Breed and anatomical predisposition for canine cutaneous neoplasia in South Africa during 2013

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Abstract

Cutaneous neoplasia occurs commonly in dogs and owners in consultation with their veterinarian must decide when to perform surgery to obtain a histopathological diagnosis. The objective of this study was to identify breed predispositions for canine cutaneous neoplasms and determine factors associated with malignancy. This retrospective case-series evaluated histopathology reports from two veterinary pathology laboratories in South Africa during a six-month study period. Breed predispositions were analysed using log-linear models and risk factors for malignancy were evaluated using binary logistic regression. Data were available for 2553 cutaneous neoplasms from 2271 dogs. The most frequent neoplasms were mast cell tumours (21.1%), histiocytoma (9.4%), haemangiosarcoma (8.3%), melanocytoma (5.8%), and lipoma (5.1%). Boxers (relative proportion = 38.9; 95% confidence interval, 2.3-646), pugs (7.6; 1.4-41.0), Staffordshire bull terriers (7.0; 1.9-26.3), boerboels (3.8; 1.3-10.7), Labrador retrievers (2.7; 1.0-7.0), and mixed breed dogs (2.2; 1.1-4.4) had a higher frequency of mast cell tumours. Jack Russell terriers (odds ratio = 2.5; 95% confidence interval, 1.8-3.5), Rottweilers (2.3; 1.3-3.9), pit bull terriers (2.2; 1.1-4.3), and Staffordshire bull terriers (1.6; 1.0-2.6) were more likely to have malignant neoplasms. Dog signalment might facilitate prognosis determination for cutaneous canine neoplasia prior to receiving a histopathological diagnosis.

Keywords: anatomic location, neoplasia, dog, malignancy, risk factors, skin

Introduction

Skin is a complex organ with multiple functions that include temperature regulation in addition to immunological, mechanical, neurosensory, endocrine and apocrine/eccrine functions.[1] Skin comprises the epidermis and associated epithelial structures within the dermis with support provided by the mesenchymal tissues of the dermis and panniculus.[2] The integument is continuously exposed to chemical and physical insults and is the system most accessible to, and therefore most closely observed by animal owners.[3] The skin is affected by a wide variety of pathological conditions, most notably, neoplasia.[4] Cutaneous neoplasia occurs commonly in dogs with increasing numbers being reported since 1964.[5]

The most common skin tumours reported for dogs in the Southern Hemisphere include mast cell tumours, histiocytomas, squamous cell carcinomas, perianal gland adenomas, fibromas, lipomas, and haemangiosarcomas.[6-8] A variety of causative factors have been implicated in the development of neoplasia in general. Chronic inflammation is thought to be at least partially responsible and examples in dogs and cats include thermal burns (carcinoma),[9] chronic parasitic infection (e.g. *Spirocerca lupi*-related oesophageal sarcomas[10; 11]), foreign material/implanted devices (e.g. fibrosarcoma,[12] osteosarcoma[13]), solar radiation (e.g. squamous cell carcinoma,[14] hemangiosarcoma[15]) and injection/vaccination[16] (e.g. some sarcomas).[17] Neoplasia typically occurs in older dogs with an exception being histiocytomas, which are often diagnosed in younger animals.[3; 5; 7; 8; 18-22]

Dog breed is an important predisposing factor for the development of some cutaneous neoplasms with boxers being particularly susceptible.[5; 23] Mast cell tumours reportedly have a strong genetic predisposition and dogs with bulldog ancestry, such as pugs, boxers and Boston terriers are at higher risk.[24; 25] However, golden retrievers, Labrador retrievers, beagles, shar pei,

Weimaraners, bullmastiffs, Staffordshire bull terriers, Rhodesian ridgebacks, and American pit-bull terriers are also commonly affected.[24; 26]

Melanocytic tumours frequently occur in breeds that have extensive cutaneous melanin pigmentation including schnauzers (standard and miniature) and Scottish terriers.[27] However, Irish setters and golden retrievers are at increased risk for nailbed melanomas and melanomas of the lip can also occur in golden retrievers.[27; 28] American pit bull terriers, bull terriers, Dalmatians, beagles and harlequin Great Danes are predisposed to developing sun-induced cutaneous neoplasms.[8; 28] Whippets, beagles, Dalmatians, American Staffordshire bull terriers, and basset hounds are at a higher risk for haemangiomas and haemangiosarcomas.[29] Golden retrievers, Staffordshire bull terriers, Rhodesian ridgebacks, Labrador retrievers, boxers, and German shepherds are predisposed for the development of mesenchymal tumours including histiocytic sarcoma, lymphangiosarcoma, haemangiosarcoma, synovial cell sarcoma, leiomyosarcoma, rhabdomyosarcoma, oral fibrosarcoma, and brachial plexus peripheral nerve sheath tumours.[30]

Familial clustering and genetic predispositions also influence the development of malignant neoplasms. For example, in one study 75% of identified melanocytic neoplasms were benign in Dobermans and miniature schnauzers compared to 85% of these tumours being malignant in miniature poodles.[31] However, anatomical tumour location might also influence the malignancy of melanocytic neoplasms.[26] The majority of cutaneous melanomas are benign but diagnosed malignant tumours are more commonly identified on the head, ventral abdomen and scrotum.[27] Melanomas also occur commonly at mucocutaneous junctions and within the oral cavity and is the second most common digital neoplasm following squamous cell carcinoma.[27]

Soft tissue sarcomas typically occur on the hind legs, forelegs, trunk, head, neck, and shoulders.[30]

Veterinary practitioners must formulate differential diagnosis lists and determine the requirement for surgery and histopathological diagnosis when confronted with masses on the skin of canine patients. An evidence-based approach can be helpful in conjunction with history, veterinarian experience and results from fine-needle aspirate biopsy. The objectives of this study were to identify breed predispositions for canine cutaneous neoplasms in South Africa and to determine factors associated with malignancy. A secondary objective was to identify the anatomic locations with increased occurrence of specific tumours. It was hypothesised that boxers would be at higher risk of cutaneous neoplasms in general while mixed-breed dogs would be at a lower risk.

Materials and Methods

Case selection

The study was designed as a case-series and scanned copies of pathologist reports pertaining to all cutaneous masses examined between 01 January and 30 June 2013 were retrieved from the records of two private veterinary pathology laboratories in South Africa. The distance between the two laboratories was approximately 550 km and both received specimens from all nine provinces of South Africa. All submissions were examined by experienced or registered specialist veterinary pathologists. Extracted data included date, province of owner residence, breed, age, sex, histopathological diagnosis, malignancy status, and anatomical location of the mass. The first author (SCT) determined malignancy status by reviewing the histopathology reports including details pertaining to cellular and nuclear pleomorphism, mitotic count, degree

of cellular differentiation, degree of tumour cellularity and necrosis, evidence of tumour emboli in vasculature, and tumour infiltration at the junction with normal tissue.[2] Cases were excluded if a diagnosis was not assigned, dog breed was not available, or if lesions were classified as non-neoplastic (e.g., inflammatory lesions). Mammary tumours were excluded because of their specialised function and the fact that they are often classified independently of the integumentary system.[2] Anal sacs were not considered part of the integumentary system and therefore associated tumours were excluded. The study was approved by the University of Pretoria's Research Ethics Committee (protocol number V008-16).

Tumour classification

Tumours were classified according to histogenesis: epidermal (EPI), apocrine (APO), follicular (FT), mesenchymal (MT), nailbed (NT), round cell (RCT), and sebaceous (ST).[28] Tumour phenotype was determined using immunohistochemistry when there was uncertainty in the final diagnosis based on morphological structure alone. The histomorphological description in the pathologist report was used to classify cutaneous mast cell tumours into low and high grade tumours to be consistent with a recent two-tier grading system.[32; 33]

Epidermal neoplasms included papillomas, squamous cell carcinomas, basal cell carcinomas, and anaplastic carcinomas. Follicular tumours included all neoplasms of follicular origin including trichoepithelioma, pilomatricoma, tricholemmoma, infundibular keratinising acanthoma, and trichoblastoma. Apocrine tumours included adenomas and carcinomas. Sebaceous tumours were classified as adenomas, carcinomas, or epitheliomas. Epitheliomas were defined as having a predominant basaloid reserve cell population with far fewer mature sebocytes.[28] Mesenchymal tumours included fibroma, fibrosarcoma, myxoma, myxosarcoma,

lipoma, liposarcoma, haemangioma, haemangiosarcoma, perivascular wall tumours, peripheral nerve sheath tumours, lymphangiosarcoma, anaplastic sarcomas, and histiocytic sarcomas. Nailbed squamous cell carcinoma, melanoma, basal cell carcinoma, and inverted papilloma were included in the category of neoplasms arising from the nailbed epithelium. Round cell tumours included mast cell tumours (low and high grades), plasma cell tumours, histiocytomas, melanoma and melanocytomas, transmissible venereal tumour, and cutaneous lymphoma. Melanocytic tumours can appear spindled, epithelioid or round but were classified within the round cell tumour category.

Anatomical region classification

The anatomical location of each skin neoplasm was classified into broad body regions. "Face" included lips, muzzle, nose, the periocular regions, cheeks, and chin. "Eyelid" and "neck" were retained as separate categories independent of "face" due to the frequency of tumours occurring in these locations. "Head" included the cranium (dorsal and ventral sides, including beneath the mandible) to the first cervical vertebra. The "dorsum" was defined as the area from the shoulders to the rump and included the tail. "Flank" was used for the lateral abdomen while "ventrum" included the ventral sternum and abdomen. "Foot" included dorsal, palmar, and plantar regions as well as the paw pads. "Legs" incorporated the area from the scapula to metacarpus (front limbs) and the hip to the metatarsus (hind limbs). The "perianal" location and "digit" were classified independently due to the frequency of neoplasms occurring in these locations.

Statistical analysis

Mixed breed dogs were classified as a single breed category for statistical analysis. Breeds with at least 50 records in the data set were identified and all remaining breeds were combined into a single reference category for comparative purposes. Categorical data were described using frequencies and age was described using the mean and standard deviation (SD) after assessment of the normality assumption by calculating descriptive statistics, plotting histograms and performing the Anderson-Darling test in available software (MINITAB Statistical Software, Release 13.32, Minitab Inc, State College, PA, USA). Data were descriptively presented using box and whisker plots and heat maps generated in the ggplot2 package[34] within R.[35] Age was compared across categorical predictors using 1-way ANOVA after restricting the data set to the first (primary) tumour per dog. Post hoc pairwise comparisons were adjusted using the Bonferroni correction of P values. The relative proportion of tumour diagnosis in each broad tumour category (APO, EPI, FT, MT, NT, RCT, and ST) was compared over categorical predictors using log-linear models assuming a Poisson error distribution. Sebaceous adenomas and the anatomical location of ventrum were set as the reference categories for all log-linear analyses. Full factorial models were analysed and inferences were made based on the modelled interaction terms between each tumour category and level of the other predictor variables. The case sampling design of the study prevented the main effect terms of the model from having a meaningful clinical interpretation. Log-linear models excluded multiple tumours of the same broad category when more than one was identified in the same dog. Exponentiation of the slope parameters for modelled interaction terms yielded relative proportions (RP) comparing the frequency of each tumour to the reference category of sebaceous adenomas. Over-representation of a specific tumour relative to the frequency of sebaceous adenomas was interpreted as an increased risk for that tumour within that category (e.g., breed) of dog.

Binary logistic regression was used to identify predictors for the malignancy status of tumours. Multivariable models were constructed that adjusted for potential confounding by dog age and diagnostic laboratory. Logistic regression models only incorporated data for the primary tumour from each individual dog. Cases were excluded from analysis on a test-by-test basis when required data were not available within laboratory records. Unless stated otherwise, all statistical analyses were performed using commercially available software (IBM SPSS Statistics Version 25, International Business Machines Corp., Armonk, NY, USA). Statistical significance was set as $P < 0.05$.

Results

A total of 2553 cutaneous neoplasms from 2271 dogs were included in the study. The most common dog breeds were mixed (n_t=361 tumours, n_d=320 dogs), Jack Russell terrier (n_t=272, n_d=239), boerboel (n_t=158, n_d=144), dachshund (n_t=145, n_d=123), Labrador retriever (n_t=138, n_d=124), Staffordshire bull terrier (n_t=127, n_d=114), boxer (n_t=94, n_d=83), Rottweiler (n_t=78, n_d=70), German shepherd (n_t=73, n_d=68), bull terrier (n_t=67, n_d=58), Rhodesian ridgeback (n_t=60, n_d=55), golden retriever (n_t=59, n_d=51), Maltese poodle (n_t=59, n_d=49), pug (n_t=54, n_d=46), and pit bull terrier (n_t=50, n_d=44). The study population included 1140 females, 1063 males, and 68 without a recorded sex. Age was recorded for 2107 dogs and the mean (standard deviation) was 7.9 (3.3) years overall. There were 526, 469, 281, 488, 437, and 353 neoplasms included for the months January-June, respectively. Laboratory 1 contributed 818 tumours and laboratory 2 provided data for 1735.

The most common tumour category was round cell tumours (RCT; n=1078) followed by mesenchymal (MT; n=795), sebaceous (ST; n=263), follicular (FT; n=204), epidermal (EPI;

n=146), apocrine (APO; n=39), and nailbed tumours (NT; n=28). During the study period, the most common specific diagnoses included low grade mast cell tumours (n=495), histiocytoma (n=239), haemangiosarcoma (n=211), melanocytoma (n=147), lipoma (n=129), squamous cell carcinoma (n=126), peripheral nerve sheath tumour (n=118), haemangioma (n=112), sebaceous adenoma (n=109), and malignant melanoma (n=84; Table 1). The age at tumour removal (or biopsy) varied among neoplastic diagnoses ($P < 0.001$) and dogs with histiocytomas were younger than dogs with all other diagnoses ($P < 0.001$ for all pairwise comparisons; Figure 1).

Rottweilers (relative proportion, RP = 18), golden retrievers (RP = 10), and mixed breed dogs (RP = 3.8) all had an increased frequency of nailbed tumours (NT) compared to the combined reference category of less common breeds (Figure 2). Staffordshire bull terriers (RP = 8.7) and Jack Russell terriers (RP = 3.5) had a higher than expected frequency of epidermal tumours (EPI). Boxers (RP = 18) and Staffordshire bull terriers (RP = 3.8) had a higher frequency while Maltese poodles (RP = 0.3) had a lower frequency of round cell tumours (RCT). Follicular tumours (FT) were more common in German shepherds (RP = 5.6) but less commonly diagnosed in Maltese poodles (RP = 0.2), Jack Russell terriers (RP = 0.3), and dachshunds (RP = 0.3).

Boxers (RP = 39), pugs (RP = 7.6), Staffordshire bull terriers (RP = 7.0), boerboels (RP = 3.8), Labrador retrievers (RP = 2.7), and mixed breed dogs (RP = 2.2) all had an increased frequency of mast cell tumours (Figure 3). Similar to having an increased frequency of epidermal tumours in general, Staffordshire bull terriers (RP = 7.8) and Jack Russell terriers (RP = 3.9) had a higher than expected frequency of squamous cell carcinomas. German shepherd dogs (RP = 8.3) were more frequently diagnosed with haemangiomas than the reference group. Maltese poodles did not have an increased diagnosis of any specific tumour but had significantly fewer

diagnoses of histiocytoma (RP = 0.2) and melanocytoma (RP = 0.2). Jack Russell terriers (odds ratio, OR = 2.5), Rottweilers (OR = 2.3), pit bull terriers (OR = 2.2), and Staffordshire bull terriers (OR = 1.6) were more likely to be diagnosed with malignant neoplasia after adjusting for the confounding effect of age (Table 2).

Tumours from the ventrum were more likely to be malignant compared to all other locations with the exception of the nailbed (all had an OR significantly less than 1; Supplemental Table 1). Follicular tumours were more likely to be found on the flank (RP = 39), dorsum (RP = 15), neck (RP = 14), and leg (RP = 9) relative to the ventrum (Figure 4). Epidermal, mesenchymal, and round cell tumours occurred more frequently on the ventrum (the ventrum had a higher proportion for the locations in which the RP was significantly less than 1).

Discussion

An evidence-based paradigm can be beneficial for diagnostic investigations within veterinary medicine. A good history from the client and the clinical experience of the veterinarian are extremely useful to formulate differential diagnosis lists and determine the likelihood of malignancy in canine cutaneous neoplasia. This information in conjunction with fine-needle aspirate biopsy results is required when advising clients concerning the requirement for surgery and formal histopathological diagnosis. The data presented here should facilitate practitioner prognostication for the scheduling of surgical removal of masses that are not currently causing discomfort to the animal. Furthermore, veterinarians are often expected to know breed predispositions for common and uncommon health conditions. The aim of this study was to provide quantitative data for an evidence-based medicine approach to the diagnostic investigation of cutaneous neoplasms in South African dogs.

The current study evaluated a large number of cutaneous neoplasms in a diverse population of dog breeds. The current findings corroborate previous results concerning the specific cutaneous neoplasms common in the Southern Hemisphere,[7] the occurrence of histiocytomas at a relatively young age,[5] the increased risk for mast cell tumours in breeds with bull dog ancestry,[24] the increased risk of Rottweilers and golden retrievers for nailbed tumours,[27; 28] the increased risk for haemangiomas in German shepherds,[30] and the increased occurrence of some malignant neoplasms on the ventrum of dogs.[27] Also as expected, boxers appeared to be at a higher risk for cutaneous neoplasms in general (darker colours in Figure 3 indicated descriptively increased risk). The risk was only significantly elevated for mast cell tumours but that might have been due to low statistical power (only 94 tumours in 83 dogs). Case-series study designs lack an unaffected group and this complicates the calculation of relative risk measures. The study presented here used sebaceous adenomas on the ventrum in a combined group of less frequent dog breeds (within the study population) as the internal comparison group for relative risk calculations. Sebaceous adenomas were chosen as the comparison group because it is a relatively common benign neoplasm without strong breed or sex predilections.[2; 28; 36] The case-series approach required using statistical procedures less commonly employed in clinical epidemiological studies. The corroboration of important findings from previous research provides evidence for the validity of the study design and statistical approach.

The validity of the epidemiological approach is important because to the authors' knowledge, some of our significant findings have not been previously published. Boerboels are a mastiff breed developed in South Africa[37] and subsequently recognised as an official breed by the American Kennel Club.[38] However, few studies have been published concerning neoplasia in this breed.[39-41] The present study provides evidence that boerboels have an increased risk for

mast cell tumours similar to breeds with bulldog ancestry. The specific breed origins of the boerboel are unclear;[37] however, their phenotypic characteristics are consistent with other mastiff breeds with some bulldog ancestry. Additionally, there was evidence that boerboels have an increased risk of spindle cell tumours, which was not identified for any other evaluated breed.

German shepherds in this study were at increased risk of developing follicular tumours in general, which included infundibular keratinising acanthoma, pilomatricoma, trichoblastoma, trichoepithelioma, and tricholemmoma. German shepherds have been recognised to be at higher risk for infundibular keratinising acanthomas but other follicular tumours were not mentioned in a previous study.[28] This finding might relate to the pedigree and specific genetics of German shepherd dogs in South Africa. Country-specific genetics has been recognised as a source of variability for the risk of cutaneous haemangiosarcoma in golden retrievers.[26]

Jack Russell terriers in our study were at a higher risk for haemangiosarcomas and squamous cell carcinomas. Solar radiation is a risk factor for these neoplasms[15] and the predominantly light colour of Jack Russell terriers is a possible explanation for this association. A limitation of the current study is that tumour histopathology was not re-evaluated for characteristic evidence of solar-induced neoplasms and therefore this explanation is speculative. However, the ventral abdomen of Jack Russell terriers is often sparsely haired and poorly pigmented and is therefore a common location for solar keratosis and the associated tumours.[15] Maltese poodles also have a predominantly light coat colour but this breed did not have an increased risk for solar radiation-associated tumours. The risk of neoplasia is multifactorial and it is likely that the increased risk for these neoplasms in Jack Russell terriers is a combination of environmental, behavioural, and hereditary causes.

Maltese poodles in our study did not have an increased risk for any cutaneous neoplasm and were, in fact, at a decreased risk for follicular tumours and round cell tumours in general. This breed category also had significantly fewer histiocytomas and melanocytomas compared to the comparison group of dogs. South Africa has diverse cultures and people with varying socioeconomic status. Our cases were extracted from commercial pathology laboratories and likely preferentially included dogs owned by people in higher income strata. However, many owned dogs in all economic strata are bred by casual breeders and only a relatively small proportion of dogs are purchased from Kennel Union of Southern Africa (KUSA) registered breeders. Owners and veterinarians typically assign breed based on phenotypic characteristics in the absence of breed registration. Maltese poodles are not a KUSA registered breed and in South Africa it is not uncommon for this name to be used for "little white fluffy dogs" without a known breed pedigree. The reduced risk for cutaneous neoplasia might be an indicator of a more diverse genetic background within this breed category.

The genetic heterogeneity of mixed breed dogs reduces the risk for hereditary conditions.[42] However, findings of the current study were not entirely consistent with this general trend. Mixed breed dogs in our study were at a higher risk for nailbed tumours, mast cell tumours, and peripheral nerve sheath tumours. Breed information was provided by referring veterinarians and it was not possible to validate this information. The observed increased risk might be attributable to the predominant breed within the mixed breed category of dogs. The risk pattern was not consistent with any single evaluated breed and it is therefore impossible to speculate on the predominant breed composition. Furthermore, it is possible that the environment of these dogs was different than the purebred dogs and it was these unrecorded environmental factors that represent the true cause for the increased risk. The magnitude of the risk increases

were relatively small suggesting the involvement of multiple pathogenic mechanisms rather than a predominant hereditary cause.

The pit bull terriers included in our study were likely dogs with the phenotypic characteristics of pit bull terriers but with few acquired from registered breeders. Previous research suggests that this breed is at higher risk for solar radiation-associated tumours including haemangiosarcoma and squamous cell carcinoma.[8; 28] In contrast, the pit bull terriers in our study were not at an increased risk for either a specific tumour category or any individual neoplasm. However, this breed was at an increased risk for malignant neoplasms in general. Jack Russell terriers, Staffordshire bull terriers, and Rottweilers were also at increased risk of malignant neoplasms but these breeds were also at a higher risk for nailbed tumours (frequently malignant) or squamous cell carcinomas (always malignant). The reason for the increased risk of malignant tumours in pit bull terriers could be due to a combination of factors including multiple neoplastic diagnoses (though too small a sample size for any single tumour to be significantly increased) and the specific anatomical locations of occurrence.

Golden retrievers had a decreased risk of malignancy despite being at a higher risk for nailbed tumours. Similarly, pugs and boxers, although having significantly increased occurrence of mast cell tumours, were not at an increased risk for malignancy. It is unclear why golden retrievers would have an increased risk for specific tumours that are frequently malignant in absence of an increased risk for malignant tumours in general. The multifactorial nature of cutaneous neoplasms suggests an influence of genetics in addition to environmental exposures. Owner characteristics likely varied among breed groups and it is possible that these differences created environmental exposure patterns that also differed by breed in this study.

The inability to evaluate environmental exposures is one limitation of the current results. Another limitation is that the study likely included a biased sample of tumours. A number of cutaneous tumours can be diagnosed by the general practitioner using fine needle aspirate biopsy and surgical removal with a formal histopathological diagnosis would not be required. The study population was therefore likely biased towards a higher prevalence of malignant tumours. Furthermore, the study population likely included few dogs from the under-resourced communities of South Africa. Our data originated from biopsy reports of the two largest veterinary diagnostic pathology laboratories in the country, which receive specimens from all nine provinces of South Africa. However, at the time of the study, veterinary care was largely inaccessible to chronically under-resourced communities in South Africa and therefore dogs from these communities were likely under-represented. The breed distribution and environmental exposures in these communities are likely different from the more affluent areas of South Africa. Concurrent data from both communities might help disentangle the influence of environmental and hereditary risk factors.

The breed distribution included in the study might have varied from the source population. The 10 most frequent breeds included in the current study were Jack Russell terrier, boerboel, dachshund, Labrador retriever, Staffordshire bull terrier, boxer, Rottweiler, German shepherd, bull terrier, and Rhodesian ridgeback. The top breeds registered with KUSA for the same year were (in descending order): Yorkshire terrier, Labrador retriever, bulldog, Rottweiler, Staffordshire bull terrier, bull terrier, golden retriever, miniature schnauzer, beagle, and Pomeranian.[43] There are some similarities between breed lists but differences are likely due to the relatively small proportion of owned dogs that are registered with KUSA and the fact that included dogs (via submitted tumours) were likely a biased sample of all dogs in South Africa. A

further limitation was that neuter status was not routinely recorded by the referring veterinarian and this potential confounder could not be accounted for in the statistical analysis. Sterilisation of dogs is recommended by veterinary practitioners in South Africa and mass sterilisation is often undertaken by government and private organisations in less affluent areas. However, despite routine veterinary recommendations, the frequency of sterilisation might have varied among breed groups due to differing owner characteristics. Additional limitations of the present study include the relatively limited time frame, the case-series design, and the lack of digital data bases at participating laboratories. The inability to review histopathology slides for tumours included in the study was another drawback and as a consequence it was only possible to apply a grading system for mast cell tumours due to inconsistencies in reporting between laboratories. The inability to apply a consistent grading system had the largest impact on the diagnosis of soft tissue sarcomas, which were very few in this study due to the classification of fibrosarcoma, mycosarcoma, myxoma, spindle cell, and peripheral nerve sheath tumours within the mesenchymal tumour category. Laboratory records were manually reviewed by one author (SCT) and the number and reasons for exclusions were not recorded at the time of data collection.

The results of the present study corroborate previous research in addition to providing new information concerning breed predispositions. An advantage of the current study is that in South Africa, histopathology is considered routine for the diagnostic investigation of cutaneous masses removed from dogs. Current findings should be generalisable to the affluent areas of South Africa but the chronically underserved communities of the country likely have different risk profiles due to variations in management and environmental exposures.

Conclusions

Dog signalment and anatomical location of cutaneous neoplasms are associated with tumour diagnosis and likelihood of malignancy. This information can be used to inform decisions related to the scheduling of biopsy and surgical tumour removal. Further research is necessary to identify genetic and environmental predictors and causal interactions in the development of cutaneous neoplasms in dogs.

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Figure legends

Figure 1. Descriptive presentation of dog age at diagnosis for the most common neoplastic diagnoses by breed for 2553 skin tumours examined from 2271 dogs at two private laboratories in South Africa over a 6-month study period during 2013. Points correspond to individual values, the box represents the interquartile (25th to 75th percentile), the horizontal line within the box corresponds to the median, and the whiskers represent to the range of values excluding outliers (1.5 times the interquartile range).

Figure 2. The association between breed and tumour categories for 2553 skin tumours examined from 2271 dogs at two private laboratories in South Africa for a 6-month study period in 2013. Lighter shading denotes negative (protective) associations and darker shading represents increased occurrence. Tumour classifications were sweat gland tumours (APO), epidermal tumours (EPI), follicular tumours (FT), mesenchymal tumours (MT), nailbed tumours (NT), round cell tumours (RCT) and sebaceous tumours (ST). Statistically significant ($P < 0.05$) relative proportion (95% confidence interval) for the combinations of breed and tumour category were: 1, 8.7 (2.2, 35.3); 2, 3.8 (1.0, 14.0); 3, 18.2 (3.5, 95.4); 4, 3.8 (1.2, 12.6); 5, 0.2 (0.1, 0.8); 6, 0.3 (0.1, 0.7); 7, 3.5 (1.6, 7.3); 8, 0.3 (0.1, 0.7); 9, 10.1 (1.1, 90.3); 10, 5.6 (1.0, 30.4); 11, 0.3 (0.1, 0.8); and 12, 18.1 (3.5, 95.4).

Figure 3. The association between breed and specific tumour diagnosis for 2553 skin tumours examined from 2271 dogs at two private laboratories in South Africa for a 6-month study period during 2013. Lighter shading denotes negative (protective) associations and darker shading

represents increased occurrence. Statistically significant ($P < 0.05$) relative proportion (95% confidence intervals) for the combinations of breed and tumour diagnosis were: 1, 7.0 (1.9, 26.3); 2, 7.8 (1.9, 32.3); 3, 7.6 (1.4, 41.0); 4, 2.2 (1.1, 4.4); 5, 2.3 (1.1, 5.2); 6, 0.2 (0.1, 0.7); 7, 0.2 (0.0, 0.9); 8, 0.2 (0.1, 0.6); 9, 2.7 (1.0, 7.0); 10, 2.7 (1.3, 5.5); 11, 0.2 (0.1, 0.7); 12, 0.5 (0.2, 0.9); 13, 3.9 (1.8, 8.4); 14, 8.3 (1.4, 48.5); 15, 38.9 (2.3, 646.1); 16, 3.8 (1.3, 10.7); and 17, 3.5 (1.1, 11.3).

Figure 4. The association between body location and tumour categories for 2553 skin tumours examined from 2271 dogs at two private laboratories in South Africa over a six-month study period during 2013. Lighter shading denotes negative (protective) associations and darker shading represents increased occurrence. Tumour classifications were sweat gland tumours (APO), epidermal tumours (EPI), follicular tumours (FT), mesenchymal tumours (MT), nailbed tumours (NT), round cell tumours (RCT) and sebaceous tumours (ST). Statistically significant ($P < 0.05$) relative proportions (95% confidence intervals) for the combinations of anatomical location and tumour category were: 1, 39.0 (5.8, 264); 2, 0.01 (0.00, 0.16); 3, 14.2 (2.4, 83.3); 4, 0.10 (0.03, 0.38); 5, 0.05 (0.02, 0.15); 6, 8.5 (1.8, 40.5); 7, 0.03 (0.01, 0.15); 8, 0.03 (0.01, 0.11); 9, 0.16 (0.05, 0.50); 10, 0.02, (0.00, 0.65); 11, 39.0 (5.6, 272); 12, 0.04 (0.01, 0.13); 13, 0.04 (0.01, 0.11); 14, 0.31 (0.12, 0.79); 15, 0.01 (0.00, 0.23); 16, 0.01 (0.00, 0.03); 17, 0.11 (0.01, 0.95); 18, 0.00 (0.00, 0.01); 19, 0.03 (0.01, 0.09); 20, 0.03 (0.01, 0.18); 21, 15.4 (2.8, 85.5); 22, 0.17 (0.05, 0.56); 23, 0.28 (0.09, 0.92); and 24, 741 (13.4, 40905).

Table 1. Number of canine cutaneous neoplasms (percent total) diagnosed at two private laboratories in South Africa over a six-month study period in 2013.

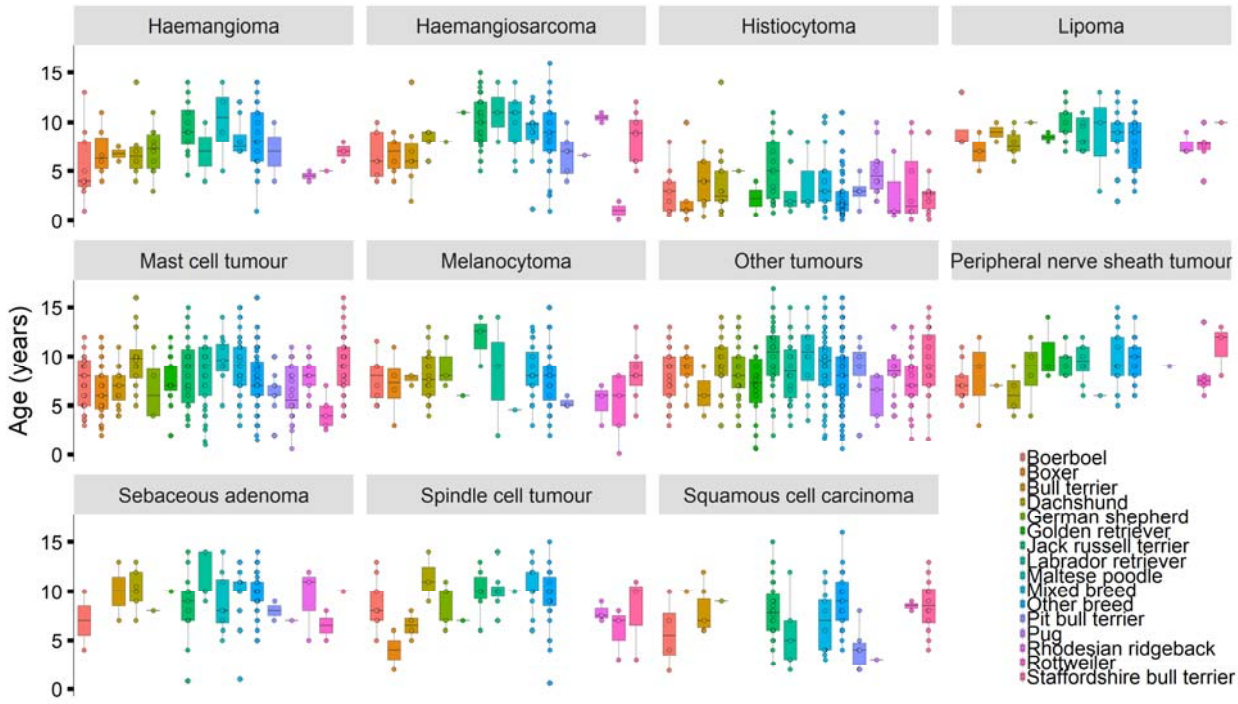
Neoplasm	Benign	Malignant	No information
Sweat gland tumours (APO)			
Apocrine adenoma	4 (0.16%)		
Apocrine adenocarcinoma		3 (0.12%)	
Apocrine carcinoma		6 (0.24%)	
Apocrine cystadenocarcinoma		1 (0.04%)	
Apocrine cystadenoma	12 (0.47%)		
Apocrine ductular adenoma	1 (0.04%)		
Apocrine ductular carcinoma		11 (0.43%)	
Mixed apocrine carcinoma		1 (0.04%)	
APO total	17 (0.67%)	22 (0.86%)	0 (0%)
Epidermal tumours (EPI)			
Anaplastic carcinoma		1 (0.04%)	
Basal cell carcinoma		1 (0.04%)	
Papilloma	1 (0.04%)		
Squamous cell carcinoma	1 (0.04%)	125 (4.90%)	
Squamous papilloma	16 (0.63%)		
Viral papilloma	1 (0.04%)		
EPI total	19 (0.74%)	127 (4.97%)	0 (0%)
Follicular tumours (FT)			
Infundibular keratinising acanthoma	32 (1.25%)		2 (0.08%)
Pilomatricoma	32 (1.25%)		
Trichoblastoma	50 (1.96%)	1 (0.04%)	
Trichoepithelioma	76 (2.98%)	3 (0.12%)	
Trichofolliculoma	3 (0.12%)		
Tricholemmoma	5 (0.20%)		
FT total	198 (7.76%)	4 (0.16%)	2 (0.08%)
Mesenchymal tumours (MT)			
Anaplastic sarcoma		6 (0.24%)	
Fibrolipoma	17 (0.67%)		
Fibroma	32 (1.25%)		
Fibrosarcoma		26 (1.02%)	
Giant cell tumour soft tissue		1 (0.04%)	
Haemangioma	112 (4.39%)		
Hemangiosarcoma		211 (8.26%)	
Histiocytic sarcoma		6 (0.24%)	
Infiltrative lipoma	14 (0.55%)		
Lipoma	129 (5.05%)		
Liposarcoma		7 (0.27%)	
Myxoma	1 (0.04%)		
Myxosarcoma		7 (0.27%)	

Peripheral nerve sheath tumour	92 (3.60%)	24 (0.94%)	2 (0.08%)
Spindle cell tumour	99 (3.88%)	9 (0.35%)	
MT total	496 (19.43%)	297 (11.63%)	2 (0.08%)
Nailbed tumours (NT)			
Nailbed keratoacanthoma	1 (0.04%)		
Nailbed melanoma		8 (0.31%)	
Nailbed SCC	1 (0.04%)	18 (0.71%)	
NT total	**2 (0.08%)**	**26 (1.02%)**	**0 (0%)**
Round cell tumours (RCT)			
Anaplastic RCT		2 (0.08%)	
Cutaneous lymphoma		5 (0.20%)	
Epitheliotropic lymphoma		13 (0.51%)	
Histiocytoma	239 (9.36%)		
Mast cell tumour	495 (19.39%)	44 (1.72%)	
Melanocytoma	147 (5.76%)		
Melanoma	5 (0.20%)	84 (3.29%)	1 (0.04%)
Non-epitheliotropic lymphoma		1 (0.04%)	
Plasma cell tumour	37 (1.45%)	2 (0.08%)	
Transmissable venereal tumour	3 (0.12%)		
RCT total	926 (36.27%)	151 (5.91%)	1 (0.04%)
Sebaceous tumours (ST)			
Perianal adenoma	82 (3.21%)		
Perianal carcinoma		7 (0.27%)	
Perianal epithelioma	6 (0.24%)		
Sebaceous adenoma	109 (4.27%)		1 (0.04%)
Sebaceous carcinoma		2 (0.08%)	
Sebaceous epithelioma	56 (2.19%)		
ST total	253 (9.91%)	9 (0.35%)	1 (0.04%)
Overall total	1911 (74.85%)	636 (24.91%)	6 (0.24%)

Table 2. Multivariable predictors of malignancy in primary skin neoplasms examined from 2016 dogs at two private laboratories in South Africa over a six-month study period in 2013.

Variable*	Parameter estimate ($\hat{\beta}$)	P value (Wald)	Odds ratio (95% CI)
Breed	—	<0.001	—
Mixed breed	0.013	0.939	1.01 (0.73, 1.41)
Jack Russell terrier	0.934	<0.001	2.54 (1.83, 3.54)
Boerboel	-0.028	0.905	0.97 (0.62, 1.54)
Dachshund	-0.294	0.270	0.75 (0.44, 1.26)
Labrador retriever	-0.169	0.507	0.85 (0.51, 1.39)
Staffordshire bull terrier	0.491	0.035	1.63 (1.04, 2.58)
Boxer	-0.195	0.535	0.82 (0.45, 1.52)
Rottweiler	0.817	0.004	2.26 (1.31, 3.92)
German shepherd	-0.060	0.852	0.94 (0.50, 1.76)
Bull terrier	0.268	0.418	1.31 (0.68, 2.50)
Rhodesian ridgeback	-0.396	0.323	0.67 (0.31, 1.48)
Golden retriever	-1.443	0.017	0.24 (0.07, 0.78)
Maltese poodle	0.024	0.947	1.02 (0.51, 2.08)
Pug	-2.482	0.015	0.08 (0.01, 0.61)
Pit bull terrier	0.771	0.029	2.16 (1.08, 4.32)
Other breed	Reference	—	—
Age	—	<0.001	—
< 3 years	-1.736	<0.001	0.18 (0.09, 0.34)
3 – 5.9 years	-0.548	0.001	0.58 (0.42, 0.80)
6 – 8.9 years	-0.281	0.042	0.76 (0.58, 0.99)
9 – 10.9 years	-0.187	0.193	0.83 (0.63, 1.10)
≥ 11 years	Reference	—	—
Laboratory			
1	-0.208	0.046	0.81 (0.66, 1.00)
2	Reference	—	—

CI = confidence interval.



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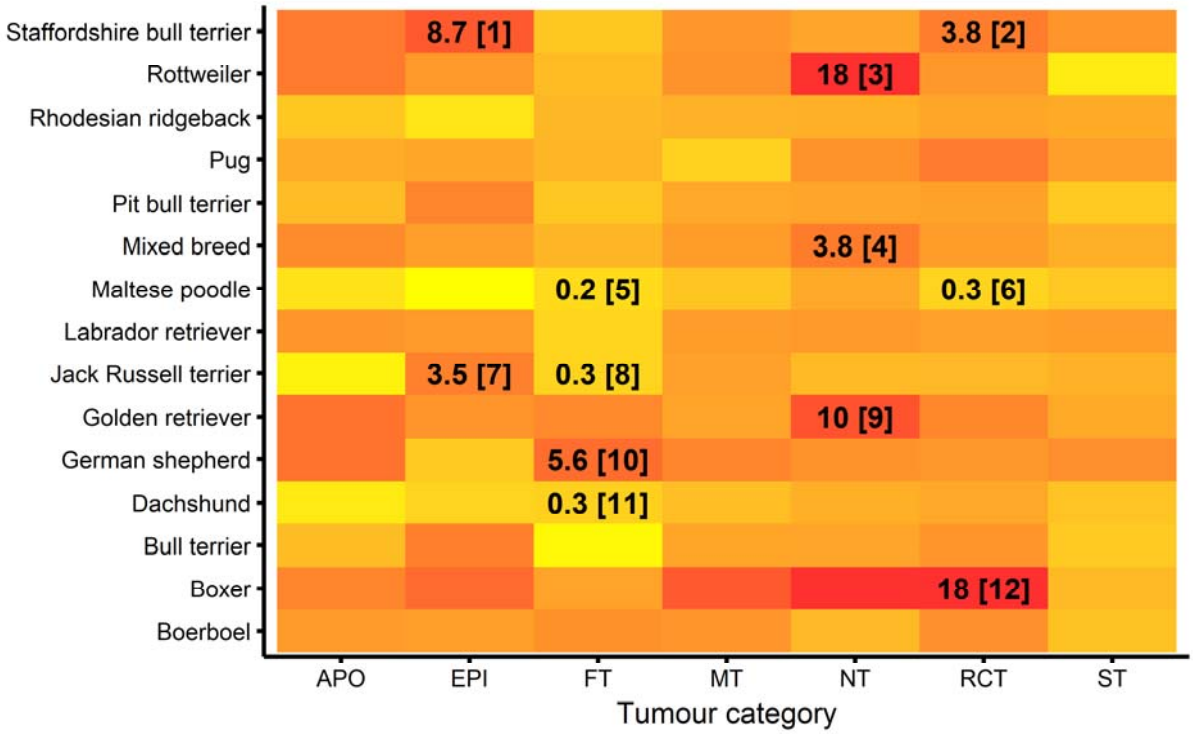

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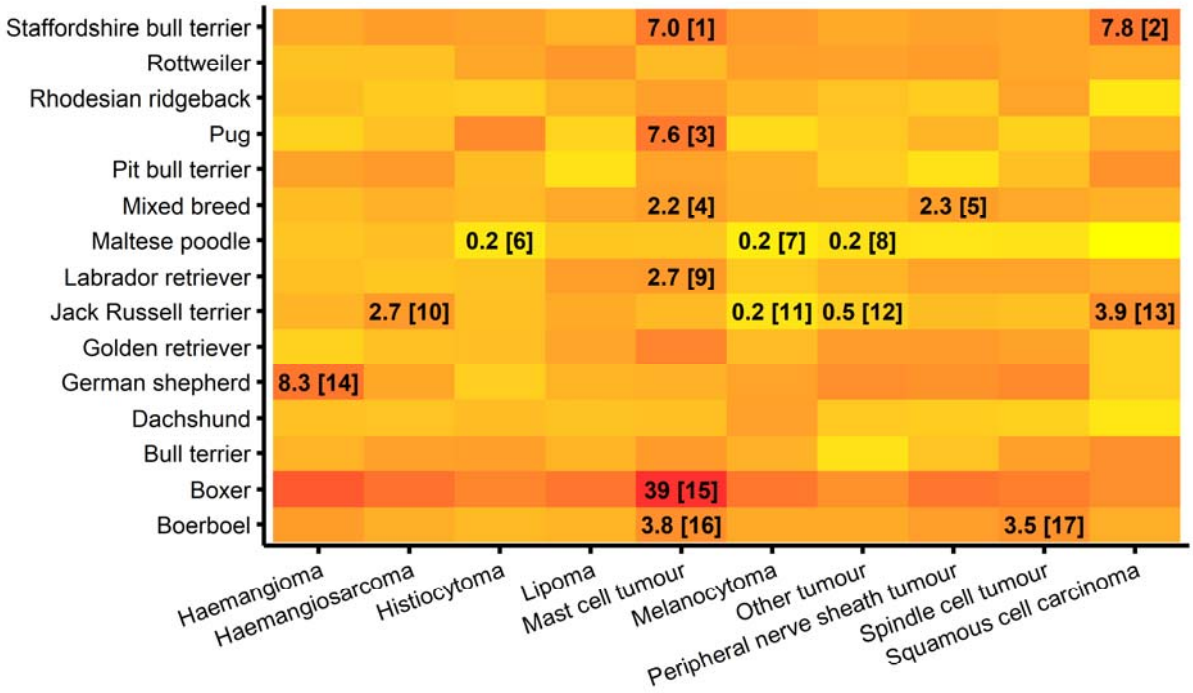

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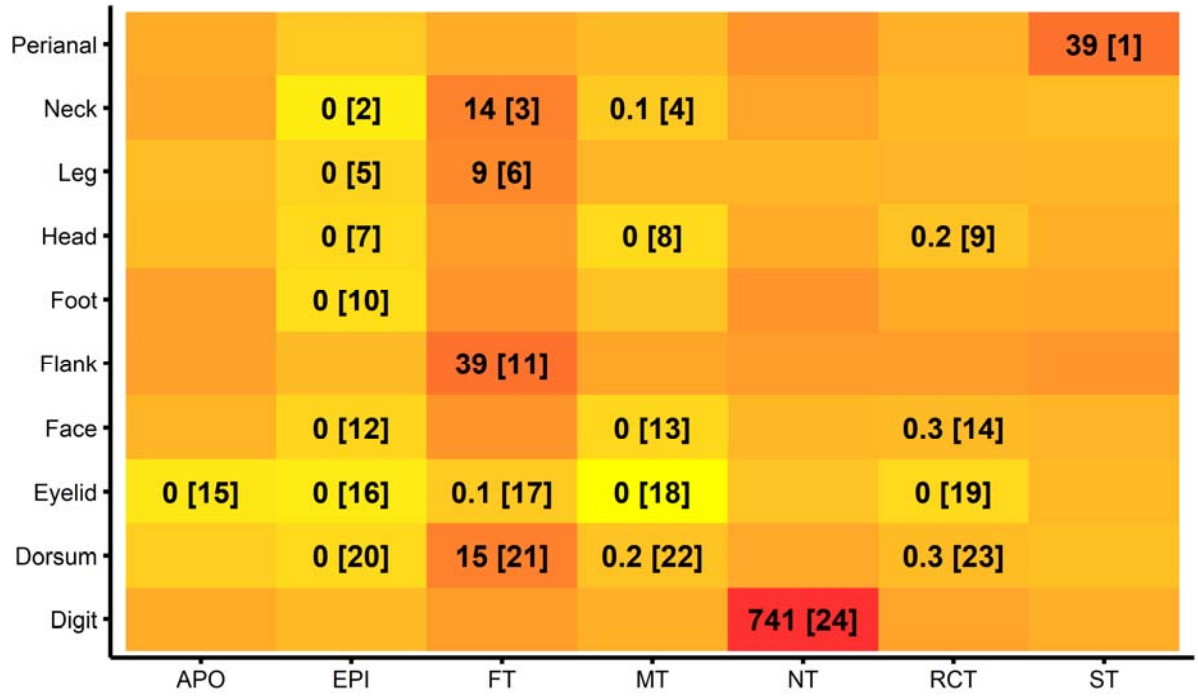

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