Recent Trends in Feline Intestinal Neoplasia: an Epidemiologic Study of 1,129 Cases in the Veterinary Medical Database from 1964 to 2004

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ABSTRACT

A retrospective epidemiologic study evaluated 1,129 feline intestinal tumor patients via data entered into the Veterinary Medical Database (VMDB) from 1964 to 2004. Cases were analyzed by breed, age, yr of diagnosis, tumor type, and location. The VMDB incidence of all intestinal tumors reported during this 40 yr period was 0.4%, with small intestinal tumors predominating. The most common intestinal tumor was lymphoma, but the most common nonlymphoid tumor was adenocarcinoma. The Siamese breed and increasing age after 7 yr conferred an increased risk. Intact males and females appeared to have a decreased risk compared with neutered patients, but this may be explained by the age difference among these patients as older patients were more likely to be neutered. Prospective studies evaluating neuter status predilection and prognosis are warranted. (*J Am Anim Hosp Assoc* 2011; 47:28–36. DOI 10.5326/JAAHA-MS-5554)

Introduction

Although feline intestinal tumors are relatively uncommon, improved veterinary care in recent years has lead to several publications regarding these neoplasms. Lymphoid tumors are considered to be the most common feline intestinal neoplasm, but reports vary regarding commonality of tumors of nonlymphoid origin as well as anatomic location.[1–7] Prior to this study, the largest retrospective study of feline alimentary tumors consisted of 122 cases and the largest report limited to intestinal tumors included 46 tumors.[1,3]

Feline alimentary neoplasia historically includes tumors of the mouth, salivary glands, esophagus, liver, and pancreas in addition to those of the gastrointestinal tract. A review of the literature revealed that alimentary tract neoplasms represent 19.7%–37.2% of feline tumors.[3,8,9] In turn, tumors of the feline intestinal tract represent approximately 19.2%–34.8% of all feline alimentary tumors and 3.8%–11.9% of all feline tumors.[3,8–10]

In contrast to their canine counterparts in which colorectal tumors are most common, feline intestinal neoplasia is reportedly more common in the small intestine with 61%–97% of all intestinal tumors, regardless of etiology, diagnosed in this location.[1,3,7,8,11–20] When evaluating intestinal lymphoma and adenocarcinoma (ACA) individually, about 79% and 82% of these tumors occur in the small intestine, respectively.[7,21] Sex predilection is controversial regarding feline intestinal tumors with some studies noting a male overrepresentation and other studies reporting equal representation among the sexes.[1,2,4,7,10,13,14,16,19,22–29] The most repeatable findings of sex predilection arise when discussing specific tumor types (e.g., lymphoma, ACA, mast cell tumor, etc). For example, intestinal lymphoma has generally been reported equally prevalent in both sexes with only an occasional study suggesting a male predominance.[11,12,16,22,25–27] In contrast, intestinal ACA is generally regarded as having an increased prevalence in males;

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CI *confidence interval;* ACA *adenocarcinoma;* DSH *domestic shorthair;* FeLV *feline leukemia virus;* OR *odds ratio;* RR *relative risk;* VMDB *Veterinary Medical Database*

*Deceased.

however two earlier studies documented approximately equal representation.[1,11,13,14,19,24] The Siamese cat is the predominant breed in multiple studies on intestinal neoplasms, especially those examining intestinal ACA.[13,14,18,19,21,24]

Cats with intestinal tumors are typically older with mean ages reported between 10.6 and 12.6 yr for gastrointestinal tumors and 8.7 and 12.3 yr for intestinal tumors alone.[1,2,11–14,16–19,21,22,26,30,31] Mean ages of 11–11.8 yr and 12.5 yr were reported for small and large intestinal tumors, respectively.[4,23,24]

Previous reports on intestinal neoplasia, though usually consistent in their data, may be flawed due to their small sample size, limited geographical distribution, or different spay/neuter practices. The purpose of this study was to determine the types, locations, and signalment associated with feline intestinal neoplasia and to determine estimates of risk for particular neoplasms within the population of cats entered in the Veterinary Medical Database (VMDB[a]) which is currently the largest database in veterinary medicine. Over 600,000 feline visits have been recorded from 1964 to 2004. The VMDB includes data acquired since 1964 that have been contributed by more than 20 veterinary schools across the United States. With such a large population and geographical distribution of cases in the VMDB, the goal of this study was to compile a more accurate representation of the total feline population in the United States. In addition, one of the strongest characteristics of the VMDB is the ability to use noncancer cases as a control population.

Materials and Methods

All feline visits from 1964 to 2004 in the VMDB were selected and analyzed using SAS[b] to eliminate all duplicate patient records due to follow-up visits or multiple diagnoses. Variables queried from the VMDB included breed, gender, age, year of diagnosis, tumor type, and topographical location. Due to the nominal occurrence of neoplasia in young cats, age was categorized as follows: <7 yr, 7–10 yr, 11–15 yr, and >15 yr of age. Year of diagnosis was separated by decade from 1964 until 2004 and also divided into 20 yr increments to look for any significant trends in incidence. Tumor type designation was based on the last four digits of the VMDB diagnostic code. The categories entered as "lymphoma" and "lymphosarcoma" were combined as were those entered as "polyp" and "papilloma."

Statistical Analyses

Observations with a diagnosis of "feline intestinal tumor" were categorized according to topographical location. Control cases consisted of any feline case entered into the VMDB for reasons other than intestinal neoplasia. The topographical pattern (small versus large intestine) of various tumor types was examined using a χ^2 test, using only those cats for which the location of neoplasia was clearly defined in the VMDB. Within the VMDB, tumor location was defined as intestine, small intestine, duodenum, jejunum, ileum, large intestine, colon, cecum, or rectum. Based on the VMDB defined locations, we defined the "small intestine" category as all tumors with identified within the duodenum, jejunum or ileum and the "large intestine" as all tumors identified within the colon, cecum, or rectum. Tumors with a location initially defined as "intestinal" or "unknown" were excluded from the topographical analysis. The specific tumor types initially considered included polyp or papilloma, carcinoid, adenocarcinoma, squamous cell carcinoma, carcinoma, lymphoma, reticular cell sarcoma, hemangiosarcoma, leiomyosarcoma, sarcoma, and mast cell tumor. The initial analysis used a χ^2 test to assess topographical pattern in a 2×11 table. Thereafter, those tumor types represented 10 or more times were analyzed for their association with either the small or large intestine. Tumor types considered as a separate category included polyp or papilloma, adenocarcinoma, carcinoma, lymphoma, and sarcoma. Significance was defined as $P<0.05$.

Data were classified into cases and controls according to the definitions given above and univariate contingency tables for each postulated risk factor were constructed. The relative risk of the diagnosis of feline intestinal tumor for each stratum was calculated relative to the strata with lowest occurrence (considered baseline). Risk factors for the occurrence of feline intestinal neoplasia that were considered included age, sex, and breed. Age groups were defined as represented in the VMDB. Strata with low occurrence were combined yielding the following age categories: <7 yr, 7–10 yr, 11–15 yr and >15 yr. Categories of sex considered were intact female, spayed female, intact male and castrated male. Breeds for which the diagnosis of feline intestinal tumor was recorded at least five times in the dataset were categorized as a specific breed group. The remaining breeds were combined to form an "other" breed category resulting in the following breed categories: mixed-breed, Abyssinian, Burmese, Himalayan, Maine Coon cat, Manx, Persian, Russian Blue, Siamese, domestic shorthair (DSH), and "other." The risk of intestinal tumors was calculated relative to baseline exposures which included the <7 yr age group, intact male gender, and "other" breed categories.

Logistic regression models were developed that predicted the probability of the diagnosis of intestinal tumor as a function of postulated risk factors. Risk factors for the occurrence of intestinal neoplasia that were considered included the same age and sex variables but we created compiled breed categories to stratify the different breeds into three groups as follows: "combo mixed-breed" (which included mixed breed and DSH), "Siamese," and "purebreed" (which included all purebreeds, other than Siamese, with a diagnosis of intestinal tumor in the VMDB).

The logistic regression method considered all variables simultaneously and included those variables in the model for which at least one category of a variable was significantly ($P<0.05$) associated with the diagnosis of intestinal tumor. Models were evaluated for goodness of fit using the Pearson χ^2 statistic and the model with the highest ratio of the χ^2 statistic divided by the degrees of freedom was deemed to have superior descriptive value. Models for which the software package identified a convergence issue were rejected. Ninety-five percent confidence intervals (95% CI) were calculated for the regression coefficient for each level of each variable included in the model. CIs that were mutually exclusive were considered indicative of differing risk of intestinal tumor. Regression coefficients were used to calculate the odds ratio (OR) for each level estimating the risk of the diagnosis of intestinal tumor relative to the defined baseline exposure. Significance was defined as $P<0.05$.

To explore the effect of breed on lymphoma and ACA incidence, a χ^2 analysis was used. To assess breed incidence, tumor type (lymphoma or ACA versus all other tumors) was compared with breed pattern including "combo mixed-breed," "purebreed," and "Siamese." Only the cases with known tumor type and breed were used in this analysis.

Results

Of the 316,244 unique feline cases entered into the VMDB between 1964 and 2004, neoplasia represented 8.2% of the cases and intestinal neoplasia comprised 0.4%. Among 26,043 feline cancer cases in the VMDB, intestinal neoplasia comprised 5%. A total of 1,311 feline intestinal tumors were identified; however, only those with a histologic diagnosis were evaluated further. The majority (79.5%) of cases were diagnosed between 1985 and 2004 with only 20.5% of cases diagnosed between 1964 and 1984. The distribution of tumor type within the equal time periods from 1964 to 1984 and 1985 to 2004 have been illustrated in **Figure 1**.

In total, 441 tumors were entered into the VMDB with a known intestinal location and 1,129 tumors with a known histologic type. Intestinal lymphoma was the most common diagnosis within the study period (**Figure 2**). The distribution by tumor type and topographical location as well as the χ^2 analysis of tumors represented $\geq$10 times have been summarized in **Table 1**. Overall breed distribution has been illustrated in **Figure 3**.

Topographically, 225 tumors were located in the small intestine, 216 were in the large intestine, and 870 tumors did not have a specific intestinal location recorded. Mast cell tumors were excluded from topographical analysis because no specific location was recorded for any of the 48 cases identified the VMDB. Also, 22 tumors in the small intestine and 44 in the large intestine were excluded because they were categorized as unknown tumor types.

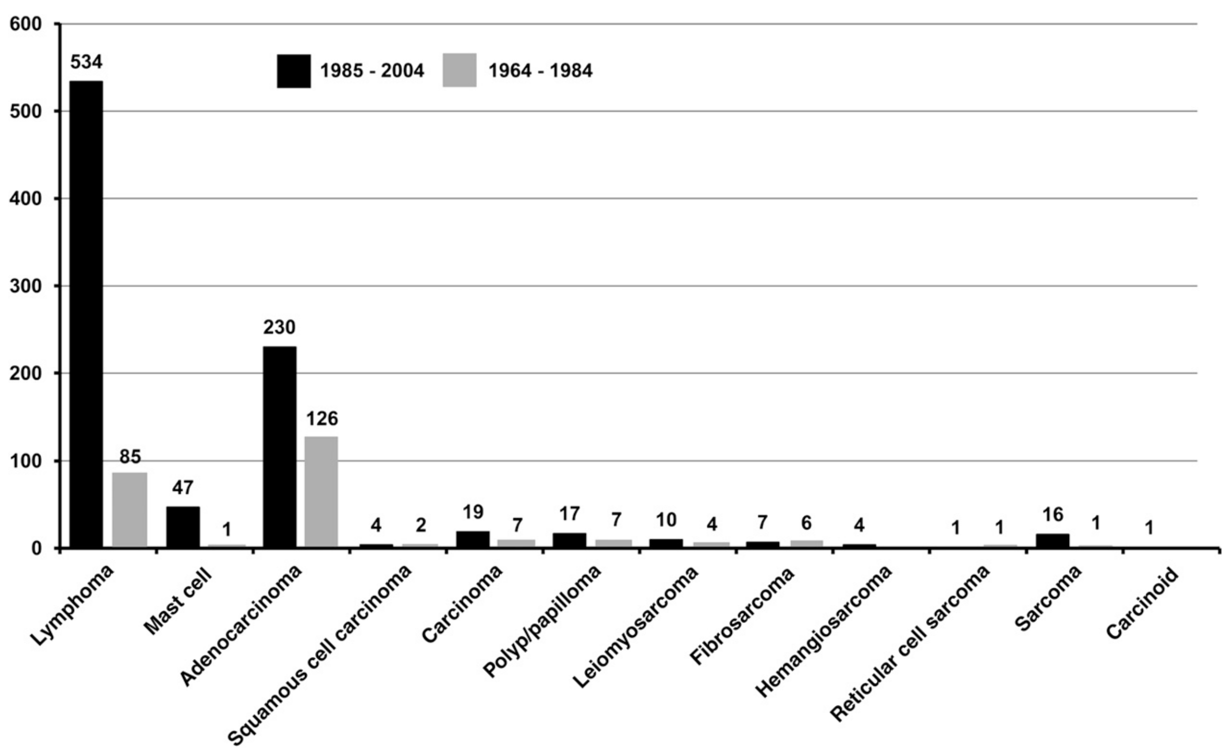

FIGURE 1 *Distribution of tumor type between 1964 and 1984, and 1985 and 2004.*

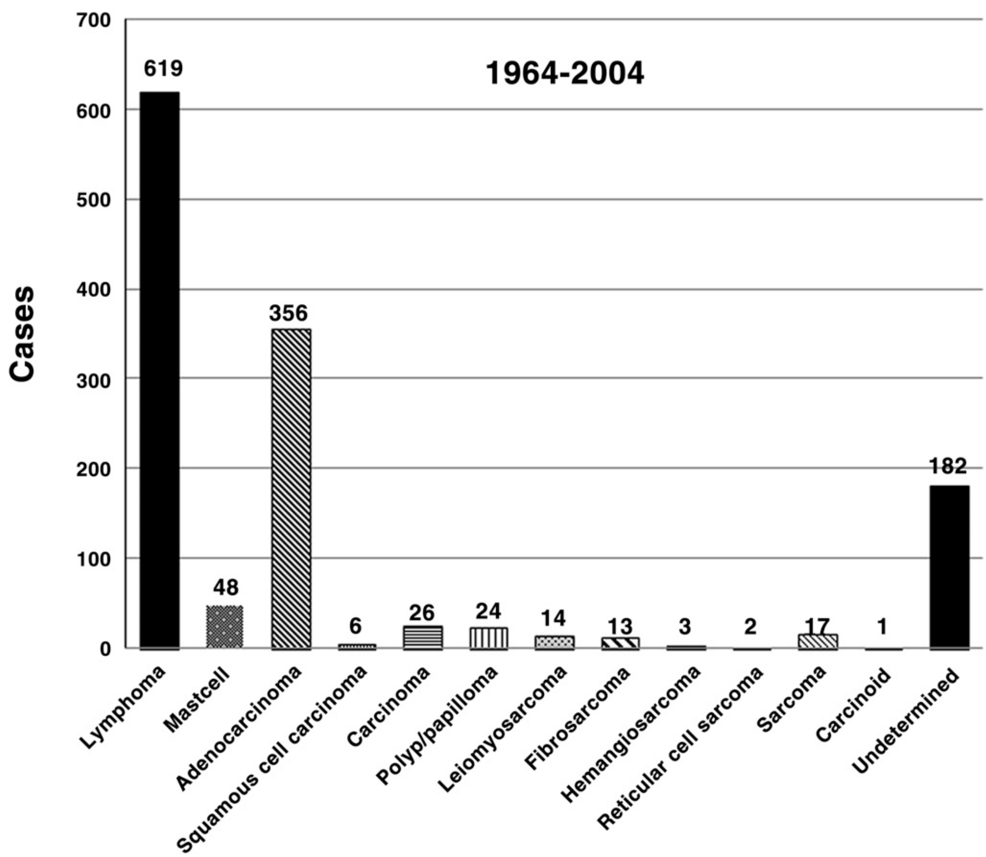

FIGURE 2 *Overall distribution of intestinal tumor types over the entire study period, including those without an etiologic diagnosis.*

Significant evidence for a predisposition for the small intestine compared with large intestine for lymphoma and sarcoma ($P<0.05$) and a predisposition for large intestine compared with small intestine was identified for polyp/papilloma and ACA ($P<0.05$). No difference in topographic distribution was noted for carcinomas.

According to the univariate analysis, (**Table 2**) the lowest risk among the age groups was in the <7 yr category (relative risk [RR]=1). The "other" breed (RR=1) and the intact male (RR=1) categories represented the lowest risk by univariate methods for their respective variables. The logistic regression model (**Table 3**) identified that age, sex, and "compiled breed" were significantly associated with a diagnosis of intestinal tumor in cats. The lowest risk of a diagnosis of intestinal tumors was in young cats <7 yr. Over the age of 7 yr, there was a gradual increase in the incidence of intestinal tumors.

The "compiled breed" category with the least risk of being diagnosed with intestinal tumors was the "purebreed" category (OR=1). There was a significant risk associated with developing intestinal tumors among the "Siamese" breed (OR=1.79, $P<0.001$) and no significant difference was noted between the "combo mixed-breed" (OR=1.1) and "purebreed" categories ($P=0.3301$). The lowest risk for the diagnosis of intestinal tumor was observed among intact male cats (OR=1). Both castrated males (OR=2.42) and spayed females (OR=2.02) were at significantly greater risk for intestinal tumors ($P<0.001$) than intact males and females (OR=1), but this could have been due to the lack of age matching in this population. For the distribution of lymphoma and ACA based on breed, there was a significantly increased risk for lymphoma in

TABLE 1

Distribution of Tumor Type by Location

Tumor type	Small intestine	Large intestine	*P* value
Polyp/papilloma	0	16	<0.001
Carcinoid	1	0	N/A
Adenocarcinoma	45	98	<0.001
Squamous cell	3	3	N/A
Carcinoma	15	11	0.862
Lymphoma	119	31	<0.001
Ret cell sarcoma	1	1	N/A
Hemangiosarcoma	0	1	N/A
Leiomyosarcoma	4	4	N/A
Fibrosarcoma	0	5	N/A
Sarcoma	15	2	0.008

N/A, not applicable

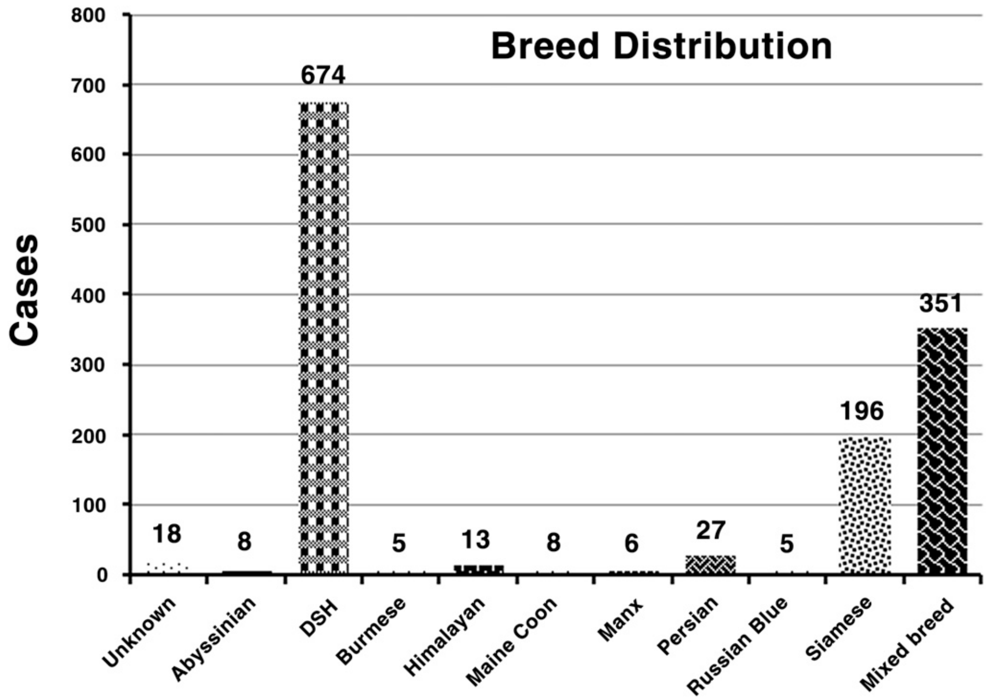

FIGURE 3 *Breed distribution among all cats with intestinal tumors.*

the "combo mixed-breed" (P=0.001) and "Siamese" breed (<0.001) compared with the other intestinal tumors. For the ACA group, a significantly increased risk was noted for the "Siamese" breed only (P<0.001). In fact, the "combo mixed-breed" had a significantly decreased risk of ACA (P<0.000) as described in **Table 4**.

For the distribution of lymphoma and ACA based on breed, there was a significantly increased risk for lymphoma in the "combo mixed-breed" and "Siamese" breed compared with the other intestinal tumors. For the ACA group, a significantly increased risk was noted for the Siamese breed only: the "combo mixed-breed" had a significantly decreased risk of ACA (Table 4).

Discussion

To the authors' knowledge, this is the largest case series of feline intestinal neoplasia presented to date and the data presented herein have proven to be fairly consistent with previously reported data. Lymphoma represents 47% of all intestinal tumors in the VMDB, consistent with the literature range of 44%–63%.[1–3] In terms of location, lymphoma represents 59% and 18% of diagnosed small and large intestinal tumors, respectively, whereas the literature cites 50% and 40%, respectively.[1,4] The anatomic distribution of intestinal lymphoma is 79% and 22% in the small and large intestine, respectively, which is similar to a previously published literature report.[7] More reported cases of intestinal tumors between the first 20 yr and last 20 yr of the study period was noted, with 79.5% of cases diagnosed in the second half of the study time period. This is likely due to a combination of more veterinary visits, improved veterinary care, and increased reporting in the VMDB. The increase in the number of lymphoma cases, specifically, could be attributable to the previously reported relative "shift" of intestinal lymphoma incidence due to implementation of FeLV testing and vaccination.[6,28,32–34] The authors propose that subsequent to the implementation of FeLV testing and vaccination, there was a decrease in the number of cats that died at a young age secondary to FeLV induced lymphoma and more FeLV negative cats were living longer to ultimately develop the naturally occurring gastrointestinal lymphoma. In contrast, the increase in lymphoma cases may also reflect more thorough diagnostic staging and a more frequent definitive diagnosis of intestinal lymphoma rather than a presumptive diagnosis of inflammatory bowel disease. A comparison of the number of lymphoma and inflammatory bowel disease entries over the 40 yr period may help discern this bias; however, this analysis is beyond the scope of this paper.

In various reports, intestinal ACA comprises 0.7%–1.2% of cats necropsied, 0.4%–3% of all feline tumors, 8% of all nonhematopoietic tumors, and 7%–27% of all alimentary tumors.[1,3,8,10,13,14,35–37] The literature cites the small intestine as the primary site of origin for intestinal ACA, but this current study found that 69% of intestinal ACA occurs in the large

TABLE 2

Initial Univariate Assessment of the Risk for the Diagnosis of Intestinal Tumor in Cats Recorded in the Veterinary Medical Database (VMDB) Between 1964 and 2004

Variable	Category	Total cases	Total controls	Occurrence	Relative risk
Age	<7 yr	181	243,266	0.001	**1***
	7–10 yr	244	26,140	0.009	12.545
	11–15 yr	658	34,304	0.019	25.780
	>15 yr	228	11,223	0.020	27.304
Breed	Other	18	8,865	0.002	**1***
	Abyssinian	8	1,434	0.006	2.748
	Domestic short hair	674	162,215	0.004	2.046
	Burmese	5	1,512	0.003	1.629
	Himalayan	13	4,429	0.003	1.446
	Maine Coon cat	8	1,258	0.006	3.132
	Manx	6	1,626	0.004	1.817
	Persian	27	10,451	0.003	1.272
	Russian Blue	5	577	0.009	4.268
	Siamese	196	25,983	0.008	3.715
	Mixed-breed	351	96,583	0.004	1.790
Sex	Intact male	72	76,919	0.001	**1***
	Intact female	71	68,345	0.001	1.110
	Spayed female	529	78,514	0.007	7.198
	Castrated male	639	91,155	0.007	7.489

*Baseline exposure strata; therefore the relative risk is defined as 1

intestine.[1,3,8,11,13,14,19,20,31,38–40] Of large intestinal tumors included in the VMDB, ACA accounts for 45% of the tumors, similar to reports of 46%–100%, which is markedly lower than occurrence of ACA in the small intestine (20%–61.5%).[1,3,4,8] Therefore, this VMDB study shows that the large intestine is the most common location for intestinal ACA and that ACA is the most common tumor occurring in the large intestine.

Mast cell tumor data were fairly consistent between literature reviews and the VMDB. Mast cell tumors reportedly make up 5% of intestinal tumors, which is similar to the 4% noted in this study.[2] The majority (65%) of mast cell tumors were diagnosed in cats 11–15 yr of age which is comparable to a mean age and range of 12.5 yr and 7–18 yr cited in published reports.[11,17,41–43] Like the VMDB, there was no previously reported breed or sex predisposition for intestinal mast cell tumors.[11,17,41–43] The usual location for intestinal mast cell tumors is the distal small intestine and colon.[41,43,44] Unfortunately, no locations were specified for any of the 48 intestinal mast cell tumors listed in the VMDB. This may be attributable to the often diffuse and progressive nature of intestinal mast cell tumors and the difficulty in discerning the site of origin with advanced stage at diagnosis.[41,42]

Intestinal leiomyosarcomas represent between 6.3% and 26.6% of all feline intestinal tumors and 10% and 30.8% of small intestinal tumors, but do not appear to occur in the colon.[1,2,4,8] The VMDB data are slightly different compared with the previous reports in that an overall incidence of 1.1% of intestinal leiomyosarcomas among intestinal tumors and equal distribution in anatomic location is evident.

TABLE 3

Summary of a Logistic Regression Model Predicting the Diagnosis of Intestinal Tumors Among Feline Submissions in the VMDB Between 1964 and 2004

Variable	Category	Odds ratio	*P* value
Age	<7 yr	1.00	*
	7–10 yr	9.36	<0.0001
	11–15 yr	19.00	<0.0001
	>15 yr	20.88	<0.0001
Compiled breed	Purebreed	1.00	*
	Combo mixed-breed	1.11	0.3301
	Siamese	1.79	<0.001
Sex	Intact male	1.00	*
	Spayed female	2.02	<0.001
	Intact female	1.00	0.9905
	Castrated male	2.42	<0.001

*Baseline exposure strata; therefore, *P* values are not provided and the odds ratio is defined as 1

TABLE 4

Distribution for Lymphoma and Adenocarcinoma According to Breed

Compiled breed category	Purebreed	Combo mixed-breed	Siamese
Lymphoma	9	130	11
Other intestinal tumor	17	162	46
***P* value**	0.709	0.001	$<$0.001
Adenocarcinoma	10	98	35
Other intestinal tumor	16	194	22
***P* value**	0.862	$<$0.000	$<$0.001

As with most neoplasms, the VMDB data shows an increased risk of intestinal neoplasia associated with increasing age (i.e., after 7 yr of age). As with previous studies, the current study reports that the Siamese breed is at an increased risk (3.7 fold) for developing any intestinal neoplasia.[7,13,14,18,24] A male overrepresentation is noted in the majority of studies, but some studies cite equal representation.[1,2,4,7,10,13,14,16,19,22–29] The VMDB data show an increased risk for castrated males and spayed females; however, this may be a direct reflection of age as older animals are more likely to be neutered. Multivariate analysis is needed to better evaluate the significance of this finding. Regardless, the benefits of castration far outweigh the risk of intestinal tumor development and would not change veterinarian's clinical recommendations regarding castration.[45–48]

Several factors should be considered when interpreting this study. As previously mentioned, due to improved veterinary practices, the majority of tumors were diagnosed between 1985 and 2004 suggesting that a representative population of patients was not obtained in the first 20 yr of the study. Of the 1,311 total cases of feline intestinal neoplasia in the VMDB over the 40 yr study period, 870 cases (66%) did not have a specified location and 182 (14%) did not have a specified tumor type. When tumors of unknown type and unknown location were removed from analysis, 375 tumors remained, representing only 29% of the original population. Of these, 375 tumors defined as "known" etiology, incomplete data existed that was used for statistical analysis. For example, in the authors' opinions, it is likely that some of the reported carcinomas were, in reality, ACA but were not defined appropriately during individual data entry. In addition, reticular cell sarcomas (n=2) are probably more appropriately categorized today as large cell lymphoma.

Reporting practices for breed predisposition should also be considered. Although the DSH was by far the most common breed to be diagnosed with intestinal neoplasia and was the most common breed in the control group, requirements for breed determination by those entering the cases into the VMDB must be considered. There was a "mixed-breed" category in the VMDB; however, in the authors' experience, "DSH" is often used as the default determination when an exact breed is neither discerned by the clinician nor suggested by the owner. This issue may have been accounted for when consolidating DSH patients with mixed-breed patients in the "combo mixed breed" category for statistical analysis.

Statistical evaluation of tumor location was challenging in this study. Intestinal lymphoma is a disease that is diffuse by nature and determining a primary site of origin may be impossible. Often, patients with intestinal neoplasia are diagnosed using mesenteric lymph node aspirates or intestinal partial- or full-thickness biopsies making site of origin difficult unless the disease is diagnosed early. This may explain why none of the 48 intestinal mast cell tumors, commonly a diffuse disease, had a defined small or large intestinal location.

One limitation of this study may be the control population. Cases entered into the VMDB are cases examined at academic institutions requiring a "referral" level of care. Even though the control population may have had some bias toward complex illnesses, these diseases include many nonneoplastic processes in addition to cancer making this bias less of a concern. Another limitation of this study takes into consideration the evaluation of risk factors. The effect of age, breed, and sex on the development of feline intestinal neoplasia was evaluated, but there are many other possible risk factors that need to be acknowledged including diet, environment (e.g., indoor/outdoor cat, smoking households, owner occupational hazards), and geographic distribution. These data were not readily and consistently available in the VMDB for the cases included in this study and were therefore excluded from statistical analysis.

The most common feline intestinal neoplasia entered in the VMDB was lymphoma. Lymphoma was the most common small intestinal tumor and the second most common large intestinal tumor after ACA. Prior to 1980, ACA was the most common small and large intestinal tumor. This finding may be attributed to the institution of FeLV testing (in the 1970s) and vaccination (in the 1980s) causing a shift in incidence from nonalimentary lymphoma (which are often diagnosed in FeLV antigen positive cats) to alimentary lymphoma (which are often diagnosed in cats which are FeLV antigen negative).[5,6,25–28,32–34,49] This shift may be a combination of two factors. First, improved diagnostic and reporting practices may have resulted in an increased frequency of diagnoses in patients that may previously have been euthanized. Secondly, with improved vaccination and testing practices in the second half of the study period, cats were presumably living longer thus allowing these animals to reach the geriatric age at which they would naturally acquire gastrointestinal lymphoma.

Conclusion

This study evaluated 1,129 cases of feline intestinal tumors to determine the major signalment predilections for the disease. Based on the results of this study, the authors found that the most common intestinal tumor was lymphoma and the most common nonlymphoid tumor was ACA. The diagnosis of intestinal neoplasia, especially intestinal lymphoma, appears to be increasing in the feline population in the United States. This may very well reflect improved veterinary care and diagnostic capability in the more recent decades. In addition, this may also be a direct result of the implementation of FeLV vaccination and testing in the 1970s and 1980s which, the authors propose, led to a decrease in lymphoma mortality in younger FeLV positive cats and thus the potential for these FeLV negative cats to develop naturally occurring gastrointestinal lymphoma later in life. High-risk variables for developing intestinal neoplasia include the Siamese breed and increasing age after 7 yr. The logistic regression analysis revealed that intact males and females appeared to have a decreased risk for intestinal neoplasia compared with neutered patients, this may be explained by the likelihood that younger patients are more likely to be intact.

Knowing the cat's breed, age, and type and anatomic distribution of intestinal tumors could help veterinarians make more informed decisions when recommending diagnostic tests and considering differential diagnoses in patients presenting with both gastrointestinal and nonspecific clinical signs.

FOOTNOTES

[a] The Veterinary Medical Databases (VMDB) available at http://www.vmdb.org/. VMDB does not make any implicit or implied opinion on the subject of this paper.

[b] PROC GEN MOD, SAS for Windows, version 9.13; SAS Institute Inc, Cary, NC

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