, however, five poodles, both toy and standard, in our study and a trend towards

TABLE 4 Distribution of dog breeds for cases with salivary neoplasia and controls

Reported Breed	Total	Case	Control
American cocker spaniel	4	1 (25%)	3 (75%)
Australian shepherd	2	1 (50%)	1 (50%)
Australian cattle dog	3	0 (0%)	3 (100%)
Chihuahua superbreed	3	0 (0%)	3 (100%)
Chow Chow	3	1 (33.3%)	2 (66.7%)
Dachshund, miniature	2	0 (0%)	2 (100%)
German shepherd	4	3 (75%)	1 (25%)
Golden retriever	4	3 (75%)	1 (25%)
Greyhound	2	0 (0%)	2 (100%)
Labrador retriever	20	8 (40%)	12 (60%)
Mixed	62	16 (25.8%)	46 (74.2%)
Pomeranian	2	0 (0%)	2 (100%)
Pug	3	2 (66.7%)	1 (33.3%)
Shetland sheepdog	4	1 (25%)	3 (75%)
Shih Tzu	3	1 (33.3%)	2 (66.7%)
Siberian husky	3	2 (66.7%)	1 (33.3%)
Standard dachshund	3	1 (33.3%)	2 (66.7%)
Standard poodle	3	3 (100%)	0 (0%)
Toy poodle	3	2 (66.7%)	1 (33.3%)
Weimaraner	4	1 (25%)	3 (75%)
Yorkshire terrier	3	1 (33.3%)	2 (66.7%)
Additional ^a	28	9 (32.1%)	19 (67.9%)
Total	168	56 (33.3%)	112 (66.7%)

^aBreeds for which there are only one representative between either the case or control population are included in this section.

TABLE 5 Conditional logistic regression analysis of salivary gland neoplasia in dogs and cats based on sex, breed and neuter status

Variable	Level	Cats (n = 60)			Dogs (n = 168)		
		Odds ratio	95% CI	p-value	Odds ratio	95% CI	p-value
Sex/Neuter	Female Spayed	1.55	0.50–4.76	.45	0.61	0.29–1.27	.26
	Female Intact	–			0.22	0.04–1.32	
	Male intact	–			0.97	0.19–4.96	
	Male Neutered	Referent			Referent		
Breed	Domestic shorthair	0.65	0.08–5.52	.53			
	American shorthair	0.32	0.06–1.62				
	All other pure bred cats	0.45	0.07–3.00				
	Mixed breed	Referent			Referent		
	Poodle				6.83	1.16–40.10	.075
	Shepherd				5.61	0.89–35.25	
	Retriever				2.29	0.81–6.46	
	Spaniel				1.18	0.19–7.45	
	All other pure bred dogs				0.88	0.37–2.10	
	Dachshund				0.42	0.40–4.52	

significance on logistic regression (5/56 dogs (0.1%); Odds ratio: 6.80, 95% CI: 1.16–40.10). A breed predisposition in poodles has previously been suggested. (Spangler & Culbertson, 1991) As with sex predilection, a larger cohort may be indicated to confirm breed disposition.

In our study, the precise location was not able to be determined in the majority of cases (90.8%). Historically, the parotid and mandibular salivary glands are most often affected and account for 75 to 80% of all salivary gland neoplasia. The zygomatic, sublingual and minor salivary glands account for the remainder of the tumours (Carberry et al., 1988; Hammer et al., 2001; Koestner & Buerger, 1965). There is inconsistency in the veterinary literature in regards to the most frequently affected salivary gland: parotid or mandibular (Koestner & Buerger, 1965; Spangler & Culbertson, 1991). A confounding factor in our study is that a high percentage of the tumours reported on VMDB were classified without a specific location. This likely skews our results as we are not sure which specific gland was affected in those cases.

As previously discussed, there are some limitations to this study. As salivary gland neoplasia is a rare disease process in both veterinary and human medicine additional data may be required to make conclusions regarding sex, location and breed predisposition. This study was retrospective which results in limitations in the information able to be obtained and evaluated. Finally, data were obtained from the VMDB in which information is contributed from participating tertiary referral centres. This may result in decreased external validity.

Much of the data used to cite demographical characteristics of dogs and cats with salivary tumours are decades old. The goal of this study was to update demographical characteristics of cats and dogs with salivary neoplasia using a much larger number of cases than has been previously reported as well as report the incidence and evaluate for sex and breed predispositions. Results from the

present study differ from previous conclusions made in regards to predisposed breeds and tumour location. Additional epidemiological studies should be performed in veterinary medicine to help determine risk factors for salivary gland neoplasia.

CONFLICT OF INTEREST

The authors of this manuscript have no conflicts of interest to declare.

ETHICAL STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as this was a retrospective epidemiological study.

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ENDNOTES

¹Pretty Random (iphone application). Version 1.0. Steven Burnett, FoxBytes; 2016.

²SAS version 9.4, SAS institute, Cary, NC.

³Stata/SE 14.2, StataCorp LLC, College Station, TX.

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